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Analysis of anesthetic effect of dexmedetomidine in femoral shaft fracture surgery

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Abstract

To investigate the effect of dexmedetomidine (DEX) on hemodynamics and recovery period after femoral shaft fracture surgery. Fifty-two patients, aged 3 to 7 years, who underwent femoral shaft fracture reduction surgery in our hospital in 2019 were randomly divided into the experimental group (n = 26) and the control group (n = 26). Both groups were given routine propofol combined with remifentanil by intravenous anesthesia. The experimental group was continuously pumped with DEX after induction of anesthesia, while the control group was continuously pumped with the same volume of normal saline. The mean arterial pressure (MAP) and heart rate (HR) were recorded before anesthesia induction (T0), when laryngeal mask was inserted (T1), when skin was cut (T2), when intramedullary needle was inserted (T3), and when laryngeal mask was removed (T4). Extubation time after anesthesia withdrawal was recorded in the 2 groups. According to the Pediatric Anesthesia Emergence Delirium score, the agitation and the incidence of agitation were recorded immediately after extubation (T5), 10 minutes after entering the recovery room (T6) and 30 minutes after entering the recovery room (T7). There was no significant difference in MAP and HR between the 2 groups at T0 and T1 time points ($P > .05$). The MAP and HR of the experimental group at T2 to T4 were significantly lower than those of the control group ($P < .05$). The extubation time of the experimental group was longer than that of the control group ($P < .05$), but the Pediatric Anesthesia Emergence Delirium score and the incidence of agitation in the recovery period of the experimental group were lower than those of the control group ($P < .05$). In femoral shaft fracture surgery, intravenous anesthesia combined with continuous pumping DEX can effectively stabilize the hemodynamics of patients, and the incidence of postoperative agitation during anesthesia recovery is low.

Abbreviations: DEX = dexmedetomidine, HR = heart rate, MAP = mean arterial pressure, PAED = Pediatric Anesthesia Emergence Delirium.

Keywords: dexmedetomidine (DEX), femoral shaft fracture, hemodynamics, recovery

1. Introduction

Femoral shaft fracture is often caused by accidents or car accidents, which is a kind of trauma with a high incidence rate. Closed or open reduction and intramedullary needle fixation is often used as the surgical method.[1] Femoral shaft fractures in children are age-selective. Due to their particularity, there are many treatment methods, including: suspension traction, splint treatment, plaster external fixation, internal fixation with steel plate, etc, but for older children (age >11), weight >49 kg, or appropriate type belong to the unstable children femoral fractures with elastic intramedullary nail fixation, but fracture end does not heal and greater incidence of complications, lower incidence of older children femoral, <2% of the total incidence of fractures in children. And mostly for high energy damage, treatment is more difficult. Patients suffer severe pain after injury, have more intraoperative blood loss, and are prone to circulatory fluctuations. The patient was young and prone to agitation due to fear and pain after surgery. This type of surgery lasts a long time, and general anesthesia is generally chosen.

Dexmedetomidine (DEX) hydrochloride can highly selectively excite α2 adrenergic receptors and has good analgesic, sedative, and anti-sympathetic effects. Moreover, due to its advantages of mild respiratory depression and stable hemodynamics, DEX hydrochloride has been widely used in clinical anesthesia maintenance, postoperative analgesia and intensive care unit sedation.[2,3] DEX is a widely used adjuvant drug for general anesthesia. Compared with midazolam, DEX can reduce stress response, postoperative agitation and postoperative pain during day surgery, and improve the comfort of patients during perioperative period. However, there are few studies on the use of DEX in traumatic surgery. In this study, the effect of DEX on intraoperative hemodynamics and postoperative recovery period in patients with femoral shaft fracture was observed by using total intravenous anesthesia combined with DEX.

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2. Materials and Methods

2.1. General information

With the increasing incidence of traffic injuries and falling injuries, the trend of femoral shaft fractures in adolescents is also increasing, accounting for 1.4 to 1.7% of all pediatric fractures, which is necessary for further attention. Therefore, we selected children as the research subject. A total of 52 patients with femoral shaft fractures undergoing emergency surgery without other trauma admitted to the department of orthopedics in our hospital from January to December 2021 were selected as the research subjects, including 28 males and 24 females. The ethics committee of The First People's Hospital of Wenling approved this study.

Inclusion criteria: All patients underwent closed reduction and intramedullary needle fixation; American Society of Anesthesiologists Class I to II; the age is 3 to 7 years; there were no significant abnormalities in preoperative hematuria, liver and kidney function, chest radiograph and electrocardiogram; all patients were given intravenous general anesthesia with propofol combined with remifentanil; and can cooperate with research independently and clearly. Exclusion criteria: combined with other trauma or organic lesions of other organs; allergic to anesthetic drugs; and the use of painkillers or other surgical trauma in the past 3 months.

2.2. Methods

The fasting time of the 2 groups before operation was 8 hours for fat, 6 hours for protein, and 2 hours for water and clear liquid.[4] Atropine (0.01 mg/kg) was injected half an hour before surgery. Before induction of anesthesia, oxygen mask was given, oxygen flow was 3 L/min, and heart rate (HR), respiratory rate, blood pressure and oxygen saturation were closely monitored. Anesthesia was induced with 0.2 ug/kg sufentanil (Yichang Renfu Pharmaceutical Co., LTD., Sinopharma H20054171), 0.3 mg/kg etomidate (Jiangsu Enhua Pharmaceutical Co., LTD., Sinopharma H20020511), and 0.5 mg/kg atracurium (Shanghai Hengrui Pharmaceutical Co., LTD., Sinopharma H20020511, Sinopharm approved H20061298). All patients were ventilated by laryngeal mask. Propofol (Astrazeneca Pharmaceutical Co., LTD., Sinopharm approved J20130163) and remifentanil (Yichang Renfu Pharmaceutical Co., LTD., Sinopharm approved H20030197) were used in both groups in the maintenance stage.

The experimental group was continuously pumped with DEX (Jiangsu Hengrui Pharmaceutical Co., LTD., Sinophosphatin approval H20130093). The loading dose was 1 ug/kg in the first 10 minutes, and then the maintenance dose was 0.5 ug/(kg/h) in the control group.[5] The control group was continuously pumped with normal saline in the same volume and time. The use of DEX and normal saline was stopped 10 minutes before the end of the operation, and the use of other intravenous maintenance drugs was stopped 5 minutes before the end of the operation. Neostigmine (0.02 mg/kg) and atropine (0.01 mg/kg) were given at the end of the operation, the respiratory tract was cleared, and the laryngeal mask was removed when the condition of extubation was reached. Steward achieves a score of 3 and is sent to the resuscitation room. Both groups were given pain relief pumps with the same drug composition according to body weight.

2.3. Observation indicators

The mean arterial pressure (MAP) were recorded at 5 time points before anesthesia induction (T0), when laryngeal mask was inserted (T1), when skin was cut (T2), when intramedullary needle was inserted (T3), and when laryngeal mask was removed (T4). The extubation time after anesthesia withdrawal was recorded in the 2 groups (from drug withdrawal to body movement, eye opening and laryngeal mask removal). Using Pediatric Anesthesia Emergence Delirium (PAED) scale scoring, the agitation score and the incidence of agitation were evaluated at 3 time points immediately after extubation (T5), 10 minutes after entering the recovery room (T6), and 30 minutes after entering the recovery room (T7).[6] The PAED scale was scored by 5 items (eye contact with the caregiver, behavioral purpose, cognition of the surrounding environment, anxiety, and restlessness). Each item had 5 grades from 0 to 4 according to the degree of performance, and the score ≥10 was considered as the presence of agitation during the awakening period.

2.4. Statistical treatment

All the data of the 2 groups were collected and analyzed by SPSS 22.0 statistical software. The measurement data of the obtained data were expressed as mean ± standard deviation. One-way analysis of variance was used to compare the measurement data of 3 or more groups. The comparison between the 2 groups was analyzed by *t* test. Count data were expressed as percentage (%) and compared by chi-square test. $P < .05$ was considered statistically significant.

3. Results

3.1. Clinical characteristics of participants

The experimental group had 15 males and 11 females, and the control group had 13 males and 13 females. The mean age of the experimental group was 5.23 ± 1.34 years, and the control group was 5.19 ± 1.36 years. The mean weight of the experimental group was 21.89 ± 4.72 kg, and the control group was 21.50 ± 4.13 kg. There was no significant difference in the baseline data ($P > .05$), as shown in Table 1.

3.2. Comparison of hemodynamic indexes between the 2 groups at different time points

In the observation group, the level of MAP and HR were significantly lower than those in the control group at T_2 to T_4 time points ($P < .05$). The MAP and HR levels of the experimental group were lower than those of the control at T_1 time point, but the differences were not statistically significant ($P = .20$ for MAP and $P = .25$ for HR). There was no significant difference in

Table 1

Comparison of general information between 2 groups.

Group	Age (yr)	Gender (male/female)	Weight (kg)
The experimental group (n = 26)	5.23 ± 1.34	15/11	21.89 ± 4.72
The control group (n = 26)	5.19 ± 1.36	13/13	21.50 ± 4.13
t/χ^2	−0.1	0.31	0.31
P	.92	.58	.76

Independent sample *t* test was used to compare the age and weight of patients in the 2 groups, and chi-square test was used to compare the gender of patients in the 2 groups.

MAP and HR between the 2 groups at T_0 time point ($P > .05$), as shown in Table 2.

3.3. Comparison of extubation time between the 2 groups

As shown in Table 3, the extubation time of the experimental group was longer than that of the control group, and the difference was statistically significant ($P = .001$).

3.4. Comparison of agitation score and agitation rate between the 2 groups

The PAED score of the experimental group was lower than those of the control group at T_5 to T_7 time point, and the differences were statistically significant ($P = .001$ for T_5, $P < .001$ for T_6, and $P = .003$ for T_7, respectively), as shown in Table 4. The agitation incidence of the experimental group was significantly lower than those of the control group at T_5 to T_7 time point ($P = .025$ for T_5, $P = .006$ for T_6, and $P = .011$ for T_7, respectively).

4. Discussion

DEX, a highly selective α2-adrenergic receptor agonist, is the only sedative that has been found to be arousable without significant respiratory depression, and can significantly reduce the dose of anesthetic drugs used during and after surgery. Femoral fracture surgery, intraoperative bleeding, pain, hemodynamic fluctuations, and because of the wound pain, fear, anesthetic drug use, easy to stir in anesthesia awakening period, especially preschool, characterized by separation of abnormal behavior, consciousness, excessive crying, limbs touch, choking cough, vomiting, drawing tube, etc, it seriously affects the postoperative recovery and physical and mental health of patients, so smooth anesthesia is very important.[7]

Propofol is the most commonly used sedative anesthetic in clinical practice at present. It is used in the induction and maintenance of anesthesia in orthopedic surgery with rapid onset of effect. Bispectral Index showed that it can quickly reach the appropriate sedation depth and has stable hemodynamics when used in the induction and maintenance of anesthesia. However, both propofol and remifentanil are short-acting anesthetics, and the blood drug concentration decreases rapidly after the operation, causing obvious pain and easy to cause postoperative agitation. Therefore, appropriate sedative and analgesic drugs should be added.[8] At the same time, to avoid airway damage caused by endotracheal intubation and reduce stress reaction, laryngeal mask insertion was used to maintain ventilation in all patients in this study.[9]

Anesthesia depth monitoring is helpful to improve anesthesia quality, ensure surgical safety, and reduce anesthesia complications. In spite of the rapid development of new drugs and techniques, the progress of monitoring anesthesia depth has been slow. In addition, the current clinical use of compound anesthesia or combined anesthesia, through the use of a variety of different anesthetics and methods to achieve sedation, hypnosis and analgesic purposes, which makes the depth of anesthesia management more complicated and difficult.

Hydrochloric acid right beauty in the clinical application of the mi in adult already very mature, as a new type of α2 adrenergic agonists, acts on the brain blue spot of G protein coupled receptor and spinal cord posterior horn postsynaptic membrane receptor α2, effectively inhibit the activity of adenylate cyclase, reduce the ion channels in the nervous system to take off the phosphorylation, reducing central sympathetic efferent. It has good sedation, analgesia and anti-anxiety effects, and also has a positive effect on maintaining the stability of intraoperative hemodynamics and reducing stress response.[10] The body's stress response will excite the sympathetic nervous system, promote the release of catecholamines, cause the body's blood pressure to rise, HR to increase, and other reactions. DEX inhibits sympathetic excitation and decreases the release of catecholamines, which decreases MAP and slows HR. It has also been analyzed that DEX excites α2 adrenoceptors, inhibits the release of norepinephrine, slows HR and lowers blood pressure, and at the same time, it excites α2 receptors on vascular smooth muscle cells, leading to vasoconstriction. The 2 effects

Table 2

Comparison of hemodynamics in the surgical operation between 2 groups.

Indicators	Group	Point in time				
		T_0	T_1	T_2	T_3	T_4
MAP (mm Hg)	The experimental group	76.45 ± 5.71	69.57 ± 5.89	71.53 ± 3.27	74.13 ± 4.51	74.59 ± 5.29
	The control group	75.23 ± 6.32	71.35 ± 3.85	74.95 ± 3.25	86.41 ± 3.97	84.35 ± 5.59
	t	−0.73	1.29	3.79	10.43	6.47
	P	.47	.2	<.001	<.001	<.001
HR (time/min)	The experimental group	106.73 ± 5.35	100.69 ± 4.55	102.15 ± 5.53	103.04 ± 3.71	105.15 ± 4.24
	The control group	107.35 ± 5.56	102.46 ± 6.35	106.15 ± 4.05	113.73 ± 5.20	116.00 ± 5.64
	t	0.41	1.16	2.98	8.53	7.84
	P	.69	.25	.004	<.001	<.001

One-way analysis of variance was used to compare the values at different time points in the same group, and independent sample *t* test was used to compare the values between the 2 groups at the same time.
HR = heart rate, MAP = mean arterial pressure.

Table 3

Comparison of extubation time between 2 groups.

Group	N	Extubation time
The experimental group	26	13.98 ± 2.49
The control group	26	11.71 ± 2.29
t	–	−3.43
P	–	.001

Independent sample *t* test was used to compare the values between the 2 groups.

Table 4

Comparison of PAED score and the incidence of delirium between 2 groups.

Indicators	Group	Point in time		
		T_5	T_6	T_7
PAED (point)	The experimental group	8.92 ± 1.81	7.46 ± 1.39	8.42 ± 1.96
	The control group	10.92 ± 2.35	9.77 ± 2.16	10.38 ± 2.50
	t	3.44	4.58	3.15
	P	.001	<.001	.003
Incidence of agitation (%)	The experimental group	27	12	23
	The control group	58	46	58
	χ^2	5.04	7.59	6.47
	P	.025	.006	.011

For measurement data, one-way analysis of variance was used to compare values at different time points in the same group, and independent sample *t* test was used to compare values between the 2 groups at the same time. For enumeration data, chi-square test was used for comparison of values at different time points in the same group and between 2 groups at the same time.
PAED = Pediatric Anesthesia Emergence Delirium.

cancel each other and keep hemodynamics relatively stable.[11] In addition, DEX can also prolong diastole, increase left ventricular coronary artery blood flow, and maintain hemodynamic stability.[10] The results of this study showed that after administration of DEX, the intraoperative MAP and HR of the patients were significantly lower than those of the control group, and the hemodynamic indexes at each time point were relatively stable.

One of the reasons why DEX alleviates agitation during recovery may be related to its mild to moderate analgesic effect. Studies have shown that DEX may inhibit the release of substance P and other nociceptive peptides in presynaptic membrane by acting on α2 receptor in locus ceruleus. It can bind to α2 receptor of spinal cord presynaptic membrane and increase the synthesis and release of acetylcholine and NO in spinal cord interneurons. Inhibiting the conduction of pain signals to the center also acts on peripheral nerves, reversibly inhibiting C and Aα fibers.[12] In addition, studies have proved that DEX can exert sedative and anti-anxiety effects on the brain stem locus ceruleus system.[13] It can effectively avoid the occurrence of sleep deprivation, facilitate the recovery and repair of neurons, and significantly reduce the agitation in the wake period.[14] The results of this study showed that the PAED score and the incidence of agitation of patients in the DEX group were significantly lower than those in the control group at each time point in the recovery period, suggesting that DEX has the effect of alleviating the recovery period agitation. However, the extubation time of patients in dexmedex group was significantly prolonged, which may be related to the synergistic effect of combined drugs and other factors.

Perioperative comfort medicine is the core part of our current clinical anesthesia most attention, to achieve psychological pleasure and physical painless feeling, and postoperative pain and anesthesia recovery period is the core of the stable. Our study found that no adverse reactions such as intraoperative awareness, postoperative behavioral changes and postoperative emotional changes occurred in all patients. It provides guiding experience for clinical practice.

The half-life of intravenous infusion of DEX is 6 minutes, the elimination half-life is about 2 hours, and the time to peak is about 25 to 30 minutes. It is suitable for patients undergoing orthopedic femoral shaft fracture reduction surgery. The receptor selectivity α2: α1 of DEX is 1620:1. Compared with clonidine (receptor selectivity α2: α1 is 220:1) and other drugs, DEX has a more efficient and selective effect, which can reduce and mitigate adverse reactions as much as possible.[11] DEX has a slight effect on patients' respiration, even if its dose accumulates continuously.[15] DEX was scheduled to be registered for use in the US in 1999. Current studies have confirmed that long-term use of DEX in adult patients is safe, and patients in intensive care units can achieve good sedative and analgesic effects with fewer adverse reactions. Ahmed et al found that when the dose of DEX reached 2 times of the commonly used clinical dose (about 2μg/kg), it had less impact on the cardiovascular system of patients and higher drug safety.[16] The Association for Sedation Research published a report on DEX in 2016, which showed that DEX has good sedative effect and low incidence of adverse reactions.[17] Recent studies have shown that DEX has a certain neuroprotective effect on the developing brain, without affecting memory, and is more suitable for the developing brain.[18] Compared with other sedative drugs, the sedation of DEX can wake up at any time, and the sedation also has a protective effect on the nervous system. Moreover, DEX can be almost completely biotransformed, and the metabolites can be completely excreted through the kidney through the mediation of glucuronidation and cytochrome P450.[19–22]

In conclusion, in femoral shaft fracture reduction surgery, propofol intravenous anesthesia combined with DEX can stabilize the hemodynamics of patients, and the postoperative anesthesia recovery period is stable, which is an ideal anesthesia method.

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