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Effects of Continuous Intravenous Infusion of Methoxamine on the Intraoperative Hemodynamics of Elderly Patients Undergoing Total Hip Arthroplasty

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Background: Hemodynamic disturbances are common during continuous epidural anesthesia in elderly patients undergoing total hip arthroplasty. This study aimed to investigate the effects of methoxamine on the intraoperative hemodynamics in elderly patients undergoing total hip arthroplasty under epidural anesthesia.

Material/Methods: This prospective study included 150 elderly patients undergoing elective total hip arthroplasty under epidural anesthesia. Patients were randomly assigned into 5 groups (n=30 per group): a control group receiving saline (Group C), a dopamine group receiving 7 µg/kg/min dopamine (Group D), and methoxamine groups receiving 1, 2, or 3 µg/kg/min methoxamine (Groups M1, M2, and M3, respectively). Hemodynamic parameters were assessed 10 min before anesthesia (T1); 10 min (T2), 20 min (T3), 30 min (T4), and 60 min (T5) after anesthesia; and at the conclusion of surgery (T6).

Results: At T2–T6, the mean arterial pressure, central venous pressure, cardiac output, stroke volume, stroke volume ratio, and pulmonary vascular resistance were higher in Groups D, M2, and M3 compared to Group C ($p < 0.05$). Compared to Group D, the heart rate and rate pressure product were significantly lower in Groups M1–M3. Infusion volume, ephedrine dose, and postoperative 24-h urine volume were significantly lower and intraoperative urine volume was significantly greater in Groups D, M2, and M3 compared with Group C. Hypertension occurred more frequently in Group M3 than in any other group.

Conclusions: Continuous intravenous infusion of 2 µg/kg/min methoxamine is safe and effective in maintaining hemodynamic stability in elderly patients undergoing total hip arthroplasty.

MeSH Keywords: **Anesthesia, Caudal • Hemodynamics • Methoxamine**

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Background

Total hip arthroplasty is often performed in elderly patients [1], whose physiological organ function reserve is decreased. The average reported age of patients undergoing total hip arthroplasty is 66 years [2]. With the growing elderly population, total hip arthroplasty is expected to be performed increasingly often. Elderly patients exhibit greater sensitivity to anesthetic agents and commonly have conditions, such as hypertension and coronary heart disease, that reduce their tolerance to anesthesia [2]. Therefore, total hip arthroplasty presents great challenges to the anesthesiologist.

Continuous epidural anesthesia is commonly used for total hip arthroplasty [3,4]. However, due to the sympathetic nerve block and the intraoperative use of bone cement, epidural anesthesia can be associated with the dilation of resistant arterioles and veins, decreased blood pressure (BP), and reduced heart rate (HR), leading to hemodynamic disturbance in patients undergoing total hip arthroplasty [3–7]. This hemodynamic disturbance can be dangerous if untreated, especially in elderly patients, because it can result in insufficient blood supply to vital organs, such as the heart and brain. Vasoactive agents, such as ephedrine and dopamine, are commonly used in the clinic to maintain stable hemodynamics during anesthesia [8]. However, these agents can result in increased HR and myocardial oxygen consumption, and their use may be unsafe for elderly patients undergoing total hip arthroplasty [9]. A reasonable alternative is an α_1 adrenoceptor agonist, such as methoxamine, which constricts peripheral vessels to increase BP but does not have a positive chronotropic effect on the heart.

Methoxamine is a direct-acting sympathomimetic agent that predominantly acts as an α_1 adrenoceptor agonist. It can cause vasoconstriction, leading to an increase in both systolic and diastolic BP. Increased BP inhibits HR via carotid baroreflex, thus reducing myocardial oxygen consumption [10]. In addition, because it cannot directly stimulate the heart, methoxamine cannot directly increase myocardial oxygen consumption. Furthermore, it can dilate the coronary arteries and increase perfusion pressure and subendocardial blood supply, thereby reducing myocardial ischemia and protecting the heart [10,11]. Therefore, methoxamine is suitable for use to maintain stable hemodynamics and myocardial oxygen supply/demand balance in elderly patients.

A single intramuscular or intravenous injection of methoxamine has been shown to have a slow onset and to cause unstable hemodynamics. The effects of continuous intravenous infusion of methoxamine on hemodynamics remain to be determined. In the present study, we investigated the effects of continuous intravenous infusion of different doses of methoxamine in elderly patients undergoing total hip arthroplasty under epidural anesthesia. The purposes of this study were to

explore the effects of methoxamine on hemodynamics during epidural anesthesia and to identify the optimal dose of methoxamine for elderly patients undergoing total hip arthroplasty. Effective maintenance of stable hemodynamics and the myocardial oxygen supply/demand balance is critical for elderly patients undergoing this procedure.

Material and Methods

Patients

The Medical Ethics Committee of The First Hospital of Dalian Medical University approved this study (No. LCKY2013-56). All patients or their relatives provided informed consent before inclusion in the study. This prospective study included 150 elderly patients (80 males and 70 females) who underwent elective total hip arthroplasty under epidural anesthesia between January 3, 2012 and October 30, 2013. Their average age was 81 ± 9 years (range, 72–90 years) and their mean body weight was 74.5 ± 12.5 kg (range, 62–87 kg). Inclusion criteria were as follows: 1) age greater than 70 years; 2) degenerative joint disease of the hip requiring total hip arthroplasty; and 3) American Society of Anesthesiology class II or III. Exclusion criteria were: 1) age less than 70 years; 2) severe liver or kidney insufficiency; 3) history of hyperthyroidism; and 4) recent administration of tricyclic antidepressants or monoamine oxidase inhibitors.

Randomization was carried out with a computer-generated random number table. Allocations were concealed in consecutively numbered, sealed envelopes. Patients were randomly assigned into 5 groups based on the assignment found in the numbered envelopes, as follows: a control group receiving saline (Group C, $n=30$); a dopamine group receiving $7 \mu\text{g}/\text{kg}/\text{min}$ dopamine (Group D, $n=30$); and methoxamine groups receiving 1, 2, or $3 \mu\text{g}/\text{kg}/\text{min}$ methoxamine (Groups M1, M2, and M3, respectively, $n=30$ each). The effectiveness of methoxamine was compared with that of dopamine.

Anesthesia procedure

All patients were deprived of food for 12 h and water for 6 h before surgery. Phenobarbital (0.1 mg) and scopolamine (3 mg) were administered intramuscularly 30 min before the procedure. Electrocardiography, HR, BP, and blood oxygen saturation were routinely monitored in the operating room. The radial artery and jugular vein were catheterized to monitor invasive arterial BP and central venous pressure (CVP), respectively. Oxygen was supplied via a low-oxygen mask. Each patient underwent continuous epidural anesthesia.

The patient was placed in the lateral decubitus position. A catheter was inserted into the epidural space through the L2/L3

Table 1. Clinical characteristics of patients (n=30 for each group).

Group	Male/female	Age (years)	Body weight(kg)	Hypertension (%)	Coronary disease (%)	Diabetes (%)	Pulmonary disease (%)	Operative time (min)
Group C	17/13	80±8	74±12	17	27	27	23	120±18
Group D	14/16	84±6	76±11	20	23	23	23	119±21
Group M1	16/14	82±8	75±10	20	27	20	27	118±21
Group M2	18/12	83±7	77±10	17	27	23	20	120±19
Group M3	15/15	81±8	75±11	23	23	27	23	121±22

intervertebral space and advanced by 3 cm in the rostral direction. After the catheter had been fixed, 2% lidocaine (3 ml) was administered through the catheter. When the anesthesia plane was at the T6–T8 level, 0.75% bupivacaine (5–10 ml) was injected through the catheter. For Group D, dopamine (lot no. 120510; Shanghai Harvest Pharmaceutical Co., Shanghai, China) was injected intravenously at an infusion rate of 7 µg/kg/min. For Groups M1, M2, and M3, methoxamine (lot no. 120901; Grandpharma Co., Wuhan, China) was administered intravenously at an infusion rate of 1, 2, or 3 µg/kg/min, respectively.

During surgery, 6% hydroxyethyl starch 130/0.4 and lactated Ringer's solution (crystal/colloidal ratio, 3:1) were injected intravenously for 20–40 min at an infusion rate of 0.5–1 ml/kg/min. Stable circulation was maintained by intravenous infusion of 6% hydroxyethyl starch 130/0.4 and lactate Ringer's solution at a rate of 0.25 ml/kg/min. If the intraoperative BP was lower than 70% of the baseline BP, the infusion rate was increased, or ephedrine (5–6 mg) was administered intravenously. Depending on each patient's condition under anesthesia, 0.75% bupivacaine (3–5 ml) was added as needed.

Anesthesia monitoring

Mean arterial pressure (MAP), CVP, cardiac output (CO), stroke volume (SV), stroke volume ratio (SVR), and pulmonary vascular resistance (PVR) were recorded 10 min before anesthesia (T1); 10 min (T2), 20 min (T3), 30 min (T4), and 60 min (T5) after induction of anesthesia; and at the conclusion of surgery (T6). The rate pressure product (RPP) was calculated as the product of HR and systolic BP. The total infusion volume, doses of ephedrine and bupivacaine, intraoperative and postoperative 24-h urine volumes, and the occurrence of pulmonary edema, hypertension, hypotension, and bradycardia were recorded.

Statistical analysis

Statistical analyses were performed using SPSS 15.0 (SPSS Inc., Chicago, IL, USA). Sample size estimation was determined by power analysis with one-way analysis of variance (ANOVA). A

sample size of 150 subjects (n=30 per group) was determined to be sufficient to detect differences in the means among the 5 groups, with a statistical power greater than 90%. All numerical values are presented as the mean and standard deviation (SD). Repeated-measures ANOVA was used to compare differences within the same group. One-way ANOVA was used to compare differences among groups. Categorical data were compared by the chi-squared test. Differences with $p < 0.05$ were considered to be statistically significant.

Results

Table 1 summarizes the clinical characteristics of patients in all groups. There were no significant differences in sex, age, or body weight among the 5 groups. The prevalence of hypertension, coronary disease, diabetes, and pulmonary disease did not differ significantly among the groups. There were no significant differences in operative time. Table 2 summarizes the hemodynamic parameters of patients in the 5 groups 10 min before anesthesia (T1), 10 min (T2), 20 min (T3), 30 min (T4), and 60 min (T5) after anesthesia, and at the conclusion of surgery (T6). There were no significant differences in MAP, HR, PRP, CVP, CO, SV, SVR, or PVR at T1 among the 5 groups.

In Group D, CPV was lower at T2–T6 compared to T1 ($p < 0.05$). In Groups C, M1, M2, and M3, HR was slower and CPV was lower at T2–T6 compared to T1 ($p < 0.05$). In Groups C and M1, MAP, CO, SV, and SVR were lower at T2–T6 compared to T1 ($p < 0.05$). In Groups C, M1, and M2, RPP was lower at T2–T6 compared to T1 ($p < 0.05$). In Groups D, M2, and M3, SVR and PVR were higher at T2–T6 compared to T1 ($p < 0.05$). In Group M3, RPP was lower at T2–T4 compared with T1 ($p < 0.05$). In Group M3, MAP and RPP were higher at T5 and T6 compared with T1 ($p < 0.05$).

At T2–T6, MAP, CVP, CO, SV, SVR, and PVR were higher in Groups D, M2, and M3 compared to Group C and in Group D compared to Group M1 (all $p < 0.05$). HR and RPP were higher in Group D compared to Groups C, M1, and M2 ($p < 0.05$). In

Table 2. Hemodynamic parameters of patients in Groups C, D, M1, M2, and M3.

Parameter	Group C (n=30)	Group D (n=30)	Group M1 (n=30)	Group M2 (n=30)	Group M3 (n=30)
MAP (mm Hg)					
T1	105±12	105±11	106±10	105±11	104±12
T2	83±9 ^a	96±9 ^c	85±8 ^{a,d}	98±10 ^c	103±10 ^c
T3	68±7 ^a	99±10 ^c	69±8 ^{a,d}	101±11 ^c	105±11 ^c
T4	74±8 ^a	101±10 ^c	71±9 ^{a,d}	103±9 ^c	107±12 ^c
T5	84±10 ^a	102±11 ^c	83±10 ^{a,d}	105±10 ^c	119±13 ^{a,c}
T6	86±11 ^a	104±12 ^c	86±10 ^{a,d}	107±12 ^c	121±14 ^{a,c}
HR (beats/min)					
T1	82±10	83±11	83±11	82±11	84±11
T2	68±6 ^a	79±10 ^c	65±7 ^{a,d}	64±7 ^{a,d}	65±7 ^{a,d}
T3	66±7 ^a	80±11 ^c	67±6 ^{a,d}	65±8 ^{a,d}	64±6 ^{a,d}
T4	69±8 ^a	80±9 ^c	67±7 ^{a,d}	64±8 ^{a,d}	66±7 ^{a,d}
T5	71±7 ^a	81±10 ^c	70±7 ^{a,d}	67±9 ^{a,d}	69±8 ^{a,d}
T6	71±9 ^a	83±11	70±8 ^{a,d}	69±7 ^{a,d}	68±8 ^{a,d}
PRP					
T1	11,652±379	11,652±379	11,659±381	11,665±382	11,567±384
T2	9451±196 ^a	11,187±265 ^c	9466±199 ^{a,d}	9945±297 ^{a,d}	9957±296 ^{a,d}
T3	9398±192 ^a	11,354±273 ^c	9402±197 ^{a,d}	9951±295 ^{a,d}	9968±297 ^{a,d}
T4	9410±185 ^a	11,421±276 ^c	9394±179 ^{a,d}	9981±297 ^{a,d}	9975±301 ^{a,d}
T5	9741±223 ^a	11,512±280 ^c	9736±219 ^{a,d}	9987±296 ^{a,d}	12,974±236 ^{a,c,d}
T6	9787±227 ^a	11,597±381 ^c	9776±226 ^{a,d}	9991±297 ^{a,d}	13,447±238 ^{a,c,d}
CVP (cm H ₂ O)					
T1	8.5±1.2	8.4±1.2	8.3±1.1	8.3±1.0	8.4±1.3
T2	3.8±1.0 ^a	4.5±1.0 ^{a,c}	3.7±0.9 ^{a,d}	4.5±0.9 ^{a,c}	4.8±1.0 ^{a,c}
T3	3.8±1.1 ^a	4.5±1.0 ^{a,c}	3.8±1.0 ^{a,d}	4.5±1.0 ^{a,c}	4.9±1.1 ^{a,c}
T4	3.9±1.2 ^a	5.1±1.1 ^{a,c}	3.8±1.1 ^{a,d}	4.9±1.1 ^{a,c}	5.1±1.0 ^{a,c}
T5	4.6±1.1 ^a	6.1±1.1 ^{a,c}	4.8±1.1 ^{a,d}	6.1±1.2 ^{a,c}	6.2±1.1 ^{a,c}
T6	4.8±1.1 ^a	6.3±1.0 ^{a,c}	4.9±1.2 ^{a,d}	6.3±1.1 ^{a,c}	6.5±1.1 ^{a,c}
CO (L/min)					
T1	7.24±1.12	7.28±1.11	7.31±1.13	7.29±1.11	7.29±1.12
T2	5.12±1.12 ^a	7.31±1.12 ^c	5.15±1.12 ^{a,d}	7.33±1.12 ^c	7.35±1.12 ^c
T3	4.89±1.07 ^a	7.36±1.12 ^c	4.91±1.08 ^{a,d}	7.41±1.13 ^c	7.43±1.15 ^c
T4	5.07±1.09 ^a	7.38±1.11 ^c	5.12±1.10 ^{a,d}	7.43±1.13 ^c	7.46±1.15 ^c
T5	5.62±1.17 ^a	7.41±1.13 ^c	5.68±1.16 ^{a,d}	7.45±1.11 ^c	7.51±1.17 ^c
T6	5.85±1.21 ^a	7.44±1.15 ^c	5.89±1.19 ^{a,d}	7.50±1.20 ^c	7.59±1.21 ^c

Table 2 continued. Hemodynamic parameters of patients in Groups C, D, M1, M2, and M3.

Parameter	Group C (n=30)	Group D (n=30)	Group M1 (n=30)	Group M2 (n=30)	Group M3 (n=30)
SV (mL/beat)					
T1	84±11	84±11	84±10	84±11	84±11
T2	65±11 ^a	79±12 ^c	66±11 ^{a,d}	84±10 ^c	83±10 ^c
T3	63±12 ^a	77±11 ^c	63±12 ^{a,d}	83±11 ^c	84±11 ^c
T4	65±12 ^a	80±11 ^c	66±11 ^{a,d}	84±12 ^c	86±12 ^c
T5	71±13 ^a	82±11 ^c	72±12 ^{a,d}	85±12 ^c	87±12 ^c
T6	73±11 ^a	83±11 ^c	74±12 ^{a,d}	87±12 ^c	88±12 ^c
SVR (dyn.sec/cm ⁵)					
T1	1231±131	1246±138	1232±136	1229±129	1248±131
T2	997±117 ^a	1471±140 ^{a,c}	1013±121 ^{a,d}	1489±139 ^{a,c}	1491±140 ^{a,c}
T3	884±109 ^a	1487±143 ^{a,c}	995±117 ^{a,d}	1495±146 ^{a,c}	1497±148 ^{a,c}
T4	912±121 ^a	1523±146 ^{a,c}	997±119 ^{a,d}	1567±148 ^{a,c}	1571±150 ^{a,c}
T5	1014±124 ^a	1543±146 ^{a,c}	1021±123 ^{a,d}	1551±148 ^{a,c}	1797±151 ^{a,c,d}
T6	1037±127 ^a	1551±151 ^{a,c}	1039±129 ^{a,d}	1559±150 ^{a,c}	1881±153 ^{a,c,d}
PVR (dyn.sec/cm ⁵)					
T1	121±11	121±10	119±11	122±12	118±10
T2	126±11	172±23 ^{a,c}	127±11 ^d	175±24 ^{a,c}	179±24 ^{a,c}
T3	129±12	191±26 ^{a,c}	130±12 ^d	194±25 ^{a,c}	198±27 ^{a,c}
T4	129±11	198±26 ^{a,c}	130±12 ^d	198±26 ^{a,c}	198±26 ^{a,c}
T5	131±12	201±28 ^{a,c}	131±12 ^d	200±25 ^{a,c}	252±31 ^{a,c,d}
T6	136±12	209±29 ^{a,c}	138±13 ^d	204±28 ^{a,c}	257±35 ^{a,c,d}

T1 – 10 min before anesthesia; T2 – 10 min after anesthesia; T3 – 20 min after anesthesia; T4 – 30 min after anesthesia; T5 – 60 min after anesthesia; T6 – conclusion of surgery. ^a $p < 0.05$ vs. T1; ^c $p < 0.05$ vs. Group C; ^d $p < 0.05$ vs. Group D.

Table 3. Occurrence of pulmonary edema, hypertension, hypotension, and bradycardia in Groups C, D, M1, M2, and M3.

Group	Hypertension (%)	Hypotension (%)	Bradycardia (%)	Pulmonary edema (%)
Group C (n=30)	0	23	27	3
Group D (n=30)	0	0 ^a	0 ^a	0 ^b
Group M1 (n=30)	0	20 ^c	27 ^c	3 ^d
Group M2 (n=30)	0	0 ^a	33 ^c	0 ^b
Group M3 (n=30)	43 ^{a,c}	0 ^a	30 ^c	0 ^b

^a $p < 0.01$ vs. Group C; ^b $p < 0.05$ vs. Group C; ^c $p < 0.01$ vs. Group D; ^d $p < 0.05$ vs. Group D.

addition, HR was higher in Group D compared to Group M3 compared to Group D, and RPP was higher in Group M3 compared to Groups C and D ($p < 0.05$). At T5 and T6, SVR and PVR were higher in Group M3 compared to Groups C and D ($p < 0.05$).

Table 4. Total infusion volume, doses of ephedrine and bupivacaine, intraoperative urine volume, and postoperative 24-h urine volume in Groups C, D, M1, M2, and M3.

Group	Infusion volume (mL)	Dose of ephedrine (mg)	Dose of bupivacaine (mg)	Intraoperative urine volume (mL)	Postoperative 24-h urine volume (mL)
Group C	2456±178	48±7	10±3	236±75	2136±148
Group D	1402±207 ^b	0 ^a	11±3	612±127 ^b	1337±174 ^b
Group M1	2447±182 ^d	47±9 ^c	10±2	242±86 ^d	2129±139 ^d
Group M2	1356±219 ^b	0 ^a	11±3	598±119 ^b	1396±166 ^b
Group M3	1334±215 ^b	0 ^a	11±2	601±121 ^b	1378±175 ^b

^a $p < 0.01$ vs. Group C; ^b $p < 0.05$ vs. Group C; ^c $p < 0.01$ vs. Group D; ^d $p < 0.05$ vs. Group D.

Because complications mainly occurred at T5 and T6, we only summarized the occurrence of complications (e.g., hypertension, hypotension, bradycardia, and pulmonary edema) at these 2 time points (Table 3). Hypotension and pulmonary edema were less frequently observed in Groups D, M2, and M3 compared to Group C ($p < 0.01$). Hypertension was more frequently observed in Group M3 than in Groups C, D, M1, and M2 ($p < 0.01$). Bradycardia was less frequently observed in Group D than in Groups C, M1, M2, and M3 ($p < 0.01$). Hypotension and pulmonary edema occurred more frequently in Group M1 than in Groups D, M2, and M3 ($p < 0.01$).

Table 4 summarizes the total infusion volume, doses of ephedrine and bupivacaine, intraoperative urine volume, and postoperative 24-h urine volume in all groups. The infusion volume, ephedrine dose, and postoperative 24-h urine volume were significantly lower and intraoperative urine volume was significantly greater in Groups D, M2, and M3 compared to Group C. The infusion volume, ephedrine dose, and postoperative 24-h urine volume were significantly greater and intraoperative urine volume was significantly lower in Group M1 compared to Group D. There was no significant difference in bupivacaine dose among the groups. No adverse effects were observed in patients from any group within 3 days after the procedure.

Discussion

Total hip arthroplasty is most commonly performed to treat joint failure caused by degenerative joint disease, especially in elderly patients. Approximately 1–3% of the elderly population (>66 years of age) is expected to undergo total hip arthroplasty [12]. With the growth of the elderly population, there is likely to be an increase in the number of elderly patients who undergo this surgery. Because elderly patients have poor physiological vital organ reserve, stable hemodynamics and the myocardial oxygen supply/demand balance must be

carefully maintained during surgery. Patients who develop hypotension during anesthesia have a 5-fold increased risk of myocardial infarction compared to those without hypotension [13]. Methoxamine increases the BP without obviously affecting the HR. Thus, it can be used to control hemodynamics during anesthesia, without increasing myocardial consumption, in elderly patients. Methoxamine exerted cardioprotective effects in elderly patients during spinal anesthesia [14].

We investigated the effects of continuous intravenous infusion of methoxamine at 1, 2, and 3 $\mu\text{g}/\text{kg}/\text{min}$ on the hemodynamic parameters of elderly patients undergoing total hip arthroplasty under epidural anesthesia. MAP, CVP, CO, SV, SVR, and PVR were higher in Groups M2 and M3 compared to Group C, suggesting that continuous intravenous infusion of methoxamine at 2 or 3 $\mu\text{g}/\text{kg}/\text{min}$ is effective in maintaining hemodynamic stability during surgery. HR was not increased in Group M2 or M3 compared with Group C, suggesting that methoxamine reduces the risk of a tachycardia-induced increase in myocardial oxygen consumption. However, the hypertension incidence was higher in Group M3 than in any other group. Therefore, even though it maintains the hemodynamic stability, continuous intravenous infusion of 3 $\mu\text{g}/\text{kg}/\text{min}$ methoxamine may not be safe for elderly patients. Overall, our findings indicate that continuous intravenous infusion of 2 $\mu\text{g}/\text{kg}/\text{min}$ methoxamine may be safe and effective in controlling hemodynamic stability of elderly patients undergoing total hip arthroplasty.

The effects of methoxamine on hemodynamic parameters were examined at several time points before and after surgery. In the control group, MAP was lower at T2–T6 compared to T1, suggesting that epidural anesthesia induced hypotension in these patients. Hypotension is the most common cardiovascular response to epidural anesthesia [15] and, in the elderly, is more likely to be associated with an increased risk of complications [13,16]. Therefore, it is important to reduce the occurrence of hypotension in these patients. Intravenous

infusion of 2 or 3 µg/kg/min methoxamine, but not 1 µg/kg/min, methoxamine prevented epidural anesthesia-induced hypotension. Compared with Group C, the incidence of hypotension during anesthesia was lower in Groups M2 and M3, but similar to that in Group M1. However, 3 µg/kg/min methoxamine increased MAP and led to a greater incidence of hypertension. Continuous intravenous infusion of methoxamine at 2 or 3 µg/kg/min did not induce an increase in HR, suggesting that methoxamine at a dose below 3 µg/kg/min should be safe for these patients. CO, SV, SVR, and PVR were higher in Group M2 than in Group C, further suggesting that continuous intravenous infusion of 2 µg/kg/min is effective in controlling hemodynamic stability in these patients.

Dopamine can be used to correct epidural anesthesia-induced hypotension [8,17]. Thus, we compared the effects of methoxamine versus dopamine on the hemodynamic parameters. Consistent with previous reports, intravenous infusion of dopamine increased MAP compared with the control. HR, CVP, CO, SV, SVR, RPP, and PVR were higher in Group D than in Group C. MAP, CVP, CO, SV, SVR, and PVR were similar in Groups D and M2, but HR was lower in Groups M1, M2, and M3 compared to Group D. These findings suggest that methoxamine can have an effect similar to that of dopamine in controlling hemodynamic stability, but it is superior to dopamine in reducing the risk of a tachycardia-induced increase in myocardial oxygen consumption in elderly patients.

In Group M1, MAP, CVP, CO, SV, SVR, and PVR were low and not different from those in Group C, suggesting that continuous intravenous infusion of 1 µg/kg/min methoxamine did not effectively control hemodynamic stability. RPP, SVR, and PVR and the incidence of hypertension during anesthesia were higher in Group M3 compared to Groups C and D, supporting the suggestion that continuous infusion of 3 µg/kg/min methoxamine is not safe for use in these patients.

Methoxamine primarily acts on resistant arterioles, leading to blood redistribution and hypoperfusion in some tissues. All of our patients had a normal CVP (indicating sufficient blood volume), suggesting that a safe blood volume can be maintained when methoxamine is used. However, pulmonary edema

occurred more frequently in Group M1 than in Groups D, M2, and M3, accompanied by an increased infusion volume. This effect was likely due to the inability of 1 µg/kg/min methoxamine to maintain hemodynamic stability, thus resulting in a large infusion volume.

In Groups D, M2, and M3 with stably controlled hemodynamics, the infusion volume, ephedrine dose, and postoperative 24-h urine volume were reduced and intraoperative urine volume was increased compared to Group C. These findings suggest that the maintenance of stable hemodynamics by these drugs may diminish the infusion volume and ephedrine use during anesthesia, as well as improve the intraoperative urine volume. However, bupivacaine usage was similar among the 5 groups, suggesting that maintenance of stable hemodynamics did not significantly affect bupivacaine use during anesthesia in elderly patients undergoing total hip arthroplasty.

Conclusions

We prospectively investigated the effects of continuous intravenous infusion of different doses of methoxamine in elderly patients undergoing total hip arthroplasty under epidural anesthesia. Continuous intravenous infusion of 2 or 3 µg/kg/min methoxamine was effective in controlling hemodynamic stability without a significant increase in HR. However, 3 µg/kg/min methoxamine resulted in a significantly higher incidence of hypertension during the procedure, indicating that this dose is not safe for these elderly patients. Continuous intravenous infusion of 2 µg/kg/min methoxamine may be safe and effective in controlling hemodynamic stability in elderly patients undergoing total hip arthroplasty.

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Declaration of interest

The authors declare that they have no conflicts of interest.

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