An Observational Study for Comparison of Perioperative Effects of Intravenous Clonidine and Dexmedetomidine as Premedication for General Anaesthesia for Thyroidectomy Patients

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ABSTRACT

BACKGROUND

Sympathetic system overactivity can result from direct laryngoscopy and intubation in general anaesthesia. This is often associated with tachycardia, hypertension, and arrhythmias and can rarely result in ischemia in susceptible individuals. Similar hemodynamic effects can result from surgical stimulation also. Deep plane of anaesthesia, intravenous opioids, beta blockers, lignocaine, dexmedetomidine, clonidine, alpha blockers, etc. are different techniques used to prevent this. There are many studies comparing various techniques but similar studies for comparing equal doses (1 mcg/Kg) of intravenous clonidine and dexmedetomidine are few.

METHODS

After obtaining institutional ethical committee clearance, a prospective observational study among 66 ASA class I and II patients was conducted and distributed among two groups with 33 in each, undergoing thyroidectomy under general anaesthesia. Patients were enrolled into two groups. The clonidine group received 1 mcg/Kg intravenous clonidine and the dexmedetomidine group 1 mcg/Kg intravenous dexmedetomidine as an infusion over 15 minutes before induction of general anaesthesia. The hemodynamic response to direct laryngoscopy and intubation, surgical incision and extubation as measured by the change in heart rate and blood pressure which were monitored in the perioperative period. At the end, duration of analgesia defined as the time of start of induction of general anaesthesia to the time of first request for rescue analgesic, or VAS (Visual Analogue Scale)= 40 mm were documented. The incidence of side effects, such as hypotension, bradycardia, were also monitored. All statistical analyses were carried out using the software Statistical Package for the Social Sciences (SPSS) Statistics version 19.0.0 with the help of a professional statistician. Data was expressed in its frequency and percentage as well as mean and standard deviation.

RESULTS

Analysis of the monitored data shows that patients in the dexmedetomidine group had more stable hemodynamic effects to direct laryngoscopy, intubation and surgical incision. The duration of analgesia of both the clonidine and dexmedetomidine were similar and did not show any significant statistical difference. Both the groups of patients had few cases of side effects like hypotension and bradycardia which were neither clinically nor statistically significant and these were easily remediable.

CONCLUSIONS

Use of dexmedetomidine is preferred to clonidine as intravenous premedication at 1 mcg/Kg dose.

KEYWORDS

Dexmedetomidine, Clonidine, Premedication, General Anaesthesia

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BACKGROUND

General anaesthesia involves direct laryngoscopy and intubation which can result in sympathetic system overactivity. Laryngoscopy and tracheal intubation are often associated with tachycardia, hypertension, and arrhythmias.[1] The hemodynamic responses to tracheal intubation are associated with an increase in plasma catecholamine concentrations[2,3] and are attenuated by β-blockers. The surgical incision also causes sympathetic stimulation.[4] This study is to compare the effects of 1 mcg/Kg clonidine and 1 mcg/Kg dexmedetomidine when used as intravenous premedication with respect to hemodynamic stability in perioperative period and analgesic effect in the postoperative period. The stress response to surgery is characterized by increased secretion of pituitary hormones and activation of the sympathetic nervous system. These can result in increased anaesthetic requirement, cerebrovascular and cardiovascular ischemic events, increased bleeding etc., Different methods are used to prevent this. Fentanyl, lignocaine, beta blockers, deep plane of anaesthesia etc., are usually used for this purpose. Some are having transient effects while others may act even in postoperative period. Intravenous as well as oral clonidine and dexmedetomidine can also be used as premedication for general anaesthesia.[5]

Aim

Aim of this observational study was to compare the perioperative hemodynamic effects and the effect on duration of analgesia between patients who received intravenous clonidine and intravenous dexmedetomidine as premedication.

Objectives

1. To compare perioperative hemodynamic effects of premedication with intravenous clonidine and dexmedetomidine as assessed by heart rate and BP changes to direct laryngoscopy, intubation and to surgical incision
2. To compare the effects on postoperative analgesia of these two drugs as assessed by visual analogue scale (VAS)

Inclusion Criteria

- ASA PS – 1 and II
- Age group between 18-60 yrs.

Exclusion Criteria

- Patients using alpha adrenergic receptor antagonist.
- Hypertensive patients controlled with multiple drugs.
- Patients on beta blockers.
- Morbidly obese patients.

Sample size was estimated by using the mean difference in postoperative analgesia duration between Dexmedetomidine and Clonidine groups from the study of Dr. Shipra Singh et al as (255.5±35.31) minutes (dexmedetomidine group) and (185.75±35.5) minutes. (clonidine group). Using these values at 95% Confidence limit and 80% power sample size of 33 was obtained in each group by using the above-mentioned formula and Med calc sample size software. With 10% nonresponse sample

$$s2SD^2 (Z_{\alpha/2}+Z_{\beta})^2 \div d^2$$

SD- Standard deviation from previous study

$Z_{\alpha/2} = Z_{1.96 = 2/0.05}$ from Z table at type 1 error of 5%= 1.96

$Z_{\beta} = Z\ 0.842_{= 0.2}$from Z table at 80% power

D= effect size= difference between mean value size of 30

+ 3 ≈ 33 cases were included in each group.

METHODS

After obtaining institutional ethical committee clearance, a prospective observational study among 66 American Society of Anesthesiologists class I and II patients was conducted and distributed among two groups with 33 each undergoing thyroidectomy under general anaesthesia. The study was conducted in the operation theatre of Govt. TD medical college, Alappuzha. Patients were educated about the study using patient information sheet. Informed written consent were taken from all patients in their mother tongue. Patients were kept nil per oral for 8 hours prior to surgery. The patients were given Tab. Ranitidine 150 mg and Tab Metoclopramide 10 mg PO on the night before surgery and early morning of surgery. In the preoperative holding room, the concept of visual analogue scale (VAS) was explained to the patients for assessment of postoperative analgesia. The patient's weight was recorded for calculation of the drug dose. Upon arrival in the operating room ECG, non-invasive blood pressure monitor, and pulse oximeter was connected and basal heart rate and BP will be recorded. Intravenous access with 18 G cannula in forearm was obtained and intravenous fluid 0.9% NS was started.

The patients received either 1 mcg/Kg of Clonidine or 1 mcg/Kg of dexmedetomidine diluted in normal saline 50 ml intravenously over 15 minutes as infusion. After the infusion the patients were premedicated with glycopyrrolate 0.2 mg and fentanyl 100 mcg iv The patients were given iv lignocaine 60 mg. The patients were induced with iv propofol 2.5 mg/Kg after 3 minutes of preoxygenation. Vecuronium 5 mg was given after checking mask ventilation. Bag and mask ventilation with oxygen were given for 3 minutes. Direct laryngoscopy and endotracheal intubation with cuffed tube of size 6.5 mm ID for female and 7.5 mm ID for male was done, and anaesthesia was maintained with 33% oxygen 66% nitrous oxide, and isoflurane 0.6%. Patients were positioned in thyroidectomy position. Muscle relaxation was maintained with intermittent dose of vecuronium 1 mg every 20 minutes. Blood pressure and heart rate were monitored every minute in the first 5 minutes and thereafter every 5 minutes until the end of surgery and in the recovery area. After the surgery patients were positioned supine. All anaesthetic agents were stopped, and the patients were reversed with neostigmine and glycopyrrolate.

In the recovery the analgesia requirement was monitored. The duration of analgesia was recorded and is defined as the time since the induction of anaesthesia until the time in the recovery when the patient requested for additional analgesia. Rescue analgesia was given with tramadol 25 mg boluses titrated to pain up to 100 mg. The patients after recovery were monitored in a high dependency unit. Hypotension defined as decrease in systolic blood pressure more than 20% of the base line value or systolic blood pressure less than 90 mm of Hg n was treated by increasing the rate of intravenous fluid administration and/or 6 mg bolus iv injection of mephentermine as and when required. Any episode of bradycardia was treated with injection atropine 0.6 mg intravenously

Statistical analysis was done using SPSS version 19.0.0 with the help of a professional statistician. Data was expressed in its frequency and percentage as well as mean and standard deviation.

RESULTS

Group	Mean (Yrs.)	SD	N	T	P
Dexmedetomidine	41.3	11.6	33	0.19	0.849
Clonidine	40.8	5.3	33		

Table 1. Age Distribution

(p value 0.849> 0.05). So patients in both dexmedetomidine group & the clonidine group were comparable with respect to age

Group	Mean (Minutes)	SD	N	T	P
Dexmedetomidine	147	14.0	33	0.26	0.795
Clonidine	149	14.3	33		

Table 2. Distribution of Duration of Surgery

(p value 0.795> 0.05). So patients in both groups were comparable with respect to duration of surgery

Time	Dexmedetomidine			Clonidine			t	p
	Mean (bpm)	SD	N	Mean (bpm)	SD	N		
Base line	71.3	9.6	33	70.6	6.9	33	0.35	0.724
0-5 mt	66.3	8.3	33	71.5	10.0	33	2.31	0.024
5-10 mt	65.0	6.8	33	72.6	10.5	33	3.51	0.001
10-15 mt	67.6	7.2	33	73.6	9.5	33	2.91	0.005
Laryngoscopy & Intubation	68.2	7.9	33	73.8	8.4	33	2.79	0.007
Incision	69.0	7.4	33	73.8	7.8	33	2.55	0.013
Incision- end of surgery	60.2	7.5	33	72.6	8.0	33	1.85	0.002
Till 3h post op	62	8.0	33	72.8	8.8	33	1.77	0.001

Table 3. Distribution of Heart Rate in the Group

Time	Dexmedetomidine			Clonidine			t	P
	Mean (mm Hg)	SD	N	Mean (mm Hg)	SD	N		
Base line	138.9	10.7	33	137.9	10.0	33	0.38	0.705
0-5 mt	107.7	18.0	33	118	11.2	33	2.81	0.007
5-10 mt	96.4	12.5	33	110	12.0	33	4.67	0.000
10-15 mt	98.4	11.5	33	112	11.8	33	5.03	0.000
Laryngoscopy & Intubation	112.9	10.7	33	124.8	15.4	33	3.41	0.001
Incision	108.8	11.9	33	114	11.4	33	2.09	0.040
Incision- end of surgery	106.2	11.5	33	116.3	12.7	33	1.57	0.012
Till 3h post op	126.7	14.0	33	130.9	15.2	33	0.25	0.009

Table 4. Distribution of Blood Pressure in the Group

Group	Mean (Min)	SD	N	T	P
Dexmedetomidine	190.5	9.2	33	9.79	0.789
Clonidine	182.6	17.0	33		

Table 5. Distribution of Time to 1st Pain (Duration of Analgesia)

The base line heart rate was comparable in both groups (p value 0.724). The heart rate after the injection of the drugs was significantly different from the injection of the drugs up to 3 hrs. post operatively (p value <0.05). The base line blood pressure was comparable in both the groups (p value 0.705> 0.05). Blood pressure was significantly lower among dexmedetomidine group than clonidine group after injection. (p value <0.05). The mean duration for the first pain to appear for dexmedetomidine group was 190.5 mins. and that of clonidine group was 182.6 mins. The duration was comparable in both groups (p value >0.05).

Two subjects from dexmedetomidine group had post-operative bradycardia, while only one subject among the clonidine group had it. The incidence of hypotension was higher among the dexmedetomidine group with 3 subjects while 1 subject in clonidine group developed it.

Symptoms	Group		Total	Chi Square	p Value
	Dexmedetomidine	Clonidine			
Hypotension	3	1	4	0.000	> 0.05
Bradycardia	2	1	3	7.661	>0.05

Table 6

DISCUSSION

Premedication is a very important part of anaesthesia aimed at making anaesthesia a pleasant and acceptable experience for the patient. The goals are to produce anxiolysis, sedation, amnesia, analgesia, salivation reduction, vagolysis, sympatholysis, reduction of gastric secretion and acidity and to prevent postoperative nausea and vomiting (PONV).[6,7] Clonidine, a centrally acting α2-agonist, has a beneficial effect on the hyperdynamic response to endotracheal intubation.[8-13] Moreover, it attenuates stress-induced sympathoadrenal responses to painful stimuli, improves the intraoperative hemodynamic stability, reduces the incidence of perioperative myocardial ischemic episodes in patients with suspected or documented coronary artery disease, and decreases anesthetic requirements during surgery.[14-18]

Dexmedetomidine is a highly selective α2 agonist. Systemic administration of dexmedetomidine has been a focus of interest for their sedative, analgesic, sympatholytic and cardiovascular stabilizing effect with reduced anesthetic requirement. It is shorter acting than clonidine and much more selective for α2 than α1. (1620:1 compared to 220:1 for clonidine).[19] One of the highest densities of α2 receptors are located in pontine locus ceruleus, an important nucleus mediating sympathetic nervous system function, vigilance, memory, analgesia and arousal. The sedative effects produced by dexmedetomidine is largely due to inhibition of this nucleus. It is a dextro isomer of pharmacologically active component medetomidine, which has been used for many years in veterinary practice for its analgesic, sedative and hypnotic properties.[20,21] Atipamezole is a specific and selective antagonist of alpha 2 receptor that effectively reverses sedative and, cardiovascular effects of IV dexmedetomidine.[21-23] but its use is restricted to veterinary practice and human trials are still going on.

Other studies have compared various aspects of clonidine dexmedetomidine premedication. Ramchandani S et al studied effect of intravenous clonidine premedication for the bloodless surgical field in patients undergoing middle ear or nasal surgery and found IV clonidine premedication in a dose of 4 and 5 µg/Kg reduces bleeding and provided a clear field for surgery. It also reduces the requirement of isoflurane, fentanyl, and metoprolol for controlled hypotension.[24] Pandazi et al studied about low dose clonidine premedication and hypotension after carotid artery surgery and concluded intravenous premedication with low-dose clonidine (1 µg/Kg) was found to be effective in preventing hypertensive episodes during carotid endarterectomy under general anaesthesia but seemed to increase the incidence of hypotension postoperatively.[25] Peden C J et al studied the effect of intravenous dexmedetomidine premedication on the dose requirement of propofol to induce loss of consciousness in patients receiving alfentanil and found dexmedetomidine caused a reduction in the overall concentration and dose of propofol required.[26]

Alka Chandra et al studied the effects of intravenous dexmedetomidine premedication on intraocular pressure and pressor response to laryngoscopy and intubation and concluded that dexmedetomidine premedication in the dose of 0.4 µg/Kg lowers the IOP and attenuates the pressor response to laryngoscopy and intubation.[27] Aindam Sarkar et al conducted study for comparison of effects of intravenous clonidine and dexmedetomidine for blunting pressor response during laryngoscopy and tracheal intubation and opined that attenuating response to hemodynamic changes were observed with dexmedetomidine and clonidine IV infusion. They also found premedication with IV infusion of dexmedetomidine can safely be recommended for attenuation of hemodynamic response to endotracheal intubation.[28]

Devang Bharti et al compared the effects of Clonidine and Dexmedetomidine on Cardiovascular Stability in Laparoscopic Cholecystectomy and found that both clonidine and dexmedetomidine favourably alter the intraoperative hemodynamics during laparoscopic cholecystectomy. Clonidine decreased intraoperative HR more than dexmedetomidine.[29]

CONCLUSIONS

Both intravenous clonidine and dexmedetomidine are safe premedications at 1 mcg/Kg. Analysis of the monitored data shows that patients in the dexmedetomidine group had clinically significant stability of haemodynamics to direct laryngoscopy, intubation and surgical incision. The duration of analgesia was similar in both the groups.

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