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The Efficacy of Dexmedetomidine 1 MCG/KG Single Infusion as an Adjuvant for General Anaesthesia

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Abstract: The purpose of this prospective study is to evaluate the efficacy of dexmedetomidine in a loading dose of 1 mcg kg^{-1} as an adjuvant to general anaesthesia. This study was carried out in Department of Anaesthesiology, Krishna Institute of Medical Sciences, Karad during a period of 2014-2016. Patients were randomly allocated into two groups of 30 patients each by coded slips for drug combinations. Later at the time of analysis, decoding of slips were done. All patients received Inj. fentanyl 0.001 mg kg^{-1} and Inj. Midazolam 0.05 mg kg^{-1} intravenously. They were induced with Inj. thiopentone sodium 5 mg kg^{-1}. Inj. vecuronium 0.12 mg kg^{-1} was used for neuromuscular blockade. After intubation anaesthesia was maintained with sevoflurane. Extubation was done in routine manner. Patients in Group D took more time compared to Group N to respond to suction catheter, to obey verbal commands and for complete extubation. Though clinically there was not much difference but statistically it was significant, ($p<0.05$).

INTRODUCTION

Intubation has been practiced following its description by Rowbatham and Magill in 1921. Till today, laryngoscopy and intubation is the Gold standard for airway management. Reid and Brace (1940) first described hemodynamic response to laryngoscopy and intubation which is exhibited in the form of changes in heart rate, blood pressure and arrhythmias. The alpha-2 receptor activation results in reduction in nor-epinephrine release which can be used therapeutically to induce sympatholysis (Jorden, 2002). Dexmedetomidine was first marketed for Intensive Care Unit (ICU) sedation, to make use of highly selective adrenergic alpha-2 receptor agonist activity.

Aim: Aim of our study is to evaluate the effect of pre-anaesthetic dexmedetomidine 1 µg kg^{-1} single infusion on sedation, haemodynamics, anaesthetic consumption and recovery profiles during general anaesthesia.

Objectives: The objective of this prospective, randomized double blind study is to evaluate the efficacy of dexmedetomidine in a loading dose of 1 mcg kg^{-1} as an adjuvant to general anaesthesia.

Literature review: Laryngoscopy and tracheal intubation are stressors stimulating inducing hypothalamic activity and causing sympathetic output leading to release of norepinephrine by post ganglionic sympathetic fibers and

secretion from adrenal medulla10 (Burstein *et al*., 1950). The very first observation made by Reid and Brace (1940) was parasympathetic predominance manifestation as bradycardia. Later in 1950 Burstein *et al*. (1950) came to a conclusion that hypertension and tachycardia are manifestation of the sympathetic response. King *et al*. (1951) suggested that they are due to a combined effect of both sympathetic and parasympathetic reflexes.

Various workers have measured the plasma catecholamine levels by using radio enzymatic assays and high pressure liquid chromatography. Laryngoscopy and intubation are stimuli of different intensity leading to different responses. Laryngoscopy alone, without intubation provides a supraglottic pressure stimulus causing increases in both systolic and diastolic pressures above the pre-induction control levels. Increases in heart rate are slight and are not significant due to laryngoscopy alone. Intubation and placement of an endotracheal tube or a catheter in the trachea, stimulates infraglottic receptors and evokes an additional cardiovascular response with a further increase in catecholamines. The hemodynamic response is much greater increasing by 36% from pre-induction control levels. The heart rate also significantly increases by about 20% with tracheal intubation where as there is little rate response to laryngoscopy alone (Forbes and Dally, 1970; Shribman *et al*., 1987). Alpha 2 agonist provide sedation, analgesia, muscle relaxation and anxiolysis. A variety of compounds have been developed for use in humans including clonidine and Dexmedetomidine. Post operated patients sedated with dexmedetomidine display similar pharmacokinetics to the pharmacokinetics seen in healthy volunteers (Venn *et al*., 2002; Iirola *et al*., 2012). For weaning patients from ventilator: the unique characteristics of dexmedetomidine in providing adequate sedation with minimal respiratory depression allows for easy weaning. It is shown to control withdrawal behaviour and allows for successful detoxification (Reves *et al*., 2010). The use of dexmedetomidine when securing the airway with a fiberoptic intubation is shown to be well tolerated with no haemodynamic compromise or respiratory depression (Grant *et al*., 2004; Scher and Gitlin, 2004). As a sole anaesthetic agent dexmedetomidine alone is infused in increasing doses (up to 10 mcg/kg/h) in patients with potential airway challenges posted for surgery until general anaesthesia attained (Ramsay and Luterman, 2004).

MATERIAL AND METHODS

The study entitled "A prospective randomized double blind study to find out the efficacy of dexmedetomidine 1µg/kg single infusion as an adjuvant for general anaesthesia" was carried out in Department of Anesthesiology, KIMS, Karad during a period 2014-16. When we were confident that the technique and the results are safe for patients in both the groups, it was converted to a double blind study with all necessary modifications from patient consent to support by qualified staff in our department willing to participate in this study.

Randomization was done with coded slips, coded for either dexmedetomidine or for normal saline. All coded slips were kept in a box and the study drug was given by picking up a coded slip by a fellow anesthesiologist by properly shaking the box. Accordingly, that study drug was given to the patient and drug code was recorded in patient's proforma. During the study conducted in a double blind procedure, the technical part was handled by one set of anesthetist and the observational part was left to different set of anaesthetist.

Preparation: All patients were kept fasting 8 hours prior to surgery. Tab. diazepam 5 mg was given orally to provide a nice sleep on the previous night of surgery. On arrival of patient to holding area of O.T in the morning i.v. line was secured with 20G cannula. Ringer Lactate infusion was started at 10 mL/kg/h rate and Inj. metoclopramide 10 mg iv and Inj. ranitidine 50 mg was administered 1 h prior to shifting patient to respective O.T suite.

Anaesthesia technique: After completion of the test drug infusion, patients were given Inj. midazolam 0.05 mg kg^{-1} and Inj fentanyl 0.001 mg kg^{-1}. After preoxygenation with 100% O_2 at 8 L min^{-1} for 5 min, all patients received Inj. thiopentone sodium 5 mg kg^{-1} intravenously and Inj. vecuronium 0.12 mg kg^{-1} intravenously for tracheal intubation. Lungs were inflated with oxygen using bag mask ventilation for 4 min. Jaw relaxation was assessed. Laryngoscopy and intubation was done with proper size cuffed endotracheal tube after complete jaw relaxation.

RESULTS AND DISCUSSION

As shown in Table 1, both groups are comparable, so far as demographic characteristics and baseline parameters are concerned.

As shown in Table 2, the Ramsay Sedation Scale in Group N and Group D were initially comparable ($p = 0.30$). After drug infusion for 10 min, none of the patients in Group N reached RSS of 3 or more. While in Group D, 9 patients reached RSS of 3, 19 patients reached RSS of 4 and 2 patients achieved RSS of 5. Applying Mann-Whitney U test it was found to be significant in Group D.

As shown in Table 3, there is no significant difference ($p = 0.34$) in baseline Systolic Blood Pressure

Table 1: Demographic parameters

Parameters	Group N	Group D
Age (Yrs)	34.53±9.09	35.66±8.07
Height (Cms)	166.1±5.73	166.23±5.26
Gender(m:f)	16:14	15:15
Weight (In Kgs)	58.83±5.36	57.9±5.74
Asa Status (i :Ii)	16:14	15:15
Baseline Heart Rate (Beats/Min)	79.23±7.29	81.4±6.62
Baseline Sbp (mm Hg)	125.1±10.42	127.2±5.97
Baseline Dbp (mm Hg)	77.13±8.22	79.2±5.26
Baseline Map (mm Hg)	93.12±8.48	95.20±8.38
Baseline Bis	97.8±0.88	97.6±1.06
Ramsay sedation scale	1.53±0.50	1.66±0.47

Table 2: Comparison of ramsay sedation scale

RSS	GROUP N	GROUP D
1	10	0
2	20	0
3	0	9
4	0	19
5	0	2

Table 3: Comparison of mean systolic BP (in mm Hg)

Variables	Group N	Group D	p-values
Baseline	125.10±10.42	127.20±5.97	= 0.340
After drug infusion	124.96±10.85	104.20±5.01	<0.000
At induction	121.0±9.79	102.06±3.17	<0.000
At intubation	143.60±10.76	111.20±4.53	<0.000
2 min	139.86±11.39	109.86±4.16	<0.000
5 min	128.40±7.41	107.33±2.98	<0.000
10 min	125.86±7.25	107.20±2.44	<0.000
15 min	122.40±5.78	107.73±2.76	<0.000
20 min	122.53±4.39	108.73±2.94	<0.000
30 min	121.13±4.68	107±2.33	<0.000
40 min	120.53±4.60	106.06±3.17	<0.000
50 min	118.6±3.93	105.40±1.83	<0.000
60 min	117.6±5.02	106.46±1.94	<0.000
80 min	116.8±3.69	111±3.18	<0.000
100 min	117±4.92	116.93±2.50	= 0.940
120 min	121.4±4.61	121.53±2.95	= 0.890

(SBP) initially between Group N (125.10±10.42) and Group D (127.20±5.97). After infusion of test drugs for 10 min, SBP in Group D (104.20±5.01) falls significantly ($p<0.0001$) as compared to Group N (124.96±10.85). At time of induction, SBP is significantly lower ($p <0.0001$) in Group D (102.06±3.17) than Group N (121.0±9.79). At the time of intubation, SBP is significantly higher ($p<0.0001$) in Group N (143.60±10.76) than Group D (111.20±4.53). SBP in Group D remained lower than Group N until 80 minutes of surgery duration ($p<0.0001$). SBP was comparable ($p >0.05$) at 100 mins and 120 mins of surgical duration (Table 4).

Initially, DBP was comparable ($p = 0.25$) in Group N (77.13±8.22) and Group D (79.2±5.26). After infusion of test drugs for 10 min, DBP in Group D (65.53±4.74) falls significantly ($p<0.0001$) as compared to Group N (77.23±8.0). At time of induction, DBP is significantly lower ($p <0.0001$) in Group D (63.96±4.00) than Group N

Table 4: Comparison of mean diastolic BP (mm Hg)

Variables	Group N	Group D	p-values
Baseline	77.13±8.22	79.2±5.26	= 0.250
After drug infusion	77.23±8.0	65.53±4.74	<0.000
At induction	74.83±8.10	63.96±4.00	<0.000
At intubation	86.8±8.47	70.86±5.16	<0.000
2 min	83.26±8.19	71.13±4.65	<0.000
5 min	79.66±6.86	71.13±3.77	<0.000
10 min	76.8±6.11	71.66±3.60	= 0.000
15 min	76.06±5.18	72.6±3.93	= 0.005
20 min	76.13±5.45	71.2±3.73	= 0.000
30 min	77.53±4.89	73.6±4.27	= 0.001
40 min	77.4±4.36	73.2±3.77	= 0.000
50 min	77.3±3.37	73.66±3.75	= 0.000
60 min	79.6±2.89	73.93±2.49	<0.000
80 min	77.8±3.94	73.73±2.14	<0.000
100 min	77.46±4.06	74.86±2.55	= 0.004
120 min	79.33±3.72	76.0±3.67	<0.000

Table 5: Comparison of mean of MAP (in mm Hg)

Variables	Group N	Group D	p-values
Baseline	93.12±8.48	95.20±8.38	= 0.343
After drug infusion	93.14±4.98	78.42±4.38	<0.000
At induction	90±8.04	77±3.29	<0.000
At intubation	105.73±8.49	84.31±4.13	<0.000
2 min	102.13±8.60	84.04±3.68	<0.000
5 min	95.91±6.47	83.20±2.75	<0.000
10 min	93.16±5.77	83.51±2.35	<0.000
15 min	91.51±4.75	84.31±2.83	<0.000
20 min	91.60±4.44	83.71±2.58	<0.000
30 min	92.07±4.40	84.73±2.78	<0.000
40 min	91.78±3.68	84.16±2.77	<0.000
50 min	91.09±3.10	84.24±2.32	<0.000
60 min	92.27±2.85	84.78±1.95	<0.000
80 min	90.80±3.28	86.16±1.78	<0.000
100 min	90.64±3.70	88.89±1.86	= 0.024
120 min	93.36±2.95	91.18±2.86	= 0.005

(74.83±8.10). At the time of intubation, DBP is significantly higher ($p<0.0001$) in Group N (86.8±8.47) than Group D (70.86±5.16). DBP in Group D remained lower than Group N throughout the surgery duration ($p<0.05$) (Table 5).

MAP was statistically comparable ($p>0.05$) in both Group N (93.12±8.48) and Group D (95.20±8.38) before infusion of test drugs. After infusion of test drugs for 10 min, MAP in Group N (93.14±4.98) falls significantly ($p<0.0001$) as compared to Group D (78.42±4.38). At time of induction, MAP remained significantly ($p<0.0001$) lower in Group D (77±3.29) than Group N (90±8.04). At the time of intubation, MAP is significantly higher ($p<0.0001$) in Group N (105.73±8.49) than Group D (84.31±4.13). MAP remained higher in Group N compared to Group D throughout the remaining duration of surgery which is statistically significant ($p>0.05$).

This study shows that preanaesthetic dexmedetomidine 1 μg kg^{-1} single infusion prevents hemodynamic changes by tracheal intubation and reduces the total cumulative consumption of sevoflurane. Study

observed BIS significantly lower in dexmedetomidine group during intubation compared to control group. The mean of BIS range in control group was 44-55 while it was from 35-38 in dexmedetomidine group. Our results are in agreement with the studies by Shin *et al*. (2013) and Ozcengiz *et al*. (2012). In our study, although, sevoflurane consumption was lesser in dexmedetomidine group, patients in dexmedetomidine group took longer time for recovery. A possible explanation is that the use of fentanyl along with dexmedetomidine might have prolonged the recovery time. Study also observed significant analgesia in the dexmedetomidine group just after shifting patient to recovery room. Among the patients who received dexmedetomidine, 63% of them showed VAS less than 4 while in control group only 16% of patients showed so. At 1st and 3rd hours after surgery both the group showed similar VAS score. The possible explanation of this may be administration of diclofenac post operatively.

Tsai *et al*. (2010) observed 10% of patients showed bradycardia and needed atropine and 5% of patients required ephedrine to treat hypotension in dexmedetomidine group while none of the patients in propofol group showed so. Among the patients who received dexmedetomidine we observed 16% showed hypotension while 20% of them showed bradycardia. This increased incidence of side effects can be because of fentanyl which was administered along with dexmedetomidine. Hypotension and bradycardia responded well to ephedrine and atropine.

Many studies have been done on dexmedetomidine using loading and different maintenance dose while our study showed that even single loading dose of dexmedetomidine has clinical benefits. It gives similar haemodynamic stability, provides anxiolysis, good analgesia, and also reduces anaesthetic agent's consumption when compared to dexmedetomidine in maintenance dosage. We also observed that it can be safely used along with fentanyl as it provides better haemodynamic stability while maintaining good anaesthetic depth without much side effects. Our study proves that dexmedetomidine in single loading dose is an economical and useful adjuvant to general anaesthesia.

CONCLUSION

Hence, we concluded that Dexmedetomidine in dose 1 μgm kg^{-1} intravenous is effective in attenuating the hemodynamic pressor responses to laryngoscopy and intubation when given as premedicant without significant side effects and provides all anxiolysis, sedation, analgesia, anaesthetic sparing and hemodynamic stability without respiratory depression during general anaesthesia.

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