Dexmedetomidine: A simple, easy, and economical adjuvant for general anesthesia

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ABSTRACT

This study examined the effect of dexmedetomidine on sedation, hemodynamic values, anesthetic consumption, and recovery from anesthesia. Forty-two female patients undergoing gynecological surgery were randomly assigned to receive IV Dex (1µg/kg; Dex group) or saline (control group) over 10 min before anesthetic induction. After tracheal intubation, anesthesia was maintained with sevoflurane, O2 (50%) N2O(50%).

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, vomiting, and visual analogue pain score were not significantly different between the groups.

In conclusion, single infusion of Dex (1 µg/kg) is a simple, easy and economical adjuvant for general anesthesia. Dex maintains stable hemodynamics and decreases anesthetic consumption without changing recovery profiles.

Introduction:
Dexmedetomidine (Dex) is an α₂- adrenergic agonist and close relative of clonidine that activates receptors distinct from the y-aminobutyric acid receptor and propofol (1,2). It has sedative and analgesic effects, and without respiratory depression (2). Dex has been used for sedation during mechanical ventilation, procedural sedation, postoperative analgesia, the prevention of emergence agitation, and the treatment of substance withdrawal (3-5). Moreover, several studies have reported several beneficial effects of Dex, including neuroprotection, cardioprotection, and renoprotection (6).

The risk of hypotension and/or bradycardia associated with Dex administration have limited its use in general anesthesia (7). Previous studies examining the efficacy and safety of Dex for general anesthesia have recommended a dose of 0.5-1µg/kg loading with 0.5-1.0 µg/kg/min infusion during IV or volatile anesthesia (8,9). In the present study, a Dex dose of 1 µg/kg loading was used as a simple anesthetic adjuvant for gynecologic surgeries.

Material & Method:
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-medicated 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-min 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 O₂ and N₂O. Ventilation was controlled to maintain an end-tidal (Et) CO₂ 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. SpO₂ 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 catheter, 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 scale (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). A P value of <0.05 was considered to be statisti-
cally significant.

**Result:**
Forty-two patients were enrolled in the study and randomized into groups, which did not differ significantly in age, height, weight, or duration of anesthesia. 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 1) 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).

End-tidal concentration (at 90 min: 2.0 ± 0.5 vol% vs. 1.4 ± 0.3 vol%, 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 vol% was significantly shorter in the Dex group compared with the Control group (Table 1); however, as shown by the recovery profiles, the time taken to respond to a suction catheter, to obey verbal commands, and to complete tracheal extubation 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 2).

**Discussion:**
The present study demonstrates that a single infusion of Dex (1 µg/kg) prevents hemodynamic changes by tracheal intubation and reduces the total cumulative consumption of sevoflurane. However, there were no differences between the Dex group and Control group in regards to recovery profiles, modified Aldrete scores, PONV, and VAS scores.

Dex is a highly selective alphabtic2 receptor agonist with sedative and anxiolytic properties. The alphabtic2-selectivity of Dex in the brain and spinal cord is approximately 7–to-8-fold greater than that of clonidine (11). Stimulation of 2 receptor subtypes mediates sedative and anti-nociceptive actions (2A), a vasoconstrictive effect (2B), and modulates dopaminergic neurotransmission, hypothermia, and a variety of behavioral responses (2C). It is the inhibition of norepinephrine release via A receptors, which controls anxiety, arousal, sleep, and opioid withdrawal (9).

It has been reported that Dex (0.5-1.0 µg/kg) induces sedation within 5 minutes and reaches its maximum effects at 15 minutes. In general, sedation induced by Dex was similar to normal sleep. Compared to other sedatives, Dex has a favourable profile due to 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 monitoring HR and 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 µg/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 (8) 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 vol% 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 of 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.

**Table 1. Characteristics of female patients participating in the study**

| 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 | 62.0 ± 7.8 |
| Type of operation (n) | TAH | 8 | 7 |
| LAWH | 11 | 13 |
| Ovarian surgery | 2 | 1 |
| Duration of anesthesia (min) | 155.8 ± 21.7 | 172.5 ± 35.8 |
| Rescue drug | Epinephrine (n) | 0 | 3 |
| Fentanyl (n) | 2 | 0 |

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

### CONCLUSION:

In conclusion, single infusion of Dex (1 µg/kg) is a good anesthetic adjuvant for general anesthesia that can attenuate the hemodynamic response 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.