ORIGINAL RESEARCH

Effect of adding dexmedetomidine and fentanyl to propofol on hemodynamics, apnoea time and insertion condition of LMA under anesthesia for chronic SDH evacuation

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ABSTRACT

Background: Laryngeal mask Airway(LMA) is commonly used as an alternative toendotracheal intubation for short surgical cases as it allows both spontaneous as well as positive pressure ventilation[1]. Propofol being well known inducing agent, is popular for its smooth induction properties. Previous studies have shown fentanyl and dexmedetomidine can be used as an adjuvant to propofol for general anaesthesia.In our study we compared the effect of dexmedetomidine and fentanyl administered before propofol, on laryngeal mask airway insertion condition, hemodynamics and apnoea time in patients posted for chronic subdural hemorrhage evacuation under general anaesthesia. **Method& materials:** This prospective randomized double blind study was carried out on 180 patients,after taking clearance from institutional ethics committee.Patients were divided into two equal groups. GroupFp (Fentanyl- Propofol group N= 90) and Group Dp (Dexmedetomidine - Propofol N= 90). Group Fp and Group Dp: Patients were given inj. fentanyl 1 mcg/kg and inj dexmedetomidine diluted in 10 ml normal saline iv over 10 minutes respectively. Thirty second after study drugs, patients were induced with inj. propofol 2mg/kg iv and PLMA was inserted after 90 seconds of inj propofol. Ease of PLMA insertion was assessed, according to Muzi scoring system such as jaw mobility, coughing, gagging or any movements were noted. In each category score $\leq$ 2 was considered optimum for PLMA insertion. HR,SBP, DBP, MAP,SPO_2 and RR were noted at baseline(BL), after administration of study drug(AASD), before PLMA insertion(BLI), after PLMA insertion(ALI),1,3,5,10 and 15 minutes after PLMAinsertion.Apnoea time is the time, from last spontaneous breath after propofol administration to first spontaneous breath of the patients was noted.In both the groups, SpO_2 was maintained throughout the study to 100%. **Result:** In the Dp group, all patients(100%), had jaw mobility which was optimal for PLMA insertion while in the Fp group 96.66% patients had acceptable score for jaw mobility. In Dp group HR, SBP, DBP and MAP was found significantly low throughout the study period following LMA insertion, while in GroupFp there was rise in the above parameters noted immediately after LMA insertion. Incidence of apnoea was significantly higher ($P < 0.0001$) in group Fp (18/20%) than Group Dp (3/3.33%).Mean duration of apnoea in Group Fp (284.5 ± 11.19 sec) was significantly higher than Group Dp (217.17 ± 16.48 sec). **Conclusion:** The addition of dexmedetomidine to propofol provides superior insertion condition and good jaw mobility for ease of insertion of PLMA in the first attempt as compared to fentanyl. Dexmedetomidine - propofol also provides better hemodynamic responses with minimal or no intraoperative and postoperative complication as compared to fentanyl-propofol.

Keywords: Laryngeal mask airway, Dexmedetomidine, Fentanyl, Propofol

INTRODUCTION

The LMA is one of the most commonly used supraglottic device[1,2]having several advantages such as easier insertion, no need for laryngoscope,better tolerated by patients, fewer hemodynamic complications,less trauma for the larynx and vocal cords also allows spontaneous ventilation as well as positive pressure ventilation.[3,4,5]Propofol has become first choice as induction agent for LMA insertion. However, propofol when used alone, may cause pain on injection, requires higher dose, more drop in blood pressure and lighter plane of anesthesia[6]may cause coughing, laryngospasm and movement[7,8]in order to eliminate or reduce propofol-induced these unwanted effects pre-mixing with an adjunct, such as benzodiazepine(Midazolam), Opioids(Fentanyl, Alfentanyl, Remifentanyl)[7] and α2-agonists(Clonidine, Dexmedetomidine) or Muscle relaxants were tried.[8]Fentanyl is commonly used opioid due to its analgesic and easy availability. Dexmedetomidine is a potent and highly selective α_2 adrenoreceptor agonist and at dose range of 0.5-1 mcg/kg iv, have found to be effective as anesthetic, analgesic, sedative and in reducing the dose of propofol during induction and maintainance of anesthesia.[9] In our study we have compared the effectiveness of combination of dexmedetomidine – propofol (Dp) and fentanyl – propofol (Fp) for ease of LMA insertion, hemodynamic stability and apnoea time in short surgeries(chronic subdural hemorrhage evacuation)under general anesthesia.

METHOD AND MATERIALS

This prospective double blind comparative study was conducted, after getting clearance from ethics committee. A Total of 180 patients of ASA Grade I & II, posted for chronic subdural hemorrhage evacuation, under general anesthesia, were divided randomly into two groups(Group Dp and Group Fp) of 90 each. Patients with history of cardiopulmonary, neurologic active hepatic and renal disease, psychiatric disorders, neck and facial burn and reduced mouth opening,Patients with risk of aspiration, Patients with head, neck, oral and nasal surgery,Patients on beta blocker therapy, heart rate < 60/min, known egg allergy,Patients with sensitivity with volatile anestheticagent or propofol or history of allergy to any known or unknown substance were excluded from the study. After detailed pre-anestheticcheckup and written informed consent, patient was taken inside the operation theatre. Baseline parameters ECG, HR, MAP,RR and SpO_2were recorded and monitoring was initiated. Patients were cannulated with 18 gauge intravenous cannula in right dorsum of hand and all patients were preloaded with 10 ml/kg bwt of ringer lactate solution over 15-20 minutes. Inj glycopyrrolate 0.2mg and inj midazolam 0.02mg/kg was given. Study drug was given by anesthesia personnel not involved in the study. Group Dp patients were given inj. dexmedetomidine 1 mcg/kg diluted in 10 ml of normal saline iv over 10 minutes. Group Fp patients were given inj. fentanyl 1 mcg/kg diluted in 10 ml normal saline iv over 10 minutes. Afterpreoxgenation, patients were induced with inj. propofol 2 mg/kg iv. PLMA was inserted after 90 seconds of injection propofol by experienced anesthesiologist who was unaware of study drug. PLMA was inserted by standard insertion technique. A 12 F Gastric drain tube was inserted through the PLMA after confirming gas leak during ventilation by placing a bolus of clear water-soluble lubrication its proximal end. The size of PLMA was selected as per patients weight and ease of insertion of PLMA was assessed according to Muzi scoring system. After PLMA insertion, cuff was inflated with its respective cuff volume. The PLMA placement was assessed by outward movement of device on cuff insertion, neck bulge on cuff inflation, adequacy of manual ventilation, passage of gastric tube and supra sternal notch test. Proper placement of PLMA was confirmed with the help of capnography and auscultation of chest for bilateral air entry. If the first attempt of PLMA placement was failed in either of the group additional dose of propofol 0.5mg/kg was given and after 30 seconds,second attempt of PLMA insertion was made. After two failed attempts the study protocol was discontinued and patients airway was managed according to standard protocol. No muscle relaxant was used in our study still if the patients remained in apnoea for more than 30 seconds after PLMA insertion the lungs were manually ventilated until spontaneous ventilation returned. General anesthesia was maintained with 1 MAC isoflurane in 60% nitrous oxide and 40% oxygen. Baseline parameter like HR, SBP, DBP, MAP, SpO_2, and RR were recorded before induction base line value (BL), after administration of study drug (AASD), before PLMA insertion (BLI), after PLMA insertion (ALI) ,1,3,5,10 and 15 minute after insertion of PLMA.Apnoea time is the time, from last spontaneous breath after propofol administration to first spontaneous breath of the patients was noted.Fall in heart rate below 60/min and systolic blood pressure below 90 mm Hg was considered bradycardia and hypotension respectively. Bradycardia and hypotension were treated with injection atropine 0.6 mg iv and injection mephenteramine 6 mg iv respectively and the patients who had bradycardia and hypotension were excluded from our study.Ease of PLMA insertion was assessed, according to Muziscoring system[10] such as jaw mobility(fully relaxed:1,mild resist:2,tight but open:3,closed:4), coughing(none:1, two/more coughs:2, three/more coughs:3, bucking/movements:4), or gagging were noted. In each category score $\leq$ 2 was considered optimum for PLMA insertion. At the end of surgery, nitrous oxide (N_2O) and isoflurane was discontinued and 100% oxygen was administered to all the patients, PLMA was removed when the patients was able to

open the mouth on commands. PLMA was inspected for blood stains and injury to lip, teeth and tongue.

STATISTICAL PLAN

Categorical variables were summarized in frequency and percent distribution and Chi-square or Fishers exact test were performed as appropriate. Continuous variables were analyzed using mean ± SD or median with inter quartile range as appropriate. Mean difference between two independent groups was analyzed by using independent t-test after normalizing the distribution, otherwise non-parametric test was applied. Odds ratio with 95% confidence limits was analyzed to find out the potential risk factors. For test the null hypothesis 0.05 Alpha and 95% confidence limit was applied.

RESULT

There was no significant differences in patients' age, weight, height, sexes, BMI, surgery duration and ASA grading in both the groups(Table 1).

TABLE 1: DEMOGRAPHIC DATA.
Source: original

Variable	Group Fp		Group Dp		P Value
	Mean	SD	Mean	SD	
Age (Years)	26.76	5.17	24.95	4.7	0.28
Weight (Kg)	53.38	5.61	54.73	5.67	0.10
Height (Cm)	147.61	7.32	149.22	6.44	0.11
Body Mass Index (Kg/M^2)	24.52	1.74	24.61	1.53	0.69
SurgeryDuration (Minutes)	40	3.75	40.05	3.70	0.92
Gender Male Female	19 71		17 73		0.70
MPC Grade I Grade II	68 22		63 27		0.40
ASA status Class 1 Class 2	82(91.11%) 88(8.88%)		83(92.22) 77(7.77%)		0.78

To compare insertion condition between both the groups, we used Muzi scoring system (Table 2).

TABLE: 2 JAW MOBILITY AND COUGH SCORE IN BOTH GROUPS
Source: original

JAW MOBILITY	GROUP Fp	GROUP Dp
Score 1	84	87
Score 2	03	03
Score 3	03	00
Score 4	00	00
COUGH SCORE	**GROUP Fp**	**GROUP Dp**
Score 1	80	87
Score 2	05	02
Score 3	03	01
Score 4	02	00

Score 1 and 2, were considered acceptable for PLMA insertion (as per Muzi scoring system). Three patients in FpGroup had jaw mobility condition which was not optimal for insertion of PLMA while in Group Dp, no patient had jaw mobility score 3 or 4. In Group Fp, total 5 patients had unacceptable cough score for PLMA insertion while in Group Dp, only 1 patients in the Group Dp had unacceptable condition for PLMA insertion in terms of cough scoring which found to be statistically insignificant as p value is 0.096 between both the groups(Table 2)**.**

On comparing ease of insertion of PLMA in both the groups, in Group Fp, 91.11% patients had acceptable condition and 8.88% patients had unacceptable condition for PLMA insertion while in Group Dp 98.88% patients had acceptable condition and 1.11% patient had unacceptable condition for PLMA insertion with significant p value of 0.016(Table 3).In the Group Fp, successful placement of PLMA with optimal insertion condition was achieved in 78 patients in the first attempt and in Group Dp, 89 patients had optimal insertion condition with successful placement of PLMA in the first attempt while second attempt required in 1 patients of Group Dp with cough score 3. In the Group Fp, second attempt of PLMA insertion was needed in total 12

patients means they received additional dose of propofol for PLMA insertion.(Table 3)

TABLE 3: PARAMETERS FOR EASE OF PLMA INSERTION (INSERTION CONDITION AND NUM OF ATTEMPT)

Source: original

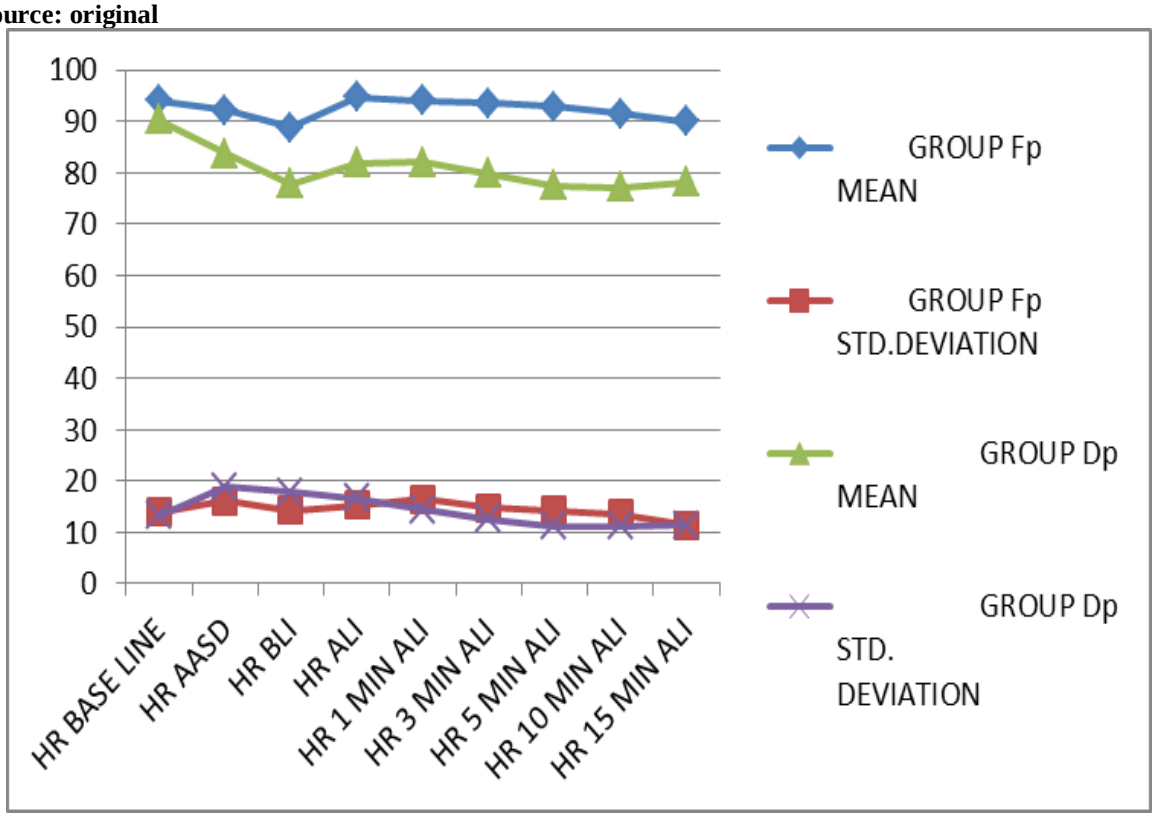
	Group Fp (%)	Group Dp (%)	P Value
1)Insertion condition			
Acceptable	82 (91.11%)	89 (98.88%)	0.016
Unacceptable	8 (8.88%)	1 (1.11%)	
2)No of Attempt			
First Attempt	78 (86.66%)	89(98.88%)	0.0015
Second Attempt	12 (13.33%)	1(1.11%)	

Baseline parameter like HR, SBP, DBP MAP, RRandSpO$_2$, were recorded before induction base line value (BL), and were insignificant (p >0.05) in both the groups.

Mean value of HR of patients in Group Fp was 92.19 ± 16.03 after administration of study drug (AASD), 88.8 ± 14.19 before PLMA insertion (BLI), 94.73 ± 15.19 after PLMA insertion (ALI), 94.02 ± 16.47 at 1 min, 93.49 ± 14.76 at 3 min, 92.8 ± 14.21 at 5 min 91.49 ± 13.56 at 10 min and 89.98 ± 11.39 at 15 min(Graph 1). In contrast to this, mean value of HR during intraoperative period for Group Dp was 83.68 ± 18.80 after administration of study drug (AASD), 77.74 ± 17.84 before PLMA insertion (BLI), 81.95 ± 16.68 after PLMA insertion (ALI), 82.03 ± 14.41 at 1 min, 79.85 ± 12.52 at 3 min, 77.55 ± 11.19 at 5 min, 77.2 ± 11.25 at 10 min and 78.14 ± 11.35 at 15 min.(Graph 1)

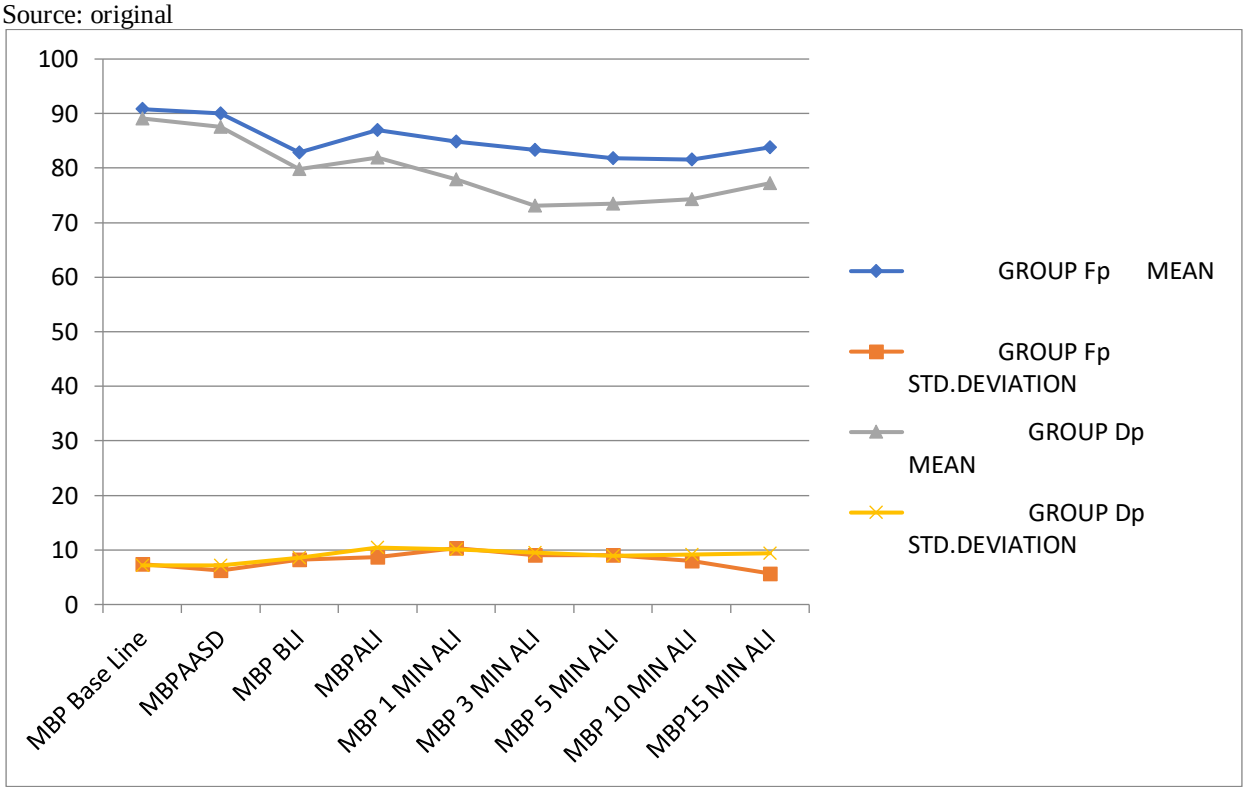
GRAPH 1: HEART RATE IN BOTH GROUPS INTRAOPERATIVLY

Source: original



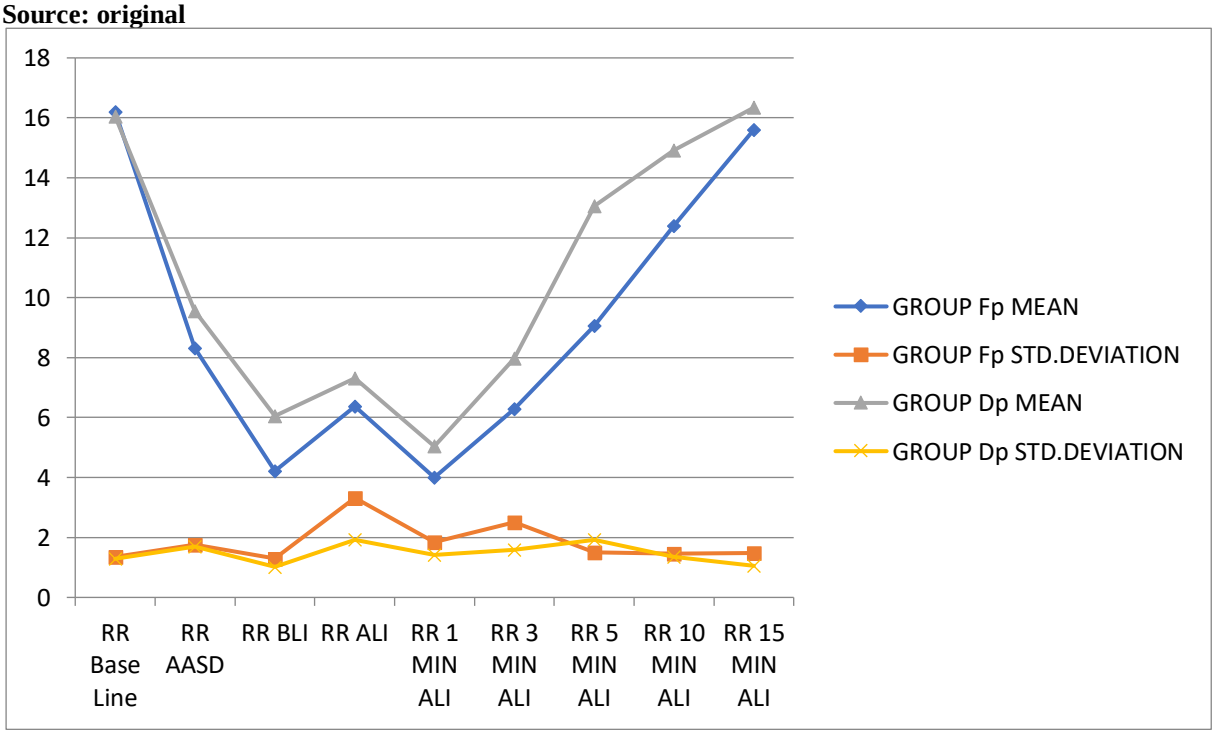
If we see Graph 2, Mean value of MAP for Group Fp was 89.99 ± 6.27 after administration of study drug (AASD), 82.91 ± 8.27 before PLMA insertion (BLI), 86.98 ± 8.65 after PLMA insertion (ALI), 84.81 ± 10.15 at 1 min, 83.37 ± 8.71 at 3 min, 81.88 ± 7.33 at 5 min, 81.56 ± 7.66 at 10 min and 83.83 ± 5.41 at 15 min.In contrast to this, mean value of MAP during intraoperative period for group Dp was 87.46 ± 7.24 after administration of study drug (AASD), 79.85 ± 8.38 before PLMA insertion (BLI), 81.96 ± 10.21 after PLMA insertion (ALI), 77.91 ± 9.65 at 1 min, 73.01 ± 7.59 at 3 min, 73.43 ± 7.32 at 5 min, 74.28 ± 7.16 at 10 min and 77.21 ± 9.00 at 15 min.Group Dp, showed significant fall in MAP with p value < 0.05 (significant) after administration of study drug, after that comparison of mean MAP at each time interval (up to 15 minutes of PLMA insertion) showed significant fall in mean blood pressure in Group Dp when compared to Group Fp with p value < 0.001 (highly significant)(Graph 2).

GRAPH 2: INTRAOPERATIVE MAP IN BOTH THE GROUPS:
Source: original



In comparision to Group Dp, Group Fp showed highly significant fall in mean of respiratory rate after administration of study drug and before PLMA insertion, after insertion of PLMA rise in RR seen in both the groups. After 1 minute of PLMA insertion respiratory rate start raising and reached to base line level after 15 minutes of PLMA insertion in Group Dp but remained below base line level in group Fp. Difference in RR at each time interval after 1 min of PLMA insertion was highly significant as p value is < 0.001(Graph 3).

GRAPH 3: INTRAOPERTIVE RESPIRATORY RATE IN BOTH GROUPS
Source: original



DISCUSSION

Laryngeal mask airway (LMA) is a useful substitute for intubation to maintain the airway.[1-3]Similar to endotracheal intubation, LMA insertion are also associated with inability to put LMA in place, lacrimation, coughing, laryngospasm(in light plane of anesthesia), aspiration (if full stomach) and also changes in hemodynamic response in form of rise in HR and BP. A study conducted by Parasa and Bapat et al[11,12]., propofol was found to be a better induction agent for PLMA insertion. In order to attenuate these responses fentanyl had been used more commonly but now dexmedetomidine is being considered for suppressing stress response. Hence we studied fentanyl and dexmedetomidine for their effects on the ease of insertion of LMA and the hemodynamic changes associated with PLMA insertion. Adequacy of mouth opening and difficult airway assessment was done by the modified Mallampati Grading which was comparable (p =0.40) in both the groups.

It has been found that LMA insertion elicits lesser hemodynamic responses than tracheal intubation, Kunisawa T. et al[13] concluded dexmedetomidine attenuate sympathetic responses to laryngoscopy and intubation. Nillore SS et al[14] concluded that dexmedetomidine 1 mcg/kg as co-induction agent with propofol not only gives excellent overall insertion condition in term of jaw relaxation and hemodynamic stability but also significantly reduces the requirement of induction as well as incremental doses of propofol when compared to Group Fp. We compared incidence of coughing between both the groups and noted higher incidence of coughing in fentanyl group.

One patient in Group Dp and 12 patients in Group Fp required a second attempt for PLMA insertion. After each unsuccessful attempts, an incremental dose of 0.5mg/kg each of propofol was given thus, Group Dp was found to be superior to Group Fp, in terms of first attempt success rate. Patients who required more than two attempts were excluded from the study. This result was similar to study done by surabhi et al[15] who reported that dexmedetomidine along with propofol provides better insertion conditions than that of fentanyl with propofol and it can be used with an advantage for insertion of PLMA during short surgical procedures.

Similar to the finding of Uzumcugil et al.[16], we observed a significant decrease in heart rate in both the groups as compared to the baseline. Group Dp showed greater decrease in heart rate as compared to Group Fp at all the time intervals, however, the episode of bradycardia and requirement of atropine were there in both the groups but those cases were excluded from this study. The administration of a single high dose of dexmedetomidine reduces norepinephrine release by stimulation of presynaptic α-2 adrenoreceptors as much as 92% in young healthy volunteers and the heart rate was decreased[17]. A second mechanism for reducing heart rate during dexmedetomidine may be by increasing vagal tone and reducing sympathetic drive, the reflex heart rate slowing to the pressor stimulus was augmented by dexmedetomidine[18,19]. Fentanyl modulates cardiovascular function, mainly by reducing sympathetic activity[20]. Fentanyl maintains cardiovascular homeostasis mainly via action on the nucleus solitarius, dorsal nucleus of the vagus, nucleus ambiguus and parabrachial nucleus. However, the predominant effect of fentanyl on the heart rate is to produce bradycardia via central vagal nucleus stimulation.

We recorded a fall in SBP, DBP and MAP in the both the groups as compared to the baseline, may be coinduction with propofol would be the reason. Kunisawa[13]and colleagues demonstrated that dexmedetomidine suppresses the decrease in blood pressure due to anesthetic induction with propofol. SBP was found to rise in Group Fp at the time of insertion of PLMA and 1 min after insertion of PLMA and this difference found to be statistically significant with p value <0.05. After 1 min of PLMA insertion SBP found to be in decreasing trend in both groups though the mean SBP in Group Fp was higher than Group Dp. These findings are resembling with study conducted by Prashanth Vadigeri et al.[21]DBP in our study had decreasing trend after induction of patient in both groups. Mean DBP in group Fp was higher in group Dp till the 15 minutes of PLMA insertion and this difference is statistically highly significant. Similar finding observed with MAP in both the groups.Group Dp showed significant fall in MAP after administration of study drug, after that comparison of mean MAP at each time interval (up to 15 minutes of PLMA insertion) showed significant fall in mean blood pressure in group Dp when compared to Group Fp.

The respiratory depression in group Fp was found to be greater than that in group Dp when compared in terms of number of patients developing apnea (20% Vs 3.33 p<0.001). In our study the RR was significantly lower in group Fp compared to group Dp. Similar to finding of apnoea in the study by Jayaram et al[22] there was higher incidence of apnea in fentanyl group in our study too. However, the percentage of patients with apnea in our study was lower than that in former study because we had used smaller induction dose of propofol. It was observed that there was no significant change in SpO_2 at any time in both the groups during or after PLMA insertion. In our study we found incidence of apnoea was significantly higher in group Fp than Group Dp. Duration of apnoea was found to be prolonged in Fp group a well-known fact behind this is dexmedetomidine does not produce respiratory depression.[23]

Though we had included more patients than previous studies but limitation of our study was that we did not include a control group in which propofol was used alone, nonavailability of BIS monitor(for assessment

of the depth of anesthesia for PLMA insertion) and PLMA insertion conditions may be assessed more accurately by the effect-site concentration of propofol using target controlled infusion which could not be done during our study.

There was no evidence of gastric regurgitation in both groups. No trauma to lips, tongue and teeth was found. The dose of propofol when used alone is neither satisfactory for smooth insertion of PLMA nor from hemodynamic point of view[24]. Thus the dexmedetomidine, used in a dose of 1 mcg/kg gives better insertion conditions, no respiratory depression and hemodynamic stability compared to fentanyl used in a dose of 1 mcg/kg.

CONCLUSION

We concluded that addition of dexmedetomidine to propofol provides superior insertion condition and good jaw mobility for ease of insertion of PLMA in the first attempt as compared to fentanyl. Dexmedetomidine - propofol also provides better hemodynamic responses with minimal or no intraoperative and postoperative complication. So dexmedetomidine appears to be a better alternative to fentanyl to co-administer with propofol for PLMA insertion.

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