ANAESTHESIA, PAIN & INTENSIVE CARE
www.apicareonline.com

ORIGINAL ARTICLE

A comparative evaluation of use of dexmedetomidine versus fentanyl for anesthesia induction with propofol for insertion of laryngeal mask airway

Shobhana Gupta, MD[1], Hina N. Gadani, MD, DA[2], Priyanka R. Shah, MBBS[3]

[1]Professor and HoD; [2]Associate Professor; [3]DNB resident

Department of Anaesthesiology, GMERS Medical College, Gandhinagar, Gujarat (India)

Correspondence: Dr Hina Niraj Gadani, 1/T, F/1, Haridham Enclave, B/H Raysan Petrol Pump, Koba-Gandhinagar highway, Raysan, Gandhinagar, Gujarat-382007 (India); Phone: +91-8690501339; E-mail: hinagadani@gmail.com

Received: 21 Nov 2017
Reviewed: 8 Jun 2018
Corrected: 21 Jun 2018
Accepted: 21 Jun 2018

ABSTRACT

Background: Airway management is one of the prime concerns for anesthesiologists. Dr Archibald Brain invented a supraglottic airway device - "Laryngeal Mask Airway" (LMA) which keeps a patient's airway open during anesthesia. When propofol is used along with either fentanyl or dexmedetomidine, it provides stable cardiorespiratory condition, diminished airway reflexes and smooth insertion of LMA.

Aim: Aim of this study is to compare the hemodynamic and respiratory parameters, apnea time and patient's response to LMA insertion between dexmedetomidine-propofol and fentanyl-propofol combinations as a primary outcome. Secondary outcome is to observe any side effect in intraoperative and postoperative period associated with the study drugs.

Methodology: Prospective, double blind, randomized clinical study in 140 healthy patients of both sex, having ASA grade I and II was carried out. Patients were demographically similar. Patients were randomized to receive either intravenous (i.v.) dexmedetomidine(1 µg/kg) –propofol(2mg/kg) injections- Group D (n = 70) or i.v. fentanyl(1 µg/kg)-Propofol(2mg/kg) injections- Group F (n = 70) for LMA insertion. Parameters like heart rate(HR), respiratory rate (RR), systolic blood pressure(SBP), diastolic blood pressure(DBP), mean arterial blood pressure(MAP), oxygen saturation(SpO2) were recorded before induction, 30 seconds after induction, 1, 3, 5, 10, 15, 30, 45 and 60 minutes (min.) after insertion of LMA. Apnea time was noted. Patient's responses to LMA insertion such as jaw mobility, coughing, gagging or any movement were noted. Other side effects were also observed.

Results: In Group-D HR, SBP, DBP and MAP showed significant decrease throughout the study period following LMA insertion, while in Group-F there was rise in the above parameters noted immediately after LMA insertion. In Group-D spontaneous respiration was well preserved and apnea time was significantly shorter compared to Group-F. LMA insertion conditions were acceptable in patients with both the Groups. Incidence of bradycardia and hypotension was higher in the patients of Group-D while incidence of nausea and vomiting was present in two patients of Group-F.

Conclusion: Dexmedetomidine 1 µg/kg with propofol 2mg/kg i.v. provides beneficial effect in attenuation of hemodynamic response to LMA insertion, better preservation of spontaneous respiration and acceptable LMA insertion conditions as compared to fentanyl 1 µg/kg with propofol 2mg/kg i.v. without major side effects.

Key words: Injection (inj.) propofol, inj. dexmedetomidine, inj. fentanyl, laryngeal mask airway, LMA insertion

Citation: Gupta S, Gadani HN, Shah PR. A comparative evaluation of use of dexmedetomidine versus fentanyl for anesthesia induction with propofol for insertion of laryngeal mask airway. Anaesth Pain & Intensive Care 2018;22(2):165-173

INTRODUCTION

Airway management is one of the prime concerns for anesthesiologists and inability to secure the airway can cause catastrophic results.[1] The best way of securing airway is by tracheal intubation. However, it is associated with many complications. In 1981, Dr Archibald Brain- A british anesthesiologist invented a supraglottic airway device named "Laryngeal Mask Airway" (LMA) which keeps a patient's airway open during anesthesia.[2] It has an airway tube that connects to an elliptical mask with a cuff. For moderate to minor surgical procedures LMA is an alternative to endotracheal tube. It is widely used and specialised LMA exist. It allows both spontaneous as well as positive pressure ventilation. Insertion of LMA requires lighter plane of anesthesia than that is required for endotracheal intubation, adequate mouth opening and minimal upper airway reflexes such as coughing, gagging or laryngospasm.[3, 17] The search to find the optimum anesthesia to provide excellent conditions for LMA insertion has been going on. Various intravenous (i.v.) and inhalational induction agents have been used.[4, 5] Since the time required for LMA insertion was longer with inhalational anesthetics, i.v. agents have been preferred. Propofol has been preferred the most because of its potential suppressor effects on upper airway reflexes. When used alone without premedication, propofol causes cardiorespiratory depression and also it lacks analgesic properties.[6, 17] In order to decrease the adverse effects of propofol, fentanyl[7] and now newer α2-agonists such as dexmedetomidine or muscle relaxants were added to reduce the propofol dose requirement. Muscle relaxants were not found to be effective and even found to increase the risk of aspiration.[8] Fentanyl is a short acting synthetic opioid agonist, 75-125 times more potent than morphine. It is most widely studied as an adjunct to anesthetic agent due to its cardiovascular stability, but associated with nausea, vomiting and respiratory depression.[9,10,11] Unfortunately, fentanyl increased the incidence and duration of apnoea. Dexmedetomidine, a highly selective α2- adrenoceptor agonist, has been shown to have sedative and analgesic properties, anxiolysis and sympatholysis via the receptors located in blood vessels, sympathetic terminals, locus ceruleus and spinal cord without producing respiratory depression.[11,12,13] Dexmedetomidine, even when used at supramaximal plasma levels, has been found to be clinically safe for respiration.[14] It was also shown to diminish airway and circulatory responses during intubation and extubation and facilitates smooth insertion of LMA,[15,16,17] rendering this compound especially suitable for anesthesia and the perioperative period.[4]

The current study was undertaken to compare the hemodynamic stability, respiratory condition, apnea time and patient's response to LMA insertion between dexmedetomidine-propofol and fentanyl-propofol combinations as a primary outcome. Secondary outcome was to observe any side effect in intraoperative and postoperative period associated with the study drugs.

METHODOLOGY

Prospective, double blind, randomized clinical study was undertaken after approval from the institution's ethical and scientific committee. Study was conducted at GMERS general hospital, Gandhinagar between December 2015 to December 2016.

Assuming the number of patients 1000 per year as per previous hospital records, with confidence interval of 12 and confidence level of 95%, calculated sample size was 63 patients. Assuming 10% of non-response, 70 patients were selected from each group.

140 healthy patients of both sex, having ASA grade I and II, aged 18-70 years, weighing 30-80 kg were selected for the study. Patients undergoing various elective minor surgical procedures under general anesthesia were recruited for the study. Patients having ASA grade III-IV, pregnant patients, smokers, patients undergoing oral and nasal surgeries, having inadequate mouth opening, patients with risk of aspiration, poorly controlled hypertension, respiratory compromises, neuromuscular diseases, hematological disorders and severe hepatic or renal insufficiency, patients allergic to any of the study drug were excluded from the study. After taking written informed consent patients were randomly allocated by a computer generated table of random numbers by a person blinded to the procedure into two groups of 70 each as Group-D (dexmedetomidine-propofol group) (n = 70) and Group-F (fentanyl-propofol group) (n = 70).

A day before surgery, a detailed pre-anesthetic checkup was carried out of history, general and systemic examination and routine investigations. All patients were asked to restrict fluids and solids by mouth at least 6 hours prior to surgery. All patients were given tablet alprazolam 0.25 mg a night before surgery. On arrival in the operation room multipara monitor was attached and baseline HR, noninvasive SBP, DBP, MAP, SpO_2 and electrocardiogram (ECG) were

recorded and monitoring was initiated. Patient was preloaded with 10 ml/kg body weight of ringer lactate solution over 15-20 min through good intravenous (i.v.) line. I.V. premedication with inj. glycopyrrolate 0.2 mg, ranitidine 1 mg/kg, ondansetron 0.08 mg/kg and midazolam 0.04 mg/kg body weight just before the procedure was given.

Group-D patients were given inj. dexmedetomidine 1 μg/kg diluted in 10 ml normal saline i.v. slowly over 2 min. Group-F patients were given inj. fentanyl 1 μg/kg diluted in 10 ml normal saline i.v. slowly over 2 min. In both the groups 30 sec later, inj. propofol 2 mg/kg was given i.v. over 30 sec for induction without any neuromuscular blocking agents. 90 sec after inj. propofol LMA was inserted by an experienced anesthesiologist who was blinded to the choice of induction and adjuvant anesthetic agents. The correct LMA placement was confirmed with the expansion of the chest wall with bag compression, with slight outward movement of the tube with LMA cuff inflation. LMA insertion conditions were evaluated by the same anesthesiologist. From the induction to insertion of LMA, patients were given 100% oxygen via face mask and ventilated if apneic. HR < 45 was considered as bradycardia and was treated with inj. atropine 0.01 mg/kg. i.v. If any movement occurred before or after LMA insertion, inj. propofol 0.5 mg/kg was administered and waited for 30 sec before next attempt at LMA placement. Baseline parameters like HR, RR, SBP, DBP, MAP, SpO_2 were recorded before induction, 30 sec after induction, 1, 3, 5, 10, 15, 30, 45 and 60 min after insertion of LMA. Apnea time that is the time from last spontaneous breath after propofol administration to first spontaneous breath of the patient was noted. Patient's response to LMA insertion such as jaw mobility, coughing, gagging or any movement were noted and scored according to the scoring system modified by Muzi et al.[18] In each category, scores ≤2 was considered optimum for LMA insertion. Other events such as spontaneous respiration, breath holding, expiratory stridor and lacrimation were also monitored.

Jaw mobility graded as-

1- Fully relaxed
2- Mild resistance
3- Tight but opens
4- Closed

Coughing/movements graded as-

1- None
2- Two or more coughs
3- Three or more coughs
4- Bucking/movement

Data obtained from observations were entered and analysed in EPI info 7. Continuous variables were expressed in mean and standard deviation. Categorical variables were expressed in percentages. t-test and chi square test were applied accordingly. P value < 0.05 was considered statistically significant and < 0.001 was considered highly significant.

RESULTS

There was no significant differences in patients' age, weight or sexes in the two groups, e.g. p = 0.34, 0.69 and 1.00 respectively (Table 1).

Table 1: Demographic data

Groups	Number of patients (n)	Sex(M:F)	Age in years (mean ± SD)	Weight in kilograms (mean ± SD)
Group D	70	39:31	34.18 ± 15.36	53.70±6.87
Group F	70	38:32	36.54±13.99	53.24±6.92
Total	140	77:63		
P value		1.00 NS	0.34 NS	0.69 NS

NS-Not significant

Table 2: Comparison of heart rate (per min)

Time (in minutes)	Group D		Group F		p value	Remark
	Mean	SD	Mean	SD		
Baseline (T_0)	88.02	5.67	86.67	6.75	0.20	NS
LMA insertion (T_L)	85.97	7.04	86.95	6.55	0.39	NS
1 min (T_1)	79.64	7.43	94.61	8.41	0.0001	HS
3 min (T_3)	71.71	8.00	92.90	5.98	0.0001	HS
5 min (T_5)	67.08	5.91	84.00	8.22	0.0001	HS
10 min (T_{10})	65.10	6.29	78.90	7.41	0.0001	HS
15 min (T_{15})	65.31	5.18	78.77	6.93	0.0001	HS
30 min (T_{30})	71.80	5.44	79.32	6.63	0.0001	HS
45 min (T_{45})	74.72	6.24	81.71	6.90	0.0001	HS
60 min (T_{60})	75.41	5.93	82.85	6.54	0.0001	HS

NS-Not significant, HS- Highly significant

There was no significant differences in baseline heart rates in the two groups (p = 0.20) and on LMA insertion (p = 0.39), but highly significant differences were noted at subsequent time intervals (p = 0.0001) (Table 2). In our study 5 patients in Group-D developed bradycardia but did not need inj. atropine. In Group-F, none of the patients had significant bradycardia.

Table 3: Comparison of systolic blood pressure (mmHg)

Time (in minutes)	Group D		Group F		p value	Remark
	Mean	SD	Mean	SD		
Baseline (T_0)	131.64	10.04	128.86	9.56	0.09	NS
LMA insertion (T_L)	127.16	10.41	130.07	9.64	0.08	NS
1 min (T_1)	123.53	10.33	133.86	10.24	0.0001	HS
3 min (T_3)	119.47	9.23	135.93	11.22	0.0001	HS
5 min (T_5)	115.21	8.24	127.23	10.57	0.0001	HS
10 min (T_{10})	111.91	6.43	121.24	9.86	0.0001	HS
15 min (T_{15})	111.86	5.97	117.87	8.75	0.0001	HS
30 min (T_{30})	119.40	7.36	120.67	8.47	0.34	NS
45 min (T_{45})	125.40	8.08	122.74	8.30	0.06	NS
60 min (T_{60})	126.71	8.79	124.81	7.94	0.18	NS

NS-Not significant, HS-Highly significant

Table 4: Comparison of diastolic blood pressure (mm of Hg)

Time (in minutes)	Group D		Group F		p value	Remark
	Mean	SD	Mean	SD		
Baseline (T_0)	84.75	8.44	85.31	8.05	0.68	NS
LMA insertion (T_L)	80.00	8.88	85.70	6.75	0.0001	HS
1 min (T_1)	76.77	7.90	88.21	6.82	0.0001	HS
3 min (T_3)	74.17	7.09	89.68	6.44	0.0001	HS
5 min (T_5)	71.41	6.16	83.28	6.58	0.0001	HS
10 min (T_{10})	68.24	5.22	78.08	6.22	0.0001	HS
15 min (T_{15})	68.30	5.97	75.98	5.08	0.0001	HS
30 min (T_{30})	73.70	5.72	78.18	4.81	0.0001	HS
45 min (T_{45})	76.92	6.17	79.58	5.08	0.006	S
60 min (T_{60})	79.34	6.81	80.34	4.99	0.32	NS

NS-Not significant, HS-Highly significant

Table 5: Comparison of mean arterial blood pressure (mmHg)

Time (in minutes)	Group D		Group F		p value	Remark
	Mean	SD	Mean	SD		
Baseline (T_0)	100.73	8.98	99.75	7.95	0.98	NS
LMA insertion (T_L)	95.68	8.84	100.44	7.41	0.0001	HS
1 min (T_1)	92.30	7.72	103.49	7.49	0.0001	HS
3 min (T_3)	89.21	6.95	105.11	7.45	0.0001	HS
5 min (T_5)	86.15	6.30	97.90	7.26	0.0001	HS
10 min (T_{10})	82.84	5.04	92.45	6.99	0.0001	HS
15 min (T_{15})	82.85	5.14	89.92	5.99	0.0001	HS
30 min (T_{30})	88.88	5.39	92.37	5.66	0.0004	HS
45 min (T_{45})	93.02	6.16	94.00	5.85	0.34	NS
60 min (T_{60})	95.77	6.53	94.75	5.77	0.33	NS

NS-Not significant, HS-Highly significant

Differences in systolic blood pressure (mm of Hg) readings were not statistically significant at baseline (T0), on LMA insertion (TL), and at 30, 45 and 60 min (p = 0.09, 0.08, 0.34, 0.06 and 0.18 respectively). But highly significant differences were noted at other time intervals (p = 0.0001) (Table 3).

Differences in diastolic blood pressure (mmHg) readings were not statistically significant at baseline (T0), and on 60 min (T60) (p = 0.68 and 0.32 respectively). But significant difference was recorded at T45 (p = 0.006), and highly significant differences were noted at other time intervals (p = 0.0001) (Table 4).

Similarly, differences in mean blood pressure (mmHg) readings were not statistically significant at baseline (T0), and at 45 min (T45) and 60 min (T60) (p = 0.98, 0.34 and 0.33 respectively). But highly significant differences were noted at other time intervals (p = 0.0001; 0.0004) (Table 5). Hypotension was noted in 3 patients of Group-D intra operatively and it was treated successfully with i.v. fluids only.

Regarding any effect on respiratory rates, no statistically significant differences were noted at baseline (T0), and at 60 min (p = 0.51 and 0.35 respectively). There was significant difference at T45 (p = 0.002), but highly significant differences were noted at other time intervals (p 0.0001) (Table 6).

Table 6: Comparison of respiratory rate (per min)

Time (in minutes)	Group D		Group F		p value	Remark
	Mean	SD	Mean	SD		
Baseline (T_0)	15.51	1.10	15.64	1.43	0.51	NS
LMA insertion (T_L)	11.91	1.03	10.10	1.11	0.0001	HS
1 min (T_1)	10.22	0.95	7.62	1.39	0.0001	HS
3 min (T_3)	10.38	0.93	8.31	1.42	0.0001	HS
5 min (T_5)	13.34	0.77	10.31	1.46	0.0001	HS
10 min (T_{10})	17.65	1.08	11.67	0.91	0.0001	HS
15 min (T_{15})	19.91	1.44	12.27	0.83	0.0001	HS
30 min (T_{30})	16.74	1.51	12.95	0.92	0.0001	HS
45 min (T_{45})	15.54	1.18	14.98	0.93	0.002	S
60 min (T_{60})	15.07	0.98	15.24	1.16	0.35	NS

NS-Not significant, HS- Highly significant, S- Significant

Table 7: Observed parameters for LMA insertion conditions

Parameter	Score	Group D	Group F	p value
Jaw mobility	Fully relaxed-1	68	66	0.63
	Mild resistence-2	2	2	NS
	Tight, but opens-3	0	2	
	Closed-4	0	0	
Coughing/ Movements	None-1	66	63	
	Two or more coughs-2	3	4	1.00
	Three or more coughs-3	1	2	NS
	Bucking/ movements-4	0	1	
Other Events	Spontaneous respiration	58	36	0.0002
	Breath holding	12	34	S
	Expiratory stridor	0	0	
	Lacrimation	0	0	

NS-Not significant, S- Significant

Data regarding observed parameters for LMA insertion conditions in both groups are given as Table 7. Breath holding was significantly more in Group-F as compared to Group-D, e.g. 34 vs. 12 respectively. Other parameter are equivalent in two groups.

Baseline SpO_2 was comparable in both the groups. ($p > 0.05$) It was observed that there was no significant change in SpO_2 at any time in both the groups during or after LMA insertion.

Postoperative nausea was observed in 2 patients of Group-F, treated with inj. ondansetron 4 mg i.v. None of the patients in both the groups had respiratory depression intraoperatively or postoperatively. Apnea was 237.78 ± 21.36 sec vs. 208.74 ± 15.69 sec in Group-F and Group-D ($p = 0.0001$; highly significant) respectively.

DISCUSSION

Apart from adequate depth of anesthesia to suppress the airway reflexes, factors which affect LMA insertion are mouth opening, MPG grade of the patient and jaw relaxation.[19] Induction of general anesthesia and LMA insertion are associated with changes in cardiovascular variables. In order to attenuate these responses fentanyl had been used more commonly but now dexmedetomidine is being considered.[20].

In our study the patients in both the groups were demographically similar.

Baseline mean HR was comparable in both the groups. The decrease in HR from the baseline towards the end of the study period was not significant in the Group-F but it was significant in Group-D. S Jayaram et al.[17] observed that 10 min. after LMA insertion, there was a significant difference in the mean HR between the two groups and the difference was statistically significant, greater fall in HR in Group-D compared to group F. The rise in HR was higher in fentanyl group as compared to dexmedetomidine group and this finding was similar to study by Surbhi Lande et al. [20.] In a similar study, Shalaka et al.[21] observed that HR decreased in both the study groups from baseline after infusion but there was a transient rise in HR during LMA insertion followed by a reduction below the baseline and rise in HR was higher in fentanyl group as compared to dexmedetomidine group. The administration of a single high dose of dexmedetomidine reduces norepinephrine release by stimulation of presynaptic alpha 2 adrenoreceptors as much as 92% in young healthy volunteers and the HR was decreased.[22] A second mechanism for reducing HR during dexmedetomidine may be by increasing vagal tone and reducing sympathetic drive, the reflex HR slowing to the pressor stimulus was augmented by dexmedetomidine.[13,23] Fentanyl modulates cardiovascular function, mainly by reducing sympathetic activity.[24] 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.[23] Fentanyl efficacy in controlling hormonal manifestations of stress response and

blunting of sympathetic response is dose dependent.[25] Although initially after LMA insertion, we observed mild increase in the HR upto 10% in group F. This might probably be because insertion of a bulky device like LMA could have caused some sympathetic response negating the effect of fentanyl on HR.[19]

Baseline mean SBP was comparable in both the groups. We observed decrease in the baseline mean SBP upto 15% following loading dose of dexmedetomidine which got stabilized by 30 min. Baseline mean SBP in group F significantly increased at 1st and 3rd min. after LMA insertion in contrast to Group-D in our study. The difference was statistically highly significant between the two groups. Our findings match with the study done by Ramswamay AH et al.[19] and Surabhi et al.[20] There was significant rise in the baseline SBP in group F at 1st min post LMA insertion in contrast to Group-D where there was no significant change. The hyperdynamic response to LMA insertion and skin incision was also not observed in Group-D. In case of fentanyl, the hyperdynamic response to the surgical stimuli was observed and there was initial rise in the SBP compared to baseline mean SBP. Our results are also consistent with other studies showing that dexmedetomidine provides hemodynamic stability and blunts sympathetic responses during critical moments of surgery.[13,15,22,26] Only 3 patients of Group-D in our study developed significant hypotension (20% decrease from baseline mean SBP) and they recovered by augmentation of i.v. fluids only. Human studies that have used intravenous boluses of dexmedetomidine show decreases in BP and cardiac output after small boluses (0.25–1 mg/kg) [21]Bradycardia and hypotension by dexmedetomidine can be counteracted by using slow infusion over 15-20 min. and by adequate preloading.[11]

The baseline mean DBP and MAP was comparable in both the groups. Patients of group-D showed fall in DBP and MAP from 1st min onward after LMA insertion, in contrast to group-F observations which showed rise in the DBP and MAP during/after LMA placement. The difference was statistically highly significant between the two groups at 1st and 3rd min. for DBP and MAP. Transient rise in the DBP has been observed primarily during the loading dose of dexmedetomidine in association with the initial peripheral vasoconstrictive effect due to peripheral alpha 2 b adrenoreceptors on vascular smooth muscles which leads to increase in the systemic vascular resistance and results into rise in the DBP and MAP. Treatment of the transient hypertension has generally not been necessary, although attenuated by a slow infusion over 10 min.[13] Dexmedetomidine inhibits release of noradrenaline and central sympathetic activity, therefore, can decrease BP and HR.[11] Plasma noradrenaline concentration is markedly reduced with dexmedetomidine.[4] Biphasic effect of dexmedetomidine is caused by the inhibition of the central sympathetic outflow overriding the direct stimulant effect.[11,13] In our case the initial rise in DBP and MAP in Group-F was noted because of the sympathetic response to the bulky device like LMA, although fentanyl is a cardiostable lipid.

The basal RR was comparable in both the groups. After LMA insertion patients of both the groups showed transient decrease in the RR, more evident with group-F. Statistically highly significant difference was found between two groups upto 30 min. ($p < 0.0001$) There was increase in the RR in group-D 10 min. onwards which gets stabilized towards the end of the procedure. Ramswamay AH et al[19] observed statistically significant increase in the RR in Group-D from 5 min. onwards after insertion of LMA which got stabilized at 22/min. by 15 min. In Group-F there was no increase in the RR further, which got stabilized at 12/min. by 15 min. after the insertion of LMA.[19] Our study co-relates with the studies done by Jayaram et al.[17] Surbhi et al.[20] and Shalaka et al.[21] Lawerence and colleagues [26] studied effects of 2 μg/kg dexmedetomidine and reported no change in respiratory rate. In group-D, 58 patients had spontaneous respiration and 12 patients showed breath holding. While in group-F, 36 patients had spontaneous respiration and 34 patients showed breath holding. The difference found was statistically significant ($p < 0.05$) suggesting better preservation of respiration in group-D. S Jayaram et al.[17] Ramswamay et al.[19] and Shalaka et al.[21] also noted better preservation of spontaneous respiration in group-D in their respective studies. Hypercapnic arousal phenomenon remains intact by dexmedetomidine, thus its sedation mimicking the natural sleep. The respiratory effect of dexmedetomidine is because one of its action on locus ceruleus, which is known to play a role in both respiratory control and sleep modulation. Dexmedetomidine is unique among sedatives as it is clinically safe from a respiratory point of view, even during doses high enough to cause unresponsiveness to vigorous stimulation and exhibiting hypercarbic arousal phenomenon similar during natural sleep.[12,19] Fentanyl is a potent respiratory depressant through mu2 receptors leading to a direct depressant effect on brainstem ventilation centers leading to prolonged pauses between breaths. It also decreases respiratory responses to carbon dioxide.[10]

In group-D patients, mean apnea time noted was

208.74 ± 15.69 sec. While in group-F patients, it was 237.78 ± 21.36 sec. The difference was statistically highly significant ($p < 0.001$). Similar findings were noted by Ramswamay AH et al.[19] In their study the duration of apnea was longer in Group-F (290 s) than in Group-D (227 s). They noted that it might be because of potentiation of the depressant effect of propofol by fentanyl on respiration. The apnea developed in patients of Group-D was probably because of the depressant effect of propofol. However, the respiratory depressant effect of propofol was not potentiated by dexmedetomidine and the apnea time was significantly shorter as compared to fentanyl. Goh et al.[7] S Jayaram et al.[17] and Shalaka et al.[21] also noted similar findings in their respective studies.

For jaw mobility in our study, only 2 patients from group-D showed mild resistance to LMA insertion while in group-F, 2 patients had mild resistance while 2 patients had tight jaw and required additional dose of inj. propofol. The difference found was statistically not significant ($p > 0.05$) and most of the patients in both the groups provided ideal LMA insertion conditions. In the study conducted by S Jayaram et al.[17] 2 patients from each group had tight jaw, while Ramswamay et al.[19] noted only 1 patient from group-F had tight jaw. Wong CM et al.[27] found that a standard fentanyl dose of 1μg/kg coadministered with propofol 2.5mg/kg provided optimal conditions in only 65% of cases and reported a higher incidence of resistance to mouth opening with use of fentanyl. Our study also showed higher incidence of jaw tightening with fentanyl group. It can be because of one of the side effects seen with opioids is muscle rigidity.[10]

Amongst 70 patients of group-D, 66 patients had no coughing, 3 patients showed 2 or more coughs and only 1 patient had 3 or more coughs. In group-F, 63 patients had no coughing, 4 patients had 2 or more coughs, 2 patients had 3 or more coughs and only 1 patient had bucking and required additional dose of inj. propofol and required reinsertion of LMA. The difference found was statistically not significant and most of the patients in our study provided acceptable LMA insertion conditions. The number of severe coughs per patient in the dexmedetomidine group was significantly decreased compared with the control group ($P < 0.05$) in the study conducted by Guler G et al.[16] In the study conducted by Ramswamay et al.[19] 1 patient from group-D and 4 patients from group-F had bucking and all 5 of them required reattempt for LMA placement. Wong et al.[27] and Phua WT et al.[28] also reported that higher doses of fentanyl were associated with a notable increase in the incidence of coughing. Liang HE et al.[29] showed that i.v. dose of dexmedetomidine (0.5μg/kg or 1 μg/kg) given immediately before administration of i.v. fentanyl (4 μg/kg) significantly reduces the fentanyl induced cough. This may be the explanation for the lower incidence of coughing on LMA insertion in dexmedetomidine group.[20] The exact cause of Reflex coughing with fentanyl is unclear but is thought to be due to imbalance between sympathetic and vagal innervation of the airways and/or stimulation of juxtacapillary irritant receptors.[10, 28]

Benefits of the current study: Stress response to endotracheal intubation is avoided in minor surgical procedures by insertion of LMA. Fentanyl is an opioid agonist and falls under the category of controlled drugs. It has administrative liability of special storage and distribution, maintain records and drug abuse. At some centers the major barrier to access/ availability to fentanyl is shortage of supply due to complicated regulations, while dexmedetomidine is easily available by hospital authority. Fentanyl is used to blunt the stress responses, but it is associated with nausea, vomiting, and respiratory depression.[11] while dexmedetomidine blunts the sympathetic responses without significant respiratory depression. Thus this study is beneficial to the consultants where limited availability of opioids, as well as to the patients to avoid side effects of opioids. Our study has some limitations such as it has not included control group that is, propofol alone for insertion of LMA, as it would be unethical because the propofol was reported several times, to be inadequate for LMA insertion when used alone and the increase in dose to make it adequate were reported to be unsafe for hemodynamics and respiration. We have not used any inhalational agents from induction till insertion of LMA, as it may affect hemodynamics, respiration and LMA insertion conditions. Study was on single dose of dexmedetomidine and fentnyl and we have not included the study concerned with its sedative and analgesic effects. Studies regarding different doses of the drugs and their sedative and analgesic effects as i.v. injection and infusion may be needed further in future. We have not studied the total requirement of inj. Propofol with the study drugs. Only experienced users inserted LMA and the results may not be applicable to less experienced personnel.

Our results showed that the effects on hemodynamics, respiration and LMA insertion conditions were more desirable in Group-D than Group-F. Propofol in combination with fentanyl has been used but it was associated with less hemodynamic stability, more apnea time and respiratory depression and more coughing with tight jaw comparable to

dexmedetomidine –propofol combination. So dexmedetomidine appears to be a potential alternative to fentanyl to co-administer with propofol for LMA insertion.

CONCLUSION

Fentanyl and dexmedetomidine both provide stable hemodynamics, diminished airway reflexes and smooth insertion of LMA along with propofol, but dexmedetomidine is superior to fentanyl in maintaining stable hemodynamics, preserving respiration and providing better LMA insertion conditions. So dexmedetomidine appears to be a potential alternative to fentanyl to co-administer with propofol for LMA insertion.

Source of support: Nil
Conflict of interest: Nil
Authors' contribution:
SG: Concept, overall supervision of the study, guide to the study, manuscript editing
HG: Concept, literature search, conduct of the study, guide and supervision of the study, manuscript writing and editing
PS: Literature search, conduct of the study, statistical analysis

REFERENCES

1. Sood J. Laryngeal mask airway and its variants. Indian Journal of Anesthesiology2005;49:275-280.
2. Brimacombe J, von Goedecke A, Keller C, Brimacombe L, Brimacombe M. The laryngeal mask airway Unique versus the Soft Seal laryngeal mask: a randomized, crossover study in paralyzed, anesthetized patients. [PubMed]
3. Brimacombe J. Anatomy. In: Laryngeal mask anesthesia: principles and practice. 2nded.2005;pp. 23-26.
4. Khanduja S, Ohri A, Panwar M. Dexmedetomidine decreases requirement of thiopentonesodium and pentazocine followed with improved recovery in patients undergoing laparoscopic cholecystectomy. J AnaesthesiolClinPharmacol. 2014;30(2):208-12. doi: 10.4103/0970-9185.130022. [PubMed][Free full text]
5. Patel MG, Swadia VN, Raghavendra S. Comparison of propofol and sevoflurane forinsertion ofPLMA.J AnaesthClinPharmacol. 2010; 26(1):74-78. cügil F, Canbay O, Celebi N, Karagoz A, Ozgen S.Comparison Of Dexmedetomidine–Propofol Vs. Fentanyl–Propofol For Laryngeal MaskInsertion. Eur J Anaesthesiol. 2008; 25(8): 675-680.doi: 10.1017/S0265021508004213[PubMed]
6. Uzümcügil F, Canbay O, Celebi N, Karagoz A, Ozgen S.Comparison Of Dexmedetomidine–Propofol Vs. Fentanyl–Propofol For Laryngeal MaskInsertion. Eur J Anaesthesiol. 2008; 25(8): 675-680.doi: 10.1017/S0265021508004213[PubMed]
7. Goh PK, Chiu CL, Wang CY, Chan YK, Loo PL. Randomised double-blind comparisonof ketamine-propofol, fentanyl-propofol and propofol-saline on haemodynamics andlaryngeal mask airway insertion conditions. Anaesth Intensive Care. 2005;33(2):223[PubMed]
8. Hemmerling TM, Beaulieu P, Jacobi KE, Babin D, Schmidt J. Neuromuscular Blockade Does Not Change The IncidenceOr Severity Of PharyngolaryngealDiscomfort After LMA Anesthesia. Can J Anesth. 2004;51(7): 728-732. [PubMed]
9. Hussain AM, Sultan ST. Efficacy of fentanyl and esmolol in the prevention ofhaemodynamic response to laryngoscopy and endotracheal intubation. J ColPhysicians Surg Pak. 2005;15(8):454-7.[PubMed]
10. Pamela Flood, James Rathmell, Steven snafer. Chapter 7 Opioid Agonists andAntagonists.Stoelting's Pharmacology & Physiology in Anesthetic Practice.5th edition.2015.p.222-225.Wolters Kluwer (India) Pvt.Ltd. New Delhi.
11. Kataria AP, Attri JP, Kashyap R, Mahajan L. Efficacy of dexmedetomidine andfentanylon pressor response and pneumoperitoneum in laproscopic cholecystectomy.AnesthEssays Res.2016;10:446-50.[PubMed][Free full text]
12. Hsu YW, Cortinez LI, Robertson KM, Keifer JC, Sum-Ping ST, Moretti EW,et al. Dexmedetomidine Pharmacodynamics: Part I: CrossoverComparisonof the Respiratory Effects of Dexmedetomidine and Remifentanil in HealthyVolunteers. Anesthesiology. 2004;101(5):1066-1076.[PubMed][Free full text]
13. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The Effects of Increasing Plasma Concentrations of Dexmedetomidine in Humans. Anesthesiology. 2000;93(2):382-394. [PubMed][Free full text]
14. Maroof M, Khan RM, Jain D, Ashraf M.Dexmedetomidine Is A UsefulAdjunct For Awake Intubation. Can J Anesth. 2005;52(7):776-777.DOI: 10.1007/BF03016576. [PubMed]
15. Guler G, Akin A, Tosun Z, Eskitascoglu E, Mizrak A, Boyaci A. Single-dosedexmedetomidine attenuates airway and circulatory reflexes during extubation. ActaAnesthesiol Scand. 2005;49(8):1088-91.[PubMed]
16. Guler G, Akin A, Tosun Z, Ors S, Esmaoglu A, Boyaci A.Single-Dose Dexmedetomidine Reduces Agitation

And Provides Smooth Extubation After PediatricAdenotonsillectomy. PediatrAnesth.2005;15(9):762-766. [PubMed]
17. Jayaram A, Janaki Subhadra P, Rao MH. Comparison of dexmedetomidine combined with propofol Vs fentanyl combined with propofol for laryngeal mask insertion.JClinSci Res. 2014;3:228-36. DOI: http://dx.doi.org/10.15380/2277- 5706.JCSR.13.032.
18. MuziM, Robinson BJ, Ebert TJ, O'Brien TJ.Induction of AnesthesiaandTracheal Intubation with Sevoflurane in Adults. Anesthesiology. 1996;85(3):536-543. [PubMed] [Free full text]
19. Ramaswamy AH,Shaikh SI. Comparison of dexmedetomidine-propofol versus fentanyl-propofol for insertion of laryngeal mask airway. JAnaesthesiol linPharmacol.2015;31(2):217-20. doi: 10.4103/0970-9185.155152. [PubMed] [Free full text]
20. SurabhiA. LandeC. P. Gadkari, A.R. Bhure, SobhanAich. Comparison ofDexmedetomidine Propofol Versus Fentanyl-Propofol for conditions of Laryngeal MaskAirway Insertion in ElectiveSurgeries. J Evol Med Dental Sci. 2014;3(15):4042-4051. DOI:10.14260/jemds/2014/239
21. Nellore SS,Waychal AD, Rustagi PS.ComparisonofDexmedetomidine-Propofol versus Fentanyl-Propofol on InsertionConditions of Proseal Laryngeal Mask Airway.J ClinDiagnRes. 2016;10(11):UC06-UC09.doi: 10.7860/JCDR/2016/23244.8934[PubMed] [Free full text]
22. Kallio A, Scheinin M, Koulu M, Ponkilainen R, Ruskoaho H, Viinamäki O,et al. Effects of dexmedetomidine, a selective α2-adrenoceptor agonist, on hemodynamic control mechanisms. ClinPharmacolTher. 1989;46(1):33-42. [PubMed]
23. Bhartia N , Pokalea SN , Balaa I, Guptab V.Analgesic efficacy ofdexmedetomidine versus fentanyl as an adjunct to thoracic epidural in patients undergoing upper abdominal surgery: a randomized controlled trial. Southern African J AnaesthAnalg. 2018;24(1):16–21.
24. Lessa MA, Tibiriçá E. Pharmacologic Evidence for the Involvement of Central andPeripheral Opioid Receptors in the Cardioprotective Effects of Fentanyl. AnesthAnalg. 2006;103(4):815-821.doi: 10.1213/01.ane.0000237284.30817.f6[PubMed]
25. Giesecke K., Hamberger B, Järnberg P, Klingstedt C, Persson B. High-And LowDose Fentanyl Anaesthesia: Hormonal And Metabolic Responses DuringCholecystectomy.Br JAnaesth. 1988;61(5):575-582.[PubMed]
26. Lawrence CJ,De Lange S. Effects of a single pre-operative dexmedetomidine dose on isoflurane requirements and peri-operative haemodynamic stability. Anaesthesia.1997;52(8):736-744. [PubMed]
27. Wong CM, Critchley LA, Lee A,Khaw KS, Ngan Kee WD.Fentanyl Dose Response Curves When Inserting The LMA Classic Laryngeal MaskAirway. Anaesthesia.2007;62:654-660. doi:10.1111/j.1365-2044.2007.05057.x. [PubMed]
28. Phua WT, Teh BT,Jong W, Lee TL, TweedWA. Tussive effect of a fentanyl bolus.Can J Anaesth. 1991;38(3):330-334.[PubMed]
29. He L, Xu JM, Dai RP. Dexmedetomidine reduces the incidence of fentanyl-inducedcough: A double-blind, randomized and placebo-controlled study. Ups JMed Sci.2012; 117: 18–21.doi: 10.3109/03009734.2011.629749[PubMed] [Free full text]

CORRIGENDUM

Please make the following corrections

1. The name of the second author of the following paper published in Vol 5, No. 1 of the journal may please be corrected;

Anaesthetist: A Perioperative Physician

Muhammad Tariq, Muhammad Naseem, Liaquat Ali

Anaesth Pain & Intensive Care 2001;5(1):35-36

For 'Muhammad Naseem'

Read 'Naseem Ahmed'