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Comparison of sedation with dexmedetomidine vs propofol during hysteroscopic surgery: Single-centre randomized controlled trial

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Summary

What is known and objective: The most appropriate sedative agent for conscious sedation in minor hysteroscopic surgeries is still unclear. Dexmedetomidine a sedative and analgesic agent, may be appropriate for outpatient procedures. The aim of our study was to compare the sedative, analgesic and hemodynamic effects of dexmedetomidine vs propofol in combination with fentanyl and midazolam in patients undergoing minor hysteroscopy surgery.

Methods: Sixty patients undergoing minor hysteroscopic surgery were randomized to receive either dexmedetomidine (n = 30) or propofol (n = 30) groups. Dexmedetomidine was infused at 1 μg/kg for 10 minutes followed by a 0.7 μg/kg/h maintenance infusion. Propofol was infused a bolus of 1.5 mg/kg followed by a 2.5 mg/kg/h maintenance infusion. Fentanyl 1.5 mcg/kg and midazolam 0.03 mg/kg were performed to all patients as premedication therapy before the hysteroscopic surgery. Post-operative pain score was assessed with visual analogue scale (VAS). Hemodynamic variables and Riker Sedation-Agitation Scale (SAS) scores were recorded for all patients.

Results: Mean arterial pressure and heart rate in the dexmedetomidine group were significantly lower than in propofol group, whereas SpO2 was similar between two groups. In addition, post-operative Riker SAS and VAS scores were significantly lower in dexmedetomidine group than in the propofol group. Bradycardia, hypotension and serious adverse events did not occur in any patients.

What is new and conclusion: Dexmedetomidine was associated with better analgesia and lower post-operative pain score than propofol in patients undergoing hysteroscopic surgery. However, arterial pressure and heart rate should be more closely monitored in patients received dexmedetomidine.

KEYWORDS
dexmedetomidine, hysteroscopy, propofol, sedative agents

1 | WHAT IS KNOWN AND OBJECTIVE

Hysteroscopy is simple, safe and one of the most common performed outpatient procedures for both diagnosis and treatment of uterine diseases. Although this procedure has many advantages, the most important disadvantage is severe pain due to uterine distention and cervical dilatation.[1] Because of increased pain and anxiety related to hysteroscopy, an effective sedation and analgesia must be provided during the procedure to achieve maximum patient comfort and cooperation.

A rapid shift from general anaesthesia to intravenous sedation has been seen in hysteroscopic surgeries. A combination of a sedative agent with an opioid analgesic is a typical approach to provide effective anaesthesia. The most commonly used sedative drug for conscious sedation is propofol due to its fast effect, easy titration and short half-life.[2] It can decrease patient anxiety and pain and increase patient comfort. However, propofol may cause some serious problems such as respiratory depression, hypotension and hemodynamic instability.[3] Therefore, determining an ideal sedative drug during hysteroscopy surgery is still essential.

Dexmedetomidine is a potent alpha-2 adrenergic receptor agonist. It has analgesic properties and provides conscious sedation and sufficient analgesia without respiratory depression.[4] It also reduces the stress response to surgery and is associated with better hemodynamic stability.[5] Therefore, dexmedetomidine has become a commonly used sedative agent especially in intensive care units.[6] Besides, it may be an important agent for outpatient procedures, such as hysteroscopy.

In previous studies, it has been demonstrated that dexmedetomidine is a more beneficial sedative agent than propofol for conscious sedation during different ambulatory surgeries.[7-11] However, there is no study comparing the effects of dexmedetomidine vs propofol in patients undergoing minor hysteroscopy surgeries. The objective of this study was to compare the sedative, analgesic and hemodynamic effects of dexmedetomidine vs propofol in patients undergoing minor hysteroscopy surgery.

2 | METHODS

A total of 60 patients scheduled for minor hysteroscopic surgery and aged between 18 and 65 years, with American Society of Anaesthesiologist (ASA) grades I or II, were enrolled in this randomized study. Randomization was performed by a computer-generated scheme (computerized sequence generation) to receive dexmedetomidine or propofol. The major exclusion criteria were as follows: (I) ASA grades III or higher; (II) previous history of hepatic, renal or cardiovascular diseases; (III) known allergy to any of the used medications; (IV) those with body mass index >30 kg/m2; (V) blood pressure >160/110 mm Hg, or <100/50 mm Hg; or (VI) heart rate >120. The local ethics committee approved the study design (date: 28.06.2012, number: 23/B), and written informed consent was obtained from all patients. The study was registered at Australian New Zealand Clinical Trials Registry (registration number: ACTRN12618001037291).

Venous access was secured using a 20-G intravenous canula and isolyte multi-electrolyte solution was started to meet the patient's basal fluid requirement. Patients were monitored, and mean arterial pressure (MAP), heart rate (HR) and oxygen saturation (SpO2) were recorded. Just before the operation, 0.03 mg/kg midazolam and 1.5 mcg/kg fentanyl intravenous bolus were given to all patients as premedication. Prophylactic oxygen (4 L/min) was provided by a suitable face mask during the operation. Patients were assigned to undergo conscious sedation with dexmedetomidine or propofol group using a computer-generated randomization schedule as follows: dexmedetomidine group (D group, n = 30) and propofol group (P group, n = 30). Patients in group D received dexmedetomidine at a loading dose of 1 μg/kg over 10 minutes, followed by a 0.7 μg/kg/h maintenance infusion. Patients in group P received a bolus of 1.5 mg/kg propofol followed by a 2.5 mg/kg/h maintenance infusion. If the sedation level was insufficient, the maintenance dexmedetomidine infusion was increased to 1 μg/kg/h and the maintenance propofol infusion was increased to 3 mg/kg/h. If the sedation level was excessive, the maintenance dexmedetomidine and propofol infusion doses were decreased by 20%. The following evaluation time points were defined: T0: preoperative (basal), T1: first minute of the initiation of sedative infusion, T2: 5 minutes after the initiation of sedative infusion, T3: 10 minutes after the initiation of sedative infusion, T4: the end of operation, T5: 1 minute after operation, T6: 15 minutes after operation, and T7: 30 minutes after operation.

Following the end of the operation, patients were taken to the Post Anesthesia Care Unit (PACU) for close monitoring until their discharge. MAP, HR and SpO2 values were monitored in the PACU. In addition to these parameters, the Riker Sedation-Agitation Scale (SAS) was used for determining the level of anxiety of the patients.[12] The modified Aldrete's scoring system was used for determining when patients were fit to leave the PACU.[13] When patients' modified Aldrete's scoring system reached ≥9 (recovery from sedation), they were discharged from the PACU. The time until the modified Aldrete's scoring system reached ≥9 was recorded for all patients in the PACU. Post-operative pain score was assessed with a 10-point visual analogue scale (VAS, 1 point = no pain, and 10 point = worst pain imaginable).[14]

2.1 | Statistical analysis

Statistical analysis was conducted with SPSS for Windows version 22.0 (SPSS Inc, Chicago, IL, USA). Continuous data were presented as mean ± standard deviation, and categorical data were presented as percentage. Normality assessment of continuous data was performed with Kolmogorov-Smirnov and/or Shapiro-Wilk tests. Continuous data were compared with Student's *t* test for parametric data and Mann-Whitney *U* test for non-parametric data. Analysis of variance was performed for the comparison of repeated measurements of hemodynamic variables. Post hoc comparisons among the repeated measures in each group were performed by the Tukey HSD

and/or LSD method, if appropriate. A value of $P < 0.05$ was considered as statistically significant.

3 | RESULTS

Thirty patients in the D group and thirty patients in the P group were assessed in this study. The baseline characteristics of the study groups are presented in Table 1. Age, weight and duration of anaesthesia were similar between two groups.

Mean arterial pressure, HR and SpO2 values at each point of time are shown in Figure 1A-C. After the administration of the sedative agents, MAP was significantly decreased from the baseline value in both groups ($P < 0.05$). However, MAP in group P was significantly lower than that in group D at T0 and T1, whereas MAP in group D was significantly lower than that in group P at T6 and T7 (Figure 1A). Similarly, after the administration of the sedative agents, HR was significantly decreased from the baseline value in both groups ($P < 0.05$). Heart rate in group D was significantly lower than that in group P at T3, T6 and T7 (Figure 1B).

However, SpO2 was not significantly changed from the baseline value in both groups, and it was similar between two groups at baseline and after the administration of the sedative agents (Figure 1C). Bradycardia (defined as heart rate lower than 60/min) and hypotension (defined as mean arterial pressure lower than 60 mm Hg) and respiratory depression were not observed in any group during the evaluation time.

Following the end of operation, patients were taken to the PACU for close monitoring. The time until modified Aldrete's scoring system ≥9 tended to be lower in group D compared to group P (6.0 ± 3.1 vs 7.5 ± 3.0, $P = 0.055$) (Table 2).

Post-operative Riker SAS and VAS are listed in Figures 2 and 3. Post-operative first minute Riker SAS score was similar between two groups. However, it was significantly lower in group D compared to in group P at 15, and 30 minutes post-operatively (Figure 2). In addition, post-operative VAS score was significantly lower in group D than in group P at 1, 15 and 30 minutes post-operatively (Figure 3). Serious adverse events did not occur in any patients and all of them were discharged as scheduled without any complication.

4 | DISCUSSION

In the present study, we compared the effects of propofol and dexmedetomidine for conscious sedation in patients undergoing minor hysteroscopic surgery. We have demonstrated that the use of dexmedetomidine was associated with lower anxiety level and lower post-operative pain compared with the use of propofol. In addition, time to discharge from PACU tended to be lower in the dexmedetomidine group. To the best of our knowledge, this is the first study comparing the effects of propofol and dexmedetomidine in patients undergoing minor hysteroscopic surgery.

TABLE 1 Baseline characteristics of the study groups

	Dexmedetomidine group (n = 30)	Propofol group (n = 30)	*P*
Age (years)	42.8 ± 12.4	45.3 ± 8.2	0.374
Weight (kg)	70.1 ± 15.4	72.6 ± 12.0	0.486
Duration of anaesthesia, min	41.7 ± 8.1	45.8 ± 11.3	0.111

Hysteroscopy is one of the most commonly performed outpatient procedures for the diagnosis and treatment of uterine diseases. Although hysteroscopy is a minimally invasive procedure, it may cause severe pain and anxiety. Therefore, the routine use of sedation during the hysteroscopic procedures is increasing worldwide. However, there is a lack of consensus with respect to the sedative agents and anaesthetic protocols during hysteroscopic surgeries.[15]

There is a rapid shift from general anaesthesia to intravenous sedation in hysteroscopic surgeries. For maximal patient comfort and cooperation, the most appropriate sedative agent should provide adequate sedation and analgesia, minimal adverse effects and rapid recovery. These factors decrease the pain and anxiety levels of the patients. The most commonly used sedative drug for conscious sedation is propofol due to its fast effect, easy titration and short half-life.[2] However, the adverse effects of propofol restrict its use in clinical practice.[3] On the other hand, studies have indicated that using dexmedetomidine in outpatient procedures for conscious sedation can increase patient comfort and safety by maintaining respiratory drive, while providing conscious sedation and analgesic effects.

Previous studies compared the effects of dexmedetomidine vs propofol in different procedures. Kaygusuz et al[8] compared the sedation with dexmedetomidine and propofol in combination with fentanyl during extracorporeal shockwave lithotripsy procedures. They reported that analgesic effects and respiratory parameters were better with dexmedetomidine compared to propofol. Wang et al[9] showed that post-operative pain score was significantly lower in the dexmedetomidine group compared to in the propofol group in patients undergoing inguinal hernia repair procedure. Akça et al[10] found that dexmedetomidine provided more stable and satisfactory sedation than propofol in patients undergoing septoplastical surgery. Finally, Xu et al[11] demonstrated that dexmedetomidine provided safer and more effective sedation than propofol in patients undergoing uvulopalatopharyngoplasty procedure.

Although the effects of dexmedetomidine and propofol were compared in the different procedures, no study so far compared the sedative and analgesic effects of dexmedetomidine vs propofol in patients undergoing minor hysteroscopic surgery. In this study, we found that post-operative pain scores were significantly lower in the dexmedetomidine group compared to the propofol group. Similar to our study, previous studies demonstrated that dexmedetomidine was associated with lower post-operative VAS score compared to the propofol.[8,10,16] We also showed that the post-operative Riker SAS score was significantly lower in the dexmedetomidine group compared to the propofol group. Based on these results, we can conclude that dexmedetomidine provides more advantages than propofol as a sedative agent during hysteroscopic surgery.

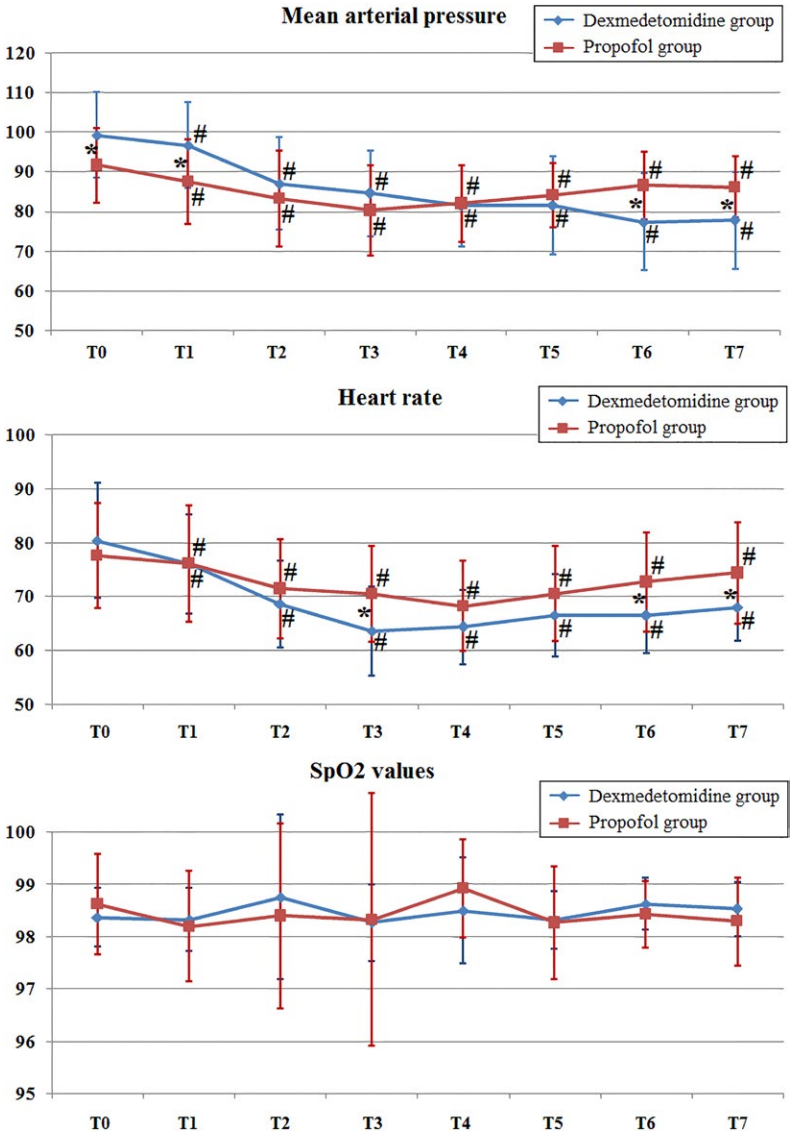

FIGURE 1 A-C, Comparison of mean arterial pressure (A), heart rate (B) and SpO2 (C) levels in dexmedetomidine and propofol groups. Data are expressed as mean ± SD. T0: preoperative (basal), T1: first minute of the initiation of sedative infusion, T2: 5 min after the initiation of sedative infusion, T3: 10 min after the initiation of sedative infusion, T4: the end of operation, T5: 1 min after operation, T6: 15 min after operation, T7: 30 min after operation. *$P < 0.05$ for the difference between the 2 groups at the same time point. #$P < 0.05$ when compared with T0 within the same group

TABLE 2 Comparison of the time until modified Aldrete's scoring ≥9 in dexmedetomidine and propofol groups

	Dexmedetomidine group (n = 30)	Propofol group (n = 30)	*P*
The time until modified Aldrete's scoring system ≥9 (min)	6.0 ± 3.1	7.5 ± 3.0	0.055

Bradycardia and hypotension are the most known adverse effects of dexmedetomidine.[17,18] These adverse effects are mainly based on the central and peripheral sympatholytic effects of dexmedetomidine. In the present study, we have also compared the hemodynamic effects of dexmedetomidine vs propofol. Although MAP and HR variability in the two groups was similar MAP and HR in dexmedetomidine group were significantly lower than in the propofol group at 15 and 30 minutes after operation. These findings suggest that hypotension and bradycardia may occur more frequently with the use of dexmedetomidine. However, we did not observe these adverse effects in any group during the follow-up period. The possible explanation for the absence of hypotension and bradycardia in our study is that we used relatively a low dose of dexmedetomidine. We propose that to avoid the adverse hemodynamic effects, low doses of dexmedetomidine should be used.

Short anaesthesia duration and rapid discharge from the hospital are important factors for outpatient procedures. In our study, duration of anaesthesia was similar between dexmedetomidine and propofol groups. However, we did not investigate the discharge time from the hospital. Nevertheless, we found that time to discharge from the PACU tended to be lower in dexmedetomidine group compared to propofol group. In addition, Karaman et al[19] demonstrated that the mean times to extubation were significantly lower in the dexmedetomidine group than in the propofol group in patients undergoing coronary artery bypass graft surgery. Further prospective studies are required to assess the discharge time from the hospital in dexmedetomidine propofol group.

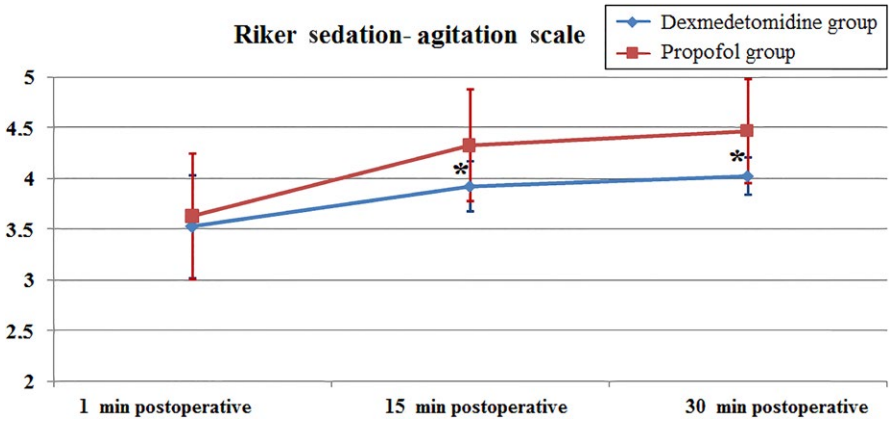

FIGURE 2 Comparison of Riker Sedation-Agitation Scale in dexmedetomidine and propofol groups. Data are expressed as mean ± SD

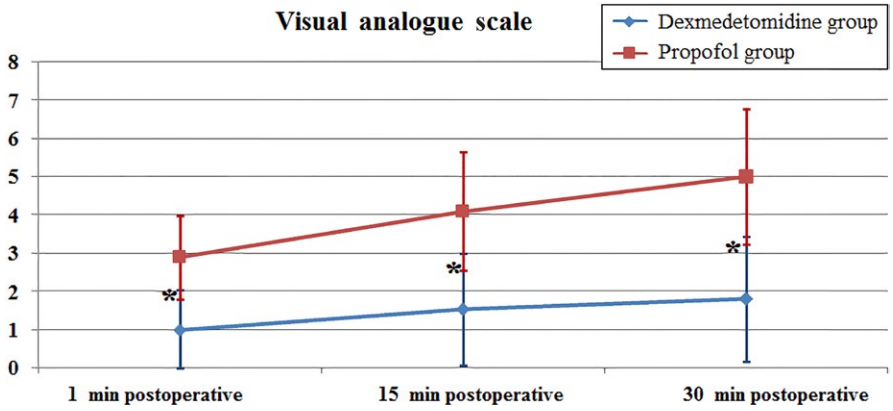

FIGURE 3 Comparison of visual analogue scale in dexmedetomidine and propofol groups. Data are expressed as mean ± SD

Our study has several limitations. First, we included just low-risk patients (ASA grades I and II) in this study. For this reason, our findings cannot be generalized to all hysteroscopic surgery patients because we excluded high-risk patients with ASA grades III or higher. Second, we did not collect some procedural adverse effects such as the frequency of nausea, vomiting and dizziness. Third, the additional doses of dexmedetomidine and propofol were not recorded during the procedure. Further prospective studies with larger participants are required to better elucidate the effects of propofol and dexmedetomidine in patients undergoing hysteroscopic surgeries.

5 | WHAT IS NEW AND CONCLUSION

Although dexmedetomidine and propofol provided sufficient and safe sedation in patients undergoing hysteroscopic surgery, we found that the use of dexmedetomidine was associated with better analgesia and lower post-operative pain scores than propofol. Therefore, we suggest that dexmedetomidine can be a useful sedative agent during hysteroscopy procedure. However, arterial pressure and heart rate should be more closely monitored in patients received dexmedetomidine because of its sympatholytic effects.

CONFLICT OF INTEREST

None to declare.

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