Dexmedetomidine versus propofol in dilatation and curettage: An open-label pilot randomized controlled trial

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ABSTRACT

Background: Traditionally propofol has been used for providing sedation in dilatation and curettage (D and C). Recently, dexmedetomidine has been tried, but very little evidence exists to support its use. **Aims:** The aim was to compare hemodynamic and recovery profile of both the drugs along with a degree of comfort experienced by patients and the usefulness of the drug to surgeons. **Settings and Design:** Tertiary care center and open-label randomized controlled trial. **Materials and Methods:** Patients posted for D and C were enrolled in two groups (25 each). Both groups received fentanyl 1 μg/kg intravenous (IV) at the beginning of the procedure. Group P received IV propofol in dose of 1.5 mg/kg over 10-15 min and Group D received dexmedetomidine at a loading dose of 1 μg/kg over 10 min, followed by 0.5 μg/kg/h infusion until Ramsay sedation score reached 3-4. Hemodynamic vitals were compared during and after the procedure. In the recovery room time to reach modified Aldrete score (MAS) of 9-10 and patient's and surgeon's satisfaction scores were also recorded and compared. **Results:** In Group D, patients had statistically significant lower heart rate at 2, 5, 10 and 15 min as compared to Group P. Hypotension was present in 52% in Group P and 4% in Group D ($P < 0.05$). MAS of 9-10 was achieved in 4.4 min in subjects in Group D in contrast to 16.2 min in Group P ($P < 0.05$). Group D showed higher patient and surgeon satisfaction scores ($P < 0.05$). **Conclusion:** Dexmedetomidine provide better hemodynamic and recovery profile than propofol. It can be a superior alternative for short surgical day care procedures.

Key words: *Conscious sedation, dexmedetomidine, dilatation and curettage, gynecologic day care procedures, propofol, sedation*

INTRODUCTION

Dilatation and curettage (D and C) is the most frequently performed minor surgery in obstetrics and gynecology. Now a days combination of sedative, hypnotic and opioid analgesic are frequently used.[1] Propofol is a widely used sedative and hypnotic agent with minimal analgesic properties. However, it also causes respiratory depression, and this effect is potentiated in the presence of opioids.[2]

Dexmedetomidine is a highly selective alpha-2-adrenergic receptor agonist that has analgesic and sedative properties without any respiratory depression and can be used for conscious sedation. Traditionally propofol has been used for D and C and there is a paucity of data for use of dexmedetomidine in D and C.

Purpose of this study was to evaluate the hemodynamic and respiratory effects (as a primary outcome) and the recovery profile and surgeons and patients satisfaction (as a secondary outcome) with dexmedetomidine sedation compared with those of propofol sedation in patients undergoing D and C. This open-label pilot randomized controlled trial (RCT) was designed to compare the safety and recovery profile of dexmedetomidine with propofol in combination with fentanyl during D and C.

MATERIALS AND METHODS

After Ethical Committee approval and written informed consent from patients, an open-label, RCT was conducted

at tertiary care center, on 50 patients, aged 18-60 years of age undergoing diagnostic and therapeutic D and C, with American Society of Anesthesiologist (ASA) Grades I and II. Patients who had ASA physical status Grade III and more, baseline oxygen saturation (SpO_2) <90%, patients with comorbid conditions such as diabetes mellitus, hypertension (HTN) or hepatic or renal insufficiency or pregnancy were excluded. Patients who had difficulty in communication (due to language problem or deafness), a known allergy to these drugs and with a history of egg or soya bean allergy were also excluded.

Preoperative check-up was done. In operating room, venous access was secured on the nondominant hand of every patient by 18G/20G cannula and intravenous (IV) fluid was started. Baseline parameters including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MAP), respiratory rate (RR) and SpO_2% were recorded. These were again recorded immediately after the loading dose (0 min) and then at 2, 5 and 10 min during the procedure and then after completion of the procedure.

Simple random sequence was generated from the computer. Subjects were randomized into two groups with a 1:1 allocation ratio. The allocated intervention was written on slips of paper, placed in serially numbered, opaque envelopes and sealed. As consecutive eligible subjects got enrolled, the envelopes were serially opened, and the allocated intervention was implemented. The chief investigator, medical and nursing personnel were not blinded as it was an open-label trial. Subjects were followed from the point of randomization until complete recovery. Complete recovery was defined as achievement of modified Aldrete score[3] (MAS) of 9-10.

Patients in both the groups received fentanyl at a dose of 1 µg/kg 5 min prior to the procedure. Patients in this study Group D received dexmedetomidine at loading dose of 1 µg/kg IV over 10 min followed by 0.5 µg/kg/h infusion until Ramsay sedation score[4] (RSS) [Table 3] reached 3-4. Group P received propofol at a dose of 1.5 mg/kg as slow IV bolus over 10-15 min till RSS reached 3-4. If the patient required more than three episode of personal restrain by an assistant during the procedure or if either patient or surgeon was uncomfortable, the rescue IV sedation was provided with IV propofol in top up incremental dose of 10 mg until patient reached RSS 3-4. During procedure any bradycardia (HR under 50 beats/min or a 20% decrease from the baseline) or tachycardia (HR over 110 or an increase in the baseline level of more than 20%) and any hypotension (MAP levels lower than 60 mmHg or 20% less than the baseline) or HTN (MAP value of over 150 mmHg

or a 20% increase from the baseline) and hypoxia (fall of RR to 8 breaths or less per minute or a fall of arterial SpO_2 value to <90%) were observed, recorded and treated accordingly. Requirement of rescue drug in each group was also recorded and compared. Possible complications, such as respiratory depression, allergies, coughing, nausea and vomiting during the procedure were also recorded and compared.

In the recovery room, MAS of patients were recorded every 5 min by anesthesiologist along with any adverse effect such as restlessness, shivering, nausea, vomiting, abdominal discomfort and respiratory depression. On achieving MAS of 9-10, patients were discharged. After the procedure, the satisfaction of the surgeon and patient was assessed using satisfaction score (4 = excellent, 3 = good, 2 = fair and 1 = poor). The duration of stay in the recovery room was also recorded. In the case of any adverse events in the recovery room such as nausea, vomiting, abdominal discomfort and respiratory depression, the patients were observed in the hospital for at least 12 h.

It was a pilot study, and a convenient sample size of 50 subjects was taken. Our primary outcome was to compare hemodynamic profile in both the groups along with patient and surgeon's satisfaction score. Descriptive statistics was used to describe the baseline characteristics. Dichotomous outcomes were compared by Chi-square test with continuity correction or Fisher's exact test as applicable. Numerical variables were compared by the Student's *t*-test or Mann-Whitney U-test, depending on the distribution. Intra-group comparison was performed using repeated measure ANOVA. Analysis was the intention to treat, that is, all subjects who were randomized were included in the analysis, irrespective of the degree of compliance. Analysis was performed using SPSS version 17 (SPSS 17, 233 South Wacker Drive, 11th Floor, Chicago, IL 60606-6412). The results were considered significant when the $P < 0.05$.

RESULTS

Demographic data and the baseline vitals were comparable in two groups [Table 1]. Group D had statistically significant ($P < 0.05$) lower HR after infusion of loading dose at 2, 5 and 10 min during procedure and immediately after procedure [Figure 1] [Table 2]. Fifteen patients (60%) in Group D and only two patients (8%) in Group P had bradycardia ($P < 0.05$) but none of the patients required any medication to treat it. Patients in Group P had lower MAP at 2, 5 and 10 min during the procedure and immediately after procedure, and the difference was statistically significant [Figure 2]. In Group P, patients had significantly more incidences of hypotension when

compared with the Group D (52% vs. 8%; $P < 0.05$). SBP and DBP were also statistically lower in Group P at 2, 5 and 10 min and also postoperatively as compared to Group D ($P < 0.05$) [Figure 3] [Table 2]. Thirteen patients in Group P and none in Group D had hypoxia (52% vs. 0; $P < 0.05$) [Table 2]. Requirement of rescue drug (propofol) during the procedure was 5.7 ± 9 mg in Group D and 23.8 ± 6.5 mg in Group P ($P < 0.05$). There was no episode of nausea and vomiting in any of the patient studied intra-operatively and in the recovery room. The recovery was quicker in Group D when compared with the Group P and result was statistically significant. Average time for recovery (MAS 9-10) was 4.4 ± 2.3 min in Group D and 16.3 ± 5.5 min in Group P ($P < 0.05$). Both the patient and surgeon's satisfaction scores were higher in Group D when compared with Group P. Group P had median value of patient and doctor satisfaction score as 2 (1.70, 2) and 3 (2, 3) whereas it was 3 (3, 3) and 4 (4, 4) in Group D

respectively. Both scores were higher in Group D and the result was statistically significant ($P < 0.001$).

DISCUSSION

A prospective RCT to compare the efficacy and safety of IV dexmedetomidine and IV propofol for conscious sedation and analgesia during D and C was conducted. Propofol (2,6-diisopropylphenol) is a short-acting, IV administered hypnotic/amnestic agent. It can be used for the induction and maintenance of general anesthesia, sedation for mechanically ventilated patients and procedural sedation. Propofol has no analgesic property, and hence opioids such as fentanyl are used as adjunct to alleviate pain.[5] Common adverse effect of propofol includes hypotension, hypoxemia, and respiratory depression. Dexmedetomidine is a new drug, which is highly selective alpha-2-adrenoceptors agonist with sympatholytic, sedative, amnestic and the analgesic properties.[6] In recent years, it has been used as a useful and safe adjunct in many clinical applications. It provides a unique "conscious sedation" (patients appear to be asleep but are readily aroused) and analgesia, without respiratory depression.

The aim of this study was to compare hemodynamic and recovery profile of both drugs in both groups. We also compared the degree of comfort experienced by patients and the usefulness of the drug to surgeons. In Group D induction dose was given by infusion in 10 min followed by maintenance, but in Group P drug was given as a slow IV bolus over 10-15 min. Doses of dexmedetomidine used our study were in the range of those used widely in previous studies to induce sedation in patients who underwent anesthesia.[7-9]

Table 1: Baseline variables

Baseline characteristics	Group D (n = 25) mean ± SD	Group P (n = 25) mean ± SD
Age (years)	40±11	42±14
Weight (kg)	65±11	66±10
ASA Grade I (n) (%)	18 (72)*	17 (68)*
Preoperative HR (per min)	89±9	90±12
Preoperative RR (per min)	15±5	14±1
SBP (mm of Hg)	133±14	141±21
DBP (mm of Hg)	88±9	83±10
MAP (mm of Hg)	103±10	102±12
SpO_2 (%)	98±2	98±2

*Figures expressed in this manner are in percentage. SBP: Systolic blood pressure, DBP: Diastolic blood pressure, ASA: American Society of Anesthesiologist, SpO_2: Oxygen saturation, HR: Heart rate, MAP: Mean arterial pressure, SD: Standard deviation, RR: Respiratory rate

Table 2: Perioperative haemodynamics variables

Timings	Groups (n = 25)	HR (per min)	RR (per min)	SBP (mm of Hg)	DBP (mm of Hg)	SpO_2 (%)
0 min (mean±SD)	Group P	89±12	14±2	141.44±20.16	83.04±9.59	98±2
	Group D	89±10	14±2	132.88±14.07	87.76±8.7	98±2
	P	0.89	0.5	0.846	0.671	0.621
2 min (mean±SD)	Group P	90±14	13±2	117±14.6	76.2±12.97	92±3
	Group D	71±14	14±2	125±13.7	81.8±9.15	98±2
	P	0.0002	0.395	0.0471	0.081	0.001
5 min (mean±SD)	Group P	85±17	11±2	110.8±14.3	72.5±14.3	90±3
	Group D	66±13	14±2	120.8±13.3	80.6±13.3	97±3
	P	0.0001	0.39	0.0137	0.046	0.0001
10 min (mean±SD)	Group P	82±17	11±2	112.5±16	74.8±14.2	89±7
	Group D	63±18	14±3	120.1±14.8	86.4±9.4	96±4
	P	0.009	0.001	0.0469	0.461	0.004
Postoperative (mean±SD)	Group P	91±14	13±2	120.3±15.4	78.9±8.8	92±2
	Group D	70±14	14±2	127.6±14.6	86.4±7.9	98±2
	P	0.006	0.0001	0.0469	0.145	0.0001

SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HR: Heart rate, RR: Respiratory rate, SD: Standard deviation, SpO_2: Oxygen saturation
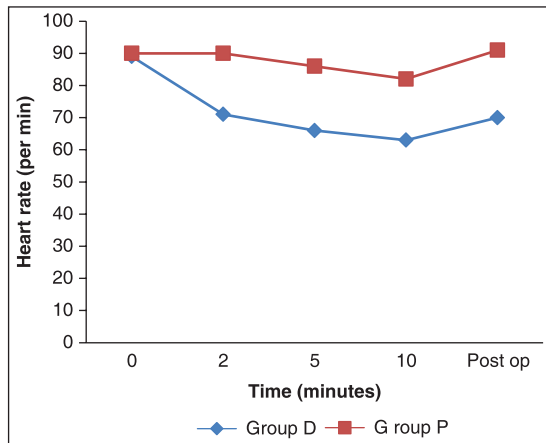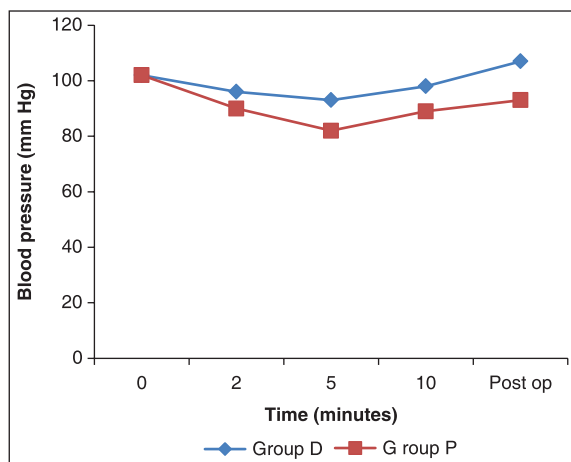
Figure 1: Trend of heart rate in both groups

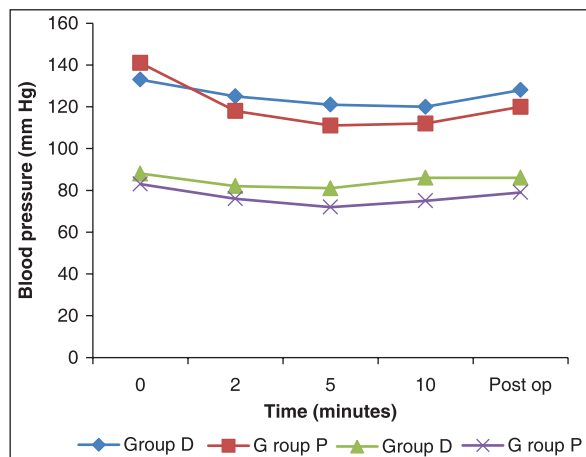**Figure 2:** Trend of mean blood pressure in both groups

Figure 3: Trend of systolic and diastolic blood pressures in both groups

There was significant difference in HR, MAP, RR and SpO_2 in Group D when compared with Group P. Patients in Group D had statistically significant lower HR after infusion of loading dose and at 2, 5, 10 and 15 min during D and C. Major side effect of alpha-2-agonist agents is bradycardia, which is mediated by activation of alpha-2-

Table 3: Ramsay sedation score
Anxious, agitated or restless
Cooperative, oriented and tranquil
Responsive to commands
Asleep, but with brisk response to light glabellar tap or loud auditory stimulus
Asleep, sluggish response to glabellar tap or auditory stimulus
Asleep, no response

adrenoceptors, especially in the solitarius nucleus tract.[10,11] Many studies had the demonstrated inhibitory effect of propofol on sympathetic outflow,[12] dexmedetomidine also has sympatholytic effects and decreases circulating catecholamine levels. Hence, a similar decrease in fall in MAP and HR was expected in both the groups.[13] The decrease in the HR might be attributed to the sympatholytic effects. In this study, we observed decrease in HR and comparatively stable blood pressure (BP) values in Group D. In Group P BP found to be lower during the procedure in subsequent measurements compared with both baseline values and Group D. It proves that dexmedetomidine has clinical advantages over propofol in controlling hemodynamic variability. Taniyama *et al.*[14] also found statistically significant lower HRs in the dexmedetomidine group and lower BP and SpO_2 in the propofol group. In this study, Group D had better SpO_2 and stable hemodynamics than Group P. Ghali *et al.*[15] also reported lower saturation levels in the propofol group. In this study, there was a significant difference between two groups regarding the requirement of propofol as rescue drug, with an increasing trend of using it in Group P ($P < 0.001$). MAS during recovery was statistically different between two groups ($P < 0.001$).

There was no intra-operative or postoperative adverse effects in the dexmedetomidine group and our results were similar to Abdellatif *et al.*[16] and Arain and Ebert[17] Abdellatif *et al.*[16] found that there were no intra-operative or postoperative side-effects as hypotension, oxygen desaturation, and nausea and vomiting in Group D. Takimoto *et al.*[18] also concluded that none of the patient in Group D had oxygen desaturation and hypotension. Thus, sedation safety of dexmedetomidine with reduced adverse effects was proved.

Patients and surgeon's satisfaction were compared by a scoring system and there was statistically significant difference between two groups ($P < 0.001$). Group D had higher satisfaction scores both for patients and surgeon. These findings were similar to findings of Arain and Ebert[17] and Takimoto *et al.*[18] as propofol sedation in this study was associated with lower patient satisfaction and more use of rescue analgesic. Arain and Ebert[17] found that surgeon's satisfaction was similar for both groups, but in the dexmedetomidine group, there was higher patient's

satisfaction compared with the propofol group. Takimoto *et al*.[18] and also mentioned that the rate of effective sedation was significantly higher in the dexmedetomidine group compared with the midazolam or propofol group in their study.

The main limitation of the study is that it is open-labeled RCT so there is always an inherent risk of bias toward intervention group. All patients were either ASA physical status I or II, results cannot be generalized to ASA physical status III and IV patients. Patients were otherwise healthy patients, free of significant comorbidities that might have exaggerated the cardiovascular side-effects of propofol or dexmedetomidine.

This study is able to demonstrate that the use of dexmedetomidine for D and C could be a superior alternative to propofol. Dexmedetomidine is a safe drug with good hemodynamic and recovery profile. Degree of satisfaction experienced by patients and surgeons was better with dexmedetomidine and very few studies are published regarding its use in D and C. However, there is need for further multicenter RCT to confirm the findings of our study. Hence that dexmedetomidine can become standard of care for day care procedures such as D and C.

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