

Research Article

A comparative study of effect of dexmedetomidine in dose of 0.7µg/kg and clonidine in doses of 2µg/kg as premedication before general anaesthesia

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ABSTRACT

Background: Alpha-2 adrenoceptor agonists have widely been used in anaesthesia and critical care as analgesics and sedatives. Both clonidine and dexmedetomidine, a more selective and specific α -2 agonist have been shown to decrease induction doses of i.v. anaesthetics and intraoperative opioid and volatile anaesthetic requirements for maintenance of anaesthesia resulting in more rapid recovery from anaesthesia and also a reduced need for pain medication in post-operative period, thereby reducing the length of stay. The current prospective randomised double blind study was undertaken to compare the effects of dexmedetomidine and clonidine, as i.v. premedication, on perioperative hemodynamics, reduction in dose of inducing agent and post-operative analgesia duration.

Methods: A total of 60 ASA class I and II patients undergoing elective surgeries under general anaesthesia were randomised into two groups. Group D- dexmedetomidine 0.7µg/kg, and group C- clonidine 2µg/kg. Drugs were given 15 minutes before induction. The cases were conducted under General anaesthesia with endotracheal intubation using Propofol, Vecuronium, N₂O and O₂. Heart rate, blood pressure, dose of inducing agent and time of rescue analgesia were recorded.

Results: The rise in mean arterial pressure and heart rate during intubation and extubation was lesser with group D as compared to group C. ($p < 0.05$). Lesser amounts of inducing agent was required with group D as compared to group C ($p < 0.0001$). Post-operative analgesia duration was more with group D as compared to group C ($p < 0.001$).

Conclusions: Study concluded that Dexmedetomidine had better control over hemodynamics as compared to clonidine when given as premedication, the drug dose used for induction was lesser and also the post-operative analgesia duration was longer with dexmedetomidine.

Keywords: Dexmedetomidine, Clonidine, Premedication, Hemodynamic changes

INTRODUCTION

Alpha-2 adrenoceptor agonists have widely been used in anaesthesia and critical care as analgesics and sedatives. Both clonidine and dexmedetomidine, a more selective and specific α -2 agonist have been shown to decrease induction doses of i.v. anaesthetics and intraoperative opioid and volatile anaesthetic requirements for maintenance of anaesthesia resulting in more rapid recovery from anaesthesia and also a reduced need for

pain medication in post-operative period, thereby reducing the length of stay.

We have compared the preoperative as well as the perioperative effects of clonidine and dexmedetomidine to determine whether dexmedetomidine being a more selective α_2 agonist ($\alpha_2:\alpha_1$ ratio: 8:1), has any advantage over clonidine.¹ Various routes of administration of alpha-2 agonists like intrathecal, epidural, nerve blocks and intravenous have been tried.^{2,3} Both the drugs have been

compared when given as infusion during perioperative period but there is paucity of studies where the two drugs have been compared as a premedicant before general anesthesia. So in this study clonidine and dexmedetomidine were compared when used in premedication. Although there are very few studies which have compared the dose equivalence of the two drugs, but it has been established in previous studies that the dose of clonidine is 1.5 to 2 times that of dexmedetomidine.⁴

Aim of the study was to compare the effect of dexmedetomidine (0.7µg/kg) and clonidine (2µg/kg) as i.v. premedication on perioperative hemodynamics, reduction in dose of inducing agent and muscle relaxant and postoperative duration of analgesia.

METHODS

After obtaining institutional ethical committee approval and written informed consent, 60 ASA status I-II patients aged 18- 60 years, of either gender, height 160-190 cm and weight 45 – 90kg scheduled for elective surgeries under general anesthesia were included in this prospective randomised double blind clinical trial. Exclusion criteria included hypertension, morbid obesity, alcohol/drug abuse, hepatic, renal, endocrine and cardiac dysfunction and patients with known drug hypersensitivity.

After fasting overnight patients were transferred to the preoperative room where continuous monitoring of ECG, heart rate, blood pressure, arterial haemoglobin oxygen saturation (SpO₂) was done. Ringer lactate 10ml/kg was given in accordance to the fasting duration. Premedication was done with inj. ranitidine 0.25 mg/kg, injection metoclopramide 0.15 mg/kg, injection glycopyrrolate 0.02 mg/kg, 45 minutes before surgery. After giving premedication patients were shifted to the operation theatre.

Patients were allocated randomly into two groups:

Group D received dexmedetomidine 0.7 µg/kg i.v. infusion dissolved in 50 ml of 0.9% NaCl over a 10 min period.

Group C received clonidine 2.0 µg/kg i.v. infusion dissolved in 50 ml of 0.9% NaCl over a 10 min period.

The double blind nature of the study was ensured by having an anaesthesiologist not participating in study; prepare dexmedetomidine and clonidine by dissolving them in 50 ml of normal saline. Measurements were made every 5 min.

Hemodynamic changes (heart rate, mean arterial pressure, spo₂) were recorded upto 15 min at 5 min intervals after which general anaesthesia was induced using injection propofol upto the loss of eyelash reflex and BIS score of 40-60. Injection vecuronium 0.1 mg/kg

was given i.v. to facilitate laryngoscopy and tracheal intubation. Drager fabius multipara monitor was used for measuring intraoperative vitals and neuromuscular monitoring. Neuromuscular monitoring was done with train of four (TOF) stimulation. Anaesthesia was maintained with propofol infusion @ 100µg/kg/min and vecuronium 0.02mg/kg was given in loading doses on return of third response in TOF.

Hypotension (mean arterial pressure <20% of baseline) was treated primarily by decreasing the infusion rate of propofol. Pulse rate <50/min was treated by a bolus dose of atropine 0.6 mg i.v. Intraoperatively pulse rate, mean arterial pressure, SpO₂, etco₂ were monitored. At the end of surgery patients were allowed to recover spontaneously from neuromuscular blockade. Reversal was done with inj. Neostigmine 0.05 mg/kg and inj. glycopyrrolate 0.02 mg/kg. Trachea was extubated when sufficient spontaneous ventilation was evident. Patients were followed up postoperatively to assess the time of rescue analgesia and post-operative nausea and vomiting if any.

The quality of analgesia was assessed every hour post-operatively in the recovery room by attending nurse using numeric rating scale (1-10). Zero was considered as no pain, 1-3 as mild pain, 4-6 as moderate pain and 7-10 as severe pain. At score of 4, rescue analgesic, injection diclofenac sodium (1.5 mg/kg) intravascular as infusion was given. Duration of analgesia was calculated from time of recovery from general anesthesia to the time of first rescue analgesic given.

Statistical analysis

The data was analysed by Statistical Package for Social Sciences software SPSS Inc., version 16 for windows. Additional to the descriptive statistical methods (Mean, Standard deviation), unpaired student's t test was used for the comparison of mean values among two groups. Normality of the data was tested by Kolomogorov-Smirnov method. During the analysis of the results p<0.05 was accepted significant in the 95 % confidence interval. P<0.001 was considered highly significant.

RESULTS

All the four groups were found to be similar regarding age, weight, height and sex (Figure 1) (p value <0.05). Rise in pulse rate was lesser with dexmedetomidine group during intubation (p<0.05). The mean pulse rate during intubation was 73.85±11.94 in group D whereas it was 80.3±7.12 in group C (P value 0.04).

After extubation the mean pulse rate in group D was 70.95 (±5.88) whereas it was 75.85(±6.55) in group C (p value <0.01) (Figure 2). During intraoperative period also there remained a significant difference between the pulse rates of the two groups, it being lesser in group D. As regards mean arterial pressure, Group D patients showed

a significant increase in MAP (7% above the baseline) about 5 minutes after premedication which again decreased to below pre-operative values 15 minutes after premedication without any treatment.

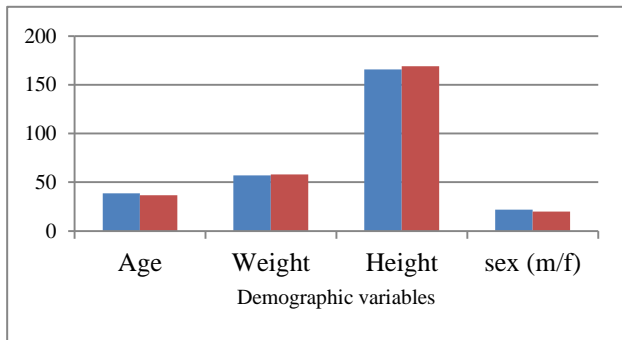


Figure 1: Distribution of patients according to age, height, weight and sex in both the groups.

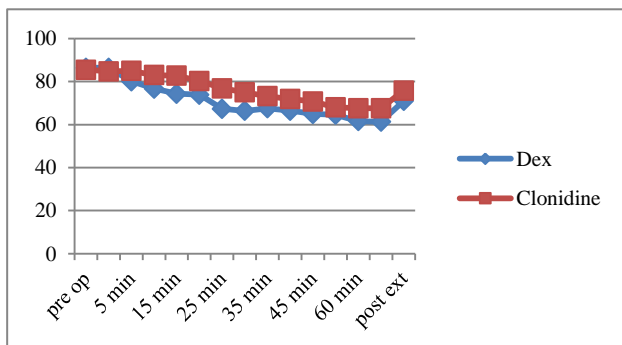


Figure 2: Pulse rate.

Mean MAP with group D was 91.1(±13.8) whereas it was 91.8(±7.33) with group C (p value <0.05) after intubation. After extubation the mean MAP was 91.35(±5.22) in group D and 94.8(±4.11) in group C patients, (p value=0.025).

During intraoperative period also the decrease in mean arterial pressure was more in group D (Figure 3).

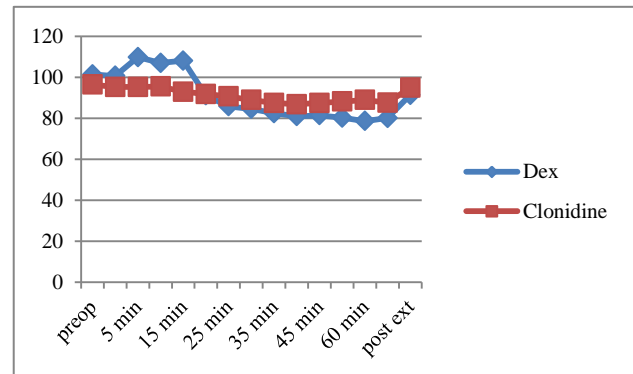


Figure 3: Mean arterial pressure.

The duration of surgery was found to be almost similar in both the groups. The inducing dose of propofol required was lesser in group D (57.5±9.1)mg as compared to group C (68±6.9) mg (p-value<0.0001 (Table 1).

Regarding postoperative analgesia duration it was more with group D patients (255.5±35.31) minutes followed by group C (185.75±35.5) minutes (p value<0.0001) (Table 2).

Table 1: Dose of inducing agent used.

Variable	Dexmedetomidine (0.7 µg/kg) D	Clonidine (2µg/kg) C	p value	Inference
Propofol (mg)	57.5 (±9.1)	68 (±6.9)	<0.0001	Extremely sig.

Table 2: Post-operative analgesia duration.

Variable	Dexmedetomidine (0.7µg/kg) D	Clonidine (2µg/kg) C	p value	Inference
Surgery duration	139 (±39.55)	110.75(±19.2)	0.0546	Not sig.
Rescue analgesia	255.5(±35.3)	185.75(±35.5)	<0.0001	extremely sig.

DISCUSSION

In this study we observed the effects as premedication before general anaesthesia of dexmedetomidine in dose of 0.7 µg/kg and clonidine in doses of 2µg/kg. Both the groups were compared with each other. We found that both the drugs cause a decrease in heart rate after laryngoscopy and intubation and after extubation in perioperative period but the decrease were more significant in group D. These results were consistent with

Taittonen and colleagues.⁵⁻⁹ The decrease in heart rate was due to the sympatholytic effect of Alpha2-adrenoceptors.¹⁰ Furthermore in present study it was observed that the rise in mean arterial pressure after laryngoscopy and intubation and after extubation was noticeably lesser with dexmedetomidine. Several studies in the past have also demonstrated that pretreatment with dexmedetomidine significantly attenuated the cardiovascular and catecholamine responses to tracheal intubation.⁷⁻¹² However; attenuation was significantly

more with the dexmedetomidine group with a quicker return to baseline.

It is a well-known fact that dexmedetomidine reduces the inducing dose of propofol and thiopentone, but in this study we tried to find out that how much beneficial it is when compared to clonidine.^{13,14} It was found that the requirement of propofol was reduced after pretreatment with dexmedetomidine as compared to clonidine. This reduction in dose was statistically significant. The reduction in dose of inducing agent can be explained by the fact that dex has sedative, analgesic and sympatholytic effect due to its action on subtype B adrenoreceptors found mainly in the CNS. Similar results were also obtained by other studies.¹⁵⁻¹⁸

In another study, it was explained that when propofol was used, dexmedetomidine decreased the propofol concentration necessary for sedation by approximately 60-80%. Plasma noradrenaline concentration was markedly reduced in patients receiving dexmedetomidine. This decrement in neuronal noradrenaline release may explain in part the reduction in inducing agent requirements.¹⁹

As regards the post-operative analgesia duration, in present study it was found that almost all the patients receiving clonidine required analgesic within 3 hours after completion of surgery while those that received dexmedetomidine experienced a longer pain free interval. The analgesia produced by α_2 -agonist is due to their action at spinal, supra-spinal, direct analgesic and/or vasoconstricting actions on blood vessels.

The locus ceruleus and the dorsal raphe nucleus are the important central neural structures where these drugs act to produce sedation and analgesia.¹⁰ Dexmedetomidine being a more selective α_2 -agonist has more analgesic properties. Bijoy panda et al obtained similar results in their study when they compared the two drugs.¹⁹

CONCLUSION

Study concluded that dexmedetomidine when given as premedication was more effective than clonidine in suppressing the pressor response during intubation and extubation as well as for longer duration of post-operative analgesia.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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