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Research Article

Intravenous dexmedetomidine infusion in adult patients undergoing open nephrolithotomy: Effects on intraoperative hemodynamics and blood loss; a randomized controlled trial

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KEYWORDS

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Abstract *Objective:* The aim of this study was to evaluate the effect of intravenous infusion of dexmedetomidine on intraoperative hemodynamics and blood loss during open nephrolithotomy under general anesthesia in adult patients.
Method: 50 male and female patients, ASA physical status I and II aged 20–60 years old scheduled for open nephrolithotomy under general anesthesia were randomly allocated into two equal groups:
Group D (n = 25): received a bolus dose of IV dexmedetomidine.
1 μg/kg over 10 min before induction of anesthesia and then IV infusion of 0.1–0.5 μg/kg/h guided by the hemodynamics.
Group P (n = 25): received a bolus dose of 10 ml Ringer lactate solution before induction of anesthesia, and infusion was continued during surgery.
General anesthesia was induced in all patients using fentanyl, propofol and atracurium. The following parameters were recorded: heart rate and systolic and diastolic arterial blood pressure: before and after induction of anesthesia and then every 15 min intraoperatively, volume of blood loss (ml), laboratory hemoglobin % and hematocrit concentration: preoperative, intraoperative and immediate postoperative and number of the transfused units of PRBCs.
Results: Intraoperative heart rate and systolic and diastolic arterial blood pressure were statistically significantly lower in group D than in group P. The intraoperative blood volume lost was statistically significantly higher in group P than in group D. A number of the transfused units of PRBCs, intraoperative and postoperative hemoglobin % and hematocrit concentration were statistically significantly lower in group P than in group D.

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Conclusion: Dexmedetomidine infusion in patients undergoing open nephrolithotomy under general anesthesia was associated with intraoperative hemodynamic stability, which decreases intraoperative blood loss and the need for intraoperative blood transfusion.

1. Introduction

Dexmedetomidine is an selective α-2 agonist with sedative, analgesic, sympatholytic cardiovascular effects, and it provided hemodynamic stability without causing respiratory depression [1,2].

Previous studies showed that dexmedetomidine decreases skin bleeding in animals, as it causes peripheral vasoconstriction, which resulted in minimal bleeding with skin incision and intraoperatively [3].

Renal stones is a common disease [4], and open surgery for renal stones is associated with blood loss which may be in large amount due to the high vascularity of the kidneys as it received 20% of the cardiac output or due to prolonged surgical time if the stone is large, thus increasing the blood loss [5] and the need for blood transfusion. A study by Khalaf et al. [6] showed that primary or secondary hemorrhage occurred in 186 patients (35%).

The decision to intraoperative blood transfusion must balance the known risks of blood transfusion with the need to provide adequate tissue oxygenation [7].

We hypothesized that intravenous infusion of dexmedetomidine in adult patients undergoing open nephrolithotomy under general anesthesia may provide better intraoperative hemodynamics, reducing bleeding and the need for blood transfusion.

The aim of this prospective randomized double-blinded controlled study was to evaluate the effect of intravenous dexmedetomidine infusion on intraoperative hemodynamics and blood loss in adult patients undergoing open nephrolithotomy under general anesthesia.

2. Patients and methods

After the approval of the ethical committee of Faculty of Medicine, Beni Suef University (FMBUS REC, Egypt), the study was registered at www.AZNCTR clinical trial registry, with registration number ACTRN12614000389606, and written informed consents were obtained from 50 patients' ASA physical status I and II, males and females aged 20–60 years old, scheduled for elective open nephrolithotomy under general anesthesia from April 2014 to November 2014.

Patients were excluded if they were ASA more than II, had a known cardiac arrhythmias, significant coagulopathy defined as (INR > 1.5), use of antiplatelet or anticoagulants, anemic patients with Hb% less than 10 g/dl.

In the operating room, two wide bore peripheral intravenous cannulae were inserted, and monitors were connected including electrocardiogram, pulse oximetry, noninvasive arterial blood pressure cuff at 5 min intervals and BIS monitor strip (BIS Sensor®; Aspect Medical Systems, USA, Toll free 1-888-BIS Index).

The study drugs were prepared by a senior anesthesia resident unaware of the study protocol.

When patients arrived to the operating theater, they were randomly assigned to one of two equally divided groups using a closed envelop technique ($n = 25$ each):

Group D: received in a separate cannula a bolus dose of dexmedetomidine (*Precedex*, *dexmedetomidine HCl injection*, 200 μg/2 ml), 1 μg/kg over 10 min before induction of anesthesia and then IV infusion of 0.1–0.5 μg/kg/h guided by the hemodynamics.

Group P: received a bolus dose of 10 ml Ringer lactate solution before induction of anesthesia and then continuous infusion till the end of the operation.

General anesthesia was induced, after preoxygenation for 3–5 min with 100% oxygen by face mask, using IV fentanyl 2 μg/kg, propofol 2 mg/kg, atracurium (0.5 mg/kg) and ventilated manually with sevoflurane 2%, oxygen 100% via a face mask, intubation with oral cuffed endotracheal tube when the BIS value reached (40–60) which indicate optimal hypnotic state [8], anesthesia was maintained with oxygen 100%, sevoflurane (according to the depth of anesthesia guided by BIS to be between 40% and 60%), muscle relaxation was maintained by additional doses of atracurium, guided by peripheral nerve stimulator (Life-Tech EZ stim II), mechanical ventilation with maintenance of end tidal carbon dioxide 36–40 mmHg. Hypotension is defined as systolic blood pressure less than 90 mmHg and it was treated by decreasing the dexmedetomidine infusion rate and/or sevoflurane concentration and ephedrine in 3 mg IV increments if needed, and bradycardia is defined as heart rate less than 60 beats per minute and was managed by decreasing the dexmedetomidine dose in D group or atropine 0.5 mg IV if needed.

At the end of surgery, 0.25% bupivacaine was injected by the surgeon at the surgical wound, neuromuscular blockade was reversed with IV neostigmine 0.04 mg/kg and atropine 0.02 mg/kg, the trachea was extubated when the patient responds to commands, and all patients were transferred to PACU, where they received oxygen via face mask for 3–4 L/min and were monitored.

The following parameters were evaluated and recorded by senior anesthesia resident unaware of the study protocol:

1. *Patient's characteristics*: age, sex, height, weight, ASA physical status and duration of surgery.
2. *Heart rate and systolic and diastolic arterial blood pressure (primary outcomes)*: before and after induction of anesthesia and then every 15 min intraoperatively.

Secondary outcomes:

3. *Volume of blood loss (ml)*: in the surgical swabs and suction bottle.
4. *Hemoglobin % and hematocrit concentration*: preoperative, intraoperative and immediate postoperative.
5. Number of the transfused units of PRBCs.

3. Statistical analysis

After a pilot study in ten patients, the mean intraoperative blood loss (SD) was 621 (143) and 782 (338) in the dexmedetomidine group and the placebo group, respectively. Therefore, the sample size was calculated using the program of Biostatistics version 3.01; twenty-five per group was needed to show a difference of intraoperative blood loss of 161 ml (SD 195 ml) between groups with the power set at 80% and the α-error level fixed at 0.05.

Data are presented as mean ± standard deviation or median (range) or numbers as appropriate. Numerical data were analyzed by using Student's unpaired *t* test. Nonparametric data were analyzed by using Mann–Whitney *U*-test. A value of $P < 0.05$ was considered statistically significant.

4. Results

All patients completed the study. Patient's characteristics and operative time showed no statistical significant difference between the two studied groups, as given in Table 1.

Intraoperative heart rate was statistically significantly lower in group D than in group P except at 60 min, as given in Table 2.

Table 1 Demographic data and operative time. Data are presented as mean ± SD, numbers.

Variables	Group D ($n = 25$)	Group P ($n = 25$)
Age (year)	39.6 ± 10.07	37.6 ± 10.87
Weight (kg)	81.52 ± 9.23	86.08 ± 9.00
Height (cm)	168.32 ± 9.33	167.36 ± 9.15
Sex (male/female)	19/6	20/5
Duration of operation (minutes)	116.6 ± 23.52	124.56 ± 14.35

Group D: dexmedetomidine group.
Group P: placebo group.
No statistically significant difference between the study groups, *P* value >0.05.

Table 2 Intraopeartive heart rate (Bpm). Data are presented as mean ± SD.

Time	Group D ($n = 25$)	Group P ($n = 25$)
Preinduction	80.44 ± 7.43	80.88 ± 9.75
After induction	71.4 ± 8.86	82.6 ± 10.35*
15 min	70.72 ± 8.27	82.36 ± 9.87*
30 min	70.68 ± 7.73	80.92 ± 10.02*
45 min	71.32 ± 8.29	81.44 ± 10.09*
60 min	76.04 ± 7.51	80.88 ± 9.75
75 min	72.36 ± 4.53	80.68 ± 9.82*
90 min	70.2 ± 3.76	80.04 ± 10.57*
105 min	70.36 ± 3.74	80.88 ± 9.75*
120 min	67.6 ± 5.26	81.36 ± 10.23*
135 min	72.88 ± 8.10	80.44 ± 10.53*

Group D: dexmedetomidine group.
Group P: placebo group.
Bpm = beat per minute.
* *P* values <0.05 are statistically significant.

Table 3 Intraoperative systolic arterial blood pressure (mmHg). Data are presented as mean ± SD.

Time	Group D ($n = 25$)	Group P ($n = 25$)
Preinduction	132.36 ± 12.93	131.44 ± 11.31
After induction	118.4 ± 11.36	121.28 ± 10.33
15 min	116.68 ± 9.70	120.84 ± 11.20
30 min	122.2 ± 7.70	117.64 ± 8.62
45 min	113.6 ± 10.20	118.04 ± 7.99
60 min	114.76 ± 8.88	119.92 ± 6.30*
75 min	116.08 ± 8.14	117.44 ± 8.42
90 min	115.68 ± 7.82	117.8 ± 8.31
105 min	115.72 ± 7.61	121.32 ± 7.79*
120 min	116.92 ± 8.11	121.64 ± 8.34*
135 min	117 ± 8.39	123.44 ± 8.43*

Group D: dexmedetomidine group.
Group P: placebo group.
* *P* values <0.05 are statistically significant.

Table 4 Intraoperative diastolic arterial blood pressure (mmHg). Data are presented as mean ± SD.

Time	Group D ($n = 25$)	Group P ($n = 25$)
Preinduction	81.76 ± 7.36	79.36 ± 7.69
After induction	74.88 ± 7.49	77.72 ± 7.54
15 min	69.24 ± 6.81	78.12 ± 7.89*
30 min	69.68 ± 5.90	77.29 ± 8.33*
45 min	68.84 ± 6.85	76.83 ± 7.92*
60 min	70.96 ± 5.62	77.45 ± 7.91*
75 min	74.4 ± 8.98	78.60 ± 8.18
90 min	68.16 ± 6.76	78.60 ± 8.18*
105 min	72.72 ± 10.24	79.83 ± 8.37*
120 min	73.88 ± 9.08	79.83 ± 8.37*
135 min	73.96 ± 9.03	77.75 ± 8.44

Group D: dexmedetomidine group.
Group P: placebo group.
* *P* values <0.05 are statistically significant.

Intraoperative systolic arterial blood pressure was statistically significantly lower in D group than in P group at 60, 105, 120, and 135 min, as given in Table 3.

Intraoperative diastolic arterial blood pressure was statistically significantly lower in D group than in P group except at 75 and 135 min, as given in Table 4.

The intraoperative blood volume lost was statistically significant higher in group P than group D, number of units of PRBCs transfused, intraoperative and postoperative hemoglobin % and hematocrit concentration were statistically significant lower in group P than group D, number of units of PRBCs transfused was statistically significantly higher in group P than group D, Table 5.

5. Discussion

Dexmedetomidine is a highly selective α 2-adrenoceptor agonist [9,10], with hemodynamic stability, analgesic and sympatholytic effects it also maintains adequate organ perfusion [11]. It attenuates the stress responses during surgery and maintains intraoperative hemodynamics [12,13].

The main finding in this study was that dexmedetomidine infusion in adult patients undergoing open nephrolithotomy

Table 5 Volume of blood loss (ml), units of PRBCs transfused, laboratory Hb%, Htc. Data are presented as mean ± SD, numbers or median (range).

Variables	Group D (n = 25)	Group P (n = 25)
Volume of blood loss (ml)	636 ± 233.86	804 ± 379.18*
Units of PRBCs transfused	0	1 (0–1) *
Hb%		
Preoperative	12.4 ± 0.90	12.10 ± 0.88
Intraoperative	9.31 ± 0.38	8.90 ± 0.53*
Postoperative	10.10 ± 0.62	9.76 ± 0.55*
Htc		
Preoperative	33.93 ± 2.28	32.19 ± 2.69
Intraoperative	28.92 ± .69	26.93 ± .91*
Postoperative	29.87 ± 1.3	28.82 ± 1.33*

Group D: dexmedetomidine group.
Group P: placebo group.
* P values <0.05 are statistically significant.

under general anesthesia was associated with intraoperative hemodynamic stability, which decreases intraoperative blood loss and the need for intraoperative blood transfusion. The heart rate and systolic and diastolic blood pressure were statistically significantly lower in dexmedetomidine group compared to the placebo group without development of bradycardia or hypotension, no patient had initial hypertension due to slow administration of dexmedetomidine bolus infusion over 10 min which was proved to decrease the initial hypertension and reflex bradycardia associated with a rapid administration of dexmedetomidine [10].

In agreement with the results of the present study, a study by Rao et al. [10] showed that patients who underwent elective surgeries under general anesthesia (e.g., oral, maxillofacial and ENT, general, orthopedic, spine, brain, thyroid, laparoscopy) and given a loading dose of dexmedetomidine 1 μg/kg and then continuous infusion of 0.5 μg/kg/h had a stable intraoperative hemodynamics, and a study by Kang et al. [14] in patients undergoing breast surgery concluded that dexmedetomidine (1 μg/kg) given before induction of anesthesia followed by infusion of (0.6 μg/kg/h) resulted in hemodynamic stability.

A study by Yacout et al. [15] showed that intravenous dexmedetomidine infusion in patients scheduled for elective major abdominal surgery under general anesthesia was associated with significantly lower heart rate and mean arterial blood pressure compared to the placebo group.

In line with the current study, Tanskanen et al. [16] showed that intraoperative infusion of dexmedetomidine at a rate of 0.4 μg/kg/h maintains heart rate and blood pressure compared to the placebo group in patients undergoing supratentorial brain tumor surgery and provided perioperative hemodynamic stability.

In this study no patient had bradycardia in dexmedetomidine group, which was in agreement with the study by Gurbet et al. [17] who reported that bradycardia did not develop in patients scheduled for total abdominal hysterectomy and received a loading dose of dexmedetomidine 1 μg/kg IV during induction of anesthesia, followed by a continuous infusion at a rate of 0.5 μg/kg/h.

Jagadish and his coworkers [18] showed that dexmedetomidine infusion 1 μg/kg before induction of anesthesia and then continuous infusion at a dose of 0.2–0.7 μg/kg/h intraoperative caused decrease in arterial blood pressure and heart rate with maintenance of hemodynamic stability in patients scheduled for elective surgeries (e.g., thyroidectomy and abdominal surgeries) under general anesthesia.

In a study by Varshali et al. [19] two patients receiving dexmedetomidine had bradycardia without decrease in arterial blood pressure and responded to IV atropine, and they concluded that dexmedetomidine maintains hemodynamic stability in patients undergoing major surgical procedure.

Dexmedetomidine causes peripheral vasoconstriction, which resulted in minimal bleeding with skin incision and intraoperative [3].

Previous studies reported that dexmedetomidine decreased bleeding during septoplasty and tympanoplasty with maintenance of intraoperative hemodynamic stability [11,20], in spine surgery, dexmedetomidine infusion reduces intraoperative blood loss and blood transfusion rate [9], and when it is used as adjuvant to general anesthesia in patients undergoing scoliosis correction surgery, it effectively decreased the amount of blood loss and was associated with stable hemodynamics [21].

A study by El-Gohary and Arafa [22] in patients underwent scoliosis correction surgery and received a bolus of dexmedetomidine IV 1 μg/kg over 10 min before induction of anesthesia and continued as 0.2–0.5 μg/kg/h infusion reduced the blood loss and the need of blood transfusion.

6. Conclusion

Dexmedetomidine infusion in patients undergoing open nephrolithotomy under general anesthesia was associated with intraoperative hemodynamic stability, which decreases intraoperative blood loss and the need for intraoperative blood transfusion.

Conflict of interest

None.

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