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A STUDY OF MAINTENANCE AND EMERGENCE CHARACTERISTICS OF INHALATIONAL ANAESTHETIC AGENTS

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ABSTRACT **Background:** Inhaled anesthetics allow rapid emergence from anesthesia because of easy titrability with inherent neuromuscular blocking effects that make them more suitable for day care anesthesia too. Aim of this study was to assess the maintenance and emergence characteristics of isoflurane, sevoflurane or desflurane in adult patients undergoing laparoscopic surgical procedures.

Methods: The study enrolled total 105 adult patients of either sex, ASA grade I or II, aged between 18-60 years.They were randomly allocated in three equal groups, Group I patients received isoflurane, group S received sevoflurane and group D received desflurane as inhalational agent. The various study parameters, side effects and complications were recorded.

Results: Overall mean dial settings required (%) were in group I was 1.09+/-0.32, in group S was 1.58+/-0.36, and in group D was 3.82+/-0.62. Mean MAC value was lower in group I as compared group S and group D, (P 0.05) while mean BIS was found to be within range of 40 to 60 in all three groups; being lowest in group I, as against group S and group D, (P <0.05).All the three agents provided almost similar (statistically insignificant difference) intraoperative hemodynamic variation, but best stability with Sevoflurane. The early and intermediate recovery time was shorter in group D than group S than group I.Study was devoid of any major side effects and complications except PONV in some patients of group S and D.

Conclusion: From the result of present study, we conclude that all three volatile agents were practically safe and useful for laparoscopic surgical procedures, Desflurane being marginally superior.

KEYWORDS : Volatile anaesthetics, Laparoscopic surgery, Dial settings, Recovery time.

INTRODUCTION

The introduction of general anesthetics into clinical practice over 150 years ago stands as one of the seminal innovations of medicine. This single discovery facilitated the development of modern surgery and spawned the speciality of Anesthesiology [1]. An ideal general anesthetic agent should provide smooth and rapid induction, optimal operating conditions, and rapid recovery with minimal side effects [2]. Inhalation anesthetics are the most common drugs used for the maintenance of general anesthesia. The rational drug selection is crucial when aiming at optimizing emergence and recovery after surgery [3].

Presently, new generation volatile halogenated anesthetic agents have evolved; like isoflurane, sevoflurane and desflurane. Isoflurane is a halogenated methyl ethyl ether. Its intermediate solubility in blood combined with a high potency permits intermediate onset and recovery from anesthesia. Sevoflurane, another volatile anesthetic agent, is halogenated ether. It has rapid induction due to low blood: gas partition (blood: gas partition coefficient of 0.65 and fat: blood solubility 48 at 37°C). Desflurane is also halogenated ether. Low solubility of desflurane in blood and body tissues (blood: gas partition coefficient of 0.42 and fat: blood solubility 27 at 37°C) leads to both rapid induction and recovery [4,5].

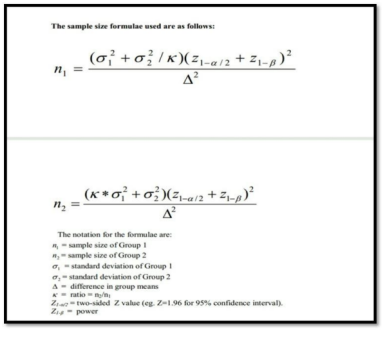
Various studies and clinical investigations have been done till date to compare efficacy of inhalational agents [6-9]. The properties of inhalational agents such as hemodynamic stability and recovery characteristics, while its use in varied surgical procedures like gynaecological, day care surgeries, bariatric surgeries and in paediatric patients were analysed in previous studies. All study results were in favour of new inhalational anaesthetic agents. Considering these studies and their positive results, our study was planned to have comparison between these commonly used inhalational agents in respect of maintenance and recovery characteristics during laparoscopic procedures.

MATERIALS AND METHODS

The present study was conducted in Department of Anaesthesiology at tertiary care institute in Maharashtra, after obtaining Institutional Ethical Committee approval and patients written inform consent.

Sample size (Selection and estimation) [2]

Haemodynamic parameters and recovery characteristics between Sevoflurane and Desflurane were the criteria considered [11]. The sample size was calculated by using the formula of – Difference between two means, and Annova test was used for comparison.



Total 105 adult patients of either sex, ASA grade I or II, age between 18-60 years, posted for elective surgical procedures by laparoscopic technique were selected for the study. Patients with ASA III and IV [9], significant cardio-respiratory disease, hepatic or renal dysfunction, psychiatric disorders, those with history of drug abuse or drug allergy, on CNS depressant drugs, pregnant, breast feeding patients, who has undergone the recent anaesthesia (within the previous 7 days) were excluded from the study.A detail history, clinical and laboratory investigations were done for all selected patients and they were randomly allocated in three equal groups by computer generated randomized sheet [9]. Group I patients received isoflurane, group S received sevoflurane and group D received desflurane as inhalational agent.

All patients were kept nil by mouth at least 8 hour prior to surgery. IV

access was obtained in non-dominant hand and IV fluid Ringer Lactate 500 ml drip was started. Premedication was given as injection ranitidine 50 mg and glycopyrrolate 4 mcg/kg, given IV 30 min prior to induction. In the operating room, baseline hemodynamic parameters were recorded using multipara monitor. Injection midazolam 0.03mg/kg as an anxiolytic agent and fentanyl 2 mcg/kg were given intravenously 5 to 10 min prior to induction. After preoxygenation with 100% oxygen for 5 minutes with fresh gas flow 6 lit / min, anaesthesia was induced with Propofol 2 mg/kg and succinylcholine 1.5 mg/kg was used as a muscle relaxants for tracheal intubation. Patients were intubated with appropriate size endotracheal tube and connected to Dragger Primus anaesthesia work station followed by mechanical ventilation with a tidal volume of 8 ml / kg. at 14 breaths/min using ventilator.

Neuromuscular blockade was achieved with injection vecuronium 0.08-0.1 mg/kg and subsequent maintenance. Anaesthesia was maintained with any one of the study inhalational agent along with 50:50% N2O and oxygen. The initial concentration to start of inhalational agent was isoflurane 1-2%, sevoflurane 1-2% and desflurane 3-6%. After initial FGF of 6 lit/min to achieve equilibrium, maintenance was on Intermediate flow rate i.e 3 lit/min with inspiratory and expiratory ratio being set 1:2 [10]. These respiratory parameters were changed in cases where hypercarbia occurred. Peak airway pressure, tidal volumes, and minute ventilation were monitored using anaesthesia ventilator with respiratory mechanics module. The set respiratory parameters were almost similar in all the three groups.

Volatile anaesthetic concentration was adjusted to maintain mean arterial pressure (MAP) and heart rate (HR) within 20 % of the pre-induction baseline values or by clinical signs of light anaesthesia (lacrimation , flushing , sweating) [6], inspired concentration of isoflurane, inspired concentration of sevoflurane and inspired concentration of desflurane were increased by increments of 1%. Intra-operatively, if MAP or HR showed persistent rise, supplemental doses of fentanyl (0.5 mcg/kg) was given. Bradycardia <55 beats /min was treated with injection atropine 0.6 mg [6]. Inhalational agent concentration was decreased only when hypotension was not responsive to intravascular volume expansion. MAC and BIS monitoring was also done.

At the end of the surgical procedures nitrous oxide was discontinued in all three groups, while volatile agent was stopped at the last port closure sutures. Controlled ventilation with 100% oxygen with 6 lit/min was continued until end tidal volatile anaesthetic concentration dropped to less than 0.1%[6]. The neuromuscular block was reversed with glycopyrrolate 8mcg/ kg, neostigmine 0.05 mg/kg and antiemetic ondansetron 4 mg was given 15 min before extubation. Tracheal extubation was done after the adequacy of reversal, consciousness, spontaneous eye opening, and responds to verbal commands. Time of discontinuation of anaesthetic agents was noted as time zero for all subsequent measurements and recovery time was determined by assessing at 1 min time interval [6]. Phase I recovery characteristics were recorded every 1 min with the help of Modified Aldrete Scoring System [10,11](Figure 1) while phase II was assessed by using Post Anaesthesia Discharge Scoring System (PADSS-Figure 2).Perioperative adverse events if any were noted.

Total consumption of inhalational agents was recorded from the anaesthesia machine software. It was also calculated by using formula, Consumption of inhalational agents (ml/hr) = fresh gas flow X 3.3 X dial setting.

Statistical Analysis

All data were analyzed by specific statistical methods applicable to various sets of data i,e. ANOVA test, chi square test. Power analysis was done for the exact differences between the groups for all variables. P value less than 0.05 was considered as statistically significant.

RESULTS

Total 105 patients with in the age group of 18 to 60 years were included in the study and randomly allocated into three groups of 35 patients in each. There were no differences between two groups with regard to patient age, sex, physical status and weight (Table-1). Mean duration of surgery and total consumption of volatile agents were also shown in table 1. The most common surgery performed in all the three groups was lap appendicectomy followed by lap cholecystectomy (Table 2).

The mean dial concentration was found to be lowest in group I as compared to the group S and group D which was statistically significant value, (P <0.05). Inspiratory and expiratory concentration achieved was lowest in group I as compared to group S and group D, (P < 0.05). The mean inspiratory concentration was low in group S than group I than group D- 0.96+/-0.39, 1.45+/-0.35, 3.32+/-3.05 respectively. Suggesting that managing of dial concentration required to maintain, steady state depth is minimal among all three groups. Mean MAC value (i.e. time to achieve surgical plane of anaesthesia) was lower in group I as compared group S and group D, which was statistically insignificant and this difference found could be due to some confounding factors like, premedication drugs, benzodiazepines, opioid used. Mean BIS was found to be within range of 40 to 60 in all three groups; being lowest in group I, as against group S and group D, which was statistically significant, (P <0.05), (Table 3).Table 4 shows the correlation in between MAC and BIS amongst three groups.

Pulse rate and systolic blood pressure were recorded at various intervals and on analysis it was comparable at all intervals in all three groups suggesting over all hemodynamic stability in all three groups (Figure 3). Adjustments of dial concentration was done to keep hemodynamics in 20% range of baseline parameters during maintenance, which was similar in all three groups, which is evident from results. The recovery time (both phase I and phase II) was earlier in both sevoflurane and desflurane group than isoflurane, earliest being in desflurane group (Table 5).Study was devoid of any major side effects and complications except PONV in some patients of group S and D.

DISCUSSION

At present, the most widely used inhalational anaesthetics are the halogenated, volatile agents halothane, enflurane, isoflurane and the gas nitrous oxide. The anaesthetic effect of these agents is related to their tension or partial pressure in the brain, represented at equilibrium by the alveolar concentration. The minimum alveolar concentration for a specific agent is remarkably constant between individuals. The uptake and distribution of inhalational anaesthetics depends on inhaled concentration, pulmonary ventilation, solubility in blood, cardiac output and tissue uptake [12-15].

With this physiological basis, in this study initial dial settings was kept in group I - 1-2%, in group S -1-2% and in group D - 3 -6% and to compare the inhalational variation in dial settings (concentration) were noted [1,9].As per the inherent property of inhalational agents, this much initial dial concentration was required to achieve early equilibrium. For initial 15 min interval there was progressive increase in the mean dial value, this was to ensure and achieve a better surgical plane so that intense surgical stimulus and insertion of trocar as well as CO2 insufflations was tolerated.

The use of nitrous oxide oxygen mixture probably helped to achieve second gas effect. It reflects the ability of high-volume uptake of one gas (First gas) to accelerate the rate of increase of the PA of a concurrently administered companion gas (second gas), the initial large-volume uptake of nitrous oxide accelerates the uptake of companion (second) gases such as oxygen and volatile anesthetics. This increased uptake of the second gas reflects increased tracheal inflow of all the inhaled gases (first and second gases) and higher concentration of the second gas or gases in a smaller lung volume (concentrating effect) due to the high-volume uptake of the first gas. [13]

Dial settings were altered as per the requirement of surgical procedures and to maintain heart rate and blood pressure within 20% of baseline values [6] and also surgical plane of anaesthesia [7]. Dial settings were altered in a state of signs of light anaesthesia like lacrimation, flushing, sweating and was decreased in response to hypotension and not responding to extra volumes of fluids other than replacement of intraoperative fluid loss [6]. The dial settings (concentration) in group I and group S were in increasing trends till maximum 10 min while in group D it was till maximum 20 min. Later on all three groups it was in steady state till 40 min, after 50 min they were in decreasing trends as the surgery proceeded towards the end. Mean dial settings in group I was 1.58+/-0.36, in group S was 1.09+/-0.32 and in group D was 3.82+/-0.62.**(Table 3& 4)**

The mean inspiratory concentration was low in group S than group I than group D. From time 0 min up to the initial 30 min of interval there was gradual increase in inspiratory concentration of all three volatile agents because initially to maintain the depth of anaesthesia for

noxious surgical stimuli and to maintain hemodynamic stability. From 30 min to 70 min there was a steady state level and after 80 min till surgery there were decreasing trends. The expired concentration was usually less as it is after utilization of patients with each breath and also absorption by circuit and absorbent during surgery.

The use of BIS helped to quantify sedative and hypnotic effect of anaesthetic and ensured adequate anaesthesia while use of MAC helped as guide to titrate volatile anaesthetics though not primary source. Group I had low BIS value as compared to group D and group S during intubation. Sudden reduction of BIS value as compared to baseline was evident after intubation till 10 min of surgery in all three groups due to synergistic effects of benzodiazepines, opioid, and induction agents used. Then from 10 min to later BIS value remain in steady state level that was in the range required to surgical plane of anaesthesia. Overall BIS value remained within the range of 40 to 60 throughout the surgery as the end of surgery BIS started to increase as dial concentration of the inhalational agent was decreased. During the initial 30 min of time interval when surgical stimulus was maximum there were a trends of increasing MAC, in groups I, S, D. It is evident that there was progressive increase in mean MAC value of all inhalational agents till about 30 min later on steady state variation as per need of the patients was noted from 30 min to 50 min, but difference among the group was statistically insignificant (p>0.05). Towards the end of surgery there was a trend towards rapid washout of desflurane in group D as compared to group S and I. Overall mean MAC in group I, S and D were. 0.85+/-0.20; 0.92+/-0.20 and 0.90+/-0.07 respectively, which was significantly less in isoflurane, suggests better potency of isoflurane. Our results were in accordance to various studies [16,17].The correlation in between MAC and BIS were depicted in table 4.During the end of surgery, the mean MAC started to decrease and mean BIS started to increase. Recovery from time of 100 to 120 min of interval was very fast in group S and group D than group I, which was significant. This observation was consistent with the greater metabolic suppression caused by isoflurane and its ability to produce a higher degree of brain electrical activity suppression[18]. The results of our study correlates with other studies [18, 19].

At 0 min, the mean pulse rate in group I and in group S increased from baseline while in group D there were slight fall in pulse rate. Thus it was evident that due to start of inhalational agents in group S and I significant rise noted, owing to its pharmacological property, i.e predominantly fall in systemic vascular resistance. At the same time insignificant fall in D group, suggests a myocardial depressant action. At 10 min of time interval the pulse rate was stable to near about baseline values, which was similar around mid of surgery that was 40 min in all three groups suggestive of overall stability. When compared among various groups the chance of decrease in group I and S were just significant, (P-0.043**)** but when group S and D was compared, desflurane has significantly better stability. By the end of procedures also patients in D group has better and significant stability while in I and S, variation in PR was almost similar.

At the start of inhalational agents, there was significantly fall in SBP from baseline in all three groups. Also, at 10 min similar findings were noted this was because, to achieve steady state concentrations and surgical plane of anaesthesia, there was gradual increase in concentration which leads to dose related myocardial depression as well as fall in peripheral vascular resistance. Due to increased potency of isoflurane and predominant, effect of dose related myocardial depression fall was significant. Once the depth of anaesthesia was achieved, maneuvering of dial concentrations in all three agents was minimal leading to improvement of systolic blood pressure and over all stability maintained. The fall in group I was still significant and difference between group D and group S was equivocal. (P=0.86). Towards end of the surgery all the three agents governed same patterns. Overall interpretation was almost stable hemodynamic. In all the three groups barring few episodes of significant fall in blood pressure and compensatory tachycardia in group I but overall both the parameters ranged in +/-20% of baseline value. Our results were similar with the study of Kaur et al [7] and Patel et al [8].

The mean time to achieve Aldrete score >/9 was 10.4+/-2.51, 4.42+/-1.09 and 3.74+/-0.65 in group I, S, and group D respectively. In group D mean time to reach Aldrete score was shortest as compared to group S and I, which was found to be statistically significant.(p=0.000). The mean time to achieve PADSS in group I, S and D was 13.34+/3.38, 4.94+/0.23, 3.91+/0.81 respectively. Here also recovery time was earliest in group D than group S than group I, which found to be statistically significant, (p=0.000). Thus group D had shorter phase I and II recovery than group S and I **(Table-6).** This study was comparable with other studies [7,8,11].

Intraoperative complications such as bradycardia, tachycardia, hypertension, hypotension, hypoxia, hypercarbia were being observed, but during the conduct of anaesthesia none of the patients had any of these. There were 4 patients each in sevoflurane and desflurane group who had post-operative nausea and vomiting. Similar results were noted by Luc et al [3].

CONCLUSION

From the results of present study, we concluded that all three volatile agents are practically safe and useful. The choice of anaesthetic for maintenance of anaesthesia should be guided by the status of the patients, the surgical procedures, types of procedure i.e routine or planned, emergency, ambulatory. Training and experience as well as availability of equipment also matters a lot. The emergence from isoflurane anaesthesia have some kind of positive correlation between duration of anaesthesia exposure owing to its better potency but need further studies to authenticate. Amongst sevoflurane and desflurane group, desflurane owes some superiority in context of recovery, which is very much useful in day care procedures.

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Table 7: Mean Time to achieve early and intermediate recovery

Tables

Table 1: Demographic data, duration of surgery and consumption of volatile agents

Parameters	Group I	Group S	Group D
Age (yrs)	32.88+/-11.55	34.34+/-11.52	38.62+/-12.07
Weight (kg)	52.68+/-9.84	55.2+/-9.06	60.62+/-7.1
Sex (Male/Female)	13/22	14/21	20/15
Duration of surgery (min)	123.71+/- 9.61	112.00+/-.39.01	114.85+/20.48
Total consumption of volatile agents (ml/hr)	10.82+/-3.23	15.71+/-3.61	37.89+/-6.23

Table 2: Surgery wise distribution of patients

Type of surgery	Group I	Group S	Group D	Total
Lap Cholecystectomy	10	13	10	33
Lap Appendicectomy	24	18	22	64
Lap IPOM **(Intra peritoneal on lay mesh)***	1	1	1	3
Lap TEP **(Total extraperitoneal Patch)****	0	3	2	5

***- Intra peritoneal on lay mesh for various Incisional hernia**

****- Total extraperitoneal Patch repair of Inguinal hernia**

TABLE N0 – 3 VARIATION OF MEAN DIAL CONCENTRATION AT VARIOUS TIME INTERVALS.

DIAL CONCENTRATION				
TIME IN MINUTE	GROUP I N=35	GROUP S N==35	GROUP D N=35	P
0	1.56+/0.60	2.01+/0.42	3.60+/0.69	0

5	1.49+/0.59	1.95+/0.43	3.94+/0.80	0
10	1.41+/0.50	1.7/0.63	4.20+/0.79	0
15	1.47+/0.47	1.75+/0.68	4.63+/1.00	0
20	1.40+/0.54	2.00+/0.60	4.5+/1.01	0
30	1.42+/0.52	1.91+/0.74	4.34+/0.96	0
40	1.52+/0.58	1.76+/0.72	4.57+/0.85	0
50	1.29+/0.700	1.85+/0.66	4.45+/0.95	0
60	1.18+0.68	1.55+/0.94	4.48+/1.14	0
80	0.97+/0.74	1.51+/0831	3.80+/1.43	0
100	0.58+/0.61	1.54+/0.68	3.65+/1.85	0
120	0.47+/0.61	0.83+/0.63	1.40+/1.98	0.06
160	-	0.25+/0.50	-	
MEAN +/-SD	1.09+/-0.32	1.58+/-0.36	3.82+/-0.62	0.000

Table 4: Concise Data of Inhalational Agents Required

	Group I	Group S	Group D	P value
Mean Dial Conc	1.09+/-0.32	1.58+/-0.36	3.82+/-0.62	0.00000
Mean Insp. Conc	1.03+/-0.30	1.50+/-0.31	3.84+/-0.43	0.00000
Mean Exp.Conc	0.81+/-0.23	1.27+/-0.31	3.50+/-0.53	0.00000
Mean MAC	0.85+/-0.20	0.92+/-0.20	0.90+/-0.07	0.2053
Mean BIS	44.83+/-4.50	50.84+/-5.90	49.04+/-3.74	0.00000

Table 5: Correlation in Between MAC and BIS

Time Interval	Group I		Group S		Group D	
	MAC	BIS	MAC	BIS	MAC	BIS
0	0.68+/-0.32	35.63+/-4.30	0.68+/-0.30	38.77+/-8.46	0.55+/-0.22	42.51+/-4.93
5	0.95+/-0.33	35.29+/-4.60	0.97+/-0.23	38.49+/-9.39	0.73+/-0.19	41.43+/-5.11
10	1.03+/-0.32	33.69+/-5.48	0.94+/-0.30	38.26+/-0.804	0.98+/-0.27	40.49+/-4.72
15	1.05+/-0.32	33.57+/-5.76	1.05+/-0.38	40.80+/-8.04	1.05+/-0.15	39.74+/-4.94
20	1.11+/-0.27	41.00+/-44.17	1.08+/-0.37	38.89+/-8.86	1.11+/-0.16	40.31+/-5.29
30	1.07+/-0.28	33.14+/-8.25	1.11+/-0.32	40.03+/-9.43	1.16+/-0.15	41.31+/-4.17
40	1.10+/-0.33	35.40+/-9.49	1.04+/-0.38	40.06+/-15.17	1.13+/-1.47	41.91+/-4.34
50	1.07+/-0.34	37.49+/-11.75	1.07+/-0.37	39.85+/-14.31	1.14+/-0.16	40.91+/-4.11
60	0.99+/-0.38	37.65+/-10.82	1.02+/-0.40	44.55+/-17.84	1.13+/-0.16	42.43+/-5.59
80	0.89+/-0.43	50.36+/-15.15	1.03+/-0.35	49.52+/-15.69	0.95+/-0.31	46.57+/-14.01
100	0.7+/-0.45	45.31+/-13.93	0.98+/-0.30	43.00+/-14.46	0.87+/-0.39	50.35+/-20.96
120	0.61+/-0.57	52.26+/-22.57	0.67+/-0.35	56.78+/-17.54	0.42+/-0.41	62.84+/-21.19
160	-	73.40+/-19.98	0.45+/-0.26	74.50+/-14.38	-	-

TABLE NO – 6 TIME RELATED VARIATION IN RECOVERY SCORE.

PHASE I – *EARLY RECOVERY* (TIME IN MIN)	GROUP I N=35 (%)	GROUP S N=35 (%)	GROUP D N=35(%)	P
</2	0 (0%)	0 (0%)	0 (0%)	
2-4	0 (0%)	14 (40%)	24 (68.57)	
4-6	1 (2.85%)	20(57.14%)	11(31.42%)	
>/6	34 (97.14)	1 (2.85%)	0 (0%)	
MEAN+/SD	**10.4+/-2.51**	**4.42+/-1.06**	**3.74+/-0.65**	**0.000**
PHASE II -*INTERMEDIATE RECOVERY* (TIME IN MIN)				
</2	0 (0%)	1 (2.85%)	0 (0%)	
2-4	0 (0%)	8 (22.85%)	22(62.85%)	
4-6	2 (5.71%)	23(65.71%)	13(37.14%)	
>/6	33 (94.28%)	3 (8.57%)	0 (0%)	
MEAN+/SD	**13.34+/-3.38**	**4.94+/-0.23**	**3.91+/-0.81**	**0.000**

Group	Phase I - Early Recovery (in min)	Phase II -Intermediate Recovery (in min)
Group I	10.40+/-2.51	13.34+/-3.38
Group S	4.43+/-1.06	4.49+/-1.73
Group D	3.74+/-0.65	3.91+/-0.81
P value	0.000	0.000

Figures

Parameter	Description of patient	Score
Activity level	Moves all extremities voluntarily/on command	2
	Moves 2 extremities	1
	Cannot move extremities	0
Respirations	Breathes deeply and coughs freely	2
	Is dyspneic, with shallow, limited breathing	1
	Is apneic	0
Circulation (blood pressure)	Is 20 mm Hg > preanesthetic level	2
	Is 20 to 50 mm Hg > preanesthetic level	1
	Is 50 mm Hg > preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation as determined by pulse oximetry	Has level >90% when breathing room air	2
	Requires supplemental oxygen to maintain level >90%	1
	Has level <90% with oxygen supplementation	0

Maximum total score is 10; a score of ≥9 is required for discharge.

Figure I Modified aldrete scoring system [-6,13.]

Figure 2 Post Anaesthesia Discharge Scoring System

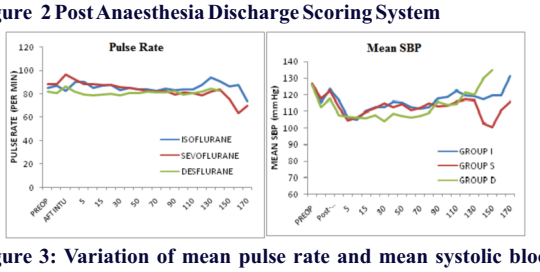

Figure 3: Variation of mean pulse rate and mean systolic blood pressure over time

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