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ORIGINAL RESEARCH ARTICLE

COMPARISON BETWEEN TOTAL INTRAVENOUS ANESTHESIA (TIVA) WITH PROPOFOL – FENTANYL AND BALANCED ANESTHESIA WITH SEVOFLURANE – FENTANYL IN TERMS OF HEMODYNAMIC CHANGES AND RECOVERY PROFILES DURING LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Background: Sevoflurane and propofol are considered to be the agents of choice in laparoscopic surgery due to their smooth induction of anesthesia, hemodynamic stability, better recovery profile and less postoperative complications. The aim of study is to compare hemodynamic changes and recovery profile of propofol with sevoflurane-based anesthesia in laparoscopic cholecystectomy.

Methods: Single blind comparative study was conducted among 132 patients aged 18-65 years, ASA-PS I & II undergoing laparoscopic cholecystectomy, randomized by computer generated random number table into two groups, 66 patients each- Group A patients induced with propofol 1.5-2.5 mg/kg IV and maintained with propofol 100-200 mcg/kg/min IV and Group B induced with sevoflurane and maintained with sevoflurane at minimum alveolar concentration of 0.7-1.3. Primary outcome were hemodynamic parameters (heart rate, systolic and diastolic blood pressure, mean arterial pressure) and recovery profile.

Results: Intraoperative heart rate and diastolic blood pressure were comparable between two groups at all times while there was a significantly lower systolic blood pressure only at 3 and 5 minutes after intubation in group B compared to group A ($p < 0.05$). Recovery profiles assessed in terms of time of eye opening (657.89 ± 172.30 s vs 453.58 ± 157.49 s), obeying command (696.79 ± 192.44s vs 481.06±164.96s), and time of extubation (706.41±166.27s vs 483.38±160.62s) were significantly faster in group B (p value < 0.001).

Conclusions: Hemodynamic changes were comparable between propofol group and sevoflurane group while sevoflurane group had faster recovery.

INTRODUCTION

Laparoscopic cholecystectomy is a standard surgical procedure for management of gallbladder stones.[1,2] Sevoflurane and propofol are considered the anesthetic agents of choice in laparoscopic cholecystectomy due to their smooth induction of anesthesia, hemodynamic stability, better recovery profile and less post-operative complications.[3] There have been several studies comparing propofol with sevoflurane in such surgeries, but very limited data are available in our population.

The purpose of this study was to compare hemodynamic changes and recovery profiles during propofol and sevoflurane-based anesthesia.

METHODS

This randomized single blind comparative study was done in patients aged 18 -65 years with American Society of Anesthesiologists physical status (ASA-PS) I and II undergoing laparoscopic cholecystectomy. It was conducted over a period of one year from March 2017 to February 2018 at B.P. Koirala Institute of Health Sciences, Dharan after clearance from the Institutional review committee (IRC) of BPKIHS (Ref No: 358/073/074-IRC) and obtaining informed written consent from the patients. Patients refusing to give the consent, conversion to open cholecystectomy and with neuromuscular disorder were excluded from the study. In the preoperative holding area, patients were randomly assigned into one of the two groups using computer generated random number either to Propofol Group (Group A) or Sevoflurane Group (Group B). Sample size was 132 patients with 66 patients in each arm considering 95% confidence interval and 80% power, based on mean time to eye opening and standard deviation in Propofol Group and Sevoflurane Group as in study by Deng and Zhu and assuming 10% drop-outs during the study period.[4] Upon arrival to the operating room, demographic details of the patients were noted. Standard monitoring equipment was applied and baseline parameters like ECG, heart rate, NIBP and SPO_2 were recorded. Intravenous access was established and Ringer's lactate 5 ml/kg was infused. All patients were preoxygenated with 100% oxygen via anatomical facemask for 3 minutes with fresh gas flow (FGF) of 6L/min.

Propofol Group patients were induced with fentanyl 1.5 µg/kg and propofol 1.5-2.5 mg/kg IV till the loss of verbal response, when the mask ventilation was confirmed, vecuronium 0.1 mg/kg IV was administered, and ventilated for 3 minutes and endotracheal intubation was done. Anesthesia was maintained with propofol 100- 200 µg/kg/min IV; starting at 100 µg/kg/min IV. Depending upon the hemodynamic responses, rate of infusion was titrated to keep the hemodynamic parameters within 20% of baseline. FGF was adjusted to 2L/min.

Sevoflurane Group patients induced with Fentanyl 1.5 µg/kg IV, FGF adjusted to 6L/min of 100% oxygen, and inhalational anesthetic agent sevoflurane was delivered initially at 2%, then increased by 1% every 2 breaths and advanced up to 8%. After the loss of eyelash reflex and bag and mask ventilation was confirmed, vecuronium 0.1 mg/kg IV was given, and manually assisted ventilation was done for 3 minutes.,then endotracheal intubation was done with appropriate size of endotracheal tube. FGF was adjusted to 2L/min. Anesthesia was maintained with sevoflurane adjusted to MAC 0.7-1.3 so as to maintain hemodynamic parameters within 20% of baseline and for further requirement in anesthetic dose beyond this range to maintain hemodynamic parameters, additional drugs were used as follows- Inj. atropine 0.6 mg IV for decrease in heart rate below 20% of baseline or HR< 60 bpm whichever was less. Phenylephrine 50 µg IV for decrease in MAP below 20 % of baseline or MAP < 60 mm Hg whichever was less. Esmolol 10 mg IV or Nitroglycerine 50 µg IV for increase in MAP above 20 percent of baseline or MAP > 120 mm Hg whichever was more. Hemodynamic parameters like HR, NIBP were recorded before induction, before intubation, immediately after intubation, and 3 mins after intubation, then every 5 min till the end of surgery. ECG, SPO_2, end tidal carbon dioxide concentration ($ETCO_2$) were monitored throughout the procedure. In patients of both the groups, Paracetamol 15mg/kg IV not exceeding 1 gm was given just before skin incision. Ketorolac 30 mg IV and ondansetron 4 mg IV were given 10 minutes before expected time of extubation and Inj. 0.25% Bupivacaine 20 ml for instillation into the gall bladder bed and 10 ml into port site for post-operative pain management. Fentanyl 0.5 µg/kg was repeated every 45 minutes till the end of surgery. Neuromuscular blockade was maintained with vecuronium (0.02 mg/kg, IV) as required throughout surgery. At the end of surgery, residual effects of neuromuscular blockade was reversed with neostigmine (0.05 mg/kg, IV) and glycopyrrolate (0.01 mg/kg, IV). Propofol infusion/ sevoflurane inhalation was discontinued with the initial skin stitch. This time of discontinuation was noted. Recovery from anesthesia was monitored every minute thereafter to awakening (opening eyes on verbal command), response to commands (protruding the tongue, squeezing the observer's hand) and this time was noted. After regaining spontaneous respiration and consciousness, patient's trachea was extubated. Mean extubation time defined as the time point from the termination of studied drug infusion/ inhalation to endotracheal extubation was noted. Agitation and sedation was assessed using Richmond Agitation and Sedation scale (RASS) just before extubation, immediately after extubation and on arrival to PACU and at 15 min, 30 min, 45 min and 60 min thereafter.[5,6] On arrival to the PACU, non-invasive blood pressure, heart rate, SpO_2, agitation and sedation were assessed by an investigator blinded to the patient allocation.

The primary outcome parameters were assessment of hemodynamic parameters- SBP, DBP, MAP, HR and comparison of recovery profiles in terms of time of eye opening, time of obeying verbal command and time of extubation. Secondary outcome parameter was incidence of postoperative agitation and sedation score.

Data were entered in Microsoft Excel 2010 and converted into Statistical package for social sciences (SPSS 11.2) for statistical analysis. Independent sample t test was used to compare the mean between two groups, paired t test to compare the mean values before and after the study drug administration within the same group, chi square test to compare the non-parametric variables. Probability value was considered significant when $p < 0.05$.

RESULTS

Out of 132 patients, with 66 patients in each group, demographic parameters, duration of anesthesia and duration of surgery were comparable between two groups (table 1).

Table 1: Comparison of demographic parameters

Characteristics		Group A (n=66)	Group B (n=66)	p- value
Age in yrs (mean ± SD)		38.97 ±13.39	40.03 ± 10.21	0.61
Sex	**Male**	14	18	0.42
	Female	52	48	
ASA-PS	**I**	55	58	0.46
	II	11	8	
Weight in Kg (mean ± SD)		55.62 ± 8.47	58.32 ± 9.45	0.09
Duration of anesthesia in min (mean ± SD)		60.55 ± 15.51	63.17 ± 19.58	0.39
Duration of Surgery in min (mean ± SD)		50.53 ± 15.20	52.30 ± 20.14	0.57

min: minutes, SD: Standard Deviation, ASA PS: American Society of Anesthesiologist Physical Status

Recovery profiles were significantly faster in sevoflurane group compared to propofol group. Time of eye opening was 657.89 ± 172.30s and 453.58 ± 157.49s, obeying command was 696.79 ± 192.44s and 481.06 ± 164.96s, and time of extubation was 706.41 ± 166.27s and 483.38 ± 160.62s in propofol group and sevoflurane group respectively and were significantly faster in sevoflurane group (p value<0.001) as compared to propofol group.

Baseline heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable in both the groups.

Compared to baseline, there was statistically significant decrease in heart rate just before intubation in both propofol and sevoflurane group by 9.758± 8.34 bpm and 7.848 ± 11.10 bpm respectively (p-value<0.001) but significant increase (p-value<0.001) occurred immediately after intubation by 4.773±10.559 and 7.955 ± 15.135 bpm. However, at 3 min there was significant increase in mean heart rate in propofol group but mean HR was unchanged in sevoflurane group. Compared to the baseline, SBP, MAP and DBP were decreased significantly just before intubation, there was no change in both the groups immediately after intubation. At 3 min and 5 min there were significant decrease in SBP and MAP in sevoflurane group whereas no change in propofol group. DBP was significantly lower in sevoflurane group at 3 min but there was no change in propofol group.

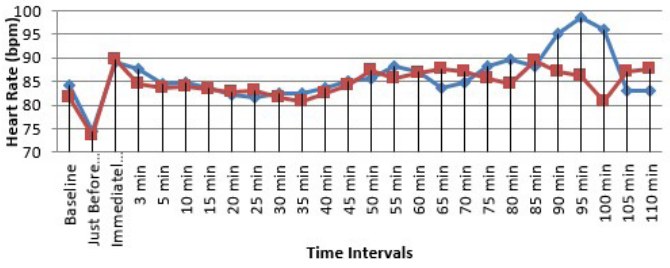
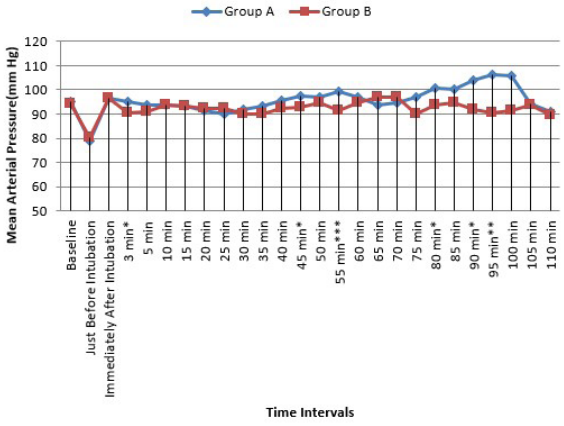


Figure 1: Comparison of Mean Heart Rate between groups

Mean HR and MAP were compared between propofol group and sevoflurane group at different time intervals- just before intubation, immediately after intubation, then at 3 min, 5 min and every 5 minutes by using independent sample t-test. Mean Heart rates were comparable between both the groups at all time intervals.

At most of the time intervals MAP were comparable in the both groups except at 3 min, 45 min, 55 min, 80 min, 90 min and 95 minutes when there was significant decrease in MAP in s



Min: Minutes,*: < 0.05, **:<0.01, ***<0.001

Figure 2: Comparison of mean arterial pressure between groups

Post-operative agitation and sedation was assessed using RASS at just before extubation, immediately after extubation, and then at 15 min, 30 min, 45 and 60 min as in Table 2.

Table 2: Richmond Agitation and Sedation (RASS)

RASS		-2 (light Sedated)	-1 (Drowsy)	0 (Alert and Calm)	+1 (Restless)	+2 (Agitated)	p-value
JBE	Group A	4	26	2	31	3	<0.001
	Group B	1	2	6	54	3	
IAE	Group A	2	31	4	29	0	<0.001
	Group B	1	9	20	35	1	

JBE: Just before Extubation; IAE: Immediately after extubation

At 15 min at PACU, three patients in propofol group and four patients in sevoflurane group were drowsy. However, rest of the patients were alert and calm in both the groups. All patients in both groups were alert and calm, when they were assessed at 30 min, 45 min and 60 min at PACU.

Only two patients in sevoflurane group were given inj. atropine 0.6 mg IV for bradycardia. Inj. nitroglycerine (NTG) was given to nine patients in propofol group and five patients in sevoflurane group which was comparable. Two patients in propofol group and 10 patients in sevoflurane group received esmolol (p value 0.015). Similarly, eight patients in propofol group and two patients in sevoflurane group were given inj. phenylephrine for hypotension, and it was found to be significant (p value 0.048). Similarly they were asked whether they had recall of intraoperative events. No patients in both groups recalled intra-operative events.

DISCUSSION

Laparoscopic cholecystectomy has gained popularity with reduced perioperative morbidity and shorter hospitalization, reduced postoperative discomfort, shortened recovery rates.[7,8] It has also been started on day care basis, where fast recovery and fully awake patient after general anaesthesia is desired.[8] Propofol, a highly lipid soluble intravenous anesthetics with rapid induction and recovery from anesthesia and minimum postoperative morbidity is popular in day care surgeries.[8] Sevoflurane with lower blood gas solubility, pleasant to inhale, offers good hemodynamic stability, and provides rapid emergence.[8]

In our study demographic variables, duration of surgery, anesthesia and baseline hemodynamic parameters were comparable in both the groups. There was significant fall in HR from baseline values after induction of anesthesia in both the groups. SBP, DBP, MAP decreased significantly (p value<0.001) from baseline values after induction of anesthesia in both the groups which was similar to the study done by Singh et al and Khare et al.[9,10] Propofol is a selective $GABA_A$ receptor modulator that decreases rate of dissociation of GABA from $GABA_A$ receptor resulting into increase chloride conductance and postsynaptic membrane hyperpolarization. Systemic vascular resistance decreases due to effect on vasoconstrictor sympathetic nerves. It also possesses negative inotropic effect by inhibiting trans-sarcolemmal influx of calcium.[11,12] Sevoflurane decreases systemic vascular resistance as well as dose-dependent decrease in MAP whereas HR increases only when minimum alveolar concentration is >1.5.[3]

There was significant increase in HR (5.67% in propofol group and 9.75% in sevoflurane group with p value < 0.001) from baseline value in both the groups similar to the finding by Shah & Adaroja immediately after intubation.[8] The decrease in blood pressure by propofol is reversed by haemodynamic effect of laryngoscopy and intubation. The intubation response lead to increase in sympathetic activity which may increase in HR in addition to that produced by sevoflurane.[13] In similar study by Tomiyasu and collegues,[14] similar increase in HR without change in SBP occurred after intubation in sevoflurane induction group but since there was no simultaneous increase in plasma epinephrine and norepinephrine concentration, they concluded sevoflurane blunts laryngoscopic response. In both the groups the intraoperative HR was comparable. MAP at most of the time intervals were comparable in both the groups which was similar to the findings by Somvanshi.[15] In few of the intervals MAP was significantly higher in propofol group. The reason being eight patients in propofol group and two patients in sevoflurane group received bolus doses of inj. Phenylephrine intraoperatively for hypotension (p value 0.048).

Recovery profiles were significantly faster in sevoflurane group than propofol group (p value < 0.001). The reason being, sevoflurane gets rapidly eliminated after it is stopped as seen from blood-gas distribution coefficient of 0.69 and moreover there is 50% decrease in anaesthetic concentration of sevoflurane in less than 5 mins irrespective of duration of anaesthesia.[13] Similar results were observed by Singh et al and Ohkushi et al.[9,16]

Rapid recovery and psychological immaturity has been considered as a reason for emergence delirium following sevoflurane anaesthesia.[17] At just before extubation, significant number of patients were restless (RASS:1), 81% in sevoflurane group and 46.96% in propofol group (p value<0.001). After 15mins in PACU, all the patients were alert and calm (RASS-0). In contrast to our study, most of the patients (63% in sevoflurane group and 70% in propofol group) were calm/cooperative/ good in study by Khare et al.[10] Reason being inclusion criteria including duration of surgery < 2 hours and infusion rate of propofol were adjusted to maintain blood pressure and HR within 15% of the baseline (20% in our study), resulting into low consumption of propofol.

CONCLUSION

Our study has shown that sevoflurane and propofol maintain intraoperative haemodynamic stability, recovery profiles are better with sevoflurane and intraoperative awareness does not occur with either drugs.

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CONFLICT OF INTEREST: None

FINANCIAL DISCLOSURE: None

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