ORIGINAL RESEARCH

Effect of dexmedetomidine infusion on Sevoflurane requirement during general anesthesia in various surgical procedures: A prospective observational study based on entropy monitoring.

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ABSTRACT

Background and Aims: Dexmede to midine is an alpha 2- adrenergic receptor agonist drug with analgesic, sedative, anxiolytic, sympatholytic, anaesthetic-sparing and hemodynamic-stabilizing properties used in perioperative anaesthesia care and has been shown to blunt the stress response to surgery as an adjuvant to general anaesthesia. The drug is claimed to decrease the requirement of inhalational anaesthetic agents thereby reducing the untoward effects of high concentrations of volatile anaesthetics on the body. Hence a study was designed toevaluate the effect of intravenous (IV) Dexmedetomidine infusion during general anesthesia for various surgical procedures on Sevoflurane requirement.

Methods: About 100 patients scheduled for various surgical procedures under general anesthesia were divided into group 1 and group 2 of 50 patients each. Group 1 received a loading dose of Dexmedetomidine IV infusion before inducing the patient at the rate of 1 µg/kg over 10 mins diluted in 100 mL normal saline, followed by maintenance rate of 0.5µg/kg/hr, till the end of surgery. Group 2 received the conventional anaesthesia without dexmedetomidine infusion. Anesthesia was maintained with nitrous oxide in oxygen and Sevoflurane on the basis of entropy level keeping it between40 and60. The dial concentration and MAC of Sevoflurane was noted during anaesthesia in both the groups and the data wasanalyzed using students t test, chi square test and Fisher Exact test as applicable.

Results: Mean hourlySevoflurane requirement in Group 1 was 11.29 ± 1.18 mL, compared to 15.53 ±1.25 mL in Group 2 and during 2nd hour mean Sevoflurane consumption in group 1 was 8.47± 1.32 ml and in group 2 was 10.75±1.38 mland was statistically significant ($P < 0.01$).Therefore, the total Sevoflurane volume required by dexmedetomidine group was significantly less when compared to the group where conventional anaesthesia was given. The study found that mean duration of surgery in Group 1 was 98.6±16.17 mins and in Group 2 it was 96.3±19.19 mins which was statistically insignificant and hence comparable($P=0.5$). In peri-operativeperiod, the mean heart rate and MAP were significantly lower in Group 1, when compared to Group 2 which was statistically significant($P< 0.01$). Patients in Group 1 were bettersedated and post-operative pain score was better in Group 1 compared to Group 2.

Conclusion: In traoperative use of Dexmedetomidine infusion as an adjuvant decreases the amount of sevoflurane requirement as compared to conventional general anaesthesia under entropy guided monitoring, without any adverse haemodynamic effects. It also provides additional postoperative analgesia as indicated by VAS score.

Key words: Adrenergic alpha-2 receptor agonists, Dexmedetomidine, Entropy, Sevoflurane

INTRODUCTION

Alpha-2 receptors are a subgroup of noradrenergic receptors that mediate the function of sympathetic nervous system. The alpha-2 receptor activation results in reduction in norepinephrine release, which can be used therapeutically to induce sympatholysis[1]. Dexmedetomidine, the pharmacologically active d-isomer of medetomidine, is a highly selective and specific alpha 2-adrenoceptor agonist.[2,3] Dexmedetomidine was first marketed for Intensive Care unit(ICU) sedation, to make use of highly selective adrenergic alpha-2 receptor agonist activity. Unlike commonly used sedatives such as propofol or midazolam, Dexmedetomidine produces an "interactive" form of sedation, in which patients can be aroused easily with stimulation, and are

cooperativeonce aroused. Because of its sympatholytic properties, dexmedetomidine was gradually developed as an anesthetic premedication, with the goal of attenuating the sympathetic response to perioperative stresses such as laryngoscopy andintubation[4] Dexmedetomidine, a highly selective alpha 2-adrenergic receptor agonist has generated lot of interest for its sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing properties with a relatively high ratio of alpha2/alpha1 activity (1620:1)[.5] In addition to sedative effects, Dexmedetomidine hasbeen labeled as "analgesia sparing" by the Food and Drug Administration (FDA). Dexmedetomidine when co-administered with opioids has no depressant effects on respiration, but its analgesic effects offer asignificant advantage for patients at risk for respiratory decompensation.[6,7] Administration and study of a drug known to decrease anesthetic requirement without monitoring the depth of anaesthesia (DOA) can leadto under-dosing of the anesthetic drugs, causing awareness underanesthesia. We included entropy as a monitoring tool to monitor the depth of anaesthesia. Entropy is a useful monitor for assessing the depth of anaesthesia. Entropy displays a high degree of specificity and sensitivity in assessingthe consciousness during anesthesia.[8] The DatexOhmeda S/5 entropy module collects a one channelraw biosignal, consisting of both the electroencephalogram (EEG) andelectromyogram (EMG) from the fronto temporal region of thepatient"s head. The biosignal is collected with a self-adhesive entropysensor consisting of three electrodes. The signal is amplified, digitizedand processed in the entropy module incorporated into the S/5 anaesthesiamonitor. Some further signal processing occurs in S/5 anaesthesiamonitor by the monitor software. In this process time frequency balancedspectral entropy content of the biosignal is calculated[.9] The analysisresults in two indices S.E. (spectral entropy) and R.E (responseentropy)[.10]. Entropy parameters range from 0 (suppression state of EEG) to100 awake for R.E and from 0 to 91 for S.E, where the differencebetween S.E and R.E corresponds to a contribution from the FEMGdominated high frequency band. Decreasing values indicate deepeninglevels of hypnosis17. As entropy detects EMG activation as a possibleresult of nociceptive stimulation during inadequate anaesthesia, use of theresponse and state entropy difference has been proposed as a tool fortitrating analgesics duringanaesthesia[.11]

AIM OF STUDY

1. To evaluate the effect of continuous infusion of Dexmedetomidine on requirement of Sevoflurane during general anesthesia with continuous monitoring of depth of anesthesia by entropy analysis.
2. To assess the effect of intravenous Dexmedetomidine infusion onperioperative hemodynamics and also post-operative analgesia on the basis of VAS score inelective surgical procedures

METHODS

This study was conducted in Postgraduate Department ofAnaesthesiology and Critical Care in Government Medical College Srinagarover a period of 2 years after getting approval from the Institutional Ethical Committee and after obtaining written informed consent from all patients. We made an observational study of two groups of patients (at least50 in each group) where Dexmedetomidine intravenous infusion was given to one group and conventionalregular anesthesia to another group. The age, gender, body weight, duration of surgery (in minutes), duration of anesthesia (in minutes) was recorded. Patients of class ASA I and IIof either sex between 20-60 years of age were included in this study and the patients on drugs affecting the heart rate and blood pressure like hypertension, diabetes, thyroid disorder, those with history of psychiatric disorders, neurological illness, cardiovascular disease, morbidly obese, CAD, heart block, history of intake of α2 agonist or α2 antagonist, pregnant and nursing women were excluded. In our observational study, a total of 100 patients were included as per our inclusion and exclusion criteria. All patients were pre-medicated with oral Alprazolam tablet 0.5 mgand tab. Ranitidine 150 mg night before surgery and a minimum of 6hours fasting state was ensured. On arrival to the operation room IVaccess was achieved with 18 G venous cannula. Monitoring consisted ofECG, pulse oximetry (SpO_2), non-invasive BP (NIBP), Capnography($EtCO_2$) and entropy. All patients received injection fentanyl 2micrograms/Kg body weight and injection Paracetamol 1gm IV foranalgesia. The patients who received Dexmedetomidine were given thedrug as an initial dose of 1mcg/kg body weight over 10 minutes. Anesthesia was induced in all patients with injpropofol tillresponse entropy dropped to 50, confirmed with loss of response to verbal commands. Atracurium 0.5 mg per kg body weight IV was administered and trachea was intubated after 03 minutes. A maintenance dose of injection Dexmedetomidine infusion was given at the rate of 0.5 mcg/kgper hour. Anesthesia was maintained with Sevoflurane and 60% N_2O inO_2 and ventilated to maintain $EtCO_2$ between 35 and 40 mmHg. Sevoflurane dial concentration was adjusted to ensure adequate depth of general anesthesia to maintain response entropy levels between 40 and 60and difference between response entropy and state entropy less than 10and also to maintain clinical variables like heart rate, NIBP, MAP within normal limits. Dexmedetomidine infusion was stopped 15 minutes priorto the expected time of completion of surgery. Sevoflurane administration was turned off at the

beginning of skin suturing. Neuromuscular blockadewas reversed with injection Neostigmine 0.5 mg/kg and injection Glycopyrrolate 10 mcg/kg body weight and trachea extubated after satisfactory recovery and presence of response to oral commands. All patients were given IV normal saline as maintainance fluid. The hemodynamic and entropy parameters were recorded every five minutes throughout the intraoperative and postoperative period. Recovery from anesthesia was assessed by the Ramsay sedation score and the post-operative pain was assessed using VAS (visual analog scale).The pain VAS is a unidimensional measure of pain intensity. The pain VAS is a continuous scale comprises a horizontal (HVAS) or vertical (VVAS) usually 10cm (100mm) in length anchored by 2 verbal descriptors one for each symptom extreme. For pain intensity the scale is most commonly anchored by no pain (score of zero) and pain as bad as it could be or worst imaginable pain (score of 100).Distribution of pain VAS scores in post-surgical patients who described their post op pain intensity as none, mild, moderate or severe the following cut points on the pain VAS have been recommended. No pain (0 to4mm)Mildpain(5to44mm)Moderatepain(45to74mm) Severe pain (74 to 100mm). We tried to prove in this study that the patients who received dexmedetomidine had lesser Sevoflurane requirements and better analgesia proving that it is a wonder drug with both anaesthesia sparing properties and analgesic properties of its own and that it also decreases the stress response to surgery. Hourly Sevoflurane requirement was calculated by Dion's method as follows: Usage of volatile anaesthetic agent (ml) = Dialed concentration (%) x duration at set concentration (min) x Total fresh gasflow (litre/min) x Molecular mass (mg) / 2412 x Density(g/ml).[13] Thefixed values in this formula include- total FGF (3 ltr /min), Molecularmass of Sevoflurane (200.055 mg) and Density of Sevoflurane at 21°C(1.52 g/ml). The changing values were Dialed concentration and Durationat set concentration. Substituting the fixed values, this equation can berewritten as: Amount of liquid Sevoflurane used (ml) = 0.00273PT,(P = Dialed concentration, T = Time in seconds).[14] The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Continuous variables were expressed as Mean ± SD and categorical variables were summarized as percentages. Student's independent t-test was employed for comparing continuous variables. Chi-square or Fischer's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar and line diagrams. A p-value of < 0.05 was considered as statistically significant. All p-values were two tailed.

RESULTS

For statistical purpose patients were categorized into two groups-

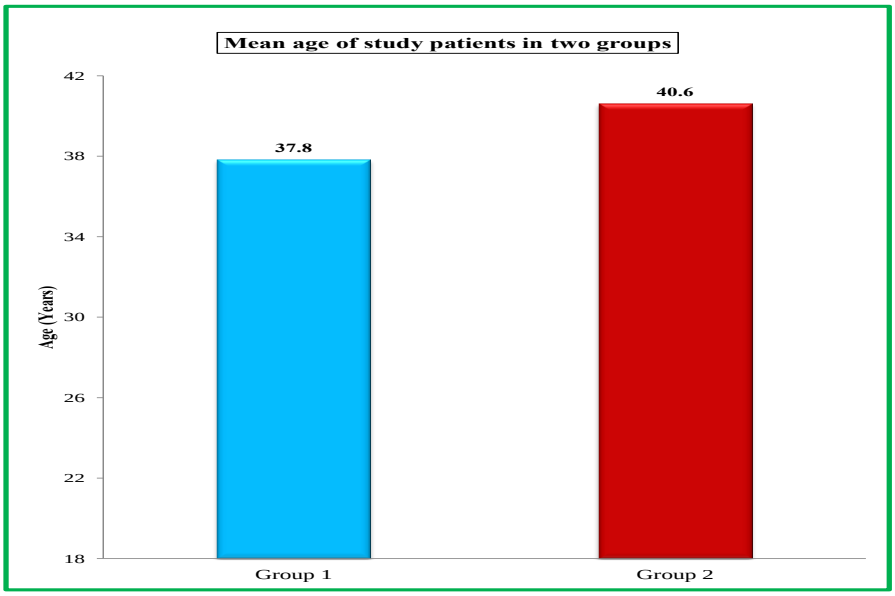
1. Group 1 included patients where the drug dexmedetomidine was used and 50 patients were observed.
2. Group 2 included patients where regular conventional anaesthesia was given and 50 patients were observed.

Age distribution in Group 1 was 20-60 years with mean of 37.8± 11.44 and in Group 2 was 21-60 years with mean of 40.6±12.59. The mean age between two groups was comparable with statistically insignificant difference (p value = 0.251)

Table 1: Age distribution of study patients in two groups

Age (Years)	N	Mean	SD	Range	P-value
Group 1	50	37.8	11.44	20-60	0.251
Group 2	50	40.6	12.59	21-60	

P-value by Student's independent t-test

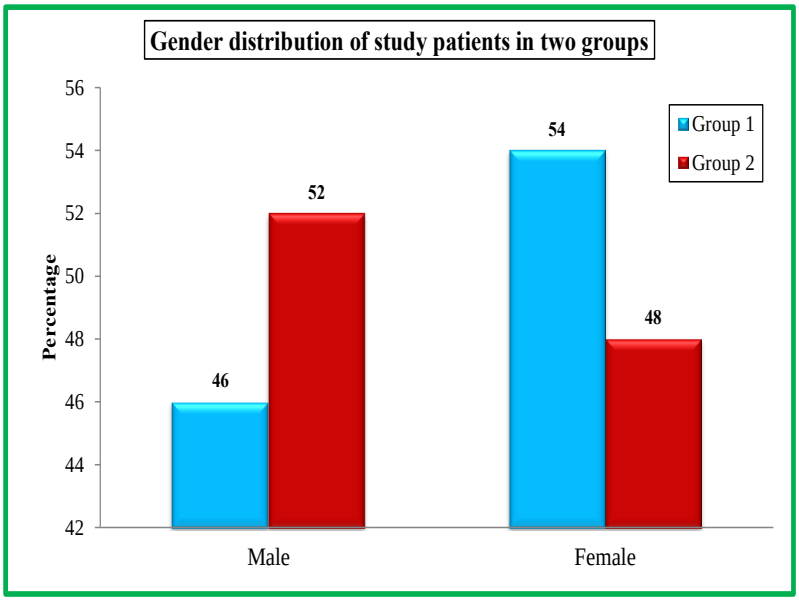


Among all patients studied 46 % were males in Group 1 and 52% were males in Group 2, 54 % were females in Group 1 and 48% were males in Group 2. As far as gender distribution was concerned between two groups it was statistically insignificant (p value =0.548).

Table 2: Gender distribution of study patients in two groups

Gender	Group 1		Group 2		P-value
	No.	%age	No.	%age	
Male	23	46	26	52	
Female	27	54	24	48	0.548
Total	50	100	50	100	

P-value by Chi-square test

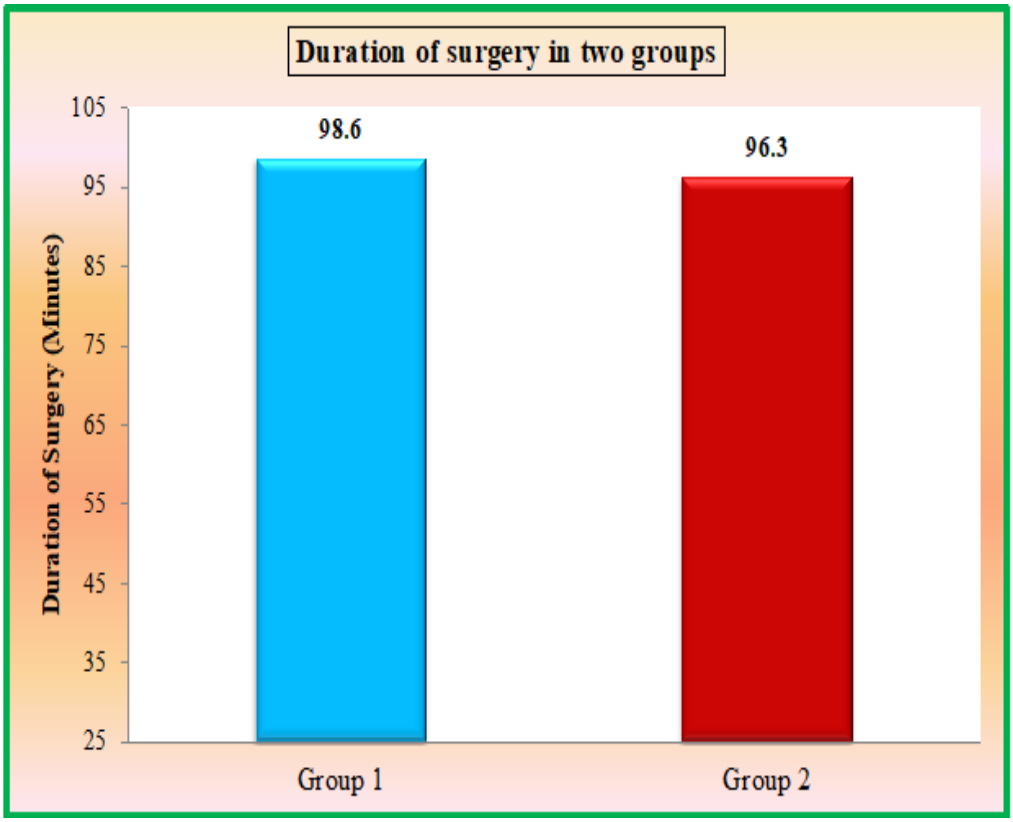


The mean duration of surgery in Group 1 was 98.6 ± 16.17 minutes and in Group 2 it was 96.3 ± 19.19 minutes. The mean duration of surgery (in minutes) between two groups was comparable with statistically insignificant difference (p value = 0.515)

Table 5: Duration of surgery (Minutes) in two groups

Duration of surgery (Minutes)	N	Mean	SD	Range	P-value
Group 1	50	98.6	16.17	60-126	0.515
Group 2	50	96.3	19.19	60-125	

P-value by Student's independent t-test

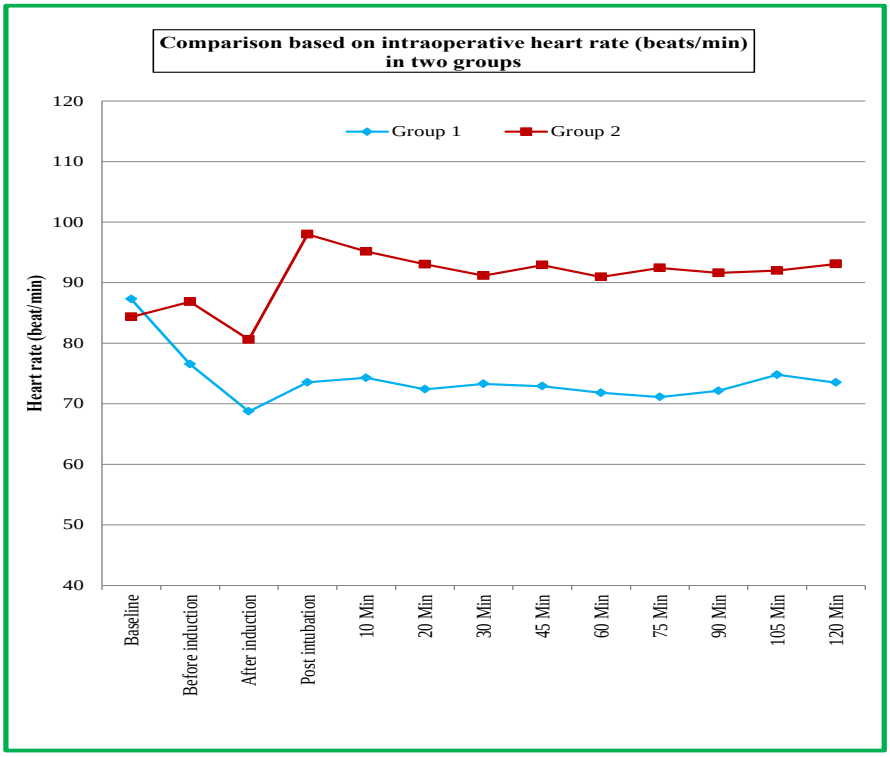


Baseline heart rate of all patients was recorded. Mean heart rate in Group 1 was 87.28 ± 10.29 bpm and in Group 2 was 84.34 ± 8.04. Difference between them was insignificant (p value =0.115). Pre induction, mean heart rate in Group 1 was 76.52 ± 10.07 bpm and in Group 2 was 86.84 ±8.85 bpm. Difference between them was statistically significant (p value < 0.001). After induction heart rate decreased in both the groups and the difference was statistically significant (p value <0.001). Post intubation heart rate increased in both the groups and the difference was statistically significant (p value <0.001) and it was also seen that heart rate increased significantly in Group 2. At 10 minute interval of time, in Group 1 heart rate was decreased and in Group 2 it was increased from baseline heart rate value and the difference was statistically significant (p value <0.001)

Table 6: Comparison based on intra-operative heart rate (beats/min) in two groups					
Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
Baseline	87.28	10.29	84.34	8.04	0.115
Pre induction	76.52	10.07	86.84	8.85	<0.001*
After induction	68.74	9.95	80.60	13.67	<0.001*
Post intubation	75.54	9.75	97.98	12.93	<0.001*
10 Min	74.28	11.47	95.14	13.60	<0.001*
20 Min	72.40	10.15	93.04	10.63	<0.001*
30 Min	73.28	11.98	91.16	11.55	<0.001*
45 Min	72.90	12.76	92.90	12.10	<0.001*
60 Min	71.82	11.36	90.94	12.07	<0.001*
75 Min	71.11	10.28	92.43	12.13	<0.001*
90 Min	72.14	9.12	91.61	14.66	<0.001*
105 Min	74.79	2.12	92.00	11.14	<0.001*
120 Min	73.50	5.32	93.08	10.25	<0.001*

*Statistically Significant Difference (P-value<0.05); P-value by Student's independent t-test

Our results showed a decrease in heart rate in Group 1 and significantly increased heart rate in Group 2 at various points of time. The p values at various time periods were < 0.001 (20 min, 30 min, 45 min, 60 min, 75 min, 90 min, 105min, 120 min) and the difference was statistically significant.

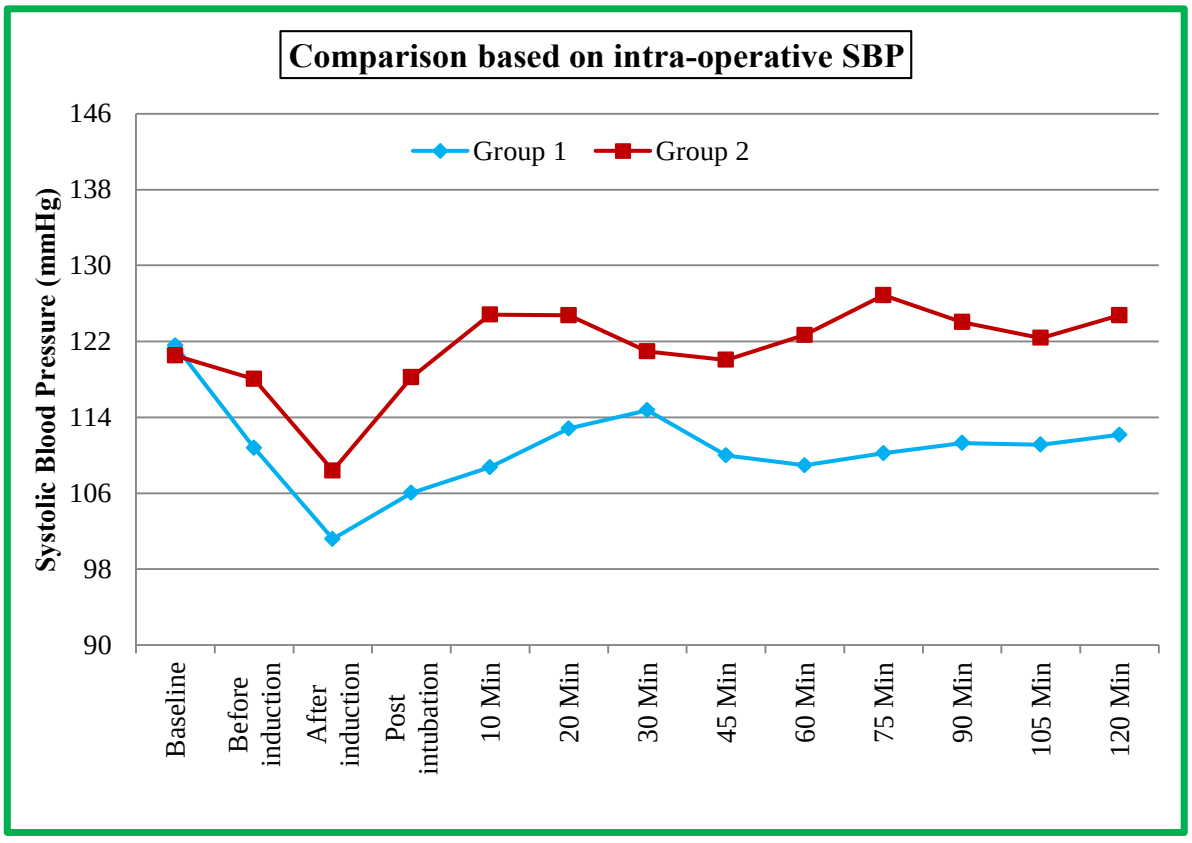


Baseline mean systolic blood pressure (SBP) of all patients was recorded. Mean SBP in Group 1 was 121.58± 11.62 mmHg and in Group 2 it was 120.52 ±14.23 mm Hg. Both the groups were comparable as far as base line SBP was concerned and the difference was insignificant (p value =0.242). Pre induction mean SBP decreased in both the groups and the difference was insignificant (p value = 0.920).

Table 7: Comparison based on intra-operative SBP (mmHg) in two groups					
Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
Baseline	121.58	11.62	120.52	14.23	0.68
Pre - induction	110.78	9.73	118.02	13.66	0.91
After induction	101.18	11.73	108.38	16.49	0.013
Post intubation	106.04	13.21	126.20	12.73	<0.001
10 Min	108.74	14.30	124.82	14.36	<0.001
20 Min	112.82	16.37	124.74	13.65	<0.01
30 Min	114.74	14.88	120.94	13.15	<0.001
45 Min	109.98	12.80	120.04	13.66	<0.001
60 Min	108.94	13.20	122.66	12.51	<0.001
75 Min	110.21	13.67	126.86	14.30	<0.001
90 Min	111.29	10.70	124.02	14.41	<0.001
105 Min	111.11	16.17	122.36	4.01	<0.001
120 Min	112.15	11.20	124.74	6.11	<0.001

P-value by Student's independent t-test

After induction mean SBP decreased in both the groups but it decreased more in Group 1 as compared to group 2 and the difference was significant (p value < 0.05). Post intubation mean SBP increased in both the groups but it increased significantly in Group 2 as compared to Group 1 and the difference was significant (p value < 0.001). Mean SBP at various points of time (10min, 20 min (p value <0.01), 30 min,45 min, 90 min, 105 min, 120 min) was decreased in Group 1 as compared to Group 2 and the difference between two groups was statistically significant (p value <0.001)



The mean baseline DBP in Group 1 was 71.66 ± 11.74 mmHg and in group 2 it was 72.32± 14.49 mmHg (p value=0.8) .Regarding baseline DBP, both the groups were comparable and the difference was statistically

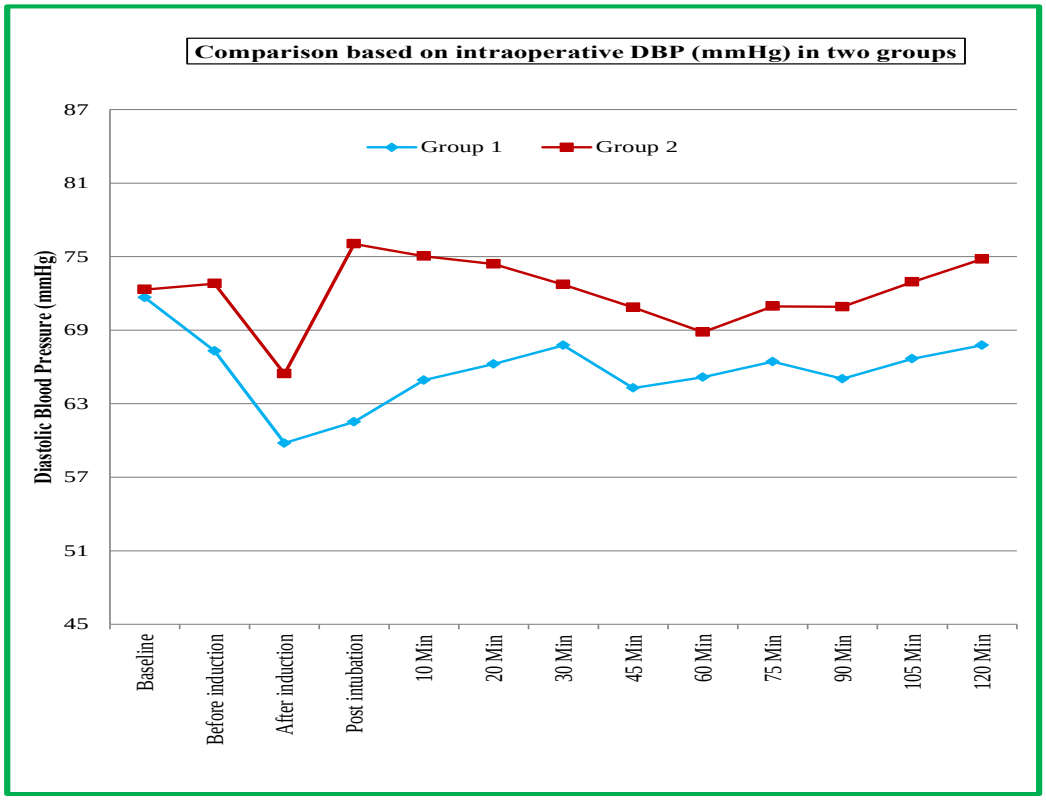
insignificant. At pre induction, the DBP in both the groups was comparable and the difference was statistically insignificant (p value = 0.53)

Table 8: Comparison based on intra-operative DBP (mmHg) in two groups

Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
Baseline	71.66	11.74	72.32	14.49	0.80
Pre - induction	67.30	12.22	72.80	11.86	0.53
After induction	59.78	12.56	65.44	12.84	<0.001
Post intubation	66.50	11.81	76.04	11.82	0.028
10 Min	64.92	12.38	75.04	12.80	<0.001
20 Min	66.24	13.37	74.40	11.63	0.001
30 Min	67.76	12.85	72.72	14.15	<0.001
45 Min	64.28	13.49	70.86	13.78	0.017
60 Min	65.16	12.50	68.84	13.66	0.001
75 Min	66.43	12.67	70.95	11.84	<0.001
90 Min	65.03	11.99	70.91	13.28	<0.001
105 Min	66.67	12.18	72.93	15.61	<0.001
120 Min	67.77	9.05	74.80	1.55	<0.001

P-value by Student's independent t-test

After that at various points of time the difference in DBP in both the groups was statistically significant with p value (<0.001) after induction, (0.028) post intubation, (<0.001) 10 min, (0.001) 20 min, (<0.001) 30 min, (0.017) 45 min, (0.001) 60 min, (0.0001), 75min (0.001) 90 min, (<0.001) 105 min and (<0.001) 120 min.

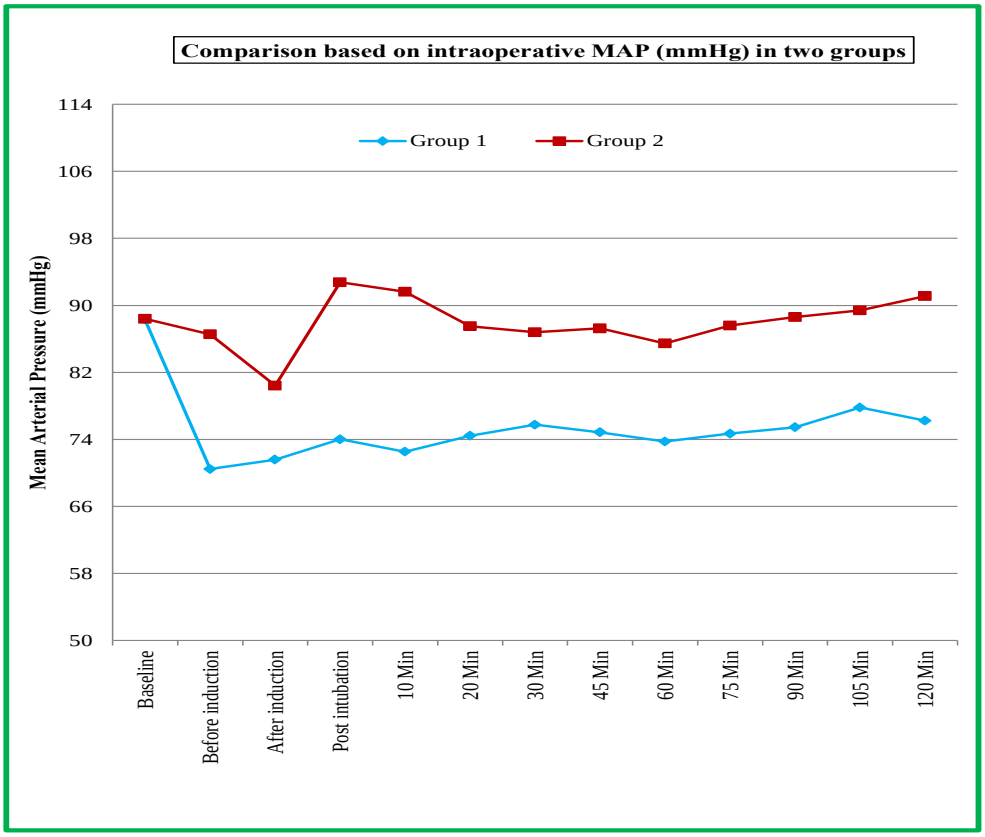


The baseline mean MAP in group 1 was 88.30 ± 11.04 mmHg and in group 2 it was 88.39±12.04 mmHg. The baseline MAP was comparable in both the groups and the difference was statistically insignificant (p value = 0.96).

Table 9: Comparison based on intra-operative MAP (mmHg) in two groups					
Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
Baseline	88.30	11.04	88.39	12.04	0.96
Pre - induction	70.46	10.50	86.54	13.33	0.65
After induction	71.58	11.76	80.42	13.39	<0.001
Post intubation	74.01	11.53	92.76	11.16	<0.001
10 Min	72.53	12.56	91.63	12.85	<0.001
20 Min	74.43	13.64	87.51	11.35	<0.001
30 Min	75.75	12.81	86.79	12.90	<0.001
45 Min	74.85	12.62	87.25	13.22	<0.001
60 Min	73.75	12.18	85.45	12.62	<0.001
75 Min	74.69	12.12	87.59	11.80	<0.001
90 Min	75.45	10.73	88.61	13.25	<0.001
105 Min	77.81	13.02	89.40	10.48	<0.001
120 Min	76.23	9.42	91.11	1.29	<0.001

P-value by Student's independent t-test

At pre induction MAP was statistically insignificant (p value = 0.65), p value was (<0.001) at 10 min ,20 min, 30 min,45 min,60 min, 75 min,90 min,105 min,120 min. The difference in MAP between two groups was statistically significant.



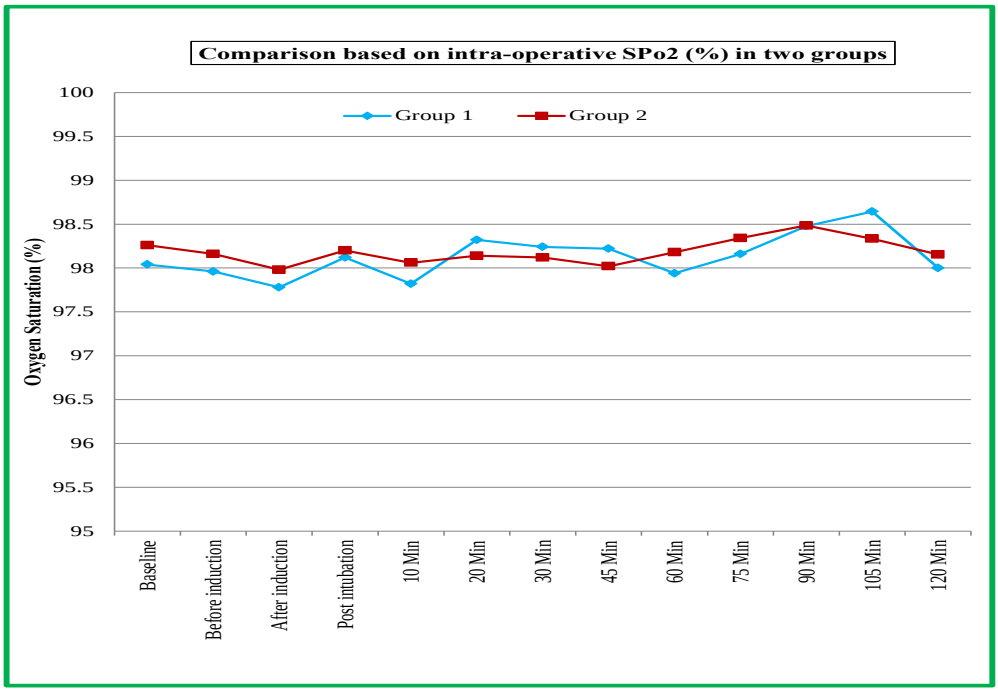
The mean base line SpO_2 level in group 1 was 98.04 ± 1.03% and in group 2 it was 98.26± 0.88% and it was comparable in both the groups and statistically insignificant (p value = 0.253).

Table 10: Comparison based on intra-operative SPo2 (%) in two groups

Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
Baseline	98.04	1.03	98.26	0.88	0.253
Before induction	97.96	1.05	98.16	0.74	0.273
After induction	97.78	1.06	97.98	0.68	0.542
Post intubation	98.12	0.98	98.20	0.81	0.657
10 Min	97.82	1.00	98.06	0.74	0.157
20 Min	98.32	0.98	98.14	0.81	0.318
30 Min	98.24	0.98	98.12	0.80	0.465
45 Min	98.22	1.02	98.02	0.87	0.563
60 Min	97.94	0.89	98.18	0.90	0.216
75 Min	98.16	0.94	98.34	0.98	0.372
90 Min	98.48	0.90	98.48	1.00	0.976
105 Min	98.64	1.15	98.33	0.49	0.310
120 Min	98.00	0.82	98.15	0.80	0.655

P-value by Student's independent t-test

The p value at various periods of time (0.273) before induction, (0.542) after induction, (0.657) post intubation, (0.157) 10 min, (0.318) 20 min, (0.465) 30 min, (0.563) 45 min, (0.216) 60 min, (0.372) 75 min, (0.976) 90 min, (0.310) 105 min, (0.655) at 120 min. The difference between two groups was statistically in significant.



After induction mean MAC of Sevoflurane in Group 1 was 1.90 ± 0.07% and in Group 2 it was 1.93 ± 0.07%. The MAC of two groups after induction was comparable and the difference was statistically insignificant (p value = 0.07). Post intubation MAC of sevoflurane in Group 1 was 1.91 ± 0.09% and in Group 2 it was 1.92 ± 0.08 %.The MAC of two groups post intubation was statistically insignificant (p value= 0.24). P value was (<0.001) at 10 min, 20 min, 30 min, 45 min, 60 min, 75 min, 90 min, 105 min, 120 min and the difference was statistically significant The baseline response entropy in in group

1 was 97.00 ± 1.00 and in group 2 it was 96.00 ± 1.00 (p value = 1.00) and the difference between two groups was statistically insignificant. Pre induction R E in group 1 was 79.67 ± 1.53 and in group 2 it was 95.67 ± 1.53 (p value = 1.00). Post induction RE in group 1 was 41.00 ± 1.00 and in group 2 it was 45.00 ± 1.00 (p value = 1.00) and the difference between two groups was statistically insignificant. p value was 0.78 (post intubation), 0.78 at 10 min, 1.00 at 20 min, 1.00 at 30 min, 1.00 at 45 min, 1.00 at 60 min, 1.00 at 75 min, 0.78 at 90 min, 0.50 at 105 min, 0.78 at 120 min and the difference between two groups was statistically insignificant.

Table 11: Comparison based on MAC (%) in two groups

Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
After induction	1.90	0.07	1.93	0.07	0.073
Post intubation	1.91	0.09	1.92	0.08	0.242
10 Min	1.62	0.08	1.89	0.08	<0.001*
20 Min	1.18	0.07	1.91	0.08	<0.001*
30 Min	0.99	0.08	1.89	0.08	<0.001*
45 Min	0.94	0.10	1.87	0.08	<0.001*
60 Min	1.04	0.11	1.91	0.08	<0.001*
75 Min	1.06	0.17	1.90	0.10	<0.001*
90 Min	1.01	0.15	1.85	0.08	<0.001*
105 Min	1.00	0.16	1.87	0.11	<0.001*
120 Min	1.10	0.16	1.88	0.11	<0.001*

**Statistically Significant Difference (P-value<0.05); P-value by Student's independent t-test*

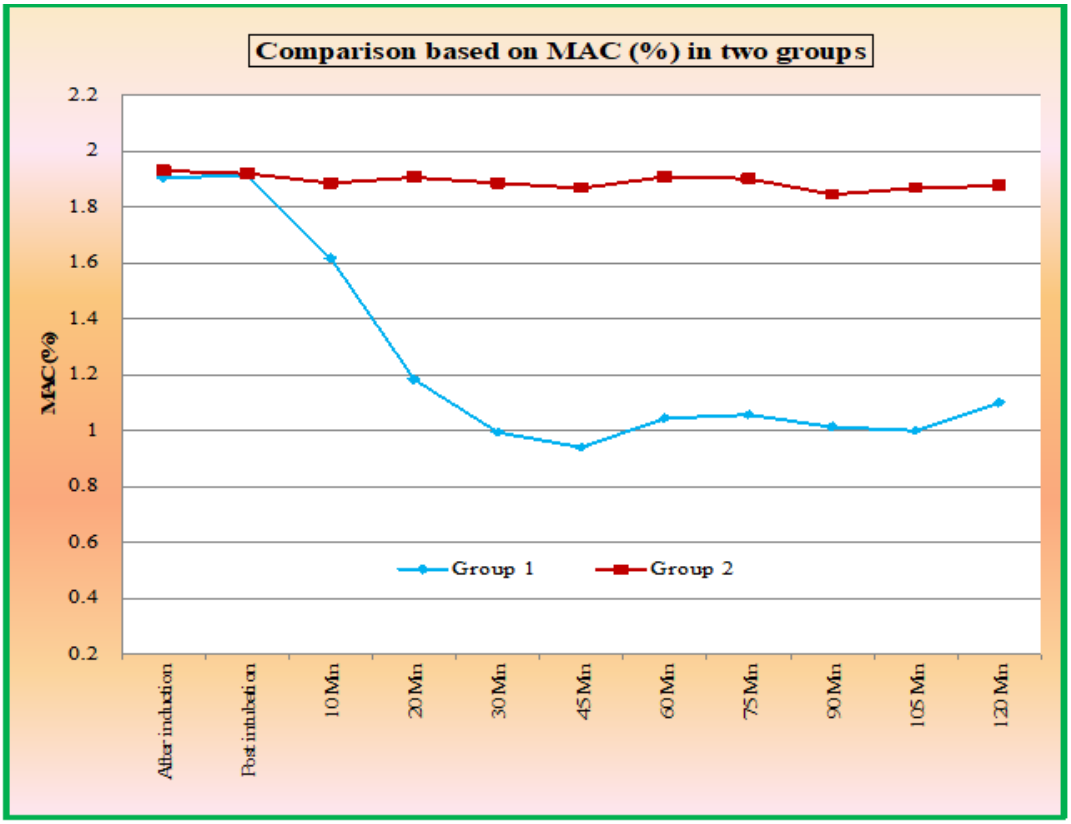
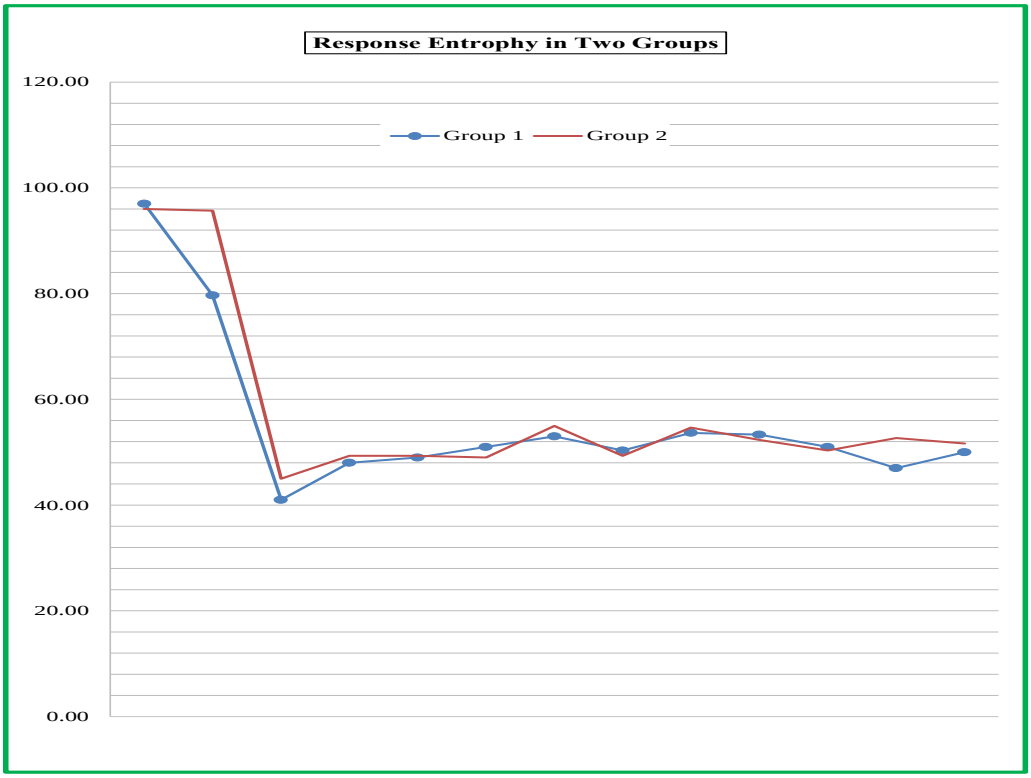


Table 12: Response Entropy in two study groups					
Time	**Group 1**	**SD**	**Group 2**	**SD**	***p* value**
Base line	97.00	1.00	96.00	1.00	1.00
Pre ind	79.67	1.53	95.67	1.53	1.00
Post ind	41.00	1.00	45.00	1.00	1.00
Post int	48.00	2.00	49.33	2.08	0.78
10 min	49.00	2.00	49.33	2.08	0.78
20 min	51.00	1.00	49.00	1.00	1.00
30 min	53.00	1.00	55.00	1.00	1.00
45 min	50.33	1.53	49.33	1.53	1.00
60 min	53.67	1.53	54.67	1.53	1.00
75 min	53.33	2.08	52.33	2.08	1.00
90 min	51.00	2.00	50.33	2.08	0.78
105 min	47.00	4.58	52.67	4.16	0.50
120 min	50.00	2.00	51.67	2.08	0.78



The baseline state entropy in group 1 was 90.67 ± 1.53 and in group 2 it was 90.00 ± 1.00 (p value = 0.99) and the difference between two groups was statistically insignificant. The pre induction state entropy in group 1 was 75.33 ± 1.15 and in group 2 it was 89.33 ± 1.53 (p value = 0.04) and the difference between two groups was statistically significant. p value was >0.99 at after induction, 0.78 at post intubation, 0.10 at 10 min, >0.99 at 20 min, >0.99 at 30 min, 0.72 at 45 min, >0.99 at 60 min, 0.06 at 75 min, >0. 99 at 90 min, 0.78 at 105 min and 0.10 at 120 min and the difference between two groups was statistically insignificant.

Table 13: State Entropy in two study groups					
Time	**Group 1**	**SD**	**Group 2**	**SD**	**P Value**
Base Line	90.67	1.53	90.00	1.00	0.99
Pre induction	75.33	1.15	89.33	1.53	0.04
After induction	41.67	1.53	43.33	1.53	>0.99
Post intubation	44.00	2.00	51.33	2.08	0.780
10 min	46.33	2.52	46.00	2.00	0.10
20 min	47.67	2.52	44.67	2.52	>0.99
30 min	50.00	2.00	44.33	2.08	>0.99
45 min	51.00	2.65	48.33	2.52	0.72
60 min	52.33	1.53	48.67	1.53	>0.99
75 min	55.00	2.00	52.67	1.53	0.06
90 min	51.67	1.53	49.33	1.53	>0.99
105 min	49.00	2.00	50.33	2.08	0.78
120 min	53.67	2.52	52.00	2.00	0.10

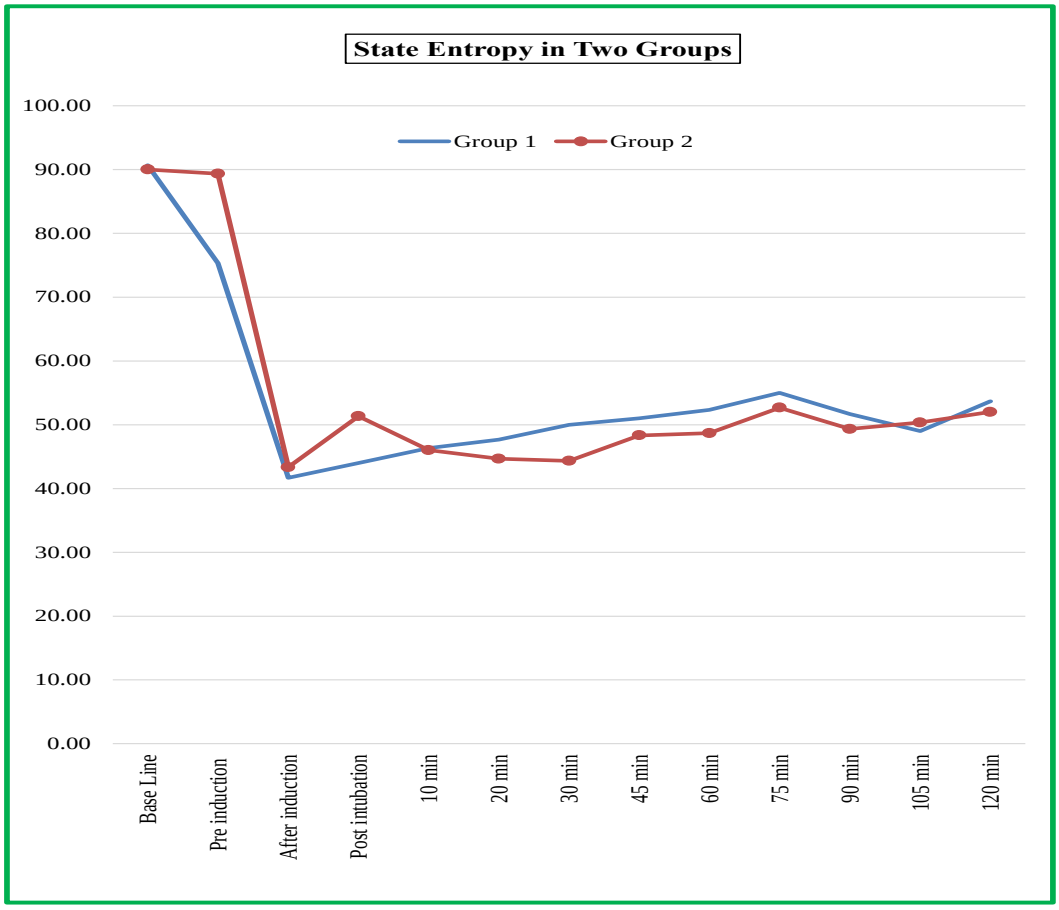


Table 15: Sevoflurane consumption in two groups					
Time interval	Group 1		Group 2		P-value
	Mean	SD	Mean	SD	
Ist hour	11.29	1.18	15.53	1.25	<0.001*
2nd Hour	8.47	1.32	10.75	1.38	<0.001*

**Statistically Significant Difference (P-value<0.05); P-value by Student's independent t-test*

The mean Sevoflurane consumption during first hour was 11.29± 1.18 ml in Group 1 patients and it was 15.53 ±1.25 ml in Group 2 patients (p value <0.001) and during 2nd hour mean sevoflurane consumption was 8.47±1.32 ml in Group 1 patients and 10.75 ±1.38 ml in group 2 patients (p value < 0.001). The difference is statistically significant.

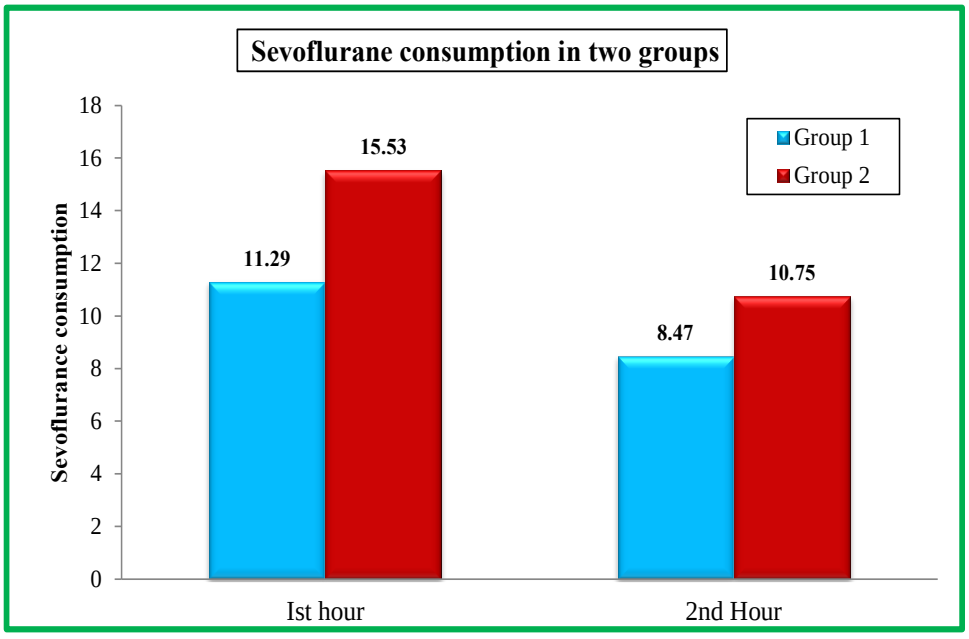


Table 16: Ramsay sedation score (RSS) at 1 hour postoperatively in two groups					
RSS	**N**	**Mean**	**SD**	**Range**	**P-value**
Group 1	50	2.48	0.505	2-3	<0.001*
Group 2	50	1.22	0.418	1-2	

**Statistically Significant Difference (P-value<0.05); P-value by Student's independent t-test*

The mean RSS at 1st hour in post operative period in Group 1 was 2.48 ± 0.505 and in Group 2 it was 1.22 ± 0.418 (p value < 0.001) and the difference between the two groups was statistically significant.

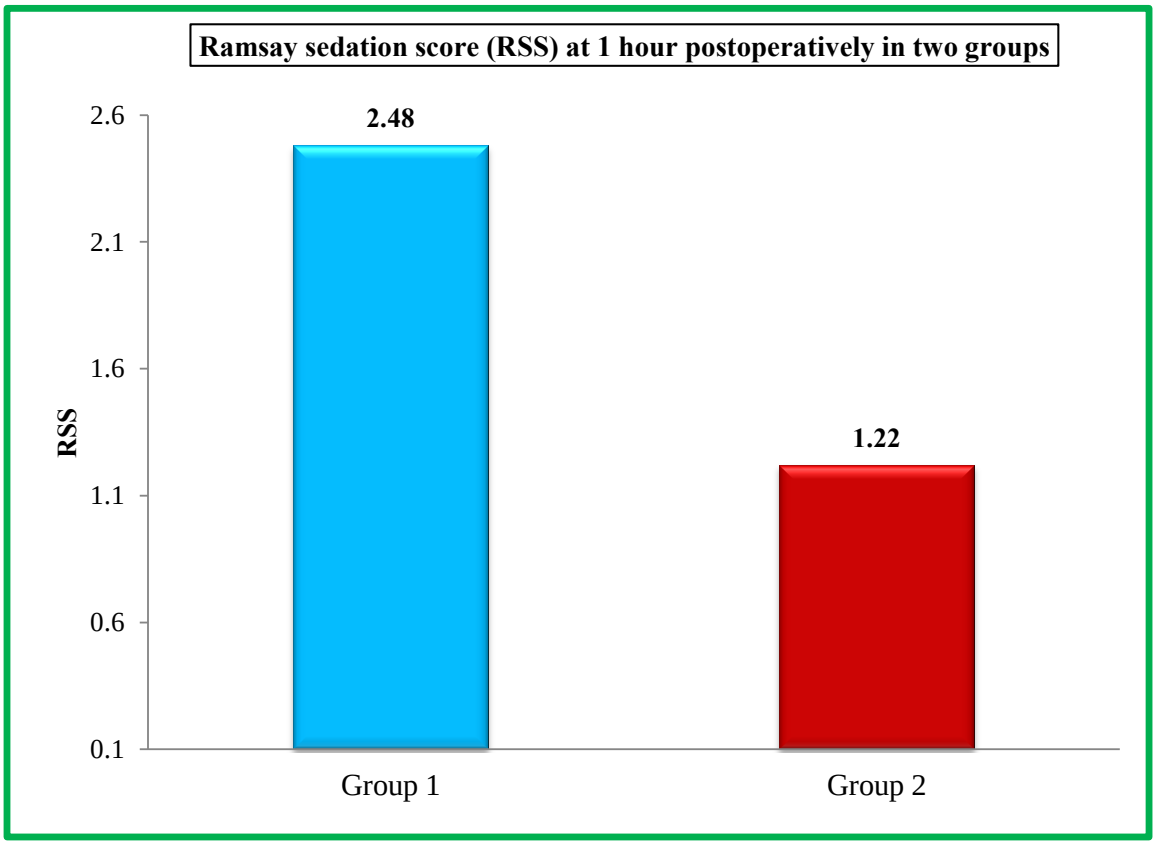


Table 17: VAS at 1 hour postoperatively in two groups					
VAS	**N**	**Mean**	**SD**	**Range**	**P-value**
Group 1	50	2.24	0.657	1-3	<0.001*
Group 2	50	3.86	0.535	3-5	

**Statistically Significant Difference (P-value<0.05); P-value by Student's independent t-test*

The mean VAS score at 1st hour in postoperative period in Group 1 was 2.24± 0.657 and in Group 2 it was 3.86 ± 0.535 (p value <0.001) and the difference between two groups was statistically significant.

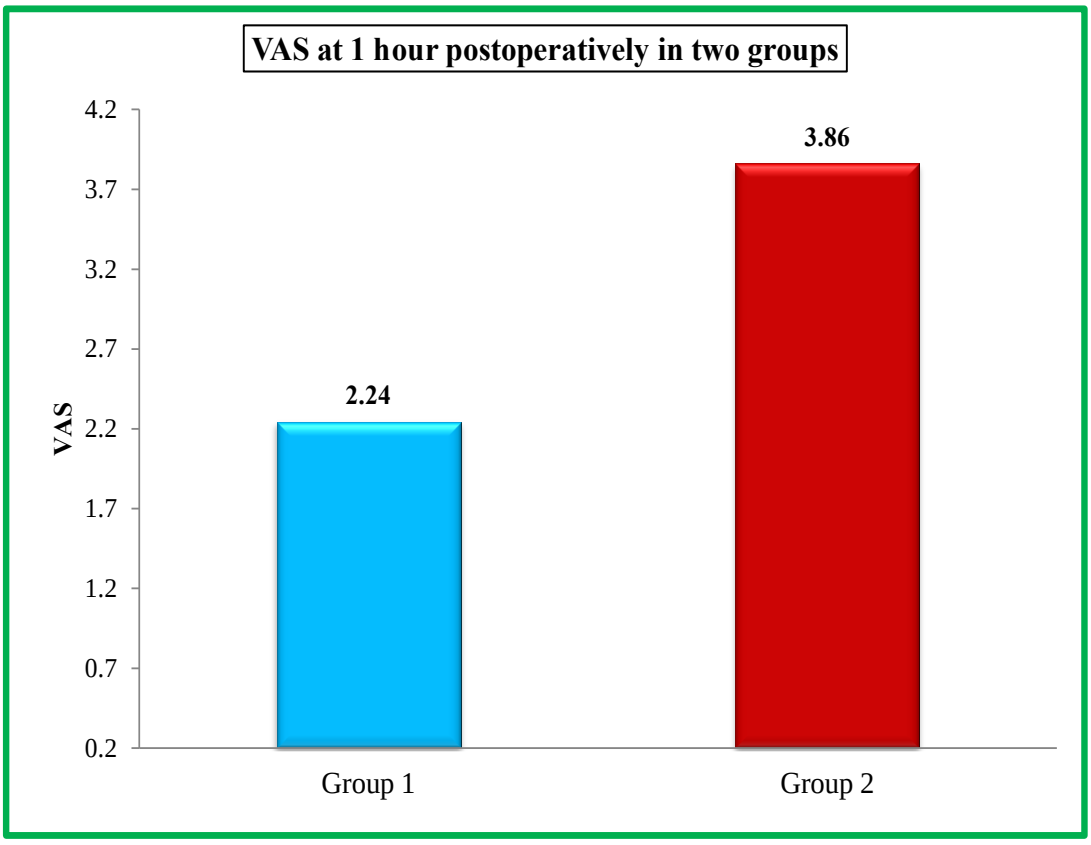
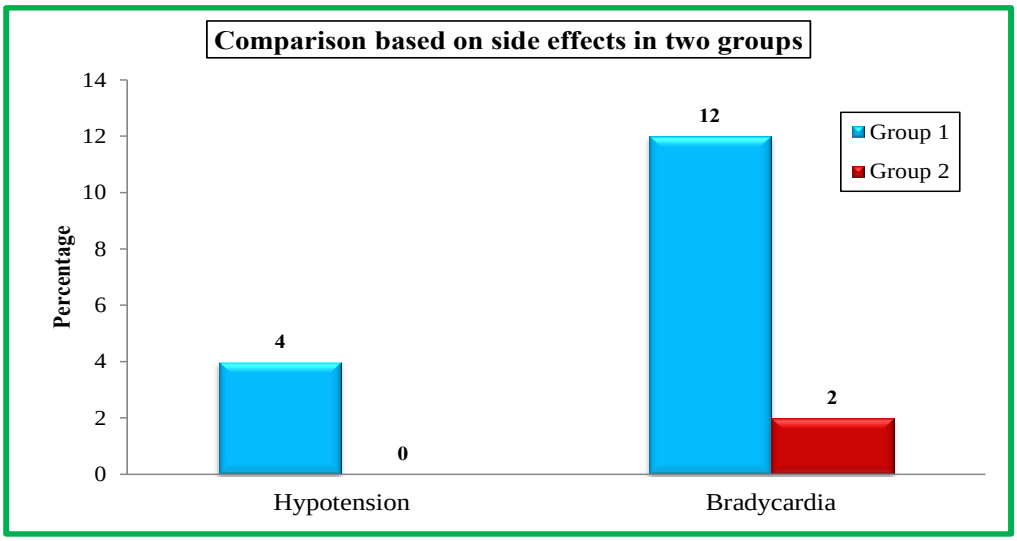


Table 18: Comparison based on side effects in two groups					
Side effects	**Group 1**		**Group 2**		**P-value**
	No.	**%age**	**No.**	**%age**	
Hypotension	2	4	0	0	0.495
Bradycardia	6	12	1	2	0.112

Hypotension was present in 4% of patients in Group 1 and there was no incidence of hypotension in Group 2 (p value = 0.495) and the difference between two groups was statistically insignificant.

Bradycardia was present in 12% of patients in group 1 and in group 2 it was present in 2% of patients (p value = 0.112) and the difference between two groups was statistically insignificant.



DISCUSSION

Dexmedetomidine, a highly selective α2-adrenergic receptoragonist has generated lot of its sedative, analgesic, perioperative sympatholytic, anaesthetic-sparing, and hemodynamic – stabilizing properties with a relatively high ratio of α2/α1 activity[15]. The hypnotic and supraspinal analgesic effects ofDexmedetomidine are mediated by suppression of neuronal firing in thelocus coeruleus, resulting in inhibition of norepinephrine release andactivity in the descending medullospinal noradrenergic pathway[15,16]. Dexmedetomidine by its sympatholytic action attenuates sympathoadrenal response to tracheal intubation. Alpha (α)2-adrenoceptor agonists have been used as adjuvant to anesthetic agents in peri-operative period for its several beneficialactions. These drugs improve hemodynamic stability during endotrachealintubation and surgical stress by its central sympatholytic action, and thusreduce anesthetic and opioids requirements. The metabolic stress response to surgical trauma is characterizedby increased serum levels of catecholamines, cortisol, sympatheticnervous system activation, insulin resistance and hyperglycemia. If thisstress response is of prolonged duration, the hyper–metabolic state canlead on to decreased resistance, delayed ambulation and

increasedmorbidity and mortality. Dexmedetomidine when administered as infusion at 0.5 µg /kg/hrhas specific analgesic effect and provides visceral pain relief. Dexmedetomidine also has anesthetic sparing effect. Entropy is a useful monitor for measuring the electroencephalographiceffects of increasing and decreasing Sevoflurane concentrationand assessing depth of anesthesia Taking this all into consideration we conducted a study in whichwe observed the effect of intraoperative dexmedetomidine infusion as anadjuvant in general anesthesia on Sevoflurane requirement and on stressresponse during entropy guided general anesthesia in various surgicalprocedures. The various parameters we observed were age, gender,weight, ASA class, duration of surgery, heart rate (intraoperative), SBP,(intraoperative), DBP (intraoperative), MAP, MAC (%) of Sevoflurane,Sevoflurane requirement per hour, SpO2 level, VAS score, , RSS and entropy. The complications observed during the study in two groups were hypotension and bradycardia. The complications observed between two study groups when compared statistically were insignificant. Hypotension was observed in 4% patients in Group 1 and there was no incidence of hypotension in Group 2 patients (p value = 0.495) and the difference between the two groups was statistically insignificant. Bradycardia was observed in 12% of patents in Group 1 and 2% of patients in Group 2 (p value = 0.112) and the difference between two groups was statistically insignificant.

CONCLUSION

Dexmedetomidine as a bolus dose before induction andintraoperative infusion significantly decreased the requirement ofSevoflurane without compromising adequate depth of anesthesia, thus ithas anesthetic sparing property. It also was effective in bluntingmetabolic stress response to major surgeries . It also attenuated the vasopressor response oflaryngoscopy and intubation. It also maintained the stable hemodynamicsand a more rapid recovery from anesthesia .The pain scores were alsolower in patients receiving Dexmedetomidine due its analgesic property.

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