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RESEARCH ARTICLE

ORIGINAL RESEARCH ARTICLE: DEXMEDETOMIDINE: A SIMPLE, EASY, AND ECONOMICAL ADJUVANT FOR GENERAL ANAESTHESIA

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ABSTRACT

Background: Since the first report of clonidine, an α_2-adrenoceptor agonist, the indications for this class of drugs have continued to expand. In December 1999, dexmedetomidine was approved as the most recent agent in this group and was introduced into clinical practice as a short-term sedative (<24 hours)
Aims & Objectives: To study the effect of dexmedetomidine on sedation, hemodynamic values, anesthetic consumption, and recovery from anesthesia.
Methodology: The study includes Forty-two female patients undergoing gynaecologic surgery were randomly assigned to receive IV Dex (1μg/kg: Dex group) or saline (control group) over 10 min before anaesthetic induction. After tracheal intubation, anaesthesia was maintained with sevoflurane, o_2 (50%) N_2o (50%).
Results: Mean arterial pressure (MAP) and heart rate (HR) after intubation were increased in Control group, but did not change in the Dex group. The HR of the Dex group was lower compared to that of the Control group during maintenance; no difference in MAP between the groups. End-tidal concentration and total cumulative consumption of sevoflurane were lower in the Dex group than in the control group. Recovery profiles, postoperative nausea, voming, and visual analogue pain score were not significantly different between the groups
Conclusion: single infusion of Dex(1 μg/kg) is a simple, easy and economical adjuvant for general anesthesia. Dex maintains stable hemodynamics and decreases anestbetic consumption without changing recovery profiles.

Key Words: Dexmedetomidine, Economics, Hemodynamics, Recovery, Sevoflurane.

INTRODUCTION

Dexmedetomidine has become of the frequently used drugs in anaesthetic armamentarium, along with routine anaesthetic drugs, due to its haemodynamic, sedative, anxiolytic, analgesic, neuroprotective and anaesthetic sparing effects. Other claimed advantages include minimal respiratory depression with cardioprotection, neuroprotection and renoprotection, thus making it useful at various situations including offsite procedures *(*Panzer *et al*., 2009*)*. α-1 to α-2 ratio of 1:1600 makes it a highly selective α-2 agonist compared to clonidine, thus reducing the unwanted side effects involving α-1 receptors. High selectivity of dexmedetomidine to α-2A receptors (which mediate analgesia and sedation) has been exploited by various authors in regional anaesthesia practice. Due to its central sympatholytic effect, dexmedetomidine is useful in blunting haemodynamic responses in perioperative period. It is successfully used in intravenous doses varying from 0.25 to 1 mcg/kg for attenuating intubation response (Bloor *et al*., 1992; Ebert *et al*., 2000; Bekker *et al*., 2008; Saðýroðlu *et al*., 2010). Optimal dose for attenuating pressor response seems to be 1 mcg/kg with lesser doses not being effective (Saðýroðlu *et al*., 2010).

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Infusion continued into the postoperative period has been associated with reduced haemodynamic fluctuations and decrease in plasma catecholamines (Ebert *et al*., 2000). Doses in the range of 0.5 mcg/kg not only blunted the extubation response but also reduced the emergence reaction and analgesic requirement to extubation following rhinoplasty and neurosurgery. There was no delay in recovery or prolonged sedation when boluses were administered before induction or before extubation. Similar was the observation when duration of infusion was within 2 hrs (Turan *et al*., 2008; Aksu *et al*., 2009). Bradycardia and hypotension are the major side effects observed following dexmedetomidine infusion.

Bradycardia is attributed to reflex response for transient hypertension during initial part of infusion. Subsequent decrease in heart rate is due to decrease in central sympathetic outflow. Hypotension is attributed to decreased central sympathetic outflow. Transient hypertensive response has been observed with higher doses (1-4 mcg/kg). This is attributed to initial stimulation of α-2B receptors present in vascular smooth muscles. This hypertensive episode settles once there is decrease in central sympathetic outflow. Mason *et al*. observed increased incidence of hypertension in children less than 1 year, undergoing magnetic resonance imaging (MRI) under dexmedetomidine sedation, and observed that younger children and multiple bolus therapies are highly significant predictors of the occurrence of hypertension (Mason *et al*., 2010).

MATERIALS AND METHODS

This study was conducted in department of gynaecology in collaboration with anaesthesia department of anaesthesia of AMC MET MEDI COLLEGE, Sheth L.G.Hospital Ahmedabad,Gujarat from January 2012-2013. The double-blinded study, Forty-two female patients scheduled for gynecologic surgery were enrolled in the study & operation time was two hours. All patients were pre-med-icated with Injglycopyrrolate (0.2 mg) before anesthesia. The study employed a multi-functional anesthetic machine that could measure the consumption of volatile anesthetics . Patients were randomized to receive a 10-minute infusion of either normal saline (10 ml; Control group) or Dex (1µg/kg; 10 ml; Dex group) before anesthetic induction . Anesthesia was maintained with sevoflurane with o_2 and n_2o . Ventilation was controlled to maintain an end-tidal (Et) CO_2 of around 30-35 mmHg. For hemodynamic stability, fentanyl (1µg/kg; IV) was administered if the patient's mean arterial pressure (MAP) was more than 20% above the baseline value while decreases in MAP of a similar magnitude were treated with ephedrine (4-8 mg; IV) and glycopyrrolate (0.1 mg; IV) if the patient's heart rate (HR) was less than 45 beats/min.

MAP, and HR were recorded at several time as follows: before induction (baseline), after the end of study drug infusion, before intubation, immediately after intubation, 10,20,30,60, and 90 minutes after intubation, and in the recovery room. SpO_2 was measured before induction (baseline) and after the end of study drug infusion. Et sevoflurane concentration and the cumulative doses of sevoflurane consumed were measured at 10,20,30,60, and 90 minutes after intubation. To assess the recovery profiles , the times taken to reach sevoflurane Et 0.8% were determined, to respond to a suction catheer, to obey verbal commands , and to complete tracheal extubation after turning off the vaporizer. The postoperative nausea/vomiting (PONV) , and postoperative pain by the was recorded visual analogue score (VAS; 0 = no pain; 10= worst possible pain).

As per power analysis, a 20 patients per study group was determined to be sufficient for identifying a 20% difference between the two groups' hemodynamic changes with a power of 0.8 and x value of 0.05 with the reference to Basaretal. (8). Data were analyzed using an unpaired t test, Fisher's exact test (rescue drug, PONV), as appropriate. The hemodynamic variable within each group were analyzed by repeated measures of analysis of variance (ANOVA). P value of <0.05 was considered to be statistically significant.

RESULTS

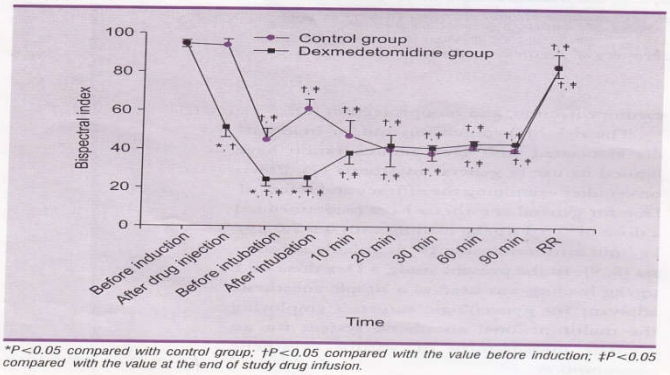
Forty-two patients were entrolled in the study and randomized into groups, which did not differ significantly in age, height, weight, or duration of anesthesia. (Table/Fig 1) After infusion of the study drug was completed, the BIS of the Dex group was significantly lower than that of Control group (51.5 ± 5.2 vs 93.9 ± 3.1 ,P = 0.000) (Figure 2) without respiratory depression (for SpO2 99.5 ± 0.8% vs 98.0 ± 1.4%, P > 0.05: control vs Dex group). After tracheal intubation, both MAP and HR significantly increased in the Control group (but remained unchanged in the Dex group. In addition, there were no significant differences in MAP between the groups during maintenance; however, the HR of the Dex group was significantly lower compared with that of Control group (Figure 2).

Table 1. Characteristics of female patients participating in the study

	Control group (n = 21)	Dexmedetomidine group (n = 21)
Age (yr)	47.8 ± 6.1	44.3 ± 6.4
Height (cm)	156.7 ± 4.6	157.1 ± 5.1
Weight (kg)	59.1 ± 9.1	62.6 ± 7.8
Type of operation (n)		
TAH	8	7
LAVH	11	13
Ovarian surgery	2	1
Duration of anesthesia (min)	155.8 ± 21.7	172.5 ± 35.8
Rescue drug		
Ephedrine (n)	0	3
Fentanyl (n)	2	0

Data are mean ± SD or number of patients (n). TAH: transabdominal hysterectomy, LAVH: laparoscopic vaginal hysterectomy.

Figure 1. Changes in the Bispectral index (BIS) during sevoflruane anesthesia



**P<0.05 compared with control group; †P<0.05 compared with the value before induction; ‡P<0.05 compared with the value at the end of study drug infusion.*

Table 2. Time taken to reach end-tidal sevoflurane 0.8 vol%, recovery profiles, modified aldrete score, postoperative nausea and vomiting (ponv), and visual analogue scale (vas) during sevoflurane anesthesia

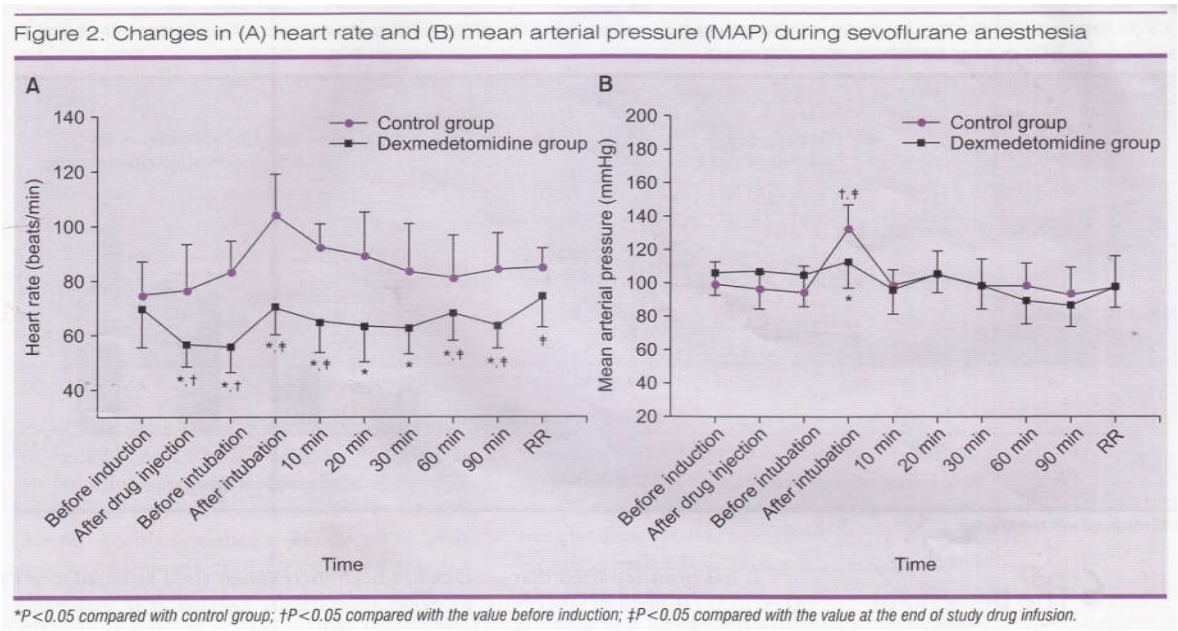
Recovery variables	Control group (n = 21)	Dexmedetomidine group (n = 21)
Time taken to reach end-tidal sevoflurane 0.8 vol% (sec)	163.8 ± 53.4	50.3 ± 35.5*
Time to suction catheter response (sec)	438.3 ± 106.0	515.1 ± 219.6
Time to obey verbal commands (sec)	643.3 ± 245.7	696.1 ± 207.3
Time to tracheal extubation (sec)	738.3 ± 205.7	743.3 ± 205.4
Modified Aldrete score arrived at recovery room	6.9 ± 1.3	7.8 ± 1.6
Time taken to modified Aldrete score 9 in the recovery room (min)	13.1 ± 7.2	14.8 ± 11.7
PONV in the recovery room (number)	3	2
VAS (0-10) in the recovery room	6.5 ± 1.0	5.0 ± 1.8

*Values are mean ± SD or or number of patients (n). Et: endtidal, *P < 0.05 versus control group.*

End-tidal concentration (at 90 min: 2.0 ± 0.5 vo1% vs 1.4 ± 0.3 vo1%, P= 0.029, P < 0.05: Control vs Dex group) and total cumulative consumption dose of sevoflurane (at 90 min; 34.6 ± 3.8 ml vs 26.5 ± 5.3 ml,P = 0.017, Control vs Dex group) WERE significantly lower in the Dex group compared with the Control group at 20 min, 30 min, 60 min, and 90 min after intubation (Figure 3). In addition, the time taken to reach sevoflurane Et 0.8 vo1% was significantly shorter in the Dex group compared with the Control group (Table/Fig 2); however, as show by the recovery profiles, the time taken to respond to a suction catheter, to obey verbal commands, and to complete tracheal extubation after turning off the vaporizer were similar between groups (Table 1). Furthermore, the time taken to reach a modified Aldrete score of 9, PONV, and VAS score in the recovery room were not different between two groups (Table/Fig 2).

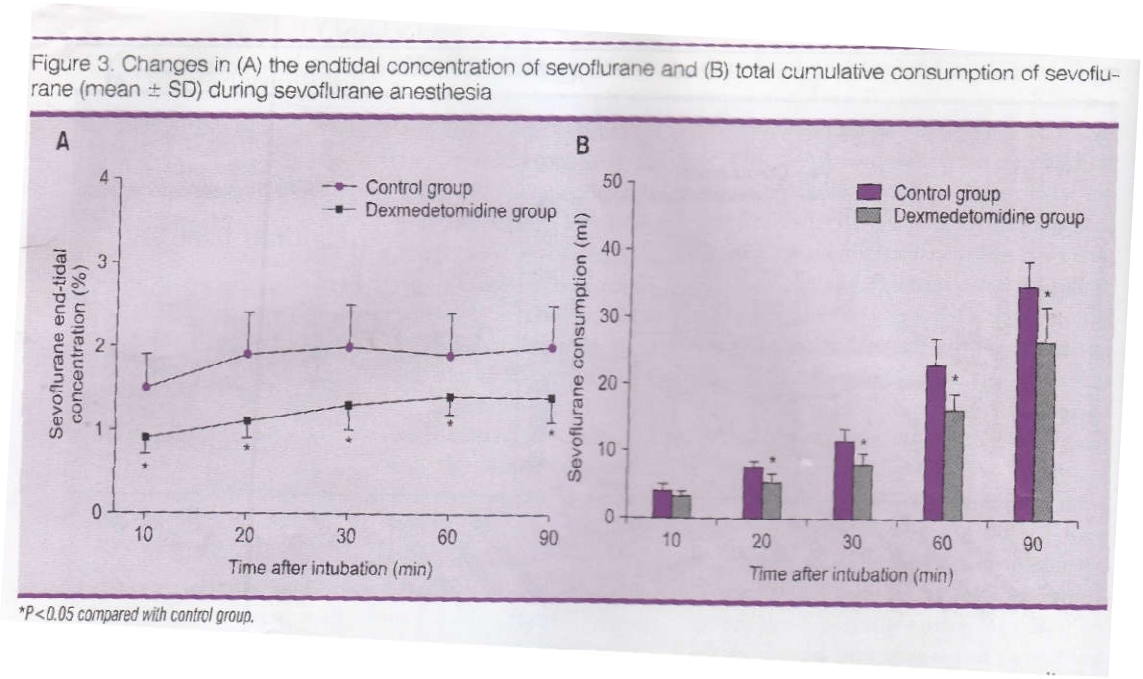
DISCUSSION

It has been reported that Dex (0.5-1.0 µg/kg) induces sedation within 5 minutes and reaches its maximum effects within 15 minutes.



*P<0.05 compared with control group; †P<0.05 compared with the value before induction; ‡P<0.05 compared with the value at the end of study drug infusion.

Figure 2. Changes in (A) heart rate and (B) mean arterial pressure (MAP) during sevoflurane anesthesia



*P<0.05 compared with control group.

Figure 3. Changes in (A) the endtidal concentration of sevoflurane and (B) total cumulative consumption of sevoflurane (mean ± SD) during sevoflurane anesthesia

In general, sedation induced by Dex was similar to normal sleep. Compared to other sedatives Dex has a favourable profile due its ability to produce good sedative outcomes without respiratory depression. Dex has not been routinely used in general anesthesia due (6,7); however, Dex has been increasingly used as an adjuvant to general anesthesia because it is associated with anesthetic sparing, hemodynamic stability , and the reduction of emergence agitation . In intubated patients, lower. Additionally, Dex has been used to successfully facilitate the withdrawal of ventilation in ICU patients who previously failed weaning attempts because of agitation.

Large doses or rapid injection of Dex have been associated with adverse events (1) such as hypotension, bradycardia and even sinus arrest in healthy young volunteers with high vagal tone secondary to the attenuation of plasma catecholamine release. Thus, Dex (over 1.0μg/kg) should be infused over 10 minutes and titrated to an adequate dosage on a case-by-case basis.

The over-infusion or over-dosage of anesthetics should be prevented by by monitoring HR BIS. Thus, the use of an anesthetic depth monitoring like BIS is essential when employing a Dex adjuvant for general anesthesia. Dex is a less appropriate adjuvant for propofol anesthesia when compared to volatile anesthetics because of the centrally mediated vagotonic or sympatholytic actions of propofol.

In the present study Dex (1 ug/kg) reduced the Et sevoflurane concentration by 30% and total consumption of sevoflurane by 23.4 compared with the Control group. Previously, studies of anesthetic consumption have shown Dex to reduce target propofol concentration by 30- 50% during propofol- anesthesia (9) and end-tidal concentration by 15-20% during volatile anesthesia. The pharmacoeconomic effect of Dex may aid in reducing the concentration of anesthetics used and preventing adverse effects such as hepatic and renal toxicity, severe myocardial depression, and the greenhouse effect.

Although the time to reach Et sevoflurane 0.8 vo1% was faster in the Dex group compared with the Control group, all patients had similar recovery profiles. A possible explanation is that the analgesic and sedative effects o f Dex may be in effect during the perioperative period, making it possible for patients in the Dex group to reach the BIS value at a lower Et sevoflurane concentration. Some studies have reported that the analgesic effect of Dex is present in the recovery room, but did not continue after recovery room discharge. McQueen-Shadfar *et al*. reported that there was no difference in pain score, analgesics, or rescue antiemetic between the Dex group and the Control group, but the Dex group stayed longer in the recovery room. Lawrence and De Lange reported reduced analgesic use, antiemetic and a higher occurrence of hypotension and bradycardia despite similar findings of perioperative hemodynamic stability and lower isoflurane concentration (10, 11).

Conclusion

In conclusion, single infusion of Dex (1 µg/kg) is a good anesthetic adjuvant for general anesthesia that can attenuate the hemodynamic respone to tracheal intubation. In addition, Dex maintains stable hemodynamics and decreases anesthetic consumption without changing recovery profiles. It is very simple, easy and economical adjuvant for general anaesthesia.

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