(International Print/Online Journal)

SJIF IMPACT FACTOR: 4.617
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume3, Issue 3, Page No: 51-58
May-June 2020

Attenuation of cardiovascular response to laryngoscopy and intubation: A comparative study between dexmedetomidine hydrochloride and fentanyl citrate

Arunkumar S Yumnam[1], Binarani M[1*], H. Kenedy Singh[2], RK. Rita Devi[2], L. Eshori Devi[3]
[1]Assistant Professor, [2]Senior Resident, [3]Associate Professor
Department of Anaesthesiology, RIMS Imphal, India 795004

***Corresponding Author:**
Dr.Binarani Maharabam
Assistant Professor, Department of Anaesthesiology, Regional Institute of Medical Sciences, Lamphelpat, Imphal, Manipur

Type of Publication: Original Research Paper
Conflicts of Interest: Nil

ABSTRACT

***Background*:** The cardiovascular responses to laryngoscopy and intubation are changes in HR, BP, cardiac rhythm and increase in CSF pressure. These responses are mediated by lifting the base of tongue and epiglottis by the laryngoscope blade and are associated with an increase in sympathoadrenal discharge and rise in catecholamine levels. In susceptible patients, these stress responses may cause deleterious effects. Various techniques have been used to attenuate this stress response including the use of lignocaine, opioids, β blockers, vasodilators, inhalation anesthetics etc. with limited success. The aim of this study was to evaluate and compare the two drugs along with saline used as control.

***Methods*:** Following institutional ethical committee approval and written informed consent, seventy five adult patients (ASA- I and II, 18-60 years of either sex) were enrolled in this study.

Patients were divided into three groups: Group I(n=25) received dexmedetomidineHcl 1µg/kg, Group II (n=25) received fentanyl citrate 2µg/kg and Group III(n=25) received saline (control). The study drugs were administered intravenously 10 min before the induction. The parameters like heart rate, blood pressure (systolic, diastolic and mean arterial pressure) were monitored every minute for the first 5 mins and then 10mins after laryngoscopy and intubation.

Results: Our study showed that the administration of 1 µg/kg dexmedetomidine infusion prior to anesthesia induction suppressed the hemodynamic response superior than that resulted from fentanyl(2µg/kg) or saline administration.

***Conclusion*:** DexmedetomidineHcl attenuates the stress response to laryngoscopy and intubation better than Fentanyl citrate

Keywords: Stress response, Laryngoscopy, Intubation, Dexmedetomidine, Fentanyl

INTRODUCTION

Laryngoscopy may be performed to facilitate tracheal intubation for general anaesthesia or cardiopulmonary resuscitation or for procedures on the larynx or other parts of the upper tracheobronchial tree. Laryngoscopy and intubation are known to cause exaggerated circulatory response.[1] These hemodynamic changes are generally transitory and without sequelae. However, in patients with pre-existing coronary artery disease, hypertension, cerebrovascular disease, presence of autonomic neuropathy in diabetic patients etc., an increase in these circulatory parameters may have deleterious respiratory, neurological and cardiovascular effects

and can precipitate myocardial ischaemia [2], arrhythmias, infarction and even cerebral hemorrhage.[3]

For all these reasons serious efforts were made to prevent these cardiovascular responses to laryngoscopy and intubation in those susceptible patients.

Opioids are also widely used to control the neurovegetative response to intubation. A linear relationship exists between increased opioid dose and cardiovascular response reduction.[4,5] Many studies have shown the effectiveness of fentanyl in blunting the pressure response to laryngoscopy and intubation. [6,7]

Use of α_2-adrenergic agonist has been shown to blunt hemodynamic response to noxious stimulation and prevent hemodynamic variability.[8] Dexmedetomidine is a highly selective α_2-adrenergic agonist that has sedative and analgesic effects. Dexmedetomidine has been used as an adjunct to general anaesthetics.[9,10]

In addition, it has been shown to decrease perioperative catecholamine concentrations and promote perioperative hemodynamic and adrenergic stability.[11] Dexmedetomidine causes a dose dependent decrease in heart rate (HR) and blood pressure (BP), produces sedative, anxiolytic and analgesic effects.[12] Few studies are available comparing the efficacy of fentanyl and dexmedetomidine in attenuation of cardiovascular response to laryngoscopy and intubation. We , therefore, plan to conduct a randomized double blind study comparing the effectiveness of dexmedetomidine and fentanyl in attenuation of stress response to laryngoscopy and intubation.

MATERIALS AND METHODS

This study was a prospective randomized and double blind placebo controlled conducted in the Department of Anesthesiology, a Tertiary Care Centre in Imphal, Manipur over a period of three years between September 2016 to August 2019. After obtaining approval from the institutional ethics committee and getting informed written consent ,75 ASA I and II (American society of Anaesthesiologist physical status I and II) adult patients of either sex, aged 18-75 years scheduled for elective surgery under general anaesthesia with endotracheal intubation were randomized based on computer generated randomization and divided into three equal groups(n=25) .Group I received inj dexmedetomidine 1µg/kg body weight, Group II received Inj fentanyl 2µg/kg body weight and Group III control group received equal volume of normal saline(NS).

Patients with predictable difficult airway, obesity (Body mass index, BMI>30), ECG (electrocardiogram) abnormalities, congestive heart failure, DM (diabetes mellitus), HTN (hypertension), coronary artery diseases, respiratory, renal, hepatic or cerebral diseases, history of drug allergy, unwilling patients, head and neck surgery, those who had taken drugs that could influence hemodynamics and autonomic functions and pregnancy were also excluded from the study.

On the day of operation all patients were pre-medicated with 0.004mg/Kg body wt. of inj. Glycopyrolate I.M .(intramuscular) 30 mins before the procedure. Intravenous (I.V.) access were secured with 18 G cannula. Monitoring and recording of BP(blood pressure) and HR(heart rate) were done by using Monitor Dragger Infinity Vista XL. The syringes containing dexmedetomidine Hcl, fentanyl citrate or NS with identical coding were prepared in a double blind fashion by a collaborator not involved in the data recording. The same collaborator administered drug while a blind observer collected the data. The study drug were administered by I.V. 10min. before induction of general anaesthesia. All patients were pre-oxygenated for 5 mins with 100% O_2 (oxygen).

For induction injection propofol 2mg/Kg body wt. were given slowly in incremental dose until the loss of eye lash reflexes, and to facilitate intubation and laryngoscopy, inj. rocuronium 0.9mg/Kg body wt. was given I.V. After 1 min of giving rucoronium, laryngoscopy and intubation were carried out by an experienced anaesthetist. Thereafter anaesthesia were maintained with nitrous oxide, oxygen and sevofluorane.

Monitoring and recording of HR and BP (SBP-systolic blood pressure, DBP-diastolic blood pressure,MAP-mean arterial pressure) were done before giving test drug (baseline), 10 min after test drug,1 min. after induction and at 1,2,3,4,5,10 mins. after laryngoscopy and intubation. After the study was over, injection diclofenac aqueous 1.5mg/Kg

Volume 3, Issue 3; May-June 2020; Page No.51-58

body wt. i.m. was given and surgeons were allowed to start the incision.The data collected were entered in a computer and statistical analysis was performed using Statistical pakage for Social Sciences (SPSS-version 20 Chicago IL, USA).Continuous data are expressed as mean±standard deviation (SD); categorical data are shown as ratios, and P value of < 0.05 is considered as significant.

DISCUSSION

Laryngoscopy and tracheal intubation is associated with cardiovascular responses like elevation of blood pressure, pulse rate, occasional dysarrhythmias, cough reflexes, increased intracranial pressure and increased intraocular pressure[1]. If no specific measures are taken to prevent hemodynamic response, the HR(heart rate) can increase from 26% to 66% depending on the method of induction and systolic blood pressure can increase from 36% to 45%.[13,14,15]

Attenuation and obtundation of pressor response during laryngoscopy and surgery has been one of the most researched topics in anaesthesia, but with only a few positive established outcomes.[9,16]

Burstein et al[17] found that the pressor response occurring at laryngoscopy and endotracheal intubation was due to augmented sympathetic response, provoked by stimulation of epipharynx and laryngopharynx. These factors were further confirmed by Prys-Roberts.[5]

Tachycardia reduces diastolic filling time thereby reducing effective stroke output. Against a higher arterial pressure the cardiac work demands more oxygen than the same workload done against a lower pressure. So, in situations like laryngoscopy and intubation which results in tachycardia and arterial hypertension, there is more oxygen demand without an increase oxygen supply with danger of myocardial insufficiency and can also cause catastrophic events such as intracerebral bleed, myocardial infarction and/ or acute heart failure.[18,19]

Numerous drugs and their combinations have been tried in the past and studies have highlighted the use of these drugs in varying doses for suppression of stress response but not without the significant incidence of quite a few side-effects especially with high doses of opioids.[20]

Recently extensive studies are conducting on dexmedetomidine administration regarding the analgesic, sedation, anxiolytic, sympatholytic and blunting of exaggerated hemodynamic responses and these are mainly mediated by the activation of α_2-receptors located in the post-synaptic terminals in the central nervous system (CNS), which causes decreased neuronal activity and augmentation of the vagal activity.[9] The role of α_2-agonists in regulating the autonomic and cardiovascular responses is well understood, whereby they inhibit release of catecholamines (nor-epinephrine) from the sympathetic nerve terminals by augmentation of a vasoconstrictive effect[21].

Sebastian B et al. compared the effect of 0.5µg/kg and 0.75µg/kg of dexmedetomidine with normal saline in attenuating stress response to laryngoscopy and intubation.They found that dexmedetomidine 0.75µg/kg attenuated the haemodynamic stress response to laryngoscopy and intubation completely compared to 0.5µg/kg.[22]

Gagan B et al. also conduced a study to compare the effect of dexmedetomidine and fentanyl in attenuating haemodynamic response to laryngoscopy and intubation by giving dexmedetomidine loading dose of 1µg/kg and maintenance dose of 0.4µg/kg/hr with fentanyl loading dose of 1µg/kg and maintenance dose of 1µg/kg/hr. They concluded that a bolus supplemented with continuous infusion of both drugs are nearly competitive in attenuation of haemodynamic without compromising patient safety and recovery from anaesthesia.[23]

In this prospective randomized study we attempt to examine whether administration of dexmedetomidine attenuates the stress response to laryngoscopy and intubation. Again comparison with fentanyl seems to be an appropriate selection for attenuating the hemodynamic response to laryngoscopy and tracheal intubation as narcotics are widely used to control the neuro-endocrine responses to intubation. A linear relationship exists between increasing opioids dose and attenuation of cardiovascular responses and most studied agents include fentanyl, sufentanil, ramifentanil and alfentanil.[4,5,12,24] Hemodynamic responses following dexmedetomidine infusion depends on dose and speed of infusion. A sequence of transient hypertension with reflex bradycardia followed by

Volume 3, Issue 3; May-June 2020; Page No.51-58

hypotension is seen in higher dose and rapid infusion. The subsequent decrease in heart rate and blood pressure may be due to decrease in central sympathetic outflow.[25] There was a minimal decrease in heart rate and blood pressure in patient receiving dexmedetomidine in our study.

The Systolic blood pressure (SBP) transiently rise after laryngoscopy and intubation in all the groups followed by a falling trend till the end of the observation period .Though statistically not significant the fall in SBP is lower in dexmedetomidine group (Group I).It could be due to the vasoconstriction caused by α_2-receptor in the vascular smooth muscle thereby minimizing the decrease in blood pressure during anaesthetic induction.[11,26] Similar findings is suggested by the study of Kunisawa T et al.[21] The same reason may explain why we could not appreciate significant difference between dexmedetomidine (Group I) and control group (GroupIII), .

However we cannot readily explain why SBP in control group(GroupIII) is not significantly higher than that of fentanly group (GroupII) except at 1min after laryngoscopy and intubation (SBP3;P=0.038). In general, the stress response starts within 5 seconds of laryngoscopy, peaks in 1 to 2mins and returns to control level within 5mins.[27] Both DBP and MAP also show similar trends. However, contemporary studies do not emphasize these parameters while studying stress response to laryngoscopy and intubation.

There were few limitations of our study. Invasive blood pressure and plasma catecholamine level monitoring were not performed due to limited facilities available at our set up.

In brief, our study showed that the administration of 1 µg/kg dexmedetomidine infusion prior to anaesthesia induction suppressed the hemodynamic response to tracheal intubation. This suppression in cardiovascular responses was found to be superior than that resulted from fentanyl(2µg/kg) or saline administration. Our study is in support of the study of Hanci V et al. He compared the effect of fentanyl and dexmedetomidine when used in combination with propofol and lidocaine for tracheal intubation without using muscle relaxant. The intubating conditions were significantly more satisfactory in dexmedetomidine group than fentanyl group.[28]

RESULTS:

A total of 50 patients of ASA Grade I and II of either sex were included in the study and divided into two equal groups. The demographic profiles of the patients like age, sex, height and weight were comparable and statistically not significant among the two groups with P value of >0.05 as shown in Table 1. The mean heart rate of the patients in the three groups is shown in table 2, drawn graphically in fig. 1. It is observed that in group I (Dexmedetomidine) heart rate falls after 6 min infusion of test drug only to rise at post laryngoscopy and intubation, thereafter it maintains a steady state. Whereas in group II (Fentanyl) heart rate rises significantly throughout the post intubation period and remains in this state till the end of our observation.

There is no significant difference between group II and group III (P=0.866). So it is quite clear that dexmedetomidine has more stabilizing effect on heart rate changes whereas fentanyl does not seem to have a controlling effect on the rise in the heart rate. As shown in table 3.and fig.2, the SBP decreased after induction from baseline in all the 3 groups . In the post intubation period SBP rises slightly only for 1min to go above the baseline reading after induction in all the groups; thereafter there is a falling trend in all the groups till the end of the study. However changes are only marginally significant (p=0.02) 2 minutes after laryngoscopy and intubation. This is due to greater fall in SBP in Fentanyl group as changes between dexmededotomidine and saline are insignificant (t=0.895;P=0.375).

CONCLUSION:

From the results of this study undertaken with the aim of comparing the effectiveness of dexmedetomidineand fentanyl citrate in attenuating the hemodynamics response to laryngoscopy and intubation and their relative effectiveness we have the following conclusion :

Intravenous dexmedetomidineHcl 1 µg/Kg body weight and intravenous fentanyl citrate 2 µg/Kg body given 10 min before induction of general anaesthesia attenuate the stress response to laryngoscopy and intubation. But dexmedetomidine is superior than fentanyl in attenuation of heart rate

Volume 3, Issue 3; May-June 2020; Page No.51-58

during laryngoscopy and intubation while both demedetomidine and fentanyl are more or less equally effective in checking blood pressure rise.

REFERENCES:

1. Reid LC., Brace DE. Irritation of the respiratory tract and its reflex effect upon heart. Surg Gynaec & Obst 1940; 70: 157-62.
2. Edwards DN, Alford AM, Dobson PMS, Peacock JE, Reilly CS.Myocardial ischaemia during tracheal intubation and extubation. Br J Anaesth 199;7:537-539.
3. Barclay K,Kluger M. Effect of bolus dose of remifentanil on haemodynamic response to tracheal intubation. Anaesth Intensive Care 2000; 28:403-7. Abraham V, Kaur B. Prevention of rise of blood pressure during induction using thiopentone immediately before intubation in normotensive patients.Ind J Anaesth 1994; 42:73-6.
4. Abraham V, Kaur B. Prevention of rise of blood pressure during induction using thiopentone immediately before intubation in normotensive patients.Ind J Anaesth 1994; 42:73-6.
5. Prys-Roberts C, Greene LT, Meloche R, Foex P. Studies of anaesthesia in relation to hypertension II Haemodynamic consequences of induction and endotracheal intubation .British Journal of Anaesthesia 1971; 43:531- 46.
6. Chraemmer-Jorgensen B, Hoilund-Carlsen PF, Marving J, Christensen V. Lack of effect of intravenous lidocaine on hemodynamic responses to rapid sequence induction of general anesthesia: a double-blind controlled clinical trial. Anesth Analg 1986; 65(10):1037-41.
7. Burstein CL, Lopinto FJ, Newman W. Electrocardiographic studies during endotracheaintubation: Effects during usual routine techniques. Anaesthesiology 1950; 11:224.
8. Kindler CH, Schumacher PG, Schneider MC, Urwyler A. Effects of intravenous lidocaine and/or esmolol on hemodynamic responses to laryngoscopy and intubation:a double-blind controlled clinical trial. Clin Anesth 1996;8(6):491-6.
9. Chung KS, Sinatra RS, Halevy JD, PAIge D, Silverman DG. A comparison of fentanyl, esmolol and their combination for blunting the haemodynamic responses during rapid-sequence induction. Can J Anaesth 1992; 39:774-9.
10. Black TE, Kay B, Healy TE. Reducing the hemodynamic responses to laryngoscopy and intubation. A comparison of alfentanil with fentanyl. Anaesthesia 1984; 39(9):883-7.
11. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous Dexmedetomidine in humans, II: Hemodynamic changes. Anesthesiology 1992;77:1134–42.
12. Bedford RF and Lt Marshal K.Cardiovascular responses to endotracheal intubation during four anaesthetic techniques.Acta Anaesthesiologica Scandinavia.1984;28:563-66.
13. Magulre AM, Kumar N,Parker JL,Rowbotham DJ,Thompson JP. Comparison of effects of remifentanil and alfentanil on cardiovascular response to tracheal intubation in hypertensive patients. Br J Anaesth 2001; 86:90-3.
14. Kautto UM. Attenuation of the circulatory response to laryngoscopy and intubation by fentanyl. Acta Anaesthesiol Scand 1982; 26(3):217-21.
15. Cork RC, Weiss JL, Hameroff SR, Bentley J. Fentanyl preloading for rapid-sequence induction of anesthesia. Anesth Analg 1984; 63(1):60-4.
16. Talke P, Richardson CA, Scheinin M. Postoperative pharmacokinetics and sympatholytic effects of dexmedetomidine. Anesth Analg 1997; 85:1136-42.
17. Flacke JW, Bloor BC, Flacke WE, Wong D, Dazza S, Stead SW et al. Reduced narcotic requirement by clonidine w ith improved hemodynamic and adrenergic stability in patients undergoing coronary bypass surgery.Anesthesiology 1987 ;67(1):11-9.
18. Jalonen J, Hynynen M, Kuitunen A, Heikkilä H, Perttilä J, Salmenperä M et al.Dexmedetomidine as an

Volume 3, Issue 3; May-June 2020; Page No.51-58

anesthetic adjunct in coronary artery bypass grafting. Anesthesiology. 1997 ;86(2):331-45.

19. Wijeysundera DN, Naik JS, Beattie WS.Alpha-2 adrenergic agonists to prevent perioperative cardiovascular complications: a meta-analysis.Am J Med 2003;114(9):742-52.
20. Yildiz M, Tavlan A, Tuncer S, Reisli R, Yosunkaya A, Otelcioglu S.Effect of dexmedetomidine on hemodynamic responses to laryngoscopy and intubation : perioperative hemodynamics and anaesthetic requirements. Drugs R D 2006;7(1):43-52.
21. Kunisawa T.Dexmedetomidine suppresses the decrease in blood pressure during anaesthetic induction and blunts the cardiovascular response to tracheal intubation.Journal of Clinical *Anesthesia* 2009;21:194-99.
22. Sebastian B,Talikoti AT,Krishnamurthy D.Attenuation of haemodynamic responses to laryngoscopy and endotracheal intubaion with intravenous dexmedetomedine: A comparision between two doses.Indian J Anaesth 2017;61:48-54.
23. Bwardwaj G, Tiwari AB, Mestha N.Fentanyl and dexmedetomidine: A comparative study of effects on haemodynamic response to laryngoscopy, intubation and peri-operative analgesia.Journal of Medical Science and Clinical Research.2019;Vol.7(1)218-227.http://dx.doi.org/10.18535/jmscr/v7il.38
24. Jeong Han Lee, Hyojoong Kim, Hyun-Tae Kim, Myoung-Hun Kim, Kwangrae Cho, Se Hun Lim, Kun Moo Lee, Young-Jae Kim and Chee-Mahn Shin.Comparison of dexmedetomidine and remifentanil for attenuation of hemodynamic responses to laryngoscopy and tracheal intubation. Korean J Anesthesiol. 2012 Aug;63(2):124-129.
25. K Sudheesh, SS Harsoor.Dexmedetomidine in anaesthesia practice: A wonder drug? IJA 2011;55(4)323-24.
26. Bekker A, Sturaitis M, Bloom M, Moric M, Golfinos J, Parker E, et al. The effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy. Anesth Analg 2008;107:1340–7.
27. Fox E, Sklar GS and Hill CH. Complications related to the pressure responses to endotracheal intubation. Anaesthesiology 1977; 47:524-25.
28. Hanci V, Erdogan G, Oxyay RD, Yurtlu BS, Ayoglu H, Baydilek Y et al. Effect of fentanyl-lidocaine-propofol and dexmedetomidine-lidocaine-propofol on tracheal intubation without use of muscle relaxant. Kaohsiung J Med Sci 2010;26(5):244-50.

Table 1: Demographicprofile:

Patient Characteristics	Group I (n=25)	Group II (n=25)	Group III (n=25)	P Value
Sex(M:F)	5:20	4:21	5:20	0.102
Age(years)	37.52±12.52	34.2±9.69	36.28±10.53	0.560
Weight(Kg)	50.72±12.37	51.64±6.79	51.56±10.96	0.921
ASA(1:2)	21:4	20:5	20:5	0.102

Volume 3, Issue 3; May-June 2020; Page No.51-58

Table 2. MeanHeart Rate(perminute)in the three groups

HR	Group I	Group II	Group III	P-Value
HR0	82.92±15.41	84.84±19.21	85.28±13.53	.872
HR1	68.88±18.62	90.04±19.41	85.44±14.51	.000
HR2	73.24±22.80	86.6±16.91	97.08±26.90	.002
HR3	88.84±20.60	103.48±12.77	103.9±15.31	.002
HR4	85.76±20.58	101±15.08	101.6±16.53	.002
HR5	82.28±18.89	98.32±16.80	101.4±15.41	.000
HR6	80.32±15.77	96.8±16.75	100.5±14.50	.000
HR7	79.64±14.81	95.12±17.30	100.7±14.80	.000
HR8	78.04±12.37	88.52±14.61	96.9±16.46	.000

Table3. Mean Systolic BP (mmHg) ingroup I,II and III

SBP	Group I (Dexmedetomidine Group)	Group II (Fentanyl Group)	Group III (Saline Group)	PValue
SBP0(Baseline)	132.48±14.22	130.36±15.90	129.04±16.20	.731
SBP1	127.12±15.35	127±13.65	124.44±16.52	.782
SBP2	122.36±14.65	113.16±19.84	110.12±19.30	.051
SBP3 (1min after laryngoscopy)	135.68±15.71	125.28±20.37ϕ	136.92±18.05ϕ	.051
SBP4 (2 min after laryngoscopy)	127.68±17.77*	115.8±17.23	123.4±15.99*	.050
SBP5	118.80±17.90	110.2±16.26	113.64±15.51	.190

Volume 3, Issue 3; May-June 2020; Page No.51-58

SBP6	113.08±18.68	105.96±15.33	108.88±14.07	.299
SBP7	108.6±18.37	102.68±13.04	105.6±13.24	.387
SBP8	100.68±16.32	100.08±14.34	103.04±10.83	.733

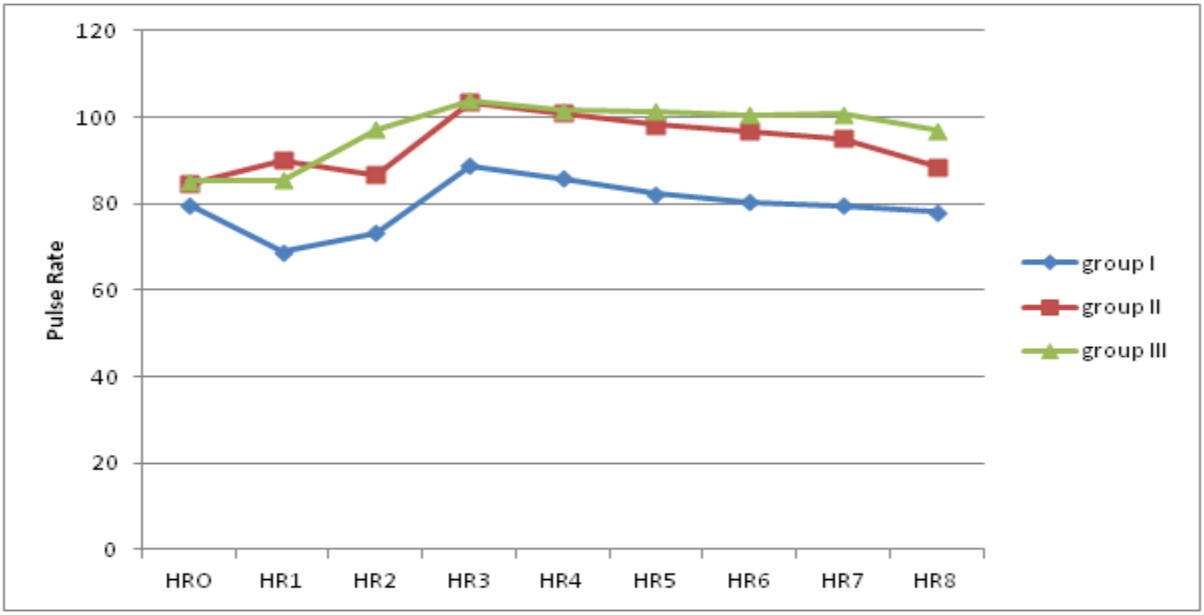

Fig 1.Graph comparing the mean heart rate among the three groups at different time period

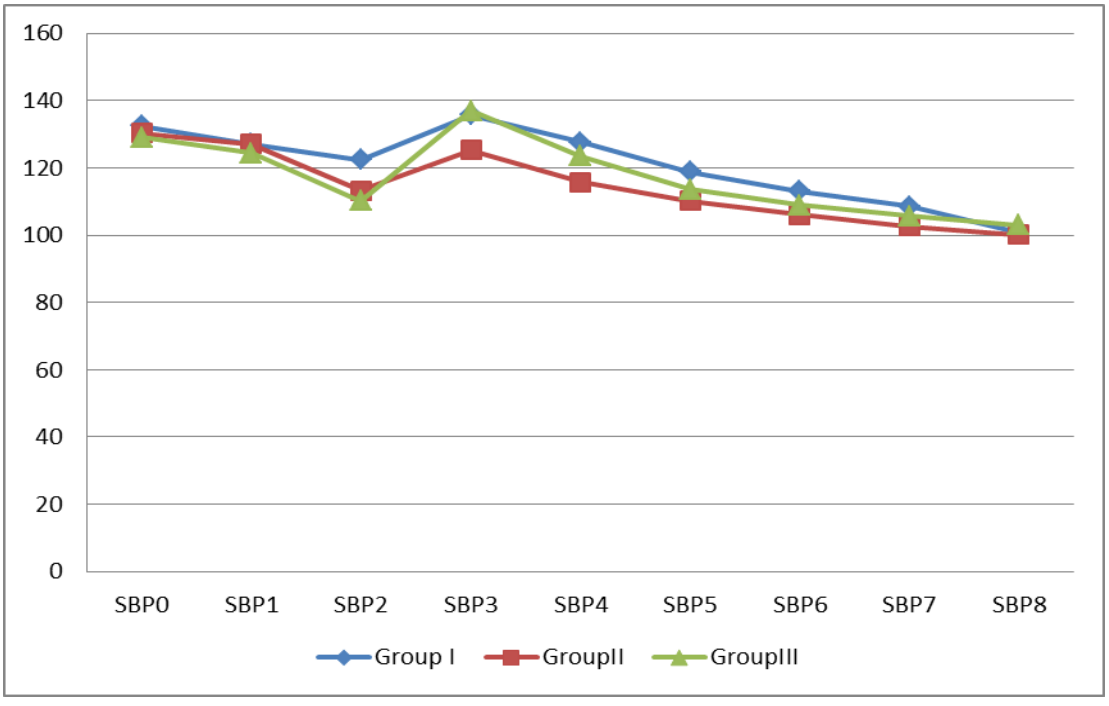

Fig 2.Graph comparing the SBP in 3 groups

Volume 3, Issue 3; May-June 2020; Page No.51-58