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## **FUTURE OF MEDICAL SCIENCES: MEDICAL FUTUROLOGY**

**Dr Janardan Bhatt**

### **Editorials**

When we observe the rapid development in technology it is often questioned what will be the future of medicine/ the medical sciences? We have to guess wildly and widely the future but be realistic let us start with infrastructure .When I was medical student, our hospital was just two floor building and today I am my working place is 10 floor building and our grand children will be studying in 30 floor sky scrapper. And due increase population, increase survival opportunity and city based global trend , hospital ward will be like 2 tire or 3 tire train coaches. Telemedicine will be hugely popular increase availability of IT technology and improve people perception of such techniques. All the medical colleges will be connected for telemedicine by satellite.It is also expected without bias that India will be super power in the world . The speed of internet will be not less than 3/4-G to 7-G.More than 80% population will be using Smart Phone .Stem cell technology will be the pioneer mode of therapy. There will be no card or any type of ID card except Biometric Card. And the Biometric techniques will be expanded and will not be limited to thumb, figure or hand but it will cornea, tongue and many more. Ambulances will be automatic without driver including public transport . Human head transplant will be possible. There will be no difference between, Ear, Eye, tongue as a special individual organs but it will be inter changeable at higher neural level .Blood tests and collection of blood will be a obsolete method of laboratory test. Saliva, Urine , tears will be enough to measure various biomedical parameters .Biomarkers of cancer will be detectable in saliva and urine and help in very early preclinical diagnosis .So Man get rid of prostate cancer & Women get rid of Breast cancer. A Patch on tongue will be enough for treatment of obesity. Early Diagnosis and preventive medicine will be key branch of medical sciences .Angioplasty will be routine in 104 years old people.

In next 20 years the Memory transplant will be possible. Skin or body part will act as mobile transmitter and receiver. Medical social network expand beyond our imagination and google will be the supportive professors. emedical goggle will come in action. Drug therapy will be Personalise on genome based and mainly Preventive one. Self measuring of various data will be limited to BP/sugar but will expand beyond.Surgical care will be taken by Robots. Robotics Hand will do all major surgery and quality neuro surgery will be significantly improved .Robo – sapien – will be total wireless and controlled by cell phone devises.Robotics based Simulation and Digital Reconstruction will be the key method of medical learning teaching method.with the awailability of 3 D Xerox techniques dissection and human bone and bodies will be dream. More real virtual near real Virtual - Simulation is the target of incoming decades and they will serve as real humans. There will not be different machines for X ray -CT- MRI- Angio but One machine alone will do CT- MRI- Angio altogether if needed and create 3 D Digital Reconstruction .and help in neuro and other complicated surgery. Mind reading,Genetic Profile will be possible in near decades. LIC-Premium will be calculated on genome profile.

Intra operative radio therapy will give more hope for cancer. Neurosurgery will be the treatment for uncontrolled diabetes ,High BP, and obesity. Deep Brain Stimulation treatment will be available for- depression- obesity .Computer /mobile - Brain network will help house visit ,Hospital care and laboratory. Mobile Phone will help to monitor in ICU parameters i.e. ECG ,EEG ,respiration including X-ray other digital images. Cough in Phone will help to diagnose Tuberculosis , Pneumonia and cancer.

Stimulation of CNS during anticipation of movement will help to control the movements of not only body but also wheel chair ,car and so on....Neural impulses of motor thought will help Biomechanical limbs and Neuro prosthetics to move desired target and the prosthesis work like virtual organs. Scientist have already succeeded in primates to create wire brain spinal interface to help paraplegic patients and spinal cord injuries. Walking movement made possible by using signal from motor cortex(pill size electrode is implanted in motor cortex to record the electrical impulses) which trigger coordinated electrical stimulation of spinal cord and spinal nerves for normal locomotion . Thus scientists and bio engineers have already succeeded reestablishment of brain spinal cord communication. Intrauterine surgery i.e. removing meningocele will be possible .

ECG and some similar apps have been already approved by the US -FDA for consumers and medical professionals will be validated in many more other clinical utilities. The apps' data are immediately analyzed, graphed, displayed on-screen updated, stored and shared to patients, doctors and consultants . The patient's phone will send pre-recorded data of ECG with interpretation to the doctor. Leadless ECG will change technique of Holter monitoring method radically . A simple ECG patch will record ECG / arrhythmia for 24 hour a day and with needful signals the data will be available to remotely located physician or cardiologist for diagnosis and management including wireless hemodynamic monitoring. Artificial Pacemaker of future generation will be wireless. This type of wireless technology will give new hopes of management of disorders of heart and brain. Smart phones will enable the video consultation though the method is waiting for approval. But the telemedicine has already given huge advantages of expertise advise at remote area. Sonography and Echocardiography will be available in the form of pocket devises.

Using wearable wireless sensors, one will use Smartphone to generate own medical data, including measuring blood-oxygen and glucose levels, blood-pressure and heart rhythm....etc. wearable necklaces will monitor heart function and check the amount of fluid in the lungs. Wearable contact lenses that will track glucose levels or intra ocular pressure. Wearable head bands that will capture EEG wave and will be used for diagnosis of epilepsy and can be used for therapeutic purpose for biofeedback methods of treatment. Wearable socks and shoes will help to analyze the human gait too for neurological disorders for diagnosis and drug monitoring .Smartphone sensors will be able to monitor exposure to radiation, air pollution or pesticides level in environment. Smartphone attachments will soon enable us to perform an array of laboratory tests via phone i.e. blood electrolytes; liver; kidney and thyroid function; analysis of breath, sweat and urine-all will be checked with small

fluid samples that plug directly into smartphones. Medical college will replace the old stethoscope to smart stethoscope where the mp4 supported tool will make heart audible to all medical students and hearing impaired physicians with additional benefit of phonocardiography i.e. visible Korotkow', and heart sounds on C.R.O. screen . It won't be long before one can take a smartphone X-ray selfie to diagnose a bone fracture send to a doctor for advice and opinion for further management.

In the next decade nano sensors which will be embedded in the bloodstream will be available. These microscopic sensors within the body can float in blood or be fixed to a micro stent in a tiny blood vessel. Nano medicine will be available in near future for cardiac and cancer care top delivery target treatment . One will also be able to keep blood under constant surveillance for the first appearance of cancer ,autoimmune attacks or vital organ damages i.e. myocardial ischemia/ infarction ,cerebro vascular diseases or tiny cracks in artery walls. People are more willing to disclose their inner thoughts to a computer avatar or "Virtual Human" than a real one. Virtual psychiatrists will provide a new approach to mental health by analysing the thoughts.

With all these new tools, it is no surprise that we are talking about possibility of "doctor less" medicine. Patient will continue to turn to doctors chiefly treatment, guidance, wisdom, experience, empathy and human touch and counselling.

Digital avatars won't replace physicians: one will still be seeing doctors, but the relationship will ultimately be radically altered. Digital/computer algorithm will the diagnosis and will give guideline to the patients management.

Chief reference:

I Lecture by Dr. Gopinath consultant Neurologist at AMA Ahmedabad

II Lectures delivered during JIC 2017

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## **A COMPARATIVE STUDY OF BUCCAL MUCOSAL CELLS FOR CYTOLOGICAL CHANGES OCCURRING IN SMOKELESS-TOBACCO EXPOSED POPULATION WITH THE NON-EXPOSED IN THE SAURASHTRA REGION OF GUJARAT STATE**

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### **Abstract:**



The study was conducted to detect the impact of consuming smokeless tobacco (in any form) on the buccal mucosal cytology of 100 male subjects (50 exposed and 50 non-exposed) of 18-60 age group. After proper ethical clearance, the samples were collected using sterile wooden spatula, fixed and stained by routine H&E technique. The cells observed for changes of multinucleation, binucleation, karyolysis and chromatin condensation of nuclei. The data obtained was compared with the previous studies done. It was concluded that, the intake of smokeless tobacco leads to an increased tendency of cytological aberrations and the buccal mucosal cytology is an easy, painless and cost effective procedure to detect these changes at an early stage and start preventive measures accordingly.

**Keyword :** *Buccal mucosa, cytology, multinucleated, binucleated, karyolytic, chromatin condensation*

### **Introduction:**

Oral cancer is one of the ten most common cancers in the world. Its high frequency in central and Southeast Asian countries like India, Bangladesh, Srilanka, Thailand, Indonesia and Pakistan, has been well documented. *In India:* for the year 2008, with estimated incidences of 9.8 cases per 1 lac population for males and 5.2 cases per 1 lac population for female, oral cancer was found to be a major problem in India. The estimated mortality was about 6.8 per lac in males and 3.6 per lac in females.<sup>(1)</sup>

Despite numerous advances in treatment, the overall long-term survival has remained at less than 50% for the past 50 years. This is due to several factors including the fact that oral cancer is often diagnosed when the disease has already reached an advanced stage.<sup>(2)</sup>

Tobacco in various form of its usage (smoking and chewing) is the major environmental cause of cancer of mouth, lung, larynx, pharynx etc.<sup>(3)</sup>

Approximately 90% of oral cancers in south East Asia are linked to tobacco chewing and tobacco smoking. During 1966-1977, a large epidemiological survey was carried out in different parts of the country. In a follow up study of 10 years on 30,000 individuals in the three districts of Ernakulum (kerela), srikakulum (andhra) and Bhavnagar (Gujarat), the results indicated that:

- a. Oral cancers and precancerous lesions occurred solely among those who smoked or chewed tobacco.
- b. Oral cancer was always preceded by some type of precancerous lesions.
- c. Cancer always occurred on the side of mouth where the tobacco quid was kept and the risk was 36 times higher than for non-chewers if the quid was kept in the mouth during sleep.<sup>(1)</sup>

### **Material and method:**

After obtaining clearance from the Institutional Ethical Committee of M. P. Shah Government Medical College, Jamnagar , samples were taken from the buccal mucosa of 100 individuals selected from the patients attending at the male - Out Patient Department in the Departments of Medicine, Guru Govind Hospital,

Jamnagar. These individuals were from a mixture of urban and rural settings from different areas of Jamnagar districts.

The subjects were divided into 2 groups as follows:

Sr. No.	Type of Addiction	No. of cases
1.	Tobacco Chewer (T)	50
3.	Control (non tobacco chewer and alcohol drinker) (C)	50
Total no. of cases		100

Only males, of 18-60 years of age who were tobacco chewers with normal appearing buccal mucosa and normal jaw mobility were included in the study. After seeking proper consent, personal details and proper history regarding tobacco chewing (mava, gutkha, khaini, jarda etc) was entered in the proforma prepared.

The subjects were asked to rinse their mouth with distilled water. A new wooden spatula was used every time to scrape the of buccal mucosa of each patient, for at least three to four times with firm pressure and the obtained sample was then spread on a clean microscopic slide coded with case number to get the smear. The smear was immediately fixed in 95% ethyl alcohol for 10-15 minutes to assure adequate fixation. Then the smears were stained with routine Haematoxyline and Eosin staining technique in the histology section of Department of Anatomy of MP Shah Govt. Medical College Jamnagar and were visualized under low power and high power of binocular microscope.

The data was summarized and statistically analyzed using SPSS software. Mean values of all parameters were compared by student's't' test to check their statistical significance and P value was obtained from it. If the P value is > 0.05 then the difference is not statistically significant. If the P value is between 0.05 and 0.01 then the difference is statistically significant. If the P value is <0.01 then the difference is statistically highly significant. The observations of the study were tabulated and interpreted for discussion in details. <sup>(4)</sup>

**Result:**

- The mean age of subjects in control group was 36.64 ± 13.5 years and in tobacco, exposed group was 39.7 ± 14.8 years.
- The mean number of multinucleated cells in control group was study group was 0.3 ± 0.8 and in tobacco exposed group was 4.0 ± 2.3 and this difference was found to be statistically highly significant (p<.01)
- The mean number of binucleated cells in control group was study group was 0.96 ± 1.7 and in tobacco exposed group was 3.8 ± 1.7 and this difference was found to be statistically highly significant (p<.01)
- mean number of karyolytic cells in control group is 0.5 ± 1.3, in tobacco exposed group is 4.0 ± 2.3, and this difference was found to be statistically highly significant (p<.01)

- The mean number of cells with chromatin condensation in control group is  $0.2 \pm 0.7$ , in tobacco exposed group is  $0.9 \pm 0.9$  and this difference was found to be statistically highly significant ( $p < .01$ )

### **Discussion:**

The subjects under study were divided in two groups of tobacco exposed (taking only smokeless tobacco without any alcohol intake) and the male subjects with similar age group without any alcohol or tobacco intake were taken as control groups.

The findings thus obtained from the present study were found in accordance with the other co-workers.

In the present study, it was found that there was an increase in the mean number of multinucleated cells in tobacco-exposed subjects and it was highly significant as compared to control groups.

These findings are in accordance to those found by Sharma VL et al (2013)<sup>(5)</sup>, who also found an increase in the incidences of Multinucleation in the subjects exposed to tobacco and the findings were highly significant when compared to controls.

Harikrishna G F (2011)<sup>(6)</sup> reported the genotoxic effect of tobacco chewing in vivo and vitro conditions and their conclusions were also similar to present study.

Bansal H et al (2012)<sup>(7)</sup> also evaluated the occurrence of micronuclei in Punjabi population and concluded the genotoxicity of tobacco chewing over buccal mucosa, which was similar to the present study.

Similar results were obtained by Kashyap B et al (2012)<sup>(8)</sup> and Jindal et al (2013)<sup>(9)</sup> who detected the alteration in buccal mucosal cells due to effect of tobacco and they concluded that these agents were carcinogenic leading to increase in number of silver stained nucleolar organizer regions and micronuclei in buccal mucosa.

In the present study it was found that there was increase in mean number of binucleated cells in tobacco exposed subjects as compared to control group and this increase was statistically highly significant.

These findings were in accordance with the study of Sharma VL et al (2013)<sup>(5)</sup> who found a significant increase in incidences of binucleated cells in tobacco chewers and it was highly significant as compared to controls.

Increased incidences of Karyolytic cells found in the present study were in accordance with the study of Sharma VL et al (2013)<sup>(5)</sup> who found that there was a significant increase in incidences of karyolytic cells in both alcohol consumers and tobacco chewers and it was highly significant as compared to controls.

Similar findings were observed by Burzlaff et al (2007)<sup>(10)</sup>, who found increase in number of anucleated cells and the cytological atypia in tobacco and alcohol exposed individuals and it was found to be statistically significant.

Reis et al (2006) <sup>(11)</sup> in their study found a non-significant increase of karyolytic cells in alcohol exposed subjects. Such differences might be because of population difference or difference in the technique used.

Sharma VL et al (2013) <sup>(5)</sup> also found cells with chromatin condensation in 1% of alcohol and tobacco exposed subjects but did not mentioned about statistical significance. It might be due to some technical error, however in the present study there was a statistically significant increase in cells with chromatin condensation found in the tobacco chewers.

### **Conclusion:**

The increased tendency of nuclear aberrations and statistical analysis suggested that buccal mucosa is susceptible to cancer in those who are consuming smokeless tobacco. The methodology used in this study was simple, rapid and painless. Such a technique is cost effective and can be practised in rural hospitals for the detection of oral cancers at the preliminary stages and in effective patient counselling for prevention.

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### 3

#### INVESTIGATING CATARACT REFERRAL PRACTICES USED BY INDIAN OPTOMETRISTS

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#### ABSTRACT

**Background:** Optometrists are primary eye care practitioner and is gaining popularity as the first point of contact with the patients. However, little is known about the cataract surgery referral criteria used by optometrists in India.

**Methods:** 2574 Optometrists from India were invited to complete an online survey on cataract referral practice. The survey elicited information on practice demographics of optometrists and cataract referral considerations.

**Results:** Total respondents in the present study were 832. Respondents stated visual acuity of  $\leq 6/12$  to  $\leq 6/18$  as the benchmark for referring the patient for cataract surgery. Considerably lower proportion used glare and contrast sensitivity testing in cataract patients. Patient centred factors such as hobbies, driving, featured in the decision to refer patients sooner.

**Conclusion:** Although the reduction in the visual acuity was considered the prime factor affecting the decision making of Indian optometrists for referral for cataract surgery, patient's visual demands also played an important role.

#### INTRODUCTION

Cataract remains the leading cause of visual impairment in all areas of the world, except for developed countries <sup>[1]</sup>. Visual impairment has been recognized as an important public health problem in India, a country that is now home to a billion inhabitants <sup>[2-9]</sup>. India was the first country in the World to launch a 100% public funded programme for the Control of blindness <sup>[10]</sup> The National Programme for

Control of Blindness has emphasized the need for cataract surgical services and refraction services to be augmented, both in quantity and quality, in order to achieve the goal of eliminating avoidable blindness by 2020 [2-9]. A major portion of referral for cataract surgery in India is made by Optometrists. Optometrists are trained in various institutes and some of them have developed their own procedures and protocols for referrals [11]. Optometrist play a critical role in the identification and appropriate referral of cataracts requiring surgery; however the criteria optometrists use for the referral of candidates for cataract surgery to ophthalmologists have not been extensively studied in India. The aim of the study was to investigate the referral considerations of cataract surgery by Indian Optometrists. This study gives insight into factors like how socioeconomic factors, remoteness to healthcare, professional experience can impact cataract referral decisions of optometrists practising in India.

## METHOD

This was a Cross-sectional Questionnaire survey of Optometrists practicing in India. A preformed questionnaire of Cataract referral practices [12] of Australia was considered. It was modified and validated to be used in Indian scenario of practices. An email containing the survey link was distributed to 2574 optometrist in November 2015, explaining the purpose of the survey and inviting participation. A reminder email was sent to the entire sample six weeks after the initial invitation and the survey closed two week later. No financial incentive was provided for participation.

The survey consisted of total 28 questions. These include questions on patient's Visual acuity, contrast, glare, and symptoms of the patients. Optometrists were asked to rate the level of importance that factors had on their decision of where to refer their patients. Response frequencies were tabulated for all survey questions. The entire filled up questionnaire was entered in Microsoft Office Excel 2007. Mean and standard deviation were computed for Quantitative variable. Odds Ratio was computed for study parameters.

## RESULT

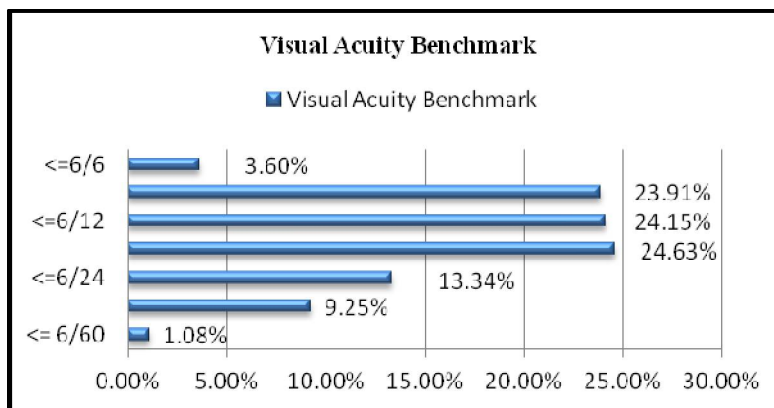
The demographic data of 832 respondents are shown in Table 1.

Characteristic		Value
Type	Intern	148
	Practitioner	684
Gender	Male	374
	Female	458

<b>Age</b>	Years	26.37 ± 5.43
<b>Years in Practice</b>	<= 5 years	607
	>= 5 years	225
<b>Main Practice Type</b>	Corporate	465
	Independent	367
<b>Professional Scope Of Practice</b>	General primary eyecare	582
	Specialty Practice	250
	Others	0

**TABLE 1: Demographic Data**

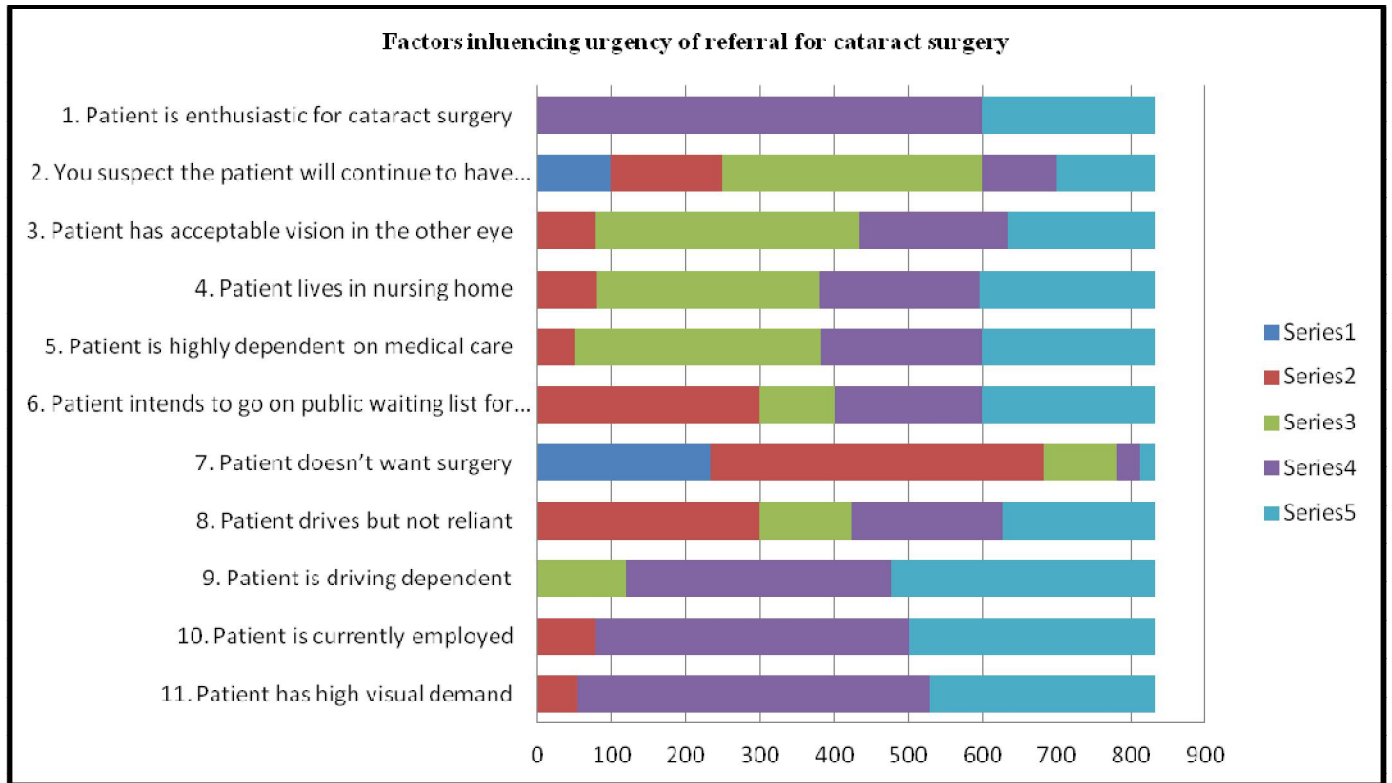
The visual acuity at which the respondents prefer to refer the patients for cataract surgery is shown in figure 1. Visual acuity between  $\leq 6/12$  and/or  $\leq 6/18$  was a common benchmark for cataract referral with 72.69% of respondents reporting referral at this level of vision. 87% of the respondents prefer not to consider contrast sensitivity testing in decision for cataract referral. 71% of the respondents consider the factor of accidental falls of the patient in the referral for surgery.



**Figure 1: Visual Acuity referral**

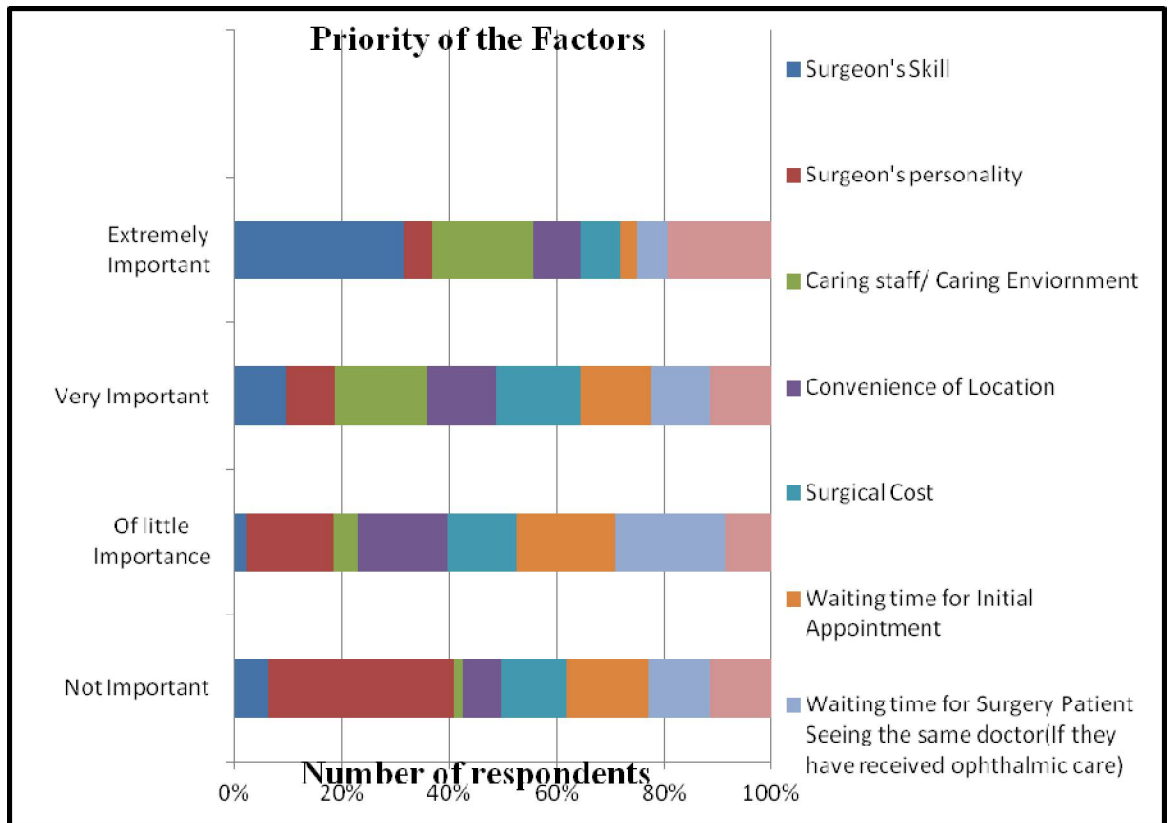
Factors affecting decision on “when to refer patients for cataract surgery” is shown in figure 2. A significant proportion of optometrists reported that patient lifestyle and health system influenced their urgency of referral for cataract surgery. Of the life style factors presented, patient’s enthusiasm (72.11%) for surgery elicited the highest percentage of respondents who would “refer urgently and refer sooner” followed by patients having high visual demand (56.85%), patient’s current employment status (50.84%) and patient’s driving dependence (42.78%) factor. There was no influence on factors of continued less vision in the eye after surgery. The factors which had the greatest influence on a decision to delay referral were

patients not wanting surgery, patient drives but not dependent, and patients wanting to go on public waiting list for cataract surgery.



**Figure 2: Factors influencing urgency for referral**

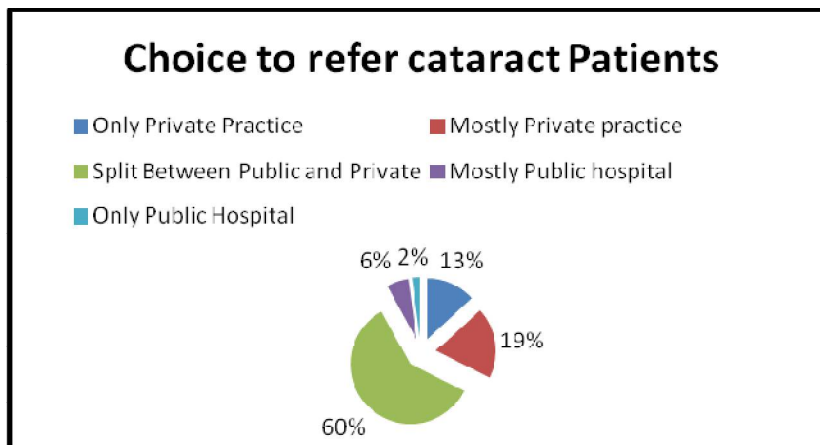




**Figure 3: Factors affecting patient referral**

Figure 3 shows factors affecting decision on “where to refer patients for cataract surgery”. Factors influencing the optometrist’s choice of referral location were also examined. Surgeon’s skill was ranked ‘extremely important’ by the highest proportion (61.53%) of optometrists in deciding where they referred patients for cataract surgery. Waiting time for patient seeing the same doctor (If they have received ophthalmic care) was ranked to be “Of little importance” (42.90%).

The opinion of the respondents as to where they chose to refer Cataract patients for surgery is shown in figure 4. Surgical cost was considered for the surgery while referring the patient. Odds ratio with respect to the referrals to private and public hospital is 1.07. This means that the specific referrals to private hospitals are 1.07 times more than public hospitals.



**Figure 4: Choice of referral**

## DISCUSSION

In our knowledge this was the first study conducted among the Indian optometrist for cataract surgery referrals. The standard guidelines for cataract surgery includes the criteria of Visual acuity, contrast sensitivity and glare testing <sup>[13]</sup>. The patterns of referrals followed by Indian optometrists are mainly based on Visual Acuity and contrast sensitivity. Glare testing is not preferred by most of the optometrist for referral. Emphasis should be equally laid on glare testing as it is affected earlier than visual acuity. Testing for glare and contrast should be performed to rule out the signs of cataract which affect the daily activities of the patient and help to maintain the record for the subsequent follow up visits to detect the changes. The aim of these guidelines is to identify good clinical practice, set standards of patient care and safety and provide a benchmark for outcomes within which high quality cataract surgery can be practiced. They represent the current understanding of the guideline development group.

In the present study the optometrists in India prefer to refer the patients having visual acuity between  $\leq 6/18$  to  $\leq 6/9$ . This criteria is close to the criteria followed by both the optometrists and ophthalmologists of West Midlands <sup>[14]</sup>

In the present study 71% respondents have considered the falling history of the patient in decision making for the referral for cataract surgery. In the study "Prospective study of the rate of falls before and after cataract surgery" by S Brannan, C Dewar et al <sup>[15]</sup> concluded that there was significant reduction in the risk of falls in patients after cataract surgery.

Patient's hobby which has high visual demand is one of the most important factors influencing the urgency of referral for cataract surgery followed by driving dependency of the patient and current employment. Comparing the present study with that of QuangDoV, Li R et al <sup>[12]</sup>, it can be said that the referral criteria is broadly similar in case of patient's hobbies for driving, visual acuity benchmark. According to the present study the specific referrals to private hospitals is 1.07 times more than public hospitals. In the study by QuangDoV, et al <sup>[12]</sup> respondents practicing in more advantaged socioeconomic areas were 2.4 times more likely to refer privately. Surgeon's skill, caring staff are the extremely important factors influencing optometrists' decisions on where to refer for cataract surgery whereas surgeon's personality has minimal importance. Priority is more for private than for public hospitals. Waiting time for surgery is also considered in selecting where to refer the patient. Socio economic status is the only predictor of whether an optometrist

chooses to refer patients publicly or privately for cataract surgeries. Factors affecting the referrals may include the surgical costs at private sector, and the large waiting times at public hospitals prior to the surgery.

The target of NPCB (State wise targets & Achievement for various eye diseases during 2015-16) cataract surgeries is 6600000 out of which 2511867 is achieved. Still 4088133 is the backlog in achieving the goal of the target surgeries in India (As per NPCB data) <sup>[16]</sup> . According to Guidelines for Quality Cataract Services- National Programme for Control of Blindness Health & Family Welfare Department Government of Gujarat 2014<sup>[17]</sup>, gave the subjective and objective criteria for patient selection for cataract surgery. Practitioners frequently make clinical decisions based on changes in visual acuity. However, acuity is recognized to be only one aspect of visual performance. High frequency contrast sensitivity charts are even more sensitive to refractive blur. Despite of proper refractive correction, some patients will complain of a visual problem but no visual anomalies. This is common with early cataract patients <sup>[18]</sup>. These guidelines are not widely followed and the awareness of these guidelines is very low.

Awareness among the optometrist regarding the referral patterns for all the eye conditions which may require the involvement of an ophthalmologist. Formation of the council to regularize the level of academic activities should be done. Hence, increasing the number of the referrals for the cataract surgery may become helpful to the programme VISION 2020: RIGHT TO SEE to achieve the target. Referrals can be increased by properly screening the patients at various sectors. However the population at the urban area is educated enough to consult an eye care practitioner, but the patients of cataract in rural areas are totally unaware of their condition. Thus, regular eye camps at such places should be conducted and the patients should be referred if needed. Coordination between the ophthalmologist and optometrist also plays an important role. Integrated eye care delivery models typically work by having ophthalmologists and optometrists together in the same practice or institution, where either can see patients at any time. Integrated models do not raise the same legal issues involving referral and postoperative care. This is the stepping stone towards achieving the goal of VISION 2020 to eradicate blindness due to cataract.

The role of optometrists as a first point of contact for patients in the cataract referral pathway places them in a key position to positively influence surgical candidate selection, the subsequent efficiency of surgical processes and the satisfaction of patients with their surgical journey and overall outcomes. By understanding and documenting the current cataract referral practices of optometrists in India, this research provides a foundation for building more effective and efficient management strategies for patients with cataracts and will help to achieve the goal of VISION:2020.

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**EFFECT OF OBESITY ON CARDIOVASCULAR AUTONOMIC  
FUNCTIONS IN SCHOOL CHILDREN**

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**ABSTRACT**

Obesity is a disorder with a multifactorial etiology resulting from a complex interaction between the environment, behaviour and genetic susceptibility. It is conceivable that one or more sub groups of obesity have an alteration in their autonomic nervous system that may promote obesity and account for several clinical consequences of obesity. In this study we performed AFT on obese and non obese children. The result of our study shows reduced E:I ( Expiration: Inspiration) ratio in obese children as compared to the normal children  $p= 0.0485$  in boys and  $p= 0.0009$  in girls. Our study also indicates higher baseline diastolic blood pressure and systolic blood pressure prior to isometric handgrip exercise and blood pressure response on lying to standing in obese group children which shows the reduced sympathetic activity in obese children ( $p= 0.0001$  for both orthostatic hypotension test and hand grip test in boys and girls.).The prevalence of obesity from our study comes 17.3% in Bikaner district.

**AIMS AND OBJECTIVE:-.** Comparative study is done to investigate the cardiovascular autonomic function test in obese school children.

**RESULT:-**Our study shows reduced parasympathetic activity (E:I ratio) and reduced sympathetic activity (orthostatic hypotension and hand grip test ) of obese children.

**CONCLUSION:-** If the autonomic nervous system dysfunction is diagnosed early by doing autonomic function test, it may prove an important aid in identification of those prone to weight gain and are at higher risk of cardio vascular complication resulting for autonomic dysfunction

### **INTRODUCTION :-**

Obesity is a disorder with a multifactorial etiology resulting from a complex interaction between the environment, behaviour and genetic susceptibility.<sup>1</sup> As the prevalence of this disorder grows worldwide, obesity is increasingly considered a major public health problem.<sup>2-4</sup>With continued rise in standards of living, obesity is emerging as a global epidemic in both children and adults. This has been called “New world syndrome” and is a reflection of massive social, economic and cultural problems currently facing developing and developed countries. The consequences of obesity in childhood and adolescence include arterial hypertension, atherosclerosis, dyslipidemia, diabetes, obstructive sleep apnea, alterations in the musculoskeletal system, depression and a reduction in quality of life.<sup>5,6</sup> Since autonomic nervous system is involved in energy metabolism and regulation of cardiovascular system.<sup>7,8</sup> It is conceivable that one or more sub groups of obesity have an alteration in their autonomic nervous system that may promote obesity and account for several clinical consequences of obesity.

Although studies demonstrate important modifications in the autonomic control of obese adults and adolescents, there is scarce information on obese children, and the findings remain inconclusive. So this study is done to investigate the cardiovascular autonomic function test in obese school children.

### **Subjects and eligibility:**

250 School children were randomly selected to obtain mixed group of children belonging to mixed socioeconomic status of age group 9-16 from various schools of Bikaner. Then they were screened to exclude underweight children by using lower cut-off limits of BMI. 50 underweight children were excluded and remaining 200 children were selected for the study. Now these 200 children were again segregated into two groups: Obese group (44) and Non obese group (156). This segregation was done using international obesity task force cutoffs because the IOTF group combined the childhood and adult definitions of overweight and obesity prevalent then, by taking at age 18 years, those percentiles that corresponded to the BMI's of 25 and 30

Kg/m<sup>2</sup>, and using these same percentiles throughout the age range for specifying overweight and obesity in childhood in girls and boys separately.

**Inclusion criteria:**

1. Children with age ranging between 9 – 16 years of both the gender.
2. Physically and mentally fit.
3. Cooperative and capable of understanding the procedure.

**Exclusion criteria:**

1. Children suffering from medical ailments or anxious, apprehensive and uncooperative.
2. Any systemic illness that is likely to affect cardiovascular autonomic functions
3. Any major psychiatric illness.

**BMI Classification tables:**

Age (years)	Boys	Girls
9	14.35	14.28
10	14.64	14.61
11	14.97	15.05
12	15.35	15.62
13	15.84	16.26
14	16.41	16.88
15	16.98	17.45
16	17.54	17.91

Table 1: International cut-off points for BMI for thinness grade 3 by sex for ages between 9 and 16 years, defined to pass through BMI of 18.5 at age 18.<sup>9</sup>

Age (years)	Boys	Girls
9	19.10	19.07
10	19.84	19.86

11	20.55	20.74
12	21.22	21.68
13	21.91	22.58
14	22.62	23.34
15	23.29	23.94
16	23.90	24.37

Table 2: International cut off points for body mass index for overweight and obesity by sex between 9 and 16 years, defined to pass through body mass index of 25 kg/m<sup>2</sup> at age 18.<sup>10</sup>

The protocol of the study was approved by the ethics committee and departmental research committee, Sardar Patel Medical College, Bikaner.

**Method:**

Informed written consent was obtained prior to data collection both from the school authorities and from the parents of the children after explaining the objectives and the method of study. Two days prior to data collection a pre tested proforma was distributed amongst the subjects to get the information on family characteristics like type of residence, type of family, education, occupation and income of parents etc. The exact age of the child was verified from the school records and rounded to the completed years. Anthropometric measurements were done utilizing the standard equipments and methodology. Weight was recorded using spring weighing machine approximated to the nearest kilogram and height was recorded using the stadiometer attached to the wall to the nearest centimetre. All the measurements were done after removing shoes and all the loose outfits of the child.

Blood pressure (BP) was recorded from the left arm in supine position after giving adequate rest to the child measured with sphygmomanometer. Body mass index (BMI) was calculated as weight in kilograms / (Height in meter)<sup>2</sup>. International Obesity Task Force (IOTF) classification was utilized for the estimation of obese subjects.

**Materials:**

**Autonomic function tests carried out by using:**



- 1) Electro cardiograph
- 2) Sphygmomanometer
- 3) Hand grip dynamometer

**Analysis of Observations:**

Standard statistical methods were applied for analysis of the observation. The mean values of various parameters were calculated separately in various groups of the subjects.

The quantitative data was expressed as Mean  $\pm$  S.D. and the student's 't' test was used to compare the differences between the respective means. All p values were 2 tailed, p value of  $<0.05$  was considered significant.

**Observations:-**

	Boy	Girl	Total
Non-Obese	95	61	156
Obese	26	18	44
Total	121	79	200

Distribution of subjects

Category	Mean $\pm$ Standard Deviation
Non-obese Boys	18.25 $\pm$ 1.915
Obese Boys	25.94 $\pm$ 4.208
Non-Obese Girls	17.7 $\pm$ 1.891
Obese Girls	24.07 $\pm$ 4.932

Mean BMI of the group

TESTS		Normal 95		Abnormal 26		t-value	P value
		Mean	SD	mean	SD		
1	30:15 ratio	1.392284	0.175183	1.399616	0.256908	0.1697	0.8655
2	Valsalva ratio	1.615921	0.296032	1.668544	0.400987	0.7408	0.4603
3	E:I ratio	1.485395	0.151245	1.411192	0.220571	1.9932	0.0485
4	Orthostatic hypotension test	6.042105	2.75185	13.07692	4.353602	10.0693	0.0001
5	Hand grip test	14.06316	2.009607	8.384615	2.3337	12.3236	0.0001

Comparison of autonomic function tests in non obese and obese boys

TESTS		Normal 61		Abnormal 18		t-value	P value
		Mean	SD	mean	SD		
1	30:15 ratio	1.389446	0.200928	1.322357	0.11609	1.3479	0.1817
2	Valsalva ratio	1.636951	0.265198	1.505988	0.242474	1.8753	0.0645
3	E:I ratio	1.492089	0.180604	1.331999	0.141933	3.4537	0.0009
4	Orthostatic hypotension test	6	2.804758	11.88889	3.968833	7.083	0.0001
5	Hand grip test	13.60656	2.471698	8.333333	1.847096	8.3722	0.0001

Comparison of autonomic function tests in non obese and obese girls

### **Parasympathetic activity:-**

The result of our study shows reduced E:I( Expiration: Inspiration) ratio in obese children as compared to the normal children. A reduction in parasympathetic activity among obese children has also been reported by other authors.

The possible mechanisms are:

1. The hypothalamus is a regulatory centre of satiety and of the ANS. Therefore, abnormalities in the hypothalamus may cause obesity and autonomic dysfunction.<sup>11,12</sup> This may explain the alterations observed in the heart rate variability indices.

2. The exact mechanism that may cause impairment of parasympathetic nerve function has not yet been clearly established. Some researchers suggested that gradual development of insulin resistance in target tissues with the beginning of excess weight gain in obesity is responsible for subsequent development of hyperinsulinaemia. This hyperinsulinaemia has got a role in low cardiac vagal activity in obese person. Though the relationship between insulin resistance and parasympathetic dysfunction is not clear, but several researchers made various suggestions such as high insulin level or insulin resistance may cause damage to autonomic nerves at any level of their reflex arc, insulin resistance may cause a deterioration of microcirculation in many tissues including nerves which may lead to neural ischemia and thereby damage of cardiac parasympathetic nerve terminals occur at the level of cardiac muscle or vascular wall.<sup>13,14</sup>

3. Valensi et al,<sup>15</sup> observed cardiac parasympathetic dysfunction present in the obese subjects could be associated with higher carbohydrate intake and lower fat and protein intake which result in parasympathetic abnormality.

4. A reduction in vagal activity is associated with an increased risk for all-cause morbidity and mortality and for the development of several risk factors. Therefore, the reduction observed in obese children may be an early sign for the prediction of the risk for cardiovascular and metabolic disease.

5. In cardiac autonomic neuropathy, the disruption of parasympathetic nervous system is usually detected earlier than that of the sympathetic nervous system. Decrease in heart rate variability is noticed as first indicator of cardiac neuropathy and *decrease in Expiration: Inspiration ratio is considered to be a sign of parasympathetic dysfunction.*<sup>16</sup>

6. Our result is also supported by Rissanen et al,<sup>17</sup> who documented that cardiac parasympathetic activity increases with weight loss in obese women. This increase may not be maintained long term if body weight is regained. The rise of cardiac parasympathetic activity is correlated with decrease of body fat mass, abdominal fat, serum insulin, and heart rate. Cardiac parasympathetic activity is not related to resting energy expenditure.

#### **Sympathetic activity:-**

The results of our study indicate higher baseline diastolic blood pressure and systolic blood pressure prior to isometric handgrip exercise and blood pressure response on lying to standing in obese group children which shows the reduced sympathetic activity in obese children.

The possible mechanisms are:

1. It is well established that stimulation of sympathetic system results in increase in arterial pressure either due to

(i) increase in heart rate and force of contraction, leading to increase in cardiac output and blood pressure or alternately

(ii) vasoconstriction and resultant increase in total peripheral resistance and blood pressure, or both.

The first effect is due to increased activity in cardiac sympathetic fibers and second due to increased activity in peripheral vasoconstrictor fibers. Such preferential activation of peripheral vasoconstrictor fibers has been attributed to cause cold induced vasoconstrictor response in normotensive population and in hypertensive.<sup>18</sup> The isometric exercise induced increase in heart rate, cardiac output and blood pressure, reported in the literature<sup>19</sup> can be explained on the basis of activity in the cardiac sympathetic fibers. The obese children showed truncated response in cardiac sympathetic activity resulting in borderline response to isometric exercise.

2. Piccirillo et al,<sup>20</sup> reported that obesity was associated with decreased sympathetic responsiveness. Obese subjects showed a higher presynaptic activation level as indicated by plasma norepinephrine levels. At the same time, postsynaptic sympathetic responsiveness was diminished in these subjects. The decreased

sympathetic reactivity to stress was thought to be a contributing factor to the higher mortality rates.

3. Peterson et al,<sup>21</sup> report an association between the increase in body fat and hypoactivity of sympathetic and parasympathetic components of ANS. The authors state that lower sympathetic activity is related to lower energy expenditure and, consequently, to a positive energy balance and increase of body weight.

4. Nagai et al,<sup>22</sup> observed that obese children possess reduced sympathetic as well as parasympathetic nerve activities. He concluded that autonomic depression, which is associated with the duration of obesity, could be a physiological factor promoting the state and development of obesity.

5. The peripheral sympathetic nervous system is a key factor in the regulation of energy balance in humans. Differences in sympathetic nervous system activity may contribute to variations in 24 h energy expenditure between individuals. beta-Adrenoceptors play a more important role than alpha-adrenoceptors in this regulation. The involvement of both beta 1- and beta 2-adrenoceptor subtypes has been demonstrated, the role of the beta 3-adrenoceptor subtype is not yet clear. Normal or increased levels of sympathetic nervous system activity and reduced reactivity appear to be present in established obesity. Furthermore, the sensitivity for beta-adrenoceptor stimulation is impaired in obesity. The blunted reactivity and sensitivity may contribute to the maintenance of the obese state. There are data to suggest that they may also play a role in the aetiology of obesity, because the impairments often remain after weight reduction. Furthermore, a negative correlation between baseline sympathetic nervous system activity and weight gain during follow-up has been found in Pima Indians. Recently, genetic evidence about the involvement of adrenoceptors in obesity has become available. Although the results of association and linkage studies on polymorphisms in the beta 2-, beta 3- and alpha 2-adrenoceptor genes are inconsistent, the functional correlates of some of these polymorphisms (changes in agonist-promoted down-regulation, protein expression levels, lipolytic sensitivity, basal metabolic rate, sympathetic nervous system activity) suggest that they may be important in the aetiology of obesity.<sup>23</sup>

So if the autonomic nervous system dysfunction is diagnosed early by doing autonomic function test, it may prove an important aid in identification of those prone to weight gain and are at higher risk of cardio vascular complication resulting for autonomic dysfunction.

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## HOMOEOSTENOSIS IN HEMATOLOGICAL PARAMETERS OF ELDERLY CITIZENS OF VADODARA CITY

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### **BSTRACT:**

**Background:** According to UN norms, India is a country with ageing population. Experts state that the available literature on hematological parameters study is scanty at home; as such, we studied hematological parameters in 70 elderly males and 40 elderly females and attempted to compare with 40 young male and 40

young female subjects respectively living in Vadodara city of Gujarat state, a favored place of retirement by many.

**Material and method:** We studied Demographic parameters like wt., height, BMI[Body Mass Index] ,and Hematological parameters-Hb, total-[ RBC,WBC, Platelets Counts], PCV [Pack Cell Volume],ESR[Erythrocyte Sedimentation Rate] and blood indices like MCH,MCHC,MCV and RDW and ESR values. The elderly had good HRQOL [Health Related Quality Of Life] in last 1year, by their self appraisal.

**Observations:** In uncomplicated ageing elderly, Hb, RBC [total], MCH, MCHC and PCV were less than in young but near lower normal limits. Total WBC and Platelets count were within normal limits. The MCV [Mean Corpuscular Volume ] was increased in elderly. We have not assessed the cause for it; also we have not done S. Creatinine value assessment.

**Conclusion:** We determined selected hematological parameters in a small sample size of elderly population of Vadodara city and found that there is definite yet mild age related homeostenosis of hematological parameters.

**Key Words:** Elderly, Hematological parameters, Homoeostenosis.

## **INTRODUCTION:-**

Aging is regarded by experts as unquestionably complex and may require systems biology approach which may combine data driven modeling and hypothesis driven experimental studies.(1)

Due to improvement in hygiene and health care, human life expectancy has been increased at a steady rate of about 2.5 years per decade since the middle of nineteenth century (2)

The term elderly has a criterion of age 60 years from UN definition (3).United Nations have declared that, when 7.0% or more than that of total population is elderly, that country population be labeled as aging population.(3).The term elderly has a criterion of age 60 years from UN definition (4)

India has 7.8% of total population as ageing population (5) so, there is need to study our ageing population in depth. Also, the hematologic profile may be playing crucial role in molecular cascades in connection to cardio-pulmonary and vascular pro inflammation and oxidative stress in ageing. Moreover, these parameters may



influence indexing of the collective dysfunctional totality suggesting homeostenotic functional reserve of elderly.

Ethnic, genetic and environmental factors being different, findings of foreign investigators with comparable series may not be suitable for Indian elderly, to establish probable reference values suitable for Indian subjects.

Keeping this view of existing paucity of such studies at home (6) in mind, we have tried to assess the values of hematological parameters in elderly citizens of Vadodara city, a city of preference of older population, located in central Gujarat, known for its good cultural, medical and tranquil environment with numerous activities for elderly population.

#### **MATERIAL AND METHOD:-**

Sample size-70 elderly males and 40 elderly females, compared with 40 young males and 40 young females respectively, having subjective self appraisal of Health Related Quality Of Life as good, selected from different areas randomly who used to visit public places, health institution or Senior Citizen spots, of age between 60 and 80 years, after screening through inclusion and exclusion criteria, complete history, clinical examination, demographic and hematological assessment, and they were arranged in 2 groups-61-70;and 71-80 years

After getting the consent of IEC(Inst. Ethical Committee), taking the consent of participants and informing through the PIS (Participant Information Sheet) the details explained to them, and the study was undertaken.

The control group consisted of no.40 of apparently healthy male and female individuals residing in Vadodara city who were in age below 20 and above 18 years who were exposed to almost comparable background

**INCLUSION CRITERIA** -\*Age-60-80 years; \*Stay- Not at high altitude in last 2 years; \*Sex-Male/Female; \*Addiction-non smoker, non alcoholic; \*Disease-no disease/H/S/O or S/S/O/ any disorder that can influence these parameters; \*Not on any drug which can affect the parameters.

**EXCLUSION CRITERIA** -\* The participant unwilling to accept the study.

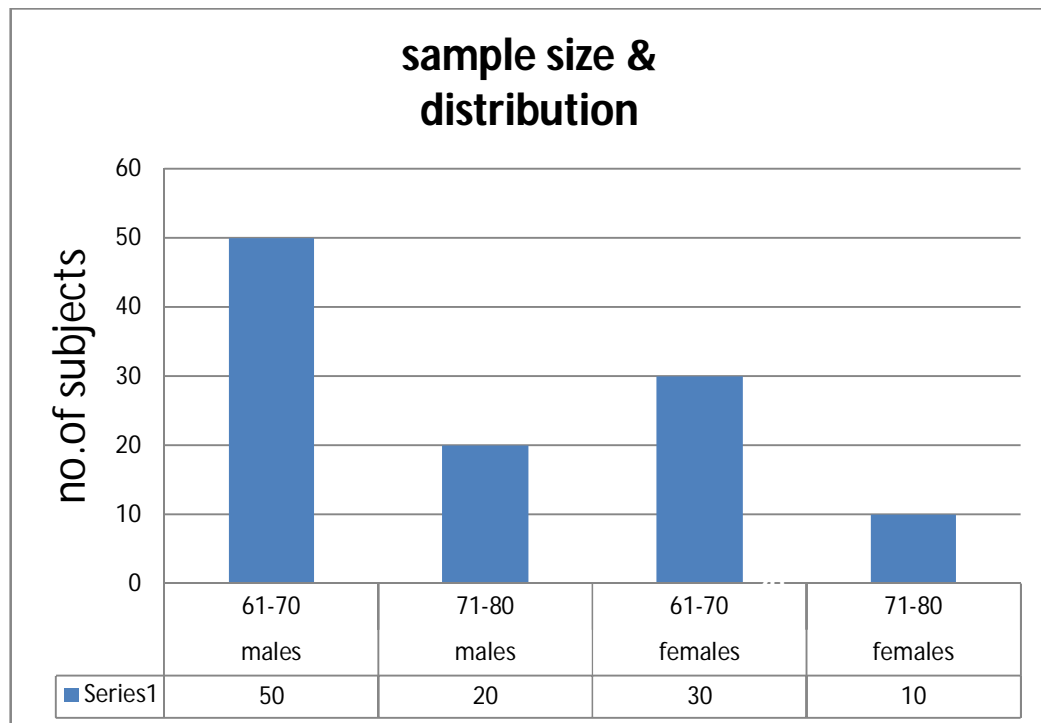
**STUDY TYPE**-Cross sectional, prospective, partly qualitative and mainly objectively assessed single time quantitative. reading .

**BLOOD SAMPLES** -Fasting 12 hours; only fresh venous 2.0ml.blood sample in EDTA bulb collected by aseptic precautions ; with max. permissible time of 2-4 hrs. in freeze between 2-8 degree Celsius; and to avoid diurnal variation, collected between 9-00a.m. and 11-00 a.m. was accepted. Approved gadgets, materials and equipments including Automatic cell counter Sysmax model, were used.

**STATISTICAL ANALYSIS** – Microsoft excel and other approved statistical software using formula of relevant nature. The degree of /% of homoeostenosis was calculated from values of mean [average] value of specific parameter of elderly and mean values of same parameter in young adults.

**OBSERVATIONS AND RESULTS**

Presented relevant data ; graphically and by tables. Mean; Standard Deviation; max-min. values, ‘p’ value; tabular ‘t’ test findings; and standard error of difference between two means presented to 5% was displayed by error bars.**Figures for homoeostenosis of RDW,ESR, total WBC count and Platelet Cell count was not determined.**



**TABLE 1 - Demographic Parameters of Elderly Participants [n =110]**

NUMBER N=	SEX	AGE GROUP	ITEM	AGE IN Yrs.	WT. IN Kg.	HT. IN Cms .	BMI
30	FEMALE	61-70	AV.	63.73	61.26	152.86	26.89
			S.D.	3.05	13.13	5.58	4.25
10	FEMALE	71-80	AV.	72.6	64.3	161	24.88
			S.D.	1.74	6.55	1.96	2.66
50	MALE	61-70	AV.	65.14	73.32	166.92	26.1
			S.D.	2.72	12.14	5.06	3.66
20	MALE	71-80	AV.	73.85	64.09	168.09	22.66
			S.D.	2.05	4.23	6.98	2.14

**TABLE 2 - Hematological Parameters of Elderly Participants [n=110]**

NUMBER N=	SEX	AGE GROUP	ITEM	HB.-G%	H.STENOSIS OF % OF Hb.	RBC[T] m./CMM.	H.STENOSIS OF RBC IN %	PCV-MM.	H.STENOSIS OF PCV IN %
30	FEMALE	61-70	Average	11.04	*12.9	4.12	*10.24	34.4	*13.83
			S.D.	2.09		0.37		5.9	
10	FEMALE	71-80	Average	11.6	*8.45	3.73	*18.74	37.7	*5.57
			S.D	0.77		0.27		1.8	
50	MALE	61-70	Average	13.68	0.7	4.62	2.95	41.76	0.48
			S.D.	1.23		0.47		4.3	
20	MALE	71-80	Average	12.29	*9.5	4.07	*11.33	40.37	*3.79
			S.D.	1.16		0.47		1.23	
40	Males control *(17)	18-20	Average	13.58		4.76		41.96	
			S.D.	1.05		0.38		4.51	
40	Females	18-20	AVERAGE	12.67		4.59		39.92	

	control *(17)						
		S.D.	1.10		0.29		2.70

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**TABLE 3 – Blood indices with % Homeostenosis in Critical Population**

NUMBER n =	SEX	AGE GROUP	ITEM	MCV $\mu$ CUBE	H.STENOSIS OF MCV- IN %	MCH PG.	H.STENOSIS OF MCH -IN %	MCHC G/DL	H.STENOSISOF MCHC -IN %
30	FEMALE	61-70	Average	83.13	4.49	26.7	0.37	31.82	---
			S.D.	11.94		4.33		1.47	
10	FEMALE	71-80	Average	101.46	*16.62	31.11	---	30.66	*3.29
			S.D	3.81		1.21		1.33	
50	MALE	61-70	Average	89.01	2.31	29.92	---	32.51	0.86
			S.D.	0.47		2.07		0.99	
20	MALE	71-80	Average	99.68	*14.57	30.15	---	30.04	*8.39
		S.D.	S.D.	11.92		2.39		1.84	
40	MALES CONTROL *(17)	18-20	Average	---		28.67		32.79	
			S.D.	---		1.90		2.24	
40	FEMALES CONTROL *(17)	18-20	average	---		27.60		31.70	

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**TABLE 4 – Data other than above Hematological parameters**

**FIGURES FOR HOMOEOSTENOSIS OF RDW, ESR, TOTAL WBC COUNT AND PLATELET CELL COUNT IS NOT DETERMINED.**

NUMBER -n =	SEX	AGE GROUP	ITEM	RDW	ESR	WBC TOTALCOUNT-IN K./CMM.	PLT CNT. IN LAC/CMM.
30	FEMALE	61-70	Average	13.22	12.76	6266	3.02
			S.D.	1.46	6.80	1399.3	.5629
10	FEMALE	71-80	Average	11.2	11.6	7500	2.554
			S.D.	1.5	2.36	2165	.7809
50	MALE	61-70	Average	12.38	10.12	6370	2.619
			S.D.	0.94	4.59	1090	0.495
20	MALE	71-80	Average	11.49	9.33	6742	2.729
		S.D.	S.D.	1.11	1.17	1321	.6067
40	MALES CONTROL *(17)	18-20	Average	46.31	--	--	--
			S.D.	4.55	--	--	--
40	FEMALES CONTROL *(17)	18-20	Average	44.04	--	--	--
			S.D.	2.67	--	--	--

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**TABLE 1. Showing Red blood profiles of Male (n=40) and Females (n=40)**

<b>Blood profile</b>	<b>Male</b>	<b>Female</b>	<b>P-value</b>
RBC Count	4.76±0.38	4.59±0.29	0.075
Hb (g/dl)	13.58±1.05	12.67±1.10	0.005*
HCT (%)	41.96±4.51	39.92±2.70	0.064
MCH(pg)	28.67±1.90	27.60±1.61	0.041*
MCHC(g/dl)	32.79±2.24	31.70±0.93	0.033
RDW (fl)	46.31±4.55	44.04±2.67	0.036*

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Table presented to compare the corresponding parameters in young males and females of Vadodara.[Acknowledgement:- given with the values.] done with same model type of auto analyzer and comparable protocols.(17),during same year at Vadodara , done by our colleagues at SBKSMI&RC in our department, because equivocally accepted standard reference values for Vadodara young individuals has not been established. As the above study has not included MCV assessment, for comparing the MCV [Mean Corpuscular Volume] we utilized the MCV value for young adults from medical book as 87µ cube, to compare with elderly value.

**TABLE-1. Demographic & Hematological parameters of elderly males 61-70 yrs. n=50**

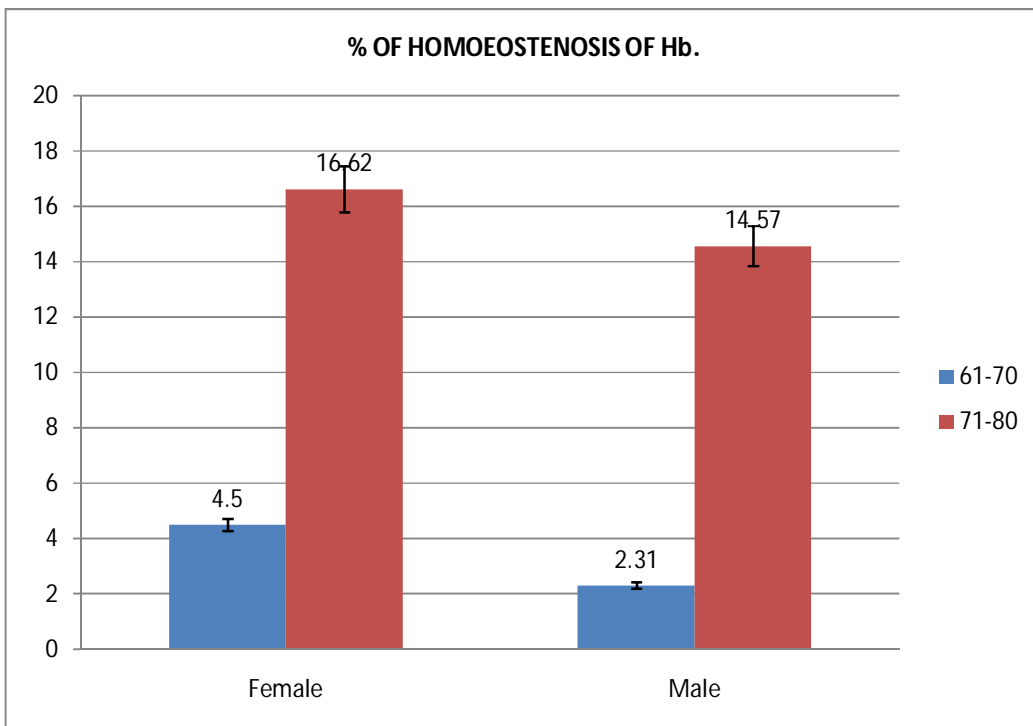
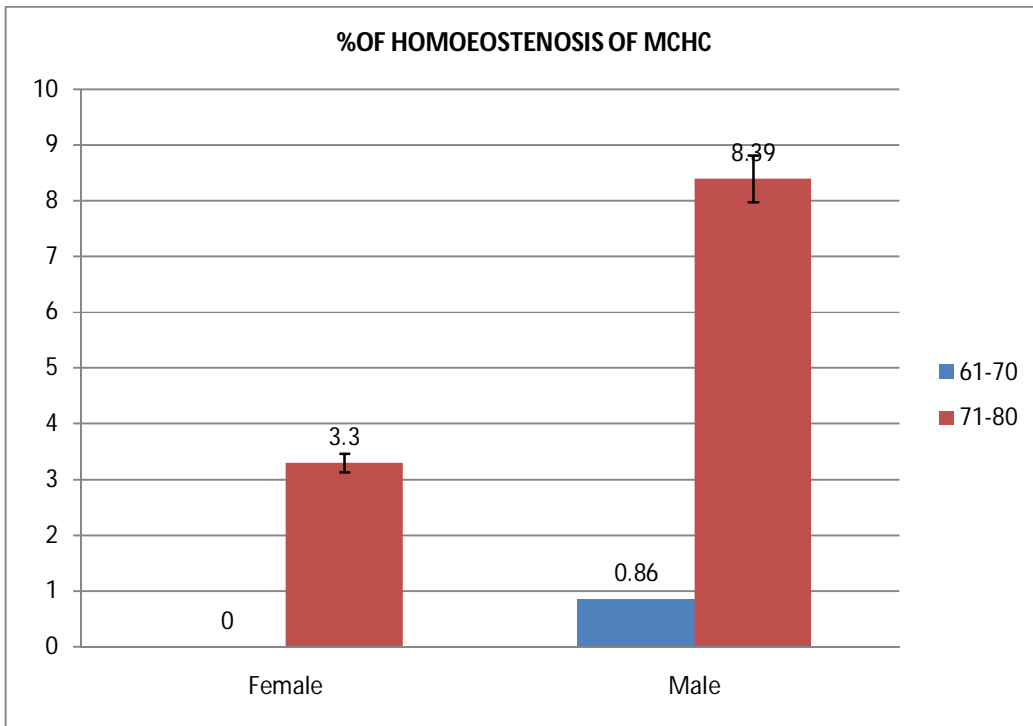
ITEM	AGE YRS.	WT.[Kg.]	HT.[Cms.]	BMI	Hb.-g%	RBC[T] m./ cmm.	WBC[T]Thousand/cm m.	PCV-mm.	MCV μ cube	MCH pg.	MCHC g/dl	RDW	ESR	PLT.CNT. L/ cmm.
AV.	65.1 4	73.3 2	166.9 2	26.1	13.6 8	4.62	6.37	41.7 6	89.0 1	29.9 2	32.5 1	12.3 8	10.1 2	2.619 2
S.D.	2.72	12.1 4	5.06	3.66	1.23	0.47	1.09	4.3	0.47	2.07	0.99	0.94	4.54	0.495

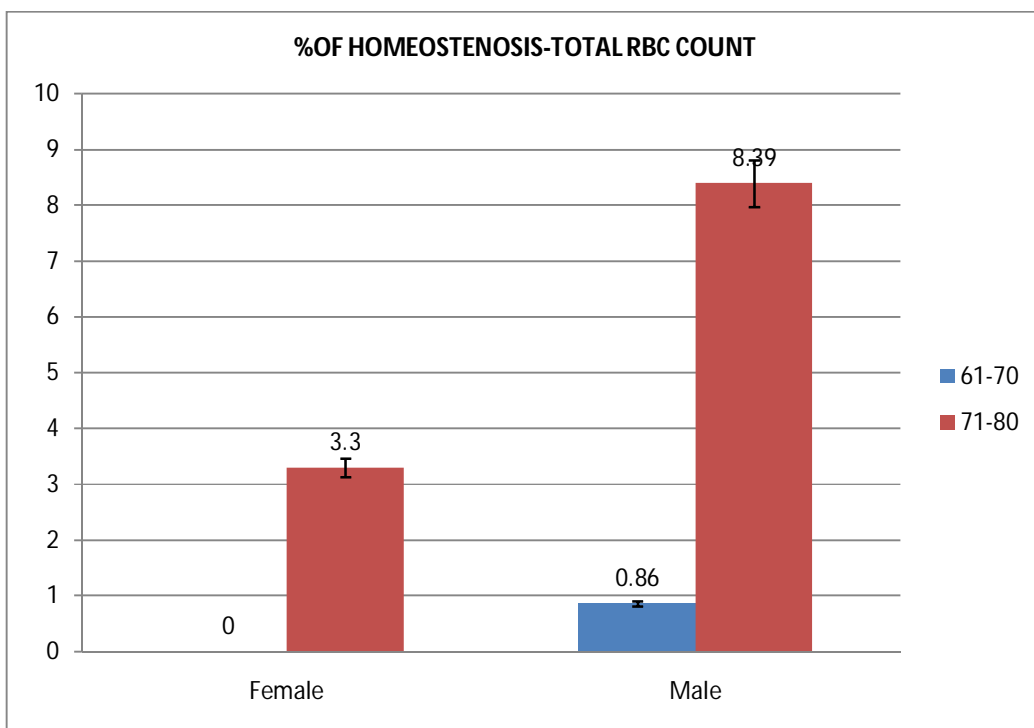
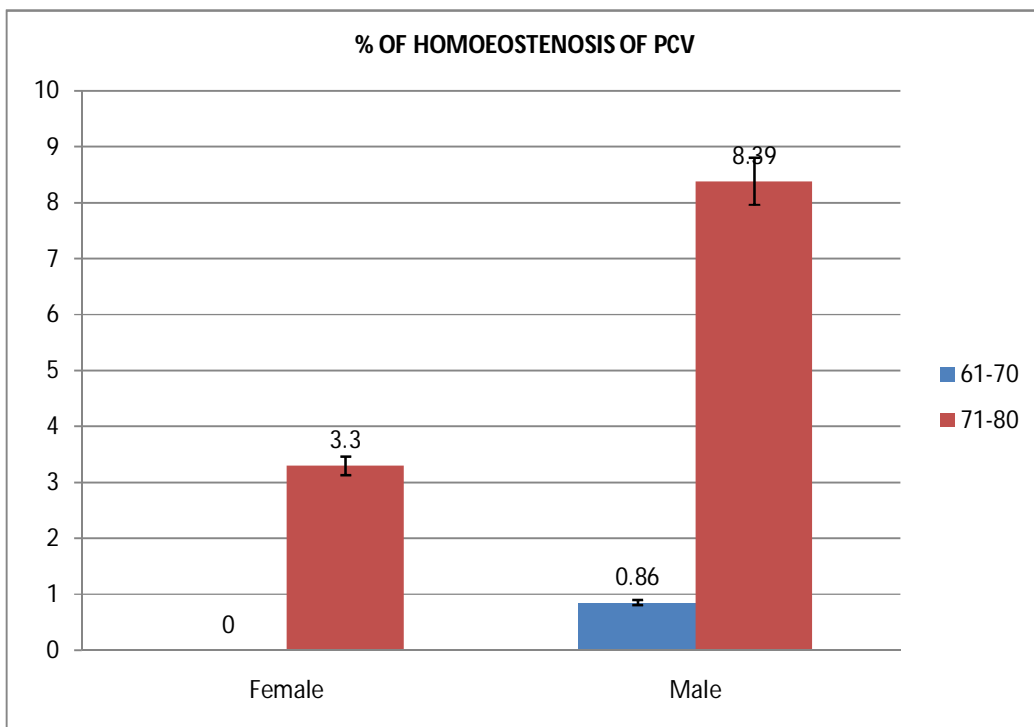
**TABLE-2. Demographic and Hematological parameters of elderly males 71-80 yrs.**

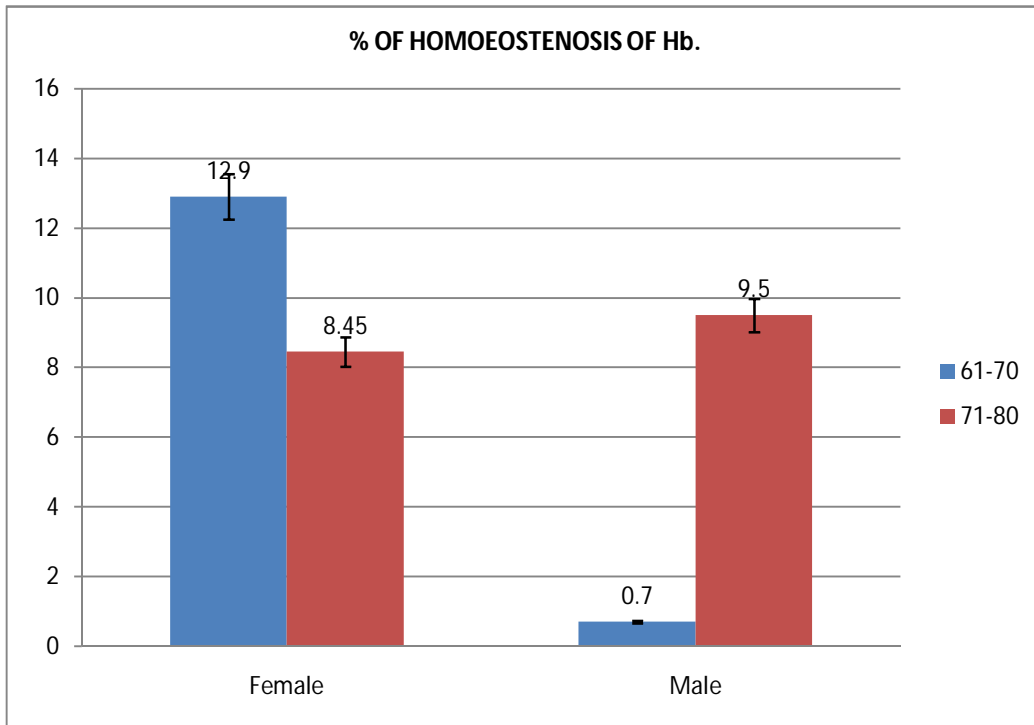
ITEM	AGE yrs	WT.[Kg.]	HT.[Cms.]	BMI	Hb.-g%	RBC[T] m/cmm	WBC[T]thousand/c mm.	PCV-mm.	MCV μcube	MCH Pg.	MCHC g/dl	RDW	ESR	PLT.CNT. L/cmm.
AV.	73.8 5	64.0 9	168.0 9	22.6 6	12.2 9	4.07	6742. 8	40.3 7	99.6 8	30.1 5	30.0 4	11.4 9	9.33	2.72 9
S.D.	2.05	4.23	6.98	2.14	1.16	0.47	1321	1.23	11.9 2	2.39	1.84	1.11	1.17	.606 7

Sr.no.	Subjects	Gender	HB.VALUE [elderly subjects]				TOTAL RBC COUNT [elderly subjects]			
			Mean	Max.	Min.	S.D.	Mean	Max.	Min.	S.D.
1	70	MALE	13.68	16	11	1.23	4.62	5.5	3.7	0.47









#### DISCUSSION:

The aging changes that influence an organism, may be caused by external agencies or the intrinsic mechanisms and the blood is also influenced by aging. An attempt is made here to assess the hematological values in this biological phenomenon in elderly population of Vadodara.. The diminished functional and structural reserves which are state of homeostenosis are seen by most of the investigators but the values presented somewhat vary in their studied series.

It is mentioned (7) that with advancing age, there is reduction in pluripotent stem cells in bone marrow. With advancing age, there is reduction in amount of trabecular bone and hemopoiesis is accompanied by increase in fat cells in sub cortical regions.(8) Average marrow cellularities at various sites are presented by Henry, who has also presented normal iliac bone marrow cellularity as given by Hartsock.(9).Also, hemopoiesis has decreased bone marrow reserves in response to high demands.(18).

It is observed that number of physiologic factors affect CBC (Complete Blood Cell) count and one of them is age Anemia is a common condition in older population. (13),here the authors have warned that, yet, taking ,the mild anemia of elderly lightly, may run a potential risk of missing an early clue to an important underlying disorder and which itself is important predictor of morbidity, performance status and mortality as a general risk factor or in states like heart failure.(13).

Chiu Wah Tsang (15) et al have studied the hematologic parameters in BMES(Blue Mount Eye Series) and also presented findings of other investigators with comparable series with large population size. BMES by CHIU WAH TSANG et al. at Uni. of Sydney[1998] group has attempted to establish healthy reference values of Hematological Indices in an older population in very large population[1382 males and 1837 females elderly participants; more over they have also assessed creatinine values. Our sample size was small, comparable to Jarnigan (15) who studied 48 women and 25 men and Zauber (15) who has studied blood indices in 50 women and 45 men;[as presented in BMES]. It comes closer to our sample size. The age group as selected by Yipp (15) and Kelly (15) is closer to the age grouping as we have done, and the findings of our values in Vadodara elderly are closer to their findings in a number of blood indices.

The assessment of similar parameters is done by Indian authors (6), (11), (12) and their findings also correlate to our observations.

.Vadodara is a favored place for retirement by elderly population but in some pockets there is likelihood for industrial pollution and urban complexities which may be feared to induce detrimental influence on health probably hematological profile.

We tried to assess a selected hematological parameters in Vadodara who were in favored situation as far as life style modification calls for, and as such their overall health related quality of life was good as per their self appraisal. [HRQOL], barring the hematological changes, none had ADL[Assisted Daily Living] or IADL[Instrumental Assisted Daily Living], and none had a transition for existing to inferior quality of life in last year. The values and patterns in Vadodara elderly are similarly showing homeostenosis in hematological parameters, like, Hb, MCH, RBC Count, PCV with rise in MCV. Also, changes in females are more significant in elderly group perhaps due to the hormonal and nutritional reasons; although the degree of severity may vary individually but the extent was not critical to degree that may call for apprehension in unmodified or uncomplicated ageing sample we studied. Elderly population should still be "monitored" for maintenance of quality of life. Indeed the sample size is small, and further study is required for programming for life style modification in elderly individuals.

## **CONCLUSION:**

The blood indices values are diminished in practically most subjects to variable extent as demonstrated by tables; except MCV however, which increased to greater or lesser degrees, as an equivocal observation. Hb and RBC counts are significantly diminished including PCV..As stated earlier these findings correlate well with findings of other studies(12);(16)

yet, the sample size being small and as we attempted examining only one area of Vadodara city, observations requires further study, in many different areas of this region having varying patterns eco biology, life style and environment.

#### **ACKNOWLEDGEMENT:**

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AND STAFF OF DEPARTMENT OF PHYSIOLOGY; SBKSMI &RC-PIPARIA GUJARAT-INDIA.

**INTREST:** Authors have no conflict of interest.

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## PERIPHERAL NERVE CONDUCTION VELOCITIES AND HANDEDNESS – IS THERE ANY CORELATION?

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### ABSTRACT:

**BACKGROUND:** Nerve conduction velocity is affected by various physiological parameters like diameter of nerve fibre, age, sex, height and temperature. Very little is known regarding the role of nerve conduction velocities in determining handedness. Present study was conducted to correlate the role of peripheral nerve conduction velocities in determining handedness.

**OBJECTIVE:** To correlate the role of peripheral nerve conduction velocities in determining handedness.

**MATERIALS and METHOD:** The study was performed on 40 right handed healthy M.B.B.S. students in the age group ranging from 18 to 25 yrs, free of neurological signs and symptoms.

The sensory and motor nerve conduction velocities of median and ulnar nerves in right and left hand were measured and compared by using “ NICOLET COMPASS PORTA BOOK II” E.M.G. machine.

The data was analysed and Z test was used to calculate the statistical significance.

**RESULT:** There was no significant statistical difference in the sensory and motor nerve conduction velocities of median and ulnar nerves in the left and right arm of an individual. The results were found to be equivocal.

### CONCLUSION:

Thus it can be concluded that the conduction velocities of the peripheral nerves do not play any role in handedness. It is determined at cerebral level and moreover training plays an important role.

**KEY WORDS:** nerve conduction velocity (NCV), Electromyography (EMG), handedness, sensory, motor, median nerve, ulnar nerve.

### INTRODUCTION:-

The nerve conduction studies are most often used to diagnose disorders of peripheral nervous system. In recent years electrophysiological methods have found a definite place in investigation and diagnosis of certain neurological disorders.

It has been proved that nerve conduction velocity depends on various factors like myelination and diameter of nerve fibers, age, sex, temperature and height. Very little is known regarding role of conduction velocities in handedness.

In our present study we have compared sensory and motor nerve conduction velocities of median and ulnar nerves of both Right and Left hand in Right handed individuals and tried to assess the correlation between handedness and nerve conduction velocity.

### **MATERIAL AND METHODS:-**

The study was conducted on 40 right handed healthy medical students in the age group ranging from 18 to 25 years, free from neurological signs and symptoms.

Edinburg Handedness Inventory (Oldfield1971) was used to assess hand preference (Tan U 1988).<sup>[9]</sup>

The motor and sensory nerve conduction velocities of the median and ulnar nerves were measured by using "Nicolet compass portabook II" E.M.G. machine.

The motor nerve conduction study involves the response of the muscle to the supramaximal stimulation of its motor nerve at two points along its course i.e at elbow and wrist. Biphasic action potential was recorded.

For measuring median nerve motor conduction velocity, the recording and the reference electrodes were placed over abductor pollicis brevis along the thenar eminence. The ground electrode was placed over the forearm between the recording and stimulating electrodes and stimulation was given along the median nerve at elbow and wrist.

Similarly to assess the ulnar motor conduction velocity, the recording and reference electrodes were placed on the abductor digiti minimi and stimulation was given along the ulnar nerve at elbow and wrist.

For measuring sensory nerve conduction velocity the ring electrodes were placed on the index finger for the median nerve and little finger for the ulnar nerve. Cathode was placed at 1<sup>st</sup> interphalangeal joint and anode 4 cms distal to it. Ground electrode was placed over the palm and stimulation was given with the help of electrodes at the wrist over the median and ulnar nerves respectively.

The response obtained varies widely in different individuals.

The latency, amplitude and duration were measured from the curve obtained and the distance between the two stimulating points was measured in mm using a flexible tape. The conduction velocity(CV) in motor fibers was calculated as follows:-



CV = Distance between proximal and distal stimulating sites(mm)

Proximal latency(msec) – Distal latency(msec)

**OBSERVATIONS AND RESULTS**

Motor and sensory conduction velocities were determined in 40 individuals, age ranging from 18 to 25 yrs. Z TEST was used to calculate statistical significance. The results are as follows.

Table 1. Motor and Sensory NCVs of Median nerve of Right and Left hand and their comparison

	Motor NCV (m/sec) (Mean ± SD)		Sensory NCV (m/sec) (Mean ± SD)	
Right hand	60.82± 4.48	Z = 0.12 (N.S)	53.40± 5.22	Z = 0.13 (N.S)
Left hand	60.70± 4.60		53.55± 4.70	

Table 2. Motor and Sensory NCVs of Ulnar nerve of Right and Left hand and their comparison

	Motor NCV (m/sec)	Sensory NCV (m/sec)

	(Mean ± SD)		(Mean ± SD)	
Right hand	60.97± 5.48	Z = 1.32 (N.S)	52.32± 7.30	Z = 0.25 (N.S)
Left hand	62.65± 5.90		51.97± 4.48	

(SD= standard deviation) (m/sec= meter/second)

**Statistical Analysis:-** The results were expressed as mean ± SD. The standard error of difference between two mean was taken. Z test was applied. By using the said test p value was found to be non significant. (p<0.05 significant)

**Result:-** There was no statistical difference in the sensory and motor nerve conduction velocity of median and ulnar in the right and left hand of an individual.

## DISCUSSION:-

Similar studies were carried out in the past by several researchers. Tan U<sup>[10]</sup> in 1985 found that there was no statistical difference in the nerve conduction velocities in the left and right hand of the subject and concluded that the nerve conduction velocities cannot contribute to the mechanism of handedness.

Kamen G., Greenstein S. S. and De Luca<sup>[6]</sup> in 1992, Trojaborg W.1964, Sathiamoorthy<sup>[8]</sup> in 1990 carried out same studies but the results were not significant.

Bhorania et al<sup>[1]</sup> in 2009 also found there was no significant difference in velocities between right and left limbs of the same individuals in relation to motor nerve conduction velocities.

Harinder J. Singh et al<sup>[4]</sup> in 2011 found limb dominance did not have any significant effect on the motor nerve conduction velocity of upper limb.

Our present study suggests that there is no statistical difference in motor and sensory nerve conduction velocity of median and ulnar nerves in right and left hand respectively in same individual.

## CONCLUSION:

The conduction studies showed that there was no significant statistical difference in motor and sensory nerve conduction velocities of median and ulnar nerves in right and left hand of an individual.

Thus it can be concluded that the conduction velocities of the peripheral nerves do not play role in handedness as it is primarily determined at the cerebral level and more or less depends on training.

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## COMPARATIVE STUDY OF ONDANSETRON,GRANISETRON AND RAMOSETRON IN PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING

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## ABSTRACT

**Introduction:** Nausea and vomiting have been associated with the use of general anesthetics for cardiac surgical procedures, with nausea, retching & vomiting as the most common postoperative complaints. The aim of the study is to compare the antiemetic effects of intravenous ondansetron, granisetron & ramosetron in a randomized double blind controlled manner for prevention of nausea and vomiting in early postoperative period in patients undergoing cardiac surgery.

**Material & methods:** Ninety patients undergoing cardiac surgery were randomly allocated into three equal groups, each receiving ondansetron, granisetron and ramosetron via intravenous route, before induction of anaesthesia. Anesthetic procedure was common to all patients. Emetic episodes in early postoperative period (first three hours) and delayed (upto 24 hours) were recorded and compared in different study groups.

**Conclusion :** Based on this study it can be concluded that in early postoperative period (first three hours) the three drugs ondansetron, granisetron and ramosetron are comparable to each other. If we consider the delayed postoperative period (upto 24 hours) ramosetron appears better than ondansetron. Effects of ramosetron and granisetron are comparable to each other.

**Keywords:** Post operative nausea & vomiting (PONV), cardiac surgery, ondansetron, granisetron and ramosetron

## **INTRODUCTION**

Nausea, retching & vomiting are common postoperative complaints occurring after general anesthesia.<sup>1</sup> It is important to minimize vomiting and retching after cardiac surgery, to avoid potential cardiovascular complications and to improve patient comfort and assist in rapid recovery.<sup>2</sup> Patients with an increased risk of postoperative nausea and vomiting (PONV) are frequently given prophylactic treatment, often with a selective 5-hydroxytryptamine-3 (5HT3) antagonist.<sup>3</sup> These 5HT3 receptor antagonists produce less sedation, extrapyramidal reactions, adverse effects on vital signs or drug interactions with other anaesthetic medications.<sup>4</sup>

This study aims to compare the efficacy of intravenous ondansetron, granisetron & ramosetron in cardiac surgery patients in prevention of post operative nausea and vomiting

## **OBJECTIVE: \**

To assesses the incidence of post operative nausea and vomiting, up to 24hours, among patients undergoing cardiac surgery, with early tracheal extubation.

To compare and evaluate the efficacy of three drugs ondansetron, granisetron and ramosetron given before induction of anaesthesia on the incidence of postoperative nausea and vomiting in adults undergoing cardiac surgery.

To assess the requirement of rescue antiemetic.

**METHODOLOGY:** This is a prospective randomized double blind controlled study performed on 90 patients undergoing cardiac surgery at a high volume tertiary care cardiac centre.

After obtaining informed written consent, using computer generated random numbers, the patients were allocated into three groups of thirty each to receive ondansetron 0.1mg/kg(group A), granisetron 40mcg/kg(group B), ramosetron 0.3 mg (group C) before induction of anaesthesia

Patient's medical history, demographic information including, height, weight, age, tobacco use, alcohol use, and menstrual history, were obtained. All adult patients in the age group of 20 – 65 undergoing elective cardiac surgery at the institute were included in the study. Patients with history of motion sickness, history of post operative nausea vomiting , vestibular disease, body mass index>30 and those who received antiemetic within 24 hrs prior to surgery were excluded from the study .

The patients were prepared by overnight fasting of 8 hours and were administered tab alprazolam 0.5mg on the night before surgery. Study drugs were injected before induction of anesthesia. In order to eliminate bias blinding was done to the extent that the investigator was not aware of the type of study drug used. The study drug was prepared by single person in 5ml syringe and was diluted up to 5ml volume using distilled water. The investigator came to know the nature of drug only once the patient was observed for 24 hours.

Anesthesia was standardized with induction with inj fentanyl 10–15  $\mu\text{g kg}^{-1}$  and inj midazolam 0.02–0.04  $\text{mg kg}^{-1}$ ,inj vecuronium was administered to facilitate tracheal intubation. A gastric tube was inserted in all patients. The lungs were ventilated with an oxygen/air mixture ( $F_{\text{O}_2}$ 0.5–0.6) with a tidal volume of 8–10  $\text{ml kg}^{-1}$  to maintain normocapnia. Anaesthesia was maintained with isoflurane, fentanyl and midazolam. Total dose of fentanyl was 20 $\mu\text{g kg}^{-1}$ and midazolam was 0.15–0.2  $\text{mg kg}^{-1}$ . After completion of surgery, patients were transferred to the ICU, where they were treated with warm air heaters

to ensure normothermia. Inotropic drugs were continued when needed. Analgesia was provided by i.v. paracetamol 15mg/kg .Weaning from the ventilator and extubation were performed according to the institute's fast-track cardiac care protocol. During 1<sup>st</sup> 24 hrs after anaesthesia all episodes of nausea, retching and vomiting were recorded by personals who were unaware of the study drug. Rescue antiemetic was given in the form of metoclopramide 0.2mg/kg i.v. Nausea was defined as unpleasant sensation associated with the awareness of urge to vomit. Retching was defined as labored, rhythmic contraction of abdominal muscles without expulsion of gastric contents. Complete response was defined as no nausea, retching or vomiting and no need of rescue medication. The results were statistically analysed using one-way analysis of variance (ANOVA) or using chi-square test. P-values obtained using Chi-square test (Fisher's Exact Probability Test). P-value<0.05 is considered to be statistically significant.

**RESULTS:**

Total 90 patients observed during this period. Divided in 3 groups of 30 patients each , ondansetron (group A), granisetron (group B), ramosetron (group C) before induction of anaesthesia.

Clinical characteristics are tabulated as below:

Demographic Profile of patients

Table 1: **Distribution of age between three study groups.**

Parameters	Group A		Group B		Group C		Group Comparisons		
	Ondansetron		Granisetron		Ramosetron		Group A vs Group B	Group A vs Group C	Group B vs Group C
	No. of patients (n)	% of patients	No. of patients (n)	% of patients	No. of patients (n)	% of patients			
<b>Age (years)</b>									

<30	6	20	7	23.3	5	16.6	0.148	0.462	0.444
30-39	6	20	13	43.3	9	30			
40-50	5	16.7	4	13.3	8	26.7			
≥50	13	43.3	6	20	8	26.7			

Table 2: Distribution of sex between three study groups.

Parameter	Group A		Group B		Group C		Between Group Comparisons		
	Ondansetron		Granisetron		Ramosetron				
Sex	No. of patients (n)	% of patients	No. of patients (n)	% of patients	No. of patients (n)	% of patients	Group A vs Group B	Group A vs Group C	Group B vs Group C
Male	11	36.7	13	43.3	13	43.3	0.598	0.598	0.999
Female	19	63.3	17	56.7	17	56.7			

Table 1 & 2 shows the distribution of age and sex is not statistically significant among three study groups.

Table 3: Distribution of anthropometric parameters between three study groups.

Parameters	Group A		Group B		Group C		Between Group Comparisons		
	Mean	S.D	Mean	S.D	Mean	S.D	Group A vs Group B	Group A vs Group C	Group B vs Group C
Height (cm)	162.4	8.3	164.8	7.3	163.6	6.6	0.438	0.808	

									0.813
Weight (kg)	58.3	11.2	59.4	10.5	61.2	8.9	0.898	0.513	0.79
B.M.I(kg/m <sup>2</sup> )	22	3.4	21.8	2.7	22.8	2.9	0.945	0.541	0.361

The distribution of anthropometric parameters was not statistically significant among three study groups.

**Table 4 : Inter-group comparison of duration of anesthesia and duration of surgery.**

Duration (Min)	Group A		Group B		Group C		Between Group Comparisons		
	Ondansetron		Granisetron		Ramosetron		(P-values)		
	Mean	S.D	Mean	S.D	Mean	S.D	Group A vs Group B	Group A vs Group C	Group B vs Group C
Duration of Anesthesia (Min)	193.5	46.1	191.3	26.9	189.7	41.6	0.453	0.36	0.985
Duration of Surgery (Min)	160.7	46.6	159	30.3	147.2	39.5	0.487	0.383	0.982

There is no statistically significant difference in the duration of surgery and anesthesia in the three study groups.

**Table 5: Comparison of early post operative nausea ,vomiting, retching and rescue antiemetic in Group A, B and C during 0-3 hr postoperatively.**



Parameters	Group A (n=30) Ondansetron		Group B (n=30) Granisetron		Group C (n=30) Ramosetron	
	0-3hrs		0-3hrs		0-3hrs	
	Number	%	Number	%	Number	%
Nausea	4	13.3	3	10.0	1	3.3
Vomiting	4	13.3	4	13.3	2	6.7
Retching	1	3.3	2	6.7	0	0.0
Rescue Antiemetic	4	13.3	4	13.3	1	3.3

Table 5a: **Statistical comparison of nausea, vomiting, retching and rescue antiemetic in Group A, B and C during early (0-3 hr) postoperative period.**

Parameters	Group A vs Group B		Group A vs Group C		Group B vs Group C	
	P value	Remarks	P value	Remarks	P value	Remarks
Nausea	0.688	NS	0.353	NS	0.612	NS
Vomiting	0.999	NS	0.671	NS	0.671	NS
Retching	0.554	NS	0.988	NS	0.492	NS
Rescue	0.999	NS	0.353	NS	0.353	NS

Antiemetic						
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P-values are obtained using Chi-square test (Fisher's Exact Probability Test). P-value<0.05 is considered to be statistically significant. Table 5 shows the percentage of patients having nausea in the 0-3 hr postoperative period as 13% with Group A, 10% with Group B and 3.3% with Group C. The percentage of patients having vomiting in the 0-3 hr postoperative period was 13.3% with Group A, 13.3% with Group B and 6.7% with Group C. The percentage of patients who needed rescue antiemetic between 0-3 hr was 13.3% in Group A, 13.3% in Group B and 3.3% in Group C. Table 5a shows that the difference between the three study groups with regards to nausea, vomiting, retching and rescue antiemetic was not statistically significant during early 0-3 hr postoperative.

**Table 6 : Comparison of post operative nausea, vomiting, retching and rescue antiemetic in Group A, B and C during delayed (3-24 hrs) postoperative period.**

Parameters	Group A Ondansetron		Group B Granisetron		Group C Ramosetron	
	Number	%	Number	%	Number	%
Nausea	6	20.0	3	10.0	1	3.3
Vomiting	7	23.3	3	10.0	2	6.7
Retching	1	3.3	1	3.3	0	0.0
Rescue Antiemetic	7	23.3	3	10.0	2	6.7

**Table 6a: Statistical comparison of post operative nausea, vomiting, retching and rescue antiemetic in Group A, B and C during delayed (3-24 hrs) postoperative period.**

Parameters	GroupA vs Group B		Group A vs Group C		Group B vs Group C	
	P value	Remarks	P value	Remarks	P value	Remarks
Nausea	0.472	NS	0.044	Significant	0.612	NS
Vomiting	0.299	NS	0.045	Significant	0.987	NS
Retching	0.999	NS	0.987	NS	0.907	NS
Rescue Antiemetic	0.313	NS	0.045	Significant	0.987	NS

Table 6 shows that during delayed (3-24 hrs) postoperative period the percentage of nausea was 20% with Group A, 10% with Group B and only 3.3% with Group C. The percentage of patients having vomiting during delayed (3-24 hrs) postoperative period was 23.3% with Group A, 10% with Group B and 6.7% with Group C. The percentage of patients who needed rescue antiemetic was 23.3% in Group A, 10% in Group B and 6.7% in Group C. Table 6a shows that there was statistically significant difference between Group A and Group C with regards to nausea, vomiting and need of rescue antiemetic. The difference between Group C versus Group B and Group A versus Group B was not statistically significant with regards to nausea, vomiting, retching and rescue antiemetic during delayed (3-24 hrs) postoperative period.

**Table 7: Intergroup comparison of complete response (no nausea, no vomiting, no retching) during delayed (3-24 hrs) postoperative period between three groups.**

Parameters	Group A Ondansetron		Group B Granisetron		Group C Ramosetron	
	Number	%	Number	%	Number	%
Complete Response	24	80.0	25	83.3	28	93.3

Table7a: **Statistical comparison of complete response during early (0-3 hr) postoperative period between three groups.**

Parameters	Group A vs Group B		Group A vs Group C		Group B vs Group C	
	P value	Remarks	P value	Remarks	P value	Remarks
Complete Response	0.739	NS	0.254	NS	0.424	NS

Table 7 shows that the complete response during early (0-3 hr) postoperative period was 80% in Group A, 83.3% in Group B, 93.3% in Group C. The results were statistically non significant (table 7a)

**Table 8 : Inter group comparison of complete response(no nausea,no vomiting, no retching) during delayed (3-24 hrs) postoperative period.**

Parameters	Group A		Group B		Group C	
	Ondansetron		Granisetron		Ramosetron	
	Number	%	Number	%	Number	%
Complete Response	21	70.0	27	90.0	28	93.3

**Table 8a: Statistical comparison of complete response during delayed (3-24 hrs) postoperative period.**

Parameters	Group A vs Group B		Group A vs Group C		Group B vs Group C	
	3-24Hrs		3-24Hrs		3-24Hrs	
	P value	Remarks	P value	Remarks	P value	Remarks
Complete Response	0.104	NS	0.042	Significant	0.987	NS

Table 8 shows that the complete response during delayed (3-24 hrs) postoperative period was 70% in Group A, 90% in Group B and 93.3% in Group C. The results were statistically significant (Table 8a) between Group A and Group C.

## DISCUSSION

Postoperative nausea and vomiting (PONV) are common sequelae of general anaesthesia and a leading cause of postoperative discomfort after cardiac surgical procedures.<sup>5</sup> The complex act of vomiting involves coordination of the respiratory, gastrointestinal, and abdominal musculature and is controlled by the emetic center.<sup>6,7</sup> The area situated in the lateral reticular formation close to the tractus solitarius in the brain stem is thought to be the emetic center.<sup>6,7</sup> Stimuli from several areas within the central nervous system can affect the emetic center. These include afferents from the pharynx, gastrointestinal tract and mediastinum, as well as afferents from the higher cortical centers (including the visual center and the vestibular portion of the eighth cranial nerve) and the chemoreceptor trigger zone (CTZ) in the area prostroma. The area prostroma of the brain is rich in dopamine, opioid,

and serotonin or 5-hydroxytryptamine (5HT<sub>3</sub>) receptors.<sup>6</sup> The four major neuro transmitter systems appear to play important roles in mediating the emetic response viz.

dopaminergic, histaminic (H<sub>1</sub>), cholinergic, muscarinic and 5HT<sub>3</sub>.<sup>6</sup> As there are four different types of receptors, there are at least four sites of action of the antiemetic drugs. Antiemetic agents may have actions at more than one receptor, but they tend to have a more prominent action at one or two receptors.<sup>6,7</sup>

Previously the standard practice was to sedate patients after cardiac surgery and to ventilate the lungs for a period of 12-

16 h after operation..A lengthy period of sedation and artificial ventilation

reduced the incidence of postoperative emesis. But recently the trend has been to extubate the trachea much earlier after surgery and have become increasingly aware of the problem of PONV.<sup>8</sup>

Using a moderate dose of fentanyl, and extubating the trachea within the first 6–8 h after cardiac surgery, the incidence of postoperative retching or vomiting was very high despite the use of hyoscine as premedication. The overall incidence of nausea and vomiting was therefore of a similar order to that after other types of major surgery.<sup>9</sup>

A large number of pharmacological and non pharmacological methods have been developed.<sup>10</sup> The non–traditional antiemetics include ephedrine, propofol and corticosteroids. Non pharmacological methods are complementary and alternative medicine (CAM) which includes acupuncture, acupressure, transcutaneous accupoint electrical stimulation, ginger, ephedera based compounds and aromatherapy Phenothiazines, butyrophenones (droperidol) and metoclopramide are associated with extrapyramidal side effects. Pharmacological agents like anticholinergics and antihistamines cause sedation and tachycardia. Phenothiazines, butyrophenones (droperidol) and metoclopramide are associated with extrapyramidal side effects Phenothiazines, butyrophenones (droperidol) and metoclopramide are associated with extrapyramidal side effects.<sup>12</sup>

The introduction of 5HT<sub>3</sub> receptor antagonist in 1990s was heralded as a major advance in the treatment of PONV because of the absence of adverse effects that were observed with commonly used traditional antiemetics.<sup>7,13</sup> The 5HT<sub>3</sub> receptor antagonists produced no sedation, extrapyramidal reactions, adverse effects on vital signs or laboratory tests or drug interactions with

other anaesthetic medications.<sup>4</sup> 5HT<sub>3</sub> receptor antagonists are routinely used nowadays to prevent PONV following cardiac surgery.

C.R. Grebenik et al has shown that using a moderate dose of fentanyl, and extubating the trachea within the first 6–8 h after cardiac surgery, the incidence of nausea was approximately 37% and that of postoperative retching or vomiting approximately 47%, despite the use of hyoscine as premedication.<sup>14</sup> In the above mentioned study, PONV appeared to be about 1.5–2 times more

common in women.<sup>14</sup> Lerman has suggested that the incidence of PONV is approximately 2–3 times greater in women than in men.<sup>15</sup> In our study no statistically significant difference was seen. While obesity has been reported to increase PONV<sup>16</sup>, in contrast with other studies, we did not find any correlation between body mass index and nausea and vomiting in our study.

Gigilo et al in their study to prevent nausea and vomiting following cancer chemotherapy concluded that both ondansetron and granisetron have similar antiemetic efficacy but dose of granisetron is much less than ondansetron.<sup>17</sup> It has been reported that using low dose granisetron

0.1 mg is effective in the treatment of PONV.<sup>18</sup> Naguib M et al showed no statistical differences between ondansetron, tropisetron and granisetron groups in lowering incidence of PONV, but concluded that ondansetron, when given prophylactically resulted in a significantly lower incidence of PONV than metoclopramide.<sup>19</sup> Wilson AJ et al concluded that granisetron is effective in the prevention of PONV and increasing the dose from 1 mg to 3 mg did not confer any additional advantage with 1 mg being the optimum dose.<sup>20</sup> Fujii Y et al showed that prophylactic therapy with ramosetron was more effective than granisetron for preventing postoperative nausea and vomiting during 0–48 hr after anesthesia.<sup>21</sup>

Our study is in accordance with studies of Noda et al.<sup>22</sup> & Koizumi et al<sup>23</sup> in which ramosetron and granisetron were found to have similar effectiveness for the prevention of postoperative nausea and vomiting. Ramosetron has been shown to have statistically significant complete response during delayed (3-24 hrs) postoperative period over ondansetron in our study.

### **Conclusion**

Based on this study it can be concluded that during early (0-3 hr) postoperative period the three drugs ondansetron, granisetron and ramosetron are comparable to each other. During delayed (3-24 hrs) ramosetron appears better than ondansetron in prevention of PONV in cardiac surgery. Effect of ramosetron and granisetron appears comparable to each other. Further studies with larger patient numbers may be required to validate the findings of this study.

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## COMPARISON OF DIFFERENT DOSES OF NITROGLYCERINE SPRAY FOR ATTENUATION OF STRESS RESPONSE TO LARYNGOSCOPY

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### Abstract

**Background** The study was done to evaluate the efficacy of NTG intranasal spray in attenuation of laryngoscopy and intubation induced hemodynamic responses and to elucidate the optimum dose.

**Material and methods** Prospective randomized controlled study was conducted in 50 ASA physical status I and II patients of both sexes, aged 20-60 years who were scheduled for elective surgery. patients were divided into 2 groups(n=25), group I received 400µg and group II received 800µg intranasally 2 minutes before laryngoscopy and endotracheal intubation after standard general anaesthesia technique and its effects on heart rate ,

systolic, diastolic, and mean arterial blood pressure were noted before and after premedication and 1-5 minutes after intubation.

**Results** Baseline mean heart rate in group I was  $97.4 \pm 28.91$  and  $81.80 \pm 6.22$  in group II . There was highly significant ( $P < 0.01$ ) increase in heart rate as compared to base line values in two groups after laryngoscopy and intubation. There was statistically significant fall in MAP after 30 seconds in Gp I which remained consistently decreased till 5 min post laryngoscopy and intubation. There was 9.97 % increase in mean arterial pressure in group II after laryngoscopy and intubation compared to baseline value, and decreased to 4.34% of baseline at 3 min after post-laryngoscopy and intubation.

**Conclusions** NTG spray in dose of 400  $\mu\text{g}$  given 2 min before general anesthesia is effective in attenuating the pressor response to laryngoscopy and intubation in normotensive patients, 800  $\mu\text{g}$  does decrease the mean arterial blood pressure but does not have an extra advantage over 400 $\mu\text{g}$ . NTG does not attenuate the rise in HR.

**keywords** Nitroglycerine intranasal spray; General anesthesia; hemodynamic responses.

## INTRODUCTION

The stress response to laryngoscopy and endotracheal intubation activates the sympathetic nervous system, which may increase myocardial oxygen demand by increasing heart rate and arterial blood pressure. Activation of the sympathetic nervous system may also cause coronary artery vasoconstriction reducing the supply of oxygen to the myocardium, which in turn would predispose to myocardial ischaemia. Therefore, attenuation of haemodynamic response to tracheal intubation such as hypertension, tachycardia and arrhythmias is important for an anaesthesiologist.(1-4)

In 1940, Reid and Brace first described a hemodynamic response to laryngoscopy and intubation.(5) It leads to an average increase in blood pressure by 40-50% and 20% increase in heart rate (HR).(6)

A wide variety of pharmacological agents were used to attenuate the hemodynamic responses to laryngoscopy and endotracheal intubation like lignocaine(7), fentanyl(8), alfentanil (9), remifentanyl (9) nifedipine(10), beta-blockers(11), Gabapentin (12), magnesium sulfate(13), verapamil, nicardipine and diltiazem (14) with varying results. The non-pharmacological methods like, appropriate premedication, smooth rapid and gentle intubation, blocking the glossopharyngeal nerve and superior laryngeal nerve have been used to attenuate the cardiovascular responses to tracheal intubation. None of these above mentioned approaches have been proved entirely satisfactory. All of them require time for preparation and administration.(15)

Glyceryl trinitrate (nitro-glycerin or NTG) relaxes vascular smooth muscles with venous dilation predominantly over arterial dilation(16), NTG had been administered intranasally (17), or parenterally as a bolus(18) or infusion(19) to attenuate hemodynamic responses during laryngoscopy and intubation but preparation, standardization and stabilization of such solution is not without problem and cost effectiveness has been questioned. (12,20,21)

Intravenous and inhalational anaesthetic agents have no appreciable effects on stress response. Nitroglycerine generates NO (nitric oxide) in vascular smooth muscles which produce vasodilatation leading to decrease in blood pressure. NTG sublingual spray is simple and easy to use formulation mainly aimed for treatment of acute anginal episodes. It is also marketed to treat acute hypertensive crisis and also to treat diabetic neuropathic pain with local application.(22-24)

Our aim was to observe the various pressor responses to laryngoscopy and intubation in normotensive patient undergoing elective surgery under general anesthesia and use of two different attenuating doses (400, 800 mcg) of intranasal nitroglycerine administered two minutes before laryngoscopy and intubation, to observe its efficacy and safety .

## **MATERIAL AND METHODS**

After institutional ethical committee approval, a prospective randomized controlled study was conducted in 50 ASA physical status I and II patients of both sexes, aged 20-60 years scheduled for elective surgery under general anesthesia. Study was undertaken to observe and compare the attenuating effects of two different doses of nitroglycerine spray administered intranasally before laryngoscopy and endotracheal intubation in normotensive patients on heart rate changes, systolic, diastolic, and mean arterial blood pressure changes. Doses of intranasal nitroglycerine used were 400 and 800  $\mu$  given two minutes prior to laryngoscopy and intubation and observed till 5 minutes after laryngoscopy and intubation every minute. Patients were watched for any complication like tachycardia, hypotension, arrhythmias, bronchospasm

All the patients under study were subjected to a detailed preanesthetic evaluation to rule out any anatomical or systemic disorders. Informed consent from each patient was taken. History of past, prolonged illness and drug therapy was elicited. Routine and relevant special investigations were carried out. patients with baseline heart rate <60 beats per minute, baseline blood pressure <100/50 mm of Hg, reactive airways disease, history of cardiac disease and hypertensive patient, treatment with adrenergic augmenting or depleting drug, contraindication to use of nitroglycerine and patient requiring two or more attempt for laryngoscopy and intubation were excluded from the study.

Patients were randomly divided into two groups of 25 each. Group I received (1 metered dose) 400  $\mu$ g and group II received (2 metered doses) 800  $\mu$ g of intranasal nitroglycerine spray two minutes before laryngoscopy and intubation. Anaesthesia technique was standardised for both the groups. On the day of surgery, in the operation theatre intravenous line was secured, pulse oxymeter, NIBP, ECG monitor were applied. Baseline parameters heart rate, systolic BP, diastolic BP were noted before administration of any drugs. Crystalloid fluid was started. All the patients were pre-medicated with inj. glycopyrolate 0.04 mg/kg, inj. ondansetron 0.15 mg/kg, and inj. fentanyl 2  $\mu$ g /kg intravenously. Nitroglycerine spray was done according to group. Patients were induced with inj. pentothal (6-7 mg/kg) i.v. and inj. suxamethonium (2 mg/kg) i.v. followed by

laryngoscopy and intubation. vitals were noted  
If intubation took more than 30 s or more than 1 attempt , it was excluded from the study.  
Anesthesia was maintained on 50% N<sub>2</sub>O and 50% O<sub>2</sub> ,1.5% MAC sevoflurane and inj.  
vecuronium bromide.

HR, SBP, DBP were recorded at T1: baseline(before premedication), T2: just before intubation, T3: just after intubation, T4:1 min after intubation, T5: 2 min after intubation, T6: 3 min after intubation, T7: 4 min after intubation, T8: 5 min after intubation. at the end of surgery patients were reversed with Inj. Neostigmine 0.05mg/kg and glycopyrolate 0.01mg/kg.

Patients were watched for any complication like tachycardia, hypotension, arrhythmias, bronchospasm.

Data were entered and analyzed .Qualitative or categorical data were presented as number (proportion) and compared using Chi-square test. Quantitative or continuous variables were presented as mean  $\pm$  standard deviation and compared using Student's *t*-test and analysis of variance. *P* < 0.05 was considered as statistically significant.

## Results

Patient's age, weight, sex, ASA grade and type of surgery were statistically comparable in three groups, *P* > 0.05

In our study baseline mean heart rate in group I was  $97.4 \pm 28.91$  and  $81.80 \pm 6.22$  in group II . There was highly significant (*P* <0.01) increase in heart rate as compared to baseline values in two groups after laryngoscopy and intubation. It went to 28.8% increase in Group I and 27.13 % increase in GroupII after one minute post intubation **Table 4**

There was significant hypotension (*P* < 0.05) in both the groups one minute after laryngoscopy and intubation compared to baseline value and consistent hypotension in group I till 5 minutes after intubation and laryngoscopy. **Table 5**

There was significant decrease in diastolic blood pressure in both the group immediately after laryngoscopy and intubation as compared to baseline value, which remained consistently significantly decreased up till 5 min after intubation and laryngoscopy. **Table 6**

There was statistically significant fall in MAP after 30 seconds in Gp I which remained consistently decreased till 5 min post laryngoscopy and intubation. There was 9.97 % increase in mean arterial pressure in group II after laryngoscopy and intubation compared to baseline value, and decreased to 4.34% of baseline at 3 min after post-laryngoscopy and intubation. ( $P < 0.05$ ) **Table 7**

## **Discussion**

Nitroglycerine is a commonly used intravenous agent in treatment of hypertension during anaesthesia. NTG is having faster onset of action (2-3 minutes), higher peak response, shorter duration of action, no need to prepare and is easy to administer as compared to any other preparation. The half-life of 4-5

minutes gives us a convenient alternative. The idea of using any drug for attenuating the hypertensive

response to tracheal intubation is that its peak effect should correspond to that of the stimulus. A 2-3 minute time gap is needed between administration of NTG spray and tracheal intubation as done in the

present study, as this time interval was found to be satisfactory.(15)

The magnitude of pressor response can be assessed by observing the rise in HR (demand), SBP (afterload), DBP (preload), and MAP. We observed that NTG spray does not attenuate the rise in HR.

The principal advantage of using NTG is that, while a desirable and transient hypotension is achieved, cardiac output is not likely to decrease. Preload reduction and accompanying decrease in ventricular end-diastolic pressure(21) reduces myocardial oxygen demand and

increases endocardial perfusion by dilating the coronary vessels, NTG may increase the coronary blood flow and oxygen delivery to the myocardium. Because of its predominantly venodilatory action, it seems to be the best choice in patients with low cardiac output and moderately elevated resistance. (16)

Myocardial oxygen consumption or demand (as measured by the pressure-rate product, tension-time index, and stroke-work index) is decreased by both the arterial and venous effects of NTG resulting in a more favorable supply-demand ratio. (21)

our findings coincided with study done by Fassoulaki A, Kaniaris P. in 1983 who gave nitroglycerine before induction of anesthesia. In comparison with the control group who received placebo, systolic blood pressure did not increase significantly immediately after intubation ( $P > 0.005$ ); while the heart rate increased significantly in both groups ( $P < 0.001$ ). According to the results of this study, nitroglycerine had an effective influence on post intubation blood pressure diminution, with no effect on heart rate (18)

Previous studies (14,21 25 -27) have also documented that NTG does not attenuate the rise in HR after intubation which can be attributed to reflex tachycardia produced by vasodilation which correlated with our study where HR increases significantly in both the groups post laryngoscopy and intubation .

Other studies have reported effective attenuation of pressor response by NTG used intravenously as bolus injection, ( <sup>14,19,20,28</sup>) and IV infusion.(29 30) .We have documented a blunting of pressor response by the intra nasal spray of NTG in doses of 400 and 800 µg. There was a trend toward fall in mean arterial blood pressure in group I from 4.98 % to 17 .20 % at 5 min and the fall in the mean arterial blood pressure started decreasing 2 min post laryngoscopy intubationie. 0.43 % to 8.11 % at 5 min which was clinically significant. The principal advantage of using NTG is that, while a desirable and transient hypotension is achieved, cardiac output is not likely to decrease. Preload reduction and accompanying



decrease in ventricular end-diastolic pressure (21) reduces myocardial oxygen demand and increases endocardial perfusion by dilating the coronary vessels, NTG may increase the coronary blood flow and oxygen delivery to the myocardium. Because of its predominantly venodilatory action, it seems to be the best choice in patients with low cardiac output and moderately elevated resistance. (16)

## **Conclusions**

We conclude that NTG spray in dose of 400 µg given 2 min before general anesthesia is effective in attenuating the pressor response to laryngoscopy and intubation in normotensive ASA I-II patients where 800 µg does decrease the mean arterial blood pressure but does not have an extra advantage over 400µg. NTG does not attenuate the rise in HR.

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Tables

<b>Table 1 : Age distribution ( yrs)</b>				
	Group 1		Group II	
	(no of patients)	%	(no of patients)	%

15-24	6	24	10	40
25-34	6	24	7	28
35-44	4	16	3	12
45-54	5	20	4	16
55-64	4	16	1	4
Total	25		25	

<b>Table 2 : Sex Distribution (no of patients)</b>				
	Group I		Group II	
	no of patients	%	no of patients	%
Male	13	52	12	48
Female	12	48	13	52

<b>Table 3 : weight distribution (kgs)</b>				
	Group I		Group II	
	No of patients	%	No of patients	%
40-49	6	24	13	52
50-59	6	24	8	32
60-69	8	32	4	16
70-79	5	20	1	4

<b>Table 4 : Heart Rate changes Mean <math>\pm</math> SD</b>				
	Group I		Group II	P value

		% Increase /decrease from base line ( increase ÷original × 100)		% Increase / decrease from base line( increase ÷original × 100)	
Before premedication	97.4 ± 28.91	Baseline	81.80 ± 6.22	baseline	<0.05
After premedication	107.1 ± 27.74	9.95	88.5 ± 6.83	8.19	<0.01
After intubation					
30 seconds	125.09 ± 22.33	28.4	102.50 ± 9.25	25.30	<0.01
1 min	125.47 ± 20.95	28.8	104 ± 9.5	27.13	<0.02
2 min	124.66 ± 19.06	27.98	102.55 ± 8.22	25.36	<0.03
3 min	122.14 ± 18.18	25.40	98.7 ± 7.13	20.66	<0.04
4 min	115 ± 17.02	18.06	96.50 ± 6.99	17.97	<0.05
5 min	113.28 ± 16.28	16.30	95.15 ± 5.10	16.32	<0.06

Table 5: Systolic blood pressure changes Mean ± SD					
	Group I		Group II		P value
		% Increase /decrease from base line ( increase ÷original		% Increase /decrease from base line ( increase ÷original	

		× 100)		× 100)	
Before premedication	135.71 ± 16.22	baseline	120.7 ± 7.40	baseline	<0.01
After premedication	127 ± 15.24	-6.41	123 ± 7.87	1.90	0.29
After intubation					
30 seconds	133.57 ± 21.93	-1.57	131.15 ± 7.11	8.65	0.64
1 min	121.23 ± 24.94	-10.66	132.8 ± 7.46	10.02	0.06
2 min	110.90 ± 24.13	-18.28	126.20 ± 7.57	4.55	<0.05
3 min	112 ± 18.90	-17.47	122.55 ± 7.27	1.5	<0.05
4 min	111.71 ± 20.95	-17.68	118.70 ± 6.46	-1.65	0.15
5 min	113.33 ± 18.07	--16.49	114.95 ± 5.52	-4.7	0.6

Table 6: Diastolic blood pressure changes Mean ± SD

	Group I		Group II		P value
		% Increase /decrease from base line ( increase ÷original × 100)		% Increase /decrease from base line ( increase ÷original × 100)	
Before premedication	86.57 ± 9.13		76.80 ± 3.96		<0.01
After premedication	83.23 ± 12.01	-3.8	77.40 ± 3.43	0.7	<0.05

After intubation					
30 seconds	85.19 ±17.16	-1.5	85.25 ± 4.63	11.00	0.99
1 min	74.61 ± 18.78	-13.81	84.75 ± 4.29	10.35	<0.05
2 min	69.57 ±19.45	-19.63	79.70 ± 4.91	3.77	<0.05
3 min	68.52 ± 16.47	-20.85	76.5 ± 5.35	-0.39	<0.05
4 min	68.19 ± 16.24	-21.23	71.85 ± 4.31	-6.44	0.4
5 min	71.2 ± 18.27	-17.75	68.55 ± 4.16	-10.74	0.4

Table 7: mean arterial blood pressure changes Mean ± SD					
	Group I		Group II		P value
		% Increase /decrease from base line ( increase ÷original × 100)		% Increase /decrease from base line ( increase ÷original × 100)	
Before premedication	102.95±11.49	Base line	91.43 ±5.10	Base line	<0.01
After premedication	97.82± 13.08	-4.98	92.6 ±4.91	1.27	<0.05
After intubation					
30 seconds	101.31±18.75	- 1.59	100.55 ±5.45	9.97	.87
1 min	90.15±20.83	- 12.43	100.76 ±5.34	10.20	<0.05



2 min	83.34±21.01	- 19.04	95.2 ±5.79	4.12	<0.05
3 min	83.01±17.28	- 19.36	91.83 ±5.99	0.43	<0.05
4 min	82.69±17.81	- 19.67	87.46 ±5.02	- 4.34	.31
5 min	85.24±18.20	- 17.20	84.01 ±4.61	-8.11	.46

Type of article : Original article

Title : Comparison of different doses of nitroglycerine spray for attenuation of stress response to laryngoscopy

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9

**COMPARITIVE STUDY OF EFFICACY AND HAEMODYNAMIC SAFETY OF LEVOSEMENDAN WITH DOBUTAMINE IN PATIENTS WITH SEVERELY REDUCED LEFT VENTRICULAR FUNTION UNDERGOING CARDIAC SURGERY.**

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## **Abstract**

**Background:** Levosimendan, a novel calcium sensitizer, improves myocardial contractility without causing an increase in myocardial oxygen demand as compared to other inotropes.

**Aims and Objectives:** We aimed to compare the hemodynamic effects of levosimendan and dobutamine in patients with EF < 30% undergoing coronary artery bypass grafting (CABG) electively on cardiopulmonary bypass (CPB).

**Materials and Methods:** 60 patients were divided into 2 groups of 30 each. Group-L patients received levosimendan 6 µg/kg loading for 10 mins followed by continuous infusion of 0.2 µg/kg/min upto 24 hrs and Group-D patients received dobutamine 5 µg/kg/min while weaning off CPB without a loading dose and continued upto 24hrs. Additional inotrope and/or vasoconstrictor were started based on hemodynamic parameters. Hemodynamic data were collected at baseline, 30 minutes after CPB, thereafter at 6, 12, 24, and 36 hours post-CPB. Mean arterial pressure (MAP), central venous pressure (CVP), Pulmonary arterial pressure (PAP), pulmonary capillary wedge pressure (PCWP), heart rate (HR), stroke volume (SV), CO (cardiac output), cardiac index (CI), systemic vascular resistance index (SVRI), pulmonary vascular resistance index (PVRI), and lactate levels were measured.

**Results:** Group-L showed increased requirement of inotropes and vasoconstrictors. The MAP, CVP, PAP were reduced more in Group-L. The CI, CO, SV were higher in Group-L when compared to Group-D, patients showed a statistically significant increase in CI, CO, SV even after 12 hrs of discontinuation of levosimendan. Compared with dobutamine group, SVRI and PVRI was significantly lower at 6, 12, 18, and 24 hour post CPB in levosimendan group, requiring additional inotropes. The HR was higher in Group-D. Lactate levels, intensive care unit stay, and duration of ventilation were similar in both groups.

**Conclusion:** Levosimendan loading dose 6 µg/kg for 10 mins followed by 0.2 µg/kg/min compared to dobutamine 5 µg/kg/min caused rapid dose-dependent improvement in hemodynamic function, showed more vasodilation and lesser inotropy in patients undergoing CABG. The requirement of another inotrope or vasopressor was frequent in levosimendan group.

**Keywords:** Hemodynamics variables, Levosimendan, dobutamine, CABG.

## **Introduction**

Intravenous positive inotropic agents play an important role in the short-term management of patients with left ventricular (LV) systolic dysfunction.<sup>18-20</sup> β-Adrenergic agonists and phosphodiesterase

inhibitors, the most commonly used positive inotropic agents, exert a positive inotropic action primarily by increasing cAMP in cardiac myocytes, although being effective positive inotropic agents, their use may be limited by increases in heart rate and the stimulation of arrhythmias limiting dosing and can result in serious adverse effects-myocardial ischemia and sudden death<sup>21-23</sup>. Secondly, because of desensitization of β-adrenergic pathway, the positive inotropic effects of agents that act through this pathway may be reduced in patients with severe LV dysfunction.<sup>24,25</sup> Calcium-sensitizing agents exert a positive inotropic action by increasing the sensitivity of the contractile apparatus to calcium.<sup>26</sup> Levosimendan is a new calcium-sensitizing agent that binds to troponin C<sup>27,28</sup>. Dobutamine was chosen as the inotropic control drug since its effects on low cardiac output syndrome following surgery involving CPB are well described.<sup>[12],[13]</sup> Surgery on cardiopulmonary bypass (CPB) with aortic clamping involves global myocardial ischemia resulting in different degrees of transitory ventricular dysfunction in the immediate post-operative period.<sup>[1],[2]</sup> β adrenergic agonists and phosphodiesterase III/IV inhibitors induce good hemodynamic improvement but

may cause myocardial ischemia, arrhythmias and are associated with high mid-term mortality.<sup>[3],[4],[5]</sup> The use of levosimendan in the treatment of heart failure with dysfunction is based on its action of improvement of myocardial contractility through the sensitization of troponin C to calcium, and systemic and coronary arterial and venous dilatation induced by activation of ATP-sensitive potassium channels of smooth muscle fibers.<sup>[3]</sup> Thus levosimendan increases cardiac output, coronary, renal blood flow also reduces the preload and afterload, has anti-arrhythmic effect, and can revert myocardial stunning.<sup>[3]</sup>

### **Aims and objectives**

The present study was aimed to compare the hemodynamic parameters and clinical outcome and safety of levosimendan and dobutamine in a group of reduced LV function patients undergoing CABG on pump. We also compared the outcomes in terms of duration of ventilation and intensive care unit stay and tissue perfusion in terms of lactate levels.

### **Materials and Methods**

The study was approved by the hospital ethics committee. Patients aged 35-60 yrs with documented LV ejection fractions of  $\leq 30\%$  by echocardiogram or radionuclide ventriculogram scheduled for CABG on CPB were recruited in the study. Patients were screened for the study if they were currently on treatment with  $\beta$  blockers, ACE (angiotensin-converting enzyme) inhibitors. The patients having other valvular pathologies, hepatic, renal dysfunction (serum creatinine  $>2$  mg/dl and/or chronic kidney disease), undergoing combined mitral valve surgery with coronary artery bypass graft surgery, redo mitral valve surgery, uncorrected thyroid disease, obstructive cardiomyopathy, pericardial disease, active myocarditis, symptomatic primary pulmonary disease, chronic obstructive pulmonary disease, requiring long-term treatment with  $\beta$ -agonists, serious arrhythmias, heart block rhythm, re-exploration for surgical causes were excluded. Written informed consent was obtained from all the patients. Randomization was done by computerized allocation of patients to both the groups. All preoperative medications were continued until the morning of surgery except ACE inhibitors stopped the day before surgery. All patients received oral alprazolam 0.5 mg and pantoprazole 40 mg previous night and on the morning of surgery. Anaesthesia, surgery and CPB were performed in accordance with standard operating procedures and hospital's routine clinical practice. Patients were induced with midazolam 0.1 mg/kg, fentanyl 4-6  $\mu$ g/kg. Vecuronium 0.1 mg/kg was used to facilitate endotracheal intubation. Routine monitoring included 5-lead ECG, pulse oximetry, capnography, invasive arterial pressure monitoring, central venous access was established using a 5-lumen swan ganz catheter for pulmonary artery pressure monitoring. CO, CI, SV were monitored using thermodilution technique with Swan ganz catheter, SVRI, PVRI was measured after obtaining CVP, PAP, PCWP. The myocardial contractility and preload were assessed by transesophageal echocardiography (TEE) at the time of separation from CPB. Surgery was performed on CPB with moderate hypothermia (28°C to 32°C) using cold blood cardioplegic cardiac arrest, LAD, LCX & RCA vessels were grafted as per the severity of stenotic lesions involved. LIMA (left internal mammary artery) and SVG (saphenous vein graft) conduits were harvested before institution of CPB. At separation from CPB, group-D patients received infusion of dobutamine 5  $\mu$ g/kg/min and group-L received levosimendan loading 6  $\mu$ g/kg for 10 mins followed by 0.2  $\mu$ g/kg/min continuous infusion till 24 hrs. The study drug levosimendan and dobutamine were diluted in such a way that equal infusion rates were achieved for comparable patients. Both the study drug syringes were prepared by another person blinded from the study. Syringes and extension tubing were covered with black paper to blind the anesthesiologist. Drugs were administered once patient was rewarmed to 34°C and aortic clamp released. In case of adverse events: HR  $>130$  or an increase in HR  $>20$  bpm above baseline for 10 minutes, symptomatic hypotension or a drop in systolic blood pressure to  $<75$  mm Hg or life threatening arrhythmias, study was abandoned Protocol and criteria for addition of another inotrope or vasopressor (adrenaline or noradrenaline) is

described below..While continuing a flow of 0.5 l/min on CPB, the CVP, the mean arterial pressure (MAP), SVRI, CI and left ventricular (LV) and right ventricular (RV) function were assessed and the vasopressor or inotropic agent was selected as described

If MAP >50 mmHg and LV , RV function adequate as assessed by TEE in mid esophageal four chamber view, the study drug was continued.

If MAP <50 mmHg, CI <1.5 dyne-sec-m<sup>2</sup>/cm<sup>5</sup> with adequate LV , RV function on TEE imaging, but SVRI <1200 units, noradrenaline 0.05 µg/kg/min was added.

If MAP <50 mmHg, CI <1.5 dyne-sec-m<sup>2</sup>/cm<sup>5</sup> with inadequate LV , RV function on TEE imaging and SVRI > 1200 units, adrenaline 0.05 µg/kg/min was added.

In both groups, the HR,MAP, CVP, PAP,PCWP,SV,CO,CI,PVRI and SVRI were monitored at baseline, at 30 minutes after CPB, thereafter at 6, 12, 24 and 36 hours after CPB. Aortic clamp time and CPB time were recorded for all patients. Tracheal extubation was performed when patients were hemodynamically stable, warm, chest tube drainage was less than 50 ml per hour, urine output more than 0.5 ml /kg / hour, and patients breathing spontaneously with adequate blood gases as per institutional protocol. Both the study drugs and additional inotrope/vasoconstrictor were tapered once the patients were extubated and hemodynamically stable after 24hrs. Presence of any arrhythmia was recorded.

## Statistics

The sample size required was determined by the criterion that an increase in the CI of >20% over baseline is obtained after 24 hours of treatment for α error of 5% and a β error of 10%. The determined sample size was 30 patients in levosimendan (L) group and 30 patients in dobutamine (D) group. Numerical results are presented as mean ± SD; mean was compared by the students 't' test; categorical data were compared using chi square test. Significance was set at a P value < 0.05.

## Results

This prospective, randomized, double-blind study included 60 patients undergoing CABG on CPB over 9 months period. The demographic data was comparable between the two groups. Both groups were comparable for ejection fraction, CPB and aortic clamp time, and surgical technique employed. The ICU stay and ventilation duration were also similar in both groups.

**TABLE 1: Clinical and demographic data of patients in study** Values expressed as mean ± standard deviation , number in parenthesis indicates % in total, LVEF- Left ventricular ejection fraction, CPB- cardio pulmonary bypass, ICU – intensive care unit, ACE- angiotensin converting enzyme, ASA- American Society of Anesthesiology, NYHA- New York Heart Association. p value <0.05 significant.

	LEVOSEMENDAN	DOBUTAMINE	P value
Number of patients	30	30	0.18
Age ( years)	49.16 ± 6.84	47.44 ±7.22	0.16
Sex - Women (%)	11 ( 36.66 )	12( 40 )	0.15
Men (%)	19 ( 63.33)	18( 60 )	0.14
Body surface area in m <sup>2</sup>	1.8 ± 0.06	1.77 ± 0.05	0.33

Body mass index ( kg/m <sup>2</sup> )	26.5 ± 5.4	27.2 ± 4.8	0.24
Pre operative beta blockers (%)	15 ( 50 )	14 ( 46.66 )	0.56
Pre operative ACE inhibitors (%)	11 ( 36.66)	12 (40 )	0.37
ASA risk classification ≥ 4 (%)	10 (33.33 )	9 ( 30 )	0.42
NYHA class 4 (%)	8 (26.66 )	8 ( 26.66)	0.31
LVEF ( % )	24 ± 5.4	24.4 ± 4.8	0.19
Duration of CPB ( mins)	76 ± 8.84	72 ± 10.4	0.23
Aortic cross clamp time ( mins)	46 ± 10.43	44 ± 8.86	0.21
Duration of ventilation ( hrs)	6.3 ± 2.1	6.8 ± 1.8	0.18
ICU stay ( hrs )	52 ± 4.2	54 ± 2.8	0.19

**Table 2** shows haemodynamic variables(HR, MAP, CVP, PAP,PCWP, SVRI,PVRI, SV,CO, CI ) in levosendan & dobutamine groups at baseline, post CPB immediately ,30 mins, 6 ,12,24,36 hrs post CPB.

Haemodynamic variables		baseline	Post CPB	30 mins	6 hours	12 hours	24 hours	36 hours
HR	GROUP L	85.3±7.4	90.5±8.8*	96.4±8.9*	76.8±6.6*	78.7±7.8*	812.8±8.44*	84.6±7.7
	GROUP D	87.4±6.6	99.9±10.2*	105.4±8.2*	88.2±7.1*	86.5±8.43*	89.8±9.23*	90.4±6.2
MAP	GROUP L	54.66±8.11	57.44±6.23*	64.78±5.32*	71.12±5.84*	75.34±7.84*	70.12±6.04	69.12±5.23
	GROUP D	53.82±7.46	64.32±7.11*	69.44±6.91*	77.34±6.51*	82.12±7.91*	75.44±5.88	72.23±4.44
CVP	GROUP L	9.3±2.3	4.4±2.3*	6.74±1.88*	7.16±1.34*	7.2±1.26*	6.92±1.56	5.84±1.66
	GROUP D	10.2±1*	6.6±2.2*	8.11±1.44*	8.9±1.44*	8.4±1.77*	7.24±1.89	6.66±1.77
PAP	GROUP L	27.0 ±3.9	22.1 ± 2.7*	20.1 ±2.9*	19.7 ±3.0*	20.0 ± 1.9*	21.1 ±2.1	20.7 ± 2.0
	GROUP D	26.2±3.2	25.3± 3.1*	24.1± 2.7*	23.4±2.4*	23.1 ± 2.7*	22.2±2.5	21.2±1.1
PCWP	GROUP L	18.0 ± 2.6	15.2±1.8	14.0 ± 2.0	12.8 ± 2.0	11.0 ± 2.6	12.0 ±2.0	12.8± 2.0
	GROUP D	17±2.8	16.5± 2.2	15.1±1.9	13.2± 2.1	12.2 ± 1.8	12.8±2.4	13.2±1.2
SV	GROUP L	40.5 ±4.6	56.6 ±8.6	58.8 ± 7.4	60.4 ± 7.8*	63.3± 6.6*	61.2±4.4*	58.3±2.1*
	GROUP D	41.1±3.4	49.3±7.2	54.8±5.4	54.3±3.4*	55.12±4.2*	56.13±2.3*	50.3±2.2*
SVRI	GROUP L	1674±138	1442±189	1486±144	1244±166*	1282±122*	1434±101*	1326±114*
	GROUP D	1784±144	1543±194	1623±178	1786± 158*	1689±145*	1549±122*	1589±158*
PVRI	GROUP L	286 ± 81	213 ± 58	200 ± 43*	203 ±45*	188±54*	186±32	190±24

	GROUP D	290±74	244±38	225±32*	228±34*	211±66*	198±38	201±20
CO	GROUP L	3.5 ±0.3	5.0 ±0.7	5.2 ± 0.7	5.3 ±0.6*	5.1±0.4*	4.9±0.2*	4.7± 0.4*
	GROUP D	3.2±0.4	4.9±0.8	4.8±0.6	4.8±0.5*	4.6±0.3*	4.3±0.2*	4.0±0.2*
CI	GROUP L	2.3±0.2	2.54±0.3	2.52±0.1	2.62±0.3*	2.77±0.3*	2.93±0.2*	3.12±0.1*
	GROUP D	2.2±0.1	2.66±0.2	2.63±0.2	2.58±0.1*	2.66±0.2*	2.79±0.1*	2.88±0.2*
Lactate	GROUP L	1.2±0.44	4.8±0.68	4.4±0.99	3.7±0.72	2.4±0.66	1.8±0.43	1.2±0.1
	GROUP D	1.32±0.32	4.4±0.84	4.8±0.83	3.99±0.66	2.9±0.72	2.2±0.44	1.1±0.2

Values expressed as mean ± standard deviation ,lactate -millimol/lit.CI – cardiac index (L/min/m<sup>2</sup>); CO – cardiac output (L/min), HR – heart rate (beats/min) MAP – mean arterial pressure (mm/hg), SV – stroke volume (mL/beat) ,CVP – central venous pressure (mmHg); PAP pulmonary artery pressure (mmHg); PCWP – pulmonary capillary wedge pressure (mmHg); PVRI (dyn·s/cm<sup>5</sup>/m<sup>2</sup>)– pulmonary vascular resistance index SVRI(dyn·s/cm<sup>5</sup>/m<sup>2</sup>); – systemic vascular resistance index, group L –levosemedan, group D- dobutamine. \* P value < 0.05- significant,

The HR was higher in D group till 24 hrs post CPB, as compared to L group, which was statistically significant and remained higher till tapering of inotropes. The MAP, CVP and PAP were reduced more in the levosimendan group compared to dobutamine group, which was statistically significant at weaning from CPB, 30 minutes, 6 hours, and 12 hours post CPB. This decrease in MAP was maintained even after levosemedan discontinuation. Treatment with dobutamine showed no significant changes in this respect. Levosimendan group patients showed a sustained increase in CO,CI and SV at 6,12, 24 and 36 hours postoperatively compared to dobutamine group, which was statistically significant. PCWP and lactate levels were comparable in both groups, although PCWP was lower in levosemedan group. SVRI and PVRI showed statistically significant sustained decrease in levosemedan group than dobutamine group at 6,12, 24 and 36 hrs post CPB.

16 patients needed adrenaline infusion, and 12 patients needed noradrenaline infusion in L group as compared to only 2 patients needing adrenaline and 8 patients needing noradrenaline infusion in D group as shown in Table-3. This difference in the requirement of inotropic agent and vasoconstrictor infusion was statistically significant. No malignant ventricular arrhythmias were recorded in any patient. Over 36 hours of double-blind drug infusion, adverse events were reported in 12% of levosimendan patients and 20% of dobutamine patients. 3 patients in group L and 4 patients in D group had nonsustained ventricular tachycardia, 2 patients from group D had increase in heart rate > 20 bpm, but was not sustained > 4 mins.

**Table -3** Concomitant use of vasoactive drugs during levosimendan and dobutamine infusion study

Inotrope or vasopressor requirement	Levosemedan group	Dobutamine group
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<b>Noradrenaline</b>	<b>16 ( 53.3% )</b>	<b>8 ( 26.67% )</b>
<b>Adrenaline</b>	<b>12 ( 40% )</b>	<b>2 ( 6.66% )</b>

## Discussion

Post-operative myocardial stunning defined as transitory myocardial dysfunction induced by ischemia through aortic clamping followed by reperfusion involves depletion of high energy phosphates, intracellular calcium overload, generation of free radicals, and impairment of the coronary microcirculation.<sup>[2]</sup> Myocardial stunning, anaesthetic agents, vasodilatation and hyperthermia caused by the inflammatory response associated with CPB, all contribute to haemodynamic instability in the early post-operative period<sup>[6]</sup>. The recovery from this phenomenon starts after one hour of termination of CPB, and continues till 24 hours post-CPB<sup>[1]</sup>. Patients with this condition usually respond to positive inotropic agents<sup>[1]</sup>. Few studies on the use of levosimendan in the immediate post-cardiac surgery patients have been undertaken<sup>[7],[8],[9],[10]</sup>. In the present study levosimendan was started at smaller loading dose of 6µg/kg/min for 10 mins followed by 0.2 µg/kg/min to avoid profound hypotension.<sup>[11]</sup> In our study, levosimendan showed sustained increase in CO, CI, SV even after 36 hrs post-CPB, helping to improve the myocardial dysfunction associated with CPB. Levosimendan increased SV,CO,CI while causing only a small increase in heart rate Julian *et al.*,<sup>[14]</sup> in their study found significant hypotension with levosimendan infusion 0.2 µg/kg/min with a bolus dose of 12 µg/kg. In our study, although we did not find significant hypotension because of smaller loading dose. In contrast to the study of Julian *et al.*<sup>[14]</sup> our study showed less increase in HR in levosimendan group compared to dobutamine group.. The prolonged effects of levosimendan are owed to the pharmacokinetic properties of its metabolites, especially the molecule known as OR-1896. This has a pharmacodynamic profile identical to that of levosimendan, with a half life of approximately 80 hours and activity period of 2 weeks.<sup>[11],[15],[16],[17]</sup> In healthy humans, levosimendan increased SV and CI without increasing heart rate.<sup>29</sup> When administered as a bolus to patients shortly after coronary bypass surgery, levosimendan increased coronary blood flow without increasing myocardial oxygen consumption.<sup>31</sup> Levosimendan increases the sensitivity of myocardial filaments to calcium.<sup>27,31,32</sup> Consistent with this thesis is the observation that levosimendan does not impair myocardial relaxation.<sup>17-20</sup> Levosimendan causes vasodilation, attributed to the activation of potassium-dependent ATP channels<sup>21</sup> and decreasing the sensitivity to calcium.<sup>22</sup> .MAP, CVP.PAP ,SVRI,PVRI were significantly lower in levosimendan group than dobutamine thus required additional inotropes more. 12 patients in levosimendan group needed adrenaline for maintaining adequate MAP and CI indicating that 0.2 µg/kg/min levosimendan did not produce enough inotropy. This might be attributed to decrease in dosage of levosimendan. 16 patients in the levosimendan group were started on nor-adrenaline infusion to increase SVRI indicating that levosimendan infusion at 0.2 µg/kg/min with a small 6 µg/kg for 10 mins bolus dose produces significant vasodilation. 2 patients needed adrenaline infusion and 8 patients needed noradrenaline infusion in dobutamine group indicating relatively less vasodilation with dobutamine. Lactate levels, intensive care unit stay, and duration of ventilation were similar in both groups.

## Conclusion

Levosimendan loading dose of 6 µg/kg followed by 0.2 µg/kg/min produces more vasodilation as compared to dobutamine 5 µg/kg/min in the post bypass period in patients undergoing CABG surgery on pump. Levosimendan showed a statistically significant increase in CI even after 12 hours of stopping the infusion when compared to dobutamine. The requirement of another inotrope or vasopressor was more frequent in levosimendan group than in dobutamine group. There was no significant difference in the lactate levels and duration of ventilation and ICU stay in both the groups. In summary, the present study

demonstrates that levosimendan is safe and efficacious drug causing rapid dose-dependent improvement in hemodynamic function in patients with reduced LV function.

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**ABSTRACT :**

**Background and objectives:** The laryngeal mask airway[LMA] provides a useful alternative for airway management during spontaneous or controlled ventilation. LMA can be inserted successfully after suppression of airway reflexes under deep anesthesia using intravenous propofol or inhalational method using sevoflurane. The anesthesiologist's priority in burns patients undergoing surgery are to maintain cardiovascular stability & secure airway.

**Methods:** A cross sectional STUDY WAS CARRIED OUT in 50 patients of ASA group I & II aged between 15-60 years of either sex having burn injury and divided into 2 groups of twenty five each in medical college in Gujarat. Induction time, quality of LMA insertion and complications during insertion as well as post operative was noted.

Patient's vitals were measured before induction, immediately after LMA insertion and 5 min, 8min, & 10 min. after LMA insertion.

**Result:** Mean induction time was 61.88±6.71 seconds in group A & 92.8±6.55 seconds in group B. LMA was successfully inserted in all cases. In group-A LMA insertion was done in 1<sup>st</sup> attempt in all patients, while in group-B 5 patients(20%) required 2<sup>nd</sup> attempt. Decrease in mean arterial pressure after LMA insertion in group-A was significant compare to group-B. *in group-A there was higher incidence of hypotension, apnoea>30 seconds and pain on injection site while in group-B there was high incidence of coughing during insertion and PONV.*

**Conclusion:** Our study found that *both propofol & sevoflurane provide good quality of anesthesia for insertion of LMA in burns patients. As sevoflurane causes less hemodynamic changes than propofol which is beneficial in burns patients. So sevoflurane is better alternative to propofol for laryngeal mask airway insertion*

**Key Words:** LMA , propofol, sevoflurane, burns patient, hemodynamic changes.

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**INTRODUCTION:-**

The laryngeal mask airway[LMA] provides a useful alternative for airway management during spontaneous or controlled ventilation<sup>1</sup>. Over last decade LMA has gained widespread acceptance. LMA can be inserted successfully after suppression of airway reflexes under deep anesthesia using intravenous propofol or inhalational method using sevoflurane<sup>2</sup>. Propofol has the advantages of rapid and smooth induction with depression of upper airway reflexes<sup>3</sup>. It provides rapid recovery with less post operative nausea and vomiting. Sevoflurane is recently introduced halogenated volatile anesthetic agent with pleasant odour and low blood gas solubility, it does not irritate the airway and allows rapid smooth induction and recovery<sup>4</sup>. The anesthesiologist's priority in burns patients undergoing surgery are to maintain cardiovascular stability & secure airway.

Abnormalities in response to depolarizing and nondepolarising muscle relaxants in thermally injured patients have been recognized for many years<sup>5</sup>. As LMA can be inserted without use of muscle relaxant it is better alternative to endotracheal intubation. Direct thermal injury to head and neck will result in difficulty in securing the airway making the use of LMA very useful. Severely contracted neck is a particular problem which may be best managed using a mask or LMA, until contracture has been surgically released before intubation<sup>5</sup>.

Therefore this study was conducted to compare intravenous method using propofol and inhalation method using sevoflurane for insertion of LMA in patient undergoing burns surgery.

## **METHOD:-**

THIS cross sectional STUDY WAS CARRIED OUT in 50 patients of ASA group I & II aged between 15-60 years of either sex having burn injury and divided into 2 groups of twenty five each. The aims of study are induction time (time required to loss of eyelash reflex), quality of LMA insertion, complications during attempted LMA insertion, analysis of hemodynamic parameters, and post operative complications.

### **EXCLUSION CRITERIA**

- 1) Cardiovascular, renal or liver dysfunction
- 2) Drug allergy
- 3) History of bronchial asthma or COPD
- 4) Potential risk of gastric regurgitation

Each patient was assessed preoperatively, explained about the procedure. A written informed consent was taken. Routine and special investigations according to history of medical illness were advised. All the patients were checked for adequate mouth opening & neck extension.

Patients were kept nil orally for at least 6 hours pre-operatively & 4 hours post-operatively. In operation theatre all routine monitors were applied. A large vein was catheterized by NO. 18 venous canula. Patients were pre-medicated by giving inj. Glycopyrolate-0.2 mg/kg I.V, inj. Midazolam -0.02mg/kg I.V and inj. Fentanyl -2microgram/kg I.V.

Pre-oxygenation with 100% O<sub>2</sub> was done for 3 min before induction. Vitals were recorded just before induction.

Induction method

GROUP-A[intravenous]

Patient received propofol [1%]2.5mg/kg[4ml/10sec] until loss of eyelash reflex.

GROUP-B[Inhalation]

Patient received a mixture of 8% sevoflurane+50% O<sub>2</sub> 8 l/min via face mask until loss of eyelash reflex.

Patient's vitals were measured before induction, immediately after LMA insertion and 5 min, 8min, & 10 min. after LMA insertion. Appropriate size laryngeal mask airway was inserted with patient in intubation position[sniffing position] after applying lignocaine gel on back surface of LMA, after inflating the cuff and connecting it to Bain circuit. The LMA was inserted after the eyelash reflex has been lost. Conditions for LMA insertion was noted with reference to jaw opening, ease of LMA insertion and attempts of insertion.

Complications during LMA insertion like Apnoea>30 sec., coughing, gagging, laryngospasm, bronchospasm, patient movements were noted. Patients were maintained using O<sub>2</sub>,N<sub>2</sub>O, propofol infusion(4mg/kg/hr) in group A & O<sub>2</sub>, N<sub>2</sub>O, sevoflurane (2-3%) in group B.

After completion of surgery, LMA was taken out under deeper plane of anesthesia after deflating the cuff and suctioning the secretions if present.

All the patients were observed for post operative complications like excitatory phenomena, pain on injection site, nausea and vomiting.

The statistical analysis of data was done by using student's t-test and chi square test was used for difference of proportions. P<0.05 was considered significant

## **Results :-**

Demographic data and physical status in both the groups were comparable. Mean induction time group-A and group-B was 61.88± 6.71 / 92.8± 6.55 seconds respectively which was statistically extremely significant(p<0.0001).

Quality of LMA insertion was noted with reference to jaw opening, ease of LMA insertion and attempt of LMA insertion as shown in table-1

Complications during LMA insertions were noted as shown in table-2. Post operative complications were noted as shown in table-3.

Hemodynamic parameters –Mean arterial pressure and Heart Rate were noted at regular interval as shown in chart -1 and chart-2 respectively. ECG findings and Spo2 remains stable throughout the surgery in both the groups.

Table-1: Quality of LMA insertion.

		Grade	Group-A	Group-B
1.Jaw opening	Full	0	23(92%)	20(80%)
	Partial	1	2(8%)	5(20%)
	Impossible	2	0	0
2.Ease of insertion	Easy	0	23(92%)	20(20%)
	Difficult	1	2(8%)	5(20%)
	Impossible	2	0	0
3.Attempts		First	25(100%)	20(80%)
		Second	0	5(20%)

Table-2: Complications during LMA insertion

	Group-A	Group-B
1.Apnoea>30sec	14(56%)	0
2.Coughing	0	5(20%)
3.Gagging	0	0
4.Laryngospasm	0	0
5.Bronchospasm	0	0
6.Patient Movement	2(8%)	2(8%)

Table-3: post operative complications.

	Group-A	Group-B
--	---------	---------

Excitatory phenomena	2(8%)	0
Pain on injection site	6(24%)	0
Nausea & vomiting	0	4(16%)

Chart-1: Analysis of mean arterial pressure changes

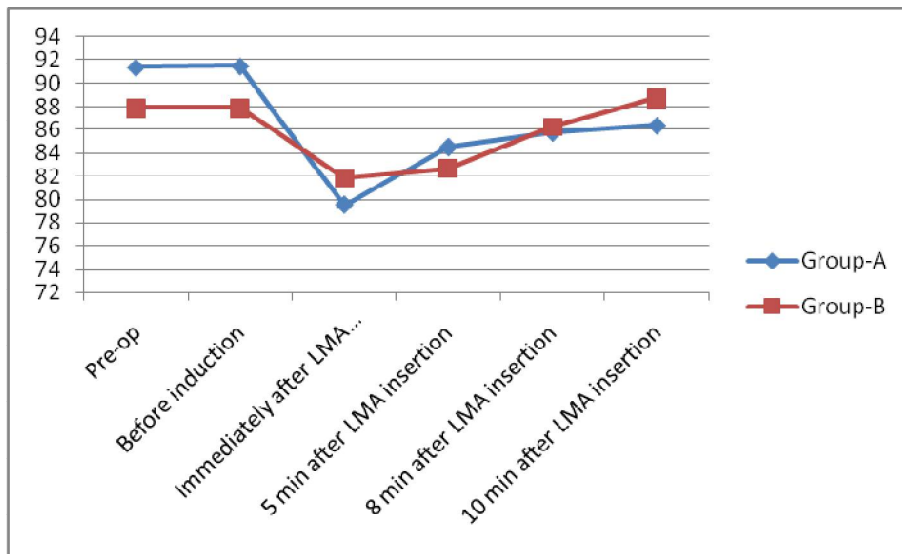
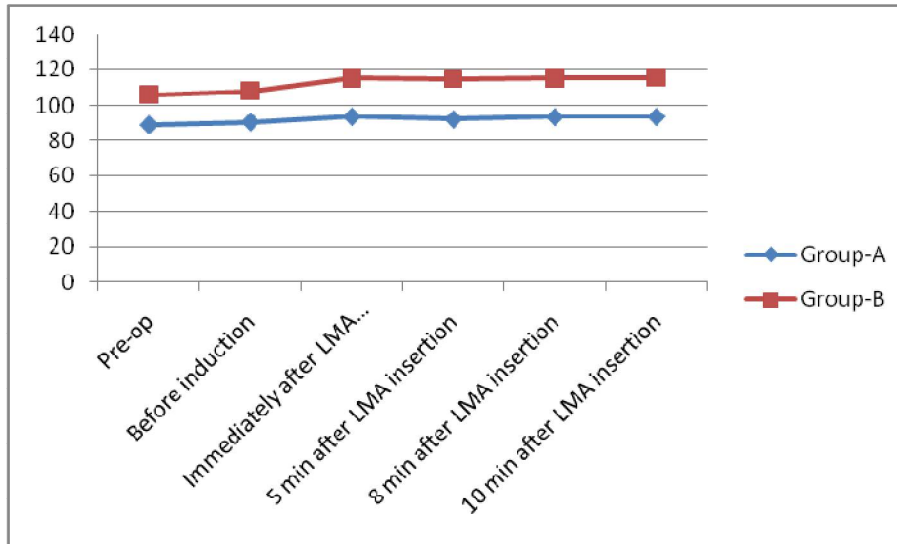


Chart-2: Analysis of heart rate changes



### Discussion:-

Anesthesia for the burns patient is great challenge to the anesthesiologist. Access to the airway is difficult because of laryngeal edema, neck contracture, facial edema etc. Burns patient often required many operative procedure in short succession. LMA is therefore most useful device to prevent tracheal tube damage in burns patient.

This study was done to compare the quality of insertion of LMA in burns patient using intravenous method (inj. Propofol 2.5 mg/kg) and inhalation method (sevoflurane 8% + O<sub>2</sub> 25% + N<sub>2</sub>O 50%, 8L/min). All patients were premedicated with inj. Glycopyrrolate, inj. Fentanyl and inj. Midazolam.

Demographic and physical status of both groups were comparable.

Mean induction time was 61.88±6.71 seconds in group A while it was 92.8±6.55 seconds in group B. Induction time was longer in sevoflurane group. In Group A shortest induction time was 50 seconds and longest time was 76 seconds. While in Group B shortest induction time was 84 seconds and longest tie was 104 seconds. Ismail Kati(2003)<sup>6</sup> in their study compared LMA insertion time, hemodynamic changes and complications in patients anesthetized by inhalation of sevoflurane with those of intravenous induction with propofol. Our results were comparable with their study.

Full jaw opening with easy LMA insertion was possible in 92% patients in group-A while 80% patients in group-B. There was partial jaw opening in 8% patients in group A while 20% patients in group B.

LMA was successfully inserted in all cases. In group-A LMA insertion was done in 1<sup>st</sup> attempt in all patients, while in group-B 5 patients (20%) required 2<sup>nd</sup> attempt. This was comparable with earlier study [Lian Kah Ti(1999)]<sup>4</sup> who compared quality and ease of LMA insertion after either single vital capacity breath of sevoflurane 8% or intravenous propofol 3mg/kg.

In group-A 14 patients (56%) had apnoea>30 seconds while none had in group B. [Lian Kah Ti(1999)] coughing was not seen in any patients in group-A while it was seen in 5 patients(20%) in group-B.

Immediately after LMA insertion in propofol group 88% patients had increase in heart <10 and 4% patients had increase in range of 11-20, while in sevoflurane group 12% patients had increase in heart rate<10 and 88% patients had heart rate increase in range of 11-20. Immediately after LMA insertion neither patient having heart rate 20/min.

Immediately after LMA insertion in propofol group 84% patients had decrease in systolic blood pressure upto 20 mm hg, hile in sevoflurane group 96% patients had decrease in systolic <10 mm Hg. Mean arterial pressure reduced significantly in group A than group B immediately after LMA insertion. Thus decrease in mean arterial pressure after LMA insertion in propofol group was extremely significant compare to sevoflurane group. This was comparable with earlier study[*Ismail Kati(2003)*].

*Pain on injection site was observed in 6 patients(24%) and excitatory phenomena in 2 patients(8%)s. nausea & vomiting was not observed in any patient in Group-A. No patient had excitatory phenomena but nausea & vomiting was observed in 4 (16%) patients in group -B.*

**Conclusion:-**

Propofol and sevoflurane both provides rapid and smooth induction of anesthesia and recovery. Propofol had shorter induction time with full jaw opening and easy LMA insertion. There was no post operative nausea & vomiting in propofol group. However propofol was associated with hypotension, apnoea>30 seconds and pain on injection site. Sevoflurane had longer induction time with comparable jaw opening and LMA insertion. There was no incidence of hypotension in sevoflurane group but has higher incidence of post operative nausea and vomiting.

*To conclude with both propofol & sevoflurane provide good quality of anesthesia for insertion of LMA in burns patients. As sevoflurane causes less hemodynamic changes than propofol which is beneficial in burns patients who are already hemodynamically compromised. So sevoflurane is better alternative to propofol for laryngeal mask airway insertion in patients undergoing burns surgery.*

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## **PACT OF AGING (ELDERLY GROUP ) ON TIME PERCEPTION , A COMPARATIVE STUDY BETWEEN YOUNG AND ELDERLY SUBJECT**

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Key words: Two minute (120 seconds) time perception test, elderly and young group. Time, perception

NSS: National service scheme ,

### **Abstract:**

**Back ground:** One side the researchers in Physics are trying to find out the true nature of time ,from where it come and when it will end .On the other hand neuro physiologist and neuro psychologists are trying to search out how brain and mind can perceive time. An old age belief “time flew as we age” is tried to validate by many scientists. It means that time pass rapidly in elderly people. Though it appears that we do not have any sense organ to perceive time as we have sense organs for i.e. touch ,taste, smell , ...And our temporal perception is a product of function of cerebrum . Illusive nature of time is very well discussed in psychology ,philosophy and metaphysics . It is understood from the studies from chrono biology that there is a internal clock in our brain to regulate circadian rhythms by getting information from suprachiasmatic nucleus of hypothalamus by receiving light information retina. The cerebrum try to synchronize the internal clock with human made external clocks. In this study we have tried to study the impact of aging on time perception by two minute (120 seconds) time perception test and compared the results similar test conducted among the healthy young volunteers and other scientists.

**Method:** The data were collected from subject attended various NSS camp set ups organized by NSS unit AMCMET medical college Ahmedabad . The subjects were divided into two groups

1  
N1: group consisting young group was medical students of mean age 19.17 sd 8.54 and 2  
N2:

elderly group was residents of elderly houses mean age 66.9 sd 8.38 Instrument required: smart phone stop watch function to calculate two minutes. Instrument required: smart phone stop watch function to calculate two minutes.

**Result:** Mean seconds perceived during two minute perception test was statistically lower significantly amongst elderly group compared by youngster group. There was a significant distortion of time perception observed amongst elderly group

### **Conclusion:**

The study concluded the fact that time perception is distorted among elderly people. Though the reliable test is awaiting for time perception more researches are required to generate the new valid tests to assess the time perception. How does the time perception matters? Time perception, chronometric capacity and its alteration with aging is a challenging research topic in physiology and medicine. The results are this study are to be dealt with caution due to methodological limitations .Though it is worth to mention that Temporal perception is essential when detecting rapidly presented stimulus information i.e. driving in traffic .Altered time perception among elderly is an issue while driving a moped or a car. As in driving in traffic, the time perception is essential for safer driving from safety of individual and general population point of view.



To understand temporal illusions a cross-multi disciplinary approach is required to develop valid tests for time perception .It further needed to develop new methods and combined with techniques employing electrophysiology, , EEG, fMRI with the hope that the time illusions will light the way to understanding general outstanding questions of time perception. Faster “internal-clock” in the older need to further documented with other neuropsychological tools to measure time perception and to study temporal perception with aging . These tests are potentially a useful tool to measure subjective perception of time. They also corroborate the hypothesis of a change in subjective time perception with aging and studies done by other scientists.

#### **Introduction:**

Throughout the life whatever behavior is conducted by human organism ,the time dimension is always there just like space dimension. Life on earth is shaped by multiple environmental cycles .Prokaryotes to humans – internal timekeepers (so called circadian clocks/rhythms) have evolved that anticipate these daily events for fine-tune physiology to the varying demands of activity and rest i.e. . The day and night. Circadian rhythms are almost omnipresent and cover all aspects of biology from behavior down to cell cycle control and chromatin modulation. In mammals, a master clock in the suprachiasmatic nuclei (SCN) of the hypothalamus is synchronised to geophysical time via visual photoreceptive systems in the retina.From the SCN, time information is transmitted to numerous peripheral clocks located throughout the body. Yet there is no known specific sensory receptor for time. So how do we have temporal perception? How the brain keeps track of time?. The brain's internal clock is commonly compared to the function of a imagery pacemaker that emits pulses at some mean rate, which then leads to the experience of subjective time.

Time is an integral part of our daily life. The time is always there, omnipresent and immaterial. . But what is time? Well it’s just a construct of our brain and mind. It doesn’t really exist without our brain and mind. Each person would perceive the flow of time. The generalized and specialized sensory receptors give rise to various perception but , there is no specific receptor for time. But the time always present with us. Without a timepiece, or even conscious awareness, people perceive the passage of time.

We all have experience that we can go to sleep without an alarm and wake up at a predetermined time. Though the experiments have proved that subjective hour is longer than an actual hour (24 hour=25 hours).virtually everyone is aware of the passage of time, and can estimate its passage. Dr. Marc Wittmann at al interviewed 499 German and Austrian older subjects and reported that the all volunteers confessed that the last decade had passed quickly. There is not a simple linear translation of perceived time into actual time. But our temporal /elementary time experiences contain duration; non-simultaneity; order; past and present; change, including the passage of time. The estimate or perception of time is less efficient and deteriorated beyond 65 years of life but is hard to prove experimentally. With all limitation of technique in this study we have compared perception of time in young healthy subjects with elderly subjects and the results are discussed.

#### **Material and method:**

The data were collected from subject attended various NSS camp set ups organized by NSS unit AMCMET medical college Ahmedabad . The subjects were divided into two groups

1  
N1: group consisting young group was medical students of mean age 19.17 sd 8.54 and 2  
N2:

elderly group was residents of elderly houses mean age 66.9 sd 8.38

Instrument required: smart phone stop watch function to calculate two minutes.

Before the test the volunteers were explained an understanding of time and the meaning of 1 second and two minutes(120 seconds). The subjects were asked to calculate mentally two minutes or one hundred and twenty seconds .The subjected were told to keep eyes closed to avoid take clue from other sources of time elapse. Standard mobile clock with stop watch was used to measure two minutes. When the subject finished mental counting, the actual elapsed times were recorded. The mean mental time or “brain clock time” were measured among both the group the young students group N1 group and elderly group N2.Mean values of observed brain times were compared amongst both the groups.

**Criteria for selection of subjects:**

All subjects must fully conscious ,  
No history of neurological disease .  
No history use of drugs i.e. anxiolytics or sedative.  
Must be cooperative to participate in study.

**Otherwise excluded.**

This study included 200 subjects, including 129 women. Two groups were formed according to age: Group N1 comprised 100 subjects, aged 17-21 years; the mean age . Group 2 comprised 100 subjects, aged the mean age

Statically tests:

Statistical analyses for comparisons between groups were performed with the student t test. All data were entered in a Microsoft excel program for the two age groups

**Research Questions**

**Does time perception differ between youngsters and elderly?..**

OBJECTIVE:

DESIGN:

Cross-sectional comparative study.

**Conflict of interest:** There is no conflict to interest to declare.

SETTING:

Data collected from camps organized by NSS Unit in AMCMET medical college at elderly houses in Ahmedabad

Subjects :200 adults 100 young and 100 elderly.

OBJECTIVE:

To study the Impact of aging on time perception as studied by 2 minute time perception test and compare result among young and elderly group

DESIGN:

Cross-sectional comparative study.

SETTING:

Data collected from camps organized by NSS Unit in AMCMET medical college in college and

elderly houses in Ahmedabad

Subjects :200: 100 young and 100 elderly.

**RESULTS and statistical test:**

**TEST RESULTS**

**P value and statistical significance:**

The two-tailed P value is less than 0.0001

By conventional criteria, this difference is considered to be extremely statistically significant.

**Confidence interval:**

The mean of n1 young group minus n2 elderly group equals 24.0989653500

95% confidence interval of this difference: From 17.9550649813 to 30.2428657187

**Intermediate values used in calculations:**

t = 7.7351

df = 198

standard error of difference = 3.116

Table 1 : Result showing mean second perceived by young student and elderly during 120 second **perception test**

Group	n1 young group	n2 elderly group
Mean	108.44	84.34
SD	22.94	21.07
SEM	2.29	2.10
N	100	100

**P < =0.001**

**Discussion:**

With all limitation of method of assessment of study time perception , the study documented that there is significant distortion of time perception in elderly groups compared to youngster’s group. Time perception is faster in elderly and is projected by this study with the help of counting “ two minutes (120 seconds )perception test” . Vanessa Fernanda Moreira ,Ferreira Gabriel ,Pina Paiva et al carried out similar study and concluded that Mental calculations of 120 seconds were shortened by an average of 24.6% in elderly individuals compared to individuals young group and further suggested fastening of time perception amongst elderly. Elżbieta Szlag and et al in their study on Aged elderly and supported similarly temporal perception decline and offered new horizons for neuro rehabilitation in elderly population in context to temporal perception .

We have a very straight forward structured and linear concept of time and time seems to speed up as we get older. The scientists have proposed “proportionality theory for time perception” . The theory uses pure mathematical model, holding that a year feels faster when you’re 40 (forty year of age) than when you’re 8(eight year of age) because it only constitutes one fortieth of your life rather than a whole one eighth of your life. Babies and toddlers have no concept of time. The awareness of time evolves during childhood as children’s attention and short-term memory capacities develop a process dependent on the gradual maturation of the prefrontal cortex. So time perception appears a learned experience. The author thinks that time perception evolves in context to learning 3D perception of space special perception/orientation and persons(i.e. close contacts friends and relatives). To gauss the time required for a task, they must pay attention to it. They must also memorize a stream of time-data without losing concentration. So children suffering from attention-deficit hyperactivity disorder find it hard to gauss time correctly. Dr. Sylvie Droit-

Volet, a psychology professor at Blaise Pascal University, in France, manipulated subjects' emotional state by showing them movies that excited fear or sadness. She then asked the subjects to estimate the duration of the visual stimulus. She found that time appears to pass more slowly when we are afraid. Here again the attention, memory and emotion play a part in our perception of time. Dr. David Eagleman at Baylor College of Medicine found that repeated stimuli appear briefer in duration than novel stimuli of equal duration. Due to aging, for old people it is difficult to perceive new stimuli as novel among the elderly compared to a younger one.

According to one more model of time mechanics of brain, time as perceived by our brains (subjective time) is synchronized with the ticking of an our watch (objective time) for measuring time. The mechanism consists of an imagery pacemaker, continuously emitting pulses (ticking), which are stored in an accumulator. Subjective duration i.e. number of pulses that have accumulated (since the beginning of the stimulus). When the internal clock speeds up, the number of pulses increases, creating the impression that time is passing more slowly. When we stop paying attention to time, pulses are blocked and no longer reach the accumulator and pulses are not counted, and time appears shorter.

While in another striatal beat-frequency model, specialized neurons in dorsal striatum of basal ganglia act as oscillator cell. Each of these brain cells has up to 30,000 connections with a series of cells in the cortex oscillating at various frequencies. The neurons in the striatum can read time codes emitted by oscillator cells in the cortex. They come into action when oscillatory activity corresponds to previously detected patterns, stored in memory. Thus the estimates of time intervals originate in neuronal activity in basal ganglia. It has further stated that when we estimate the timing of a visual stimulus visual cortex is activated. Doing motor act, primary motor cortex is come into action and so auditory cortex estimate the length of a sound stimulus. Dopamine is the main neurotransmitter involved in time processing. Dopamine receptors agonists tend to speed up our perception of time, which passes more quickly. This is also the case for certain drugs, such as cocaine, which enhances the effect of dopamine. On the contrary, narcoleptics -dopamine antagonist make time passing more slowly and so in Parkinson' disease. Duration and integration of time is lengthened in schizophrenias. Suggesting defects in the brain's time keeping mechanisms. Relation between Type A behavior/personality and heart disease is well known and there is moderate correlation between the pace of life and the rate of death from heart disease.

Perception of time passage was accelerated in aging due to a lack of new experiences and reduction in dopamine neurotransmission amongst elderly group and need further documentation and studies.

### **Conclusion:**

The study concluded the fact that time perception is distorted among elderly people. How does the time perception matters? Time perception, chronometric capacity and its alteration with aging is a challenging research topic in physiology and medicine. Though the reliable tests are awaiting for time perception. More researches are required generate the new valid tests to assess the time perception.

The results of this study are to be dealt with caution due to methodological limitations. Though it is worth to mention that Temporal perception is essential when detecting rapidly presented stimulus information i.e. driving in traffic. Altered time perception among elderly is an issue while driving a moped or car. As in driving in traffic, the time perception is essential for safer driving from safety of individual and general population point of view.

To understand temporal illusions a cross-multi disciplinary approach is required to develop valid tests for time perception. It further needed to develop new methods and combined with techniques employing electrophysiology, EEG, fMRI with the hope that the

time illusions will light the way to understanding general outstanding questions of time perception. Faster “internal-clock” in the older need to further documented with other neuropsychological tools to measure time perception and to study temporal perception with aging . Mean while the test we used is potentially a useful tool to measure subjective perception of time. They also corroborate the hypothesis of a change in subjective time perception with aging and studies done by other scientists.

Another area of interest in context to time perception is “can we slow down time passage?” Scientists have suggested constantly learning new ideas, subjects and skills is the method to slow down the time. So we recommend to remain life time a student to maintain normal time perception.

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12

# 10th ACADEMIC MEET 2017

## ON TIME AND MEDICINE

16 & 17th September 2017

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&

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**Abstract** For both paper and poster presentation abstract must be submitted on or before 30 August 2016 before the conference

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1] Name of authors 2] Affiliation with college/Hospital 3] Name of PG teacher 4]

Name of topic 5] Key words 6] Introduction 7] Methods 8] Results 9] Name of statistical test

10] conclusions. 11] Refs

**Speakers** can send abstract of their presentation and will be published in Souvenir /Abstract book.

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