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Original Article

Effects of dexmedetomidine and combined spinal and epidural anesthesia on the hemodynamics and SAS of patients undergoing total hip replacement

Jun Yang[1], Minghua Jin[1], Jing Zhang[2]

[1]Department of Anesthesiology, Shangrao People's Hospital, Shangrao 330046, Jiangxi, China; [2]Department of Anesthesiology, The Second Affiliated Hospital of Nanchang University, Nanchang 330000, Jiangxi, China

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Abstract: Objective: This study was to explore the effects of dexmedetomidine and combined spinal and epidural anesthesia (CSEA) on the hemodynamics and adverse emotions of patients undergoing total hip replacement. Method: 142 patients undergoing total hip replacement in our hospital were divided into the Study Group (SG, n=80, routine spinal anesthesia + intraoperative intravenous drip of Dexmedetomidine) and the Control Group (CG, n=62, routine spinal anesthesia). Following indicators were compared between them: mean blood pressure (MBP) and heart rate (HR) at T0 (when anesthesia began), T1 (5 min before the operation), T2 (when the operation began), T3 (5 min after the operation began), T4 (30 min after the operation began) and T5 (at the end of the operation), levels of cortisol (Cor), noradrenaline (NE) and epinephrine (E) before anesthesia, at the end of and 24 h after the operation, the scores of Visual Analogue Scale (VAS), Ramsay Sedation Scale (RSS) and Self-rating Anxiety Scale (SAS) at 24 h after the operation, the time to recover from anesthesia and the incidences of adverse reactions after the operation. Results: In comparison with the CG, the SG had higher RSS score and required more time to recover from anesthesia ($P<0.05$). The MBP and HR at T1-T5 ($P<0.05$), the levels of Cor, NE and E at the end of and 24 h after the operation ($P<0.05$), the scores of VAS and SAS at 24 h after the operation and the incidence of complications after the operation ($P<0.05$) were significantly lower in the SG as compared with these of the CG ($P<0.05$). Conclusion: Dexmedetomidine combined with CSEA could achieve preferable anesthesia and sedation effects in patients undergoing total hip replacement by maintaining the stable hemodynamics, regulating the hormone level, relieving anxiety after the operation and reducing the incidence of complications associated with anesthesia.

Keywords: Dexmedetomidine, CSEA, total hip replacement, hemodynamics, SAS score, effects

Introduction

According to the results of recent social investigation, in the constantly aging Chinese society, the incidences of various degenerative diseases have been increasing year by year. Among these diseases, hip joint disease is frequently reported. As found in clinical investigation, hip joint is an important articulationes cotylica playing a significant role in maintaining the normal activities of the lower limbs. Hip fracture is the primary cause of the movement disorder of the elderly as evidenced by data. It is predicted that as the global population is aging, the global case number of hip fracture will rise from 4.5 million to 21.3 million by 2050, in which, about 45% will be from Asia [1-4].

Total hip replacement is one of the commonly adopted surgical methods in the clinic to treat patients with hip joint disease at the terminal stage. It can not only reduce pains effectively, but also recover the functions of hip joint maximally and then improve patients' quality of life. Based on the practice, as a common but major orthopedic operation, hip replacement is often associated with high blood loss, high invasiveness and high postoperative amount of drainage. It shall be specially noted that patients requiring hip replacement are usually at a senior age with many underlying diseases. Changes in hemodynamics due to stress in the operation may raise the incidences of complications and pain after the operation or even affect the cerebral metabolic rate of oxygen (CMRO2), lead-

ing to increased incidences of cardiovascular and cerebrovascular complications and risky events. As a result, it should be more prudent to select anesthetics. The principle of maintaining anesthesia effects and stabilizing hemodynamics shall be observed [5-8]. As an α2 adrenergic receptor agonist, dexmedetomidine has a receptor selectivity about seven times higher than clonidine. Meanwhile, its high internal activity and short half-life period contribute to the better effects of sedation, analgesia and inhibition of sympathetic activity [9]. This study aimed to analyze the effects of dexmedetomidine combined with CSEA on the hemodynamics of patients undergoing total hip replacement, in order to build a theoretical basis for facilitating postoperative recovery and reducing the incidence of adverse emotions in this type of patients.

Materials and methods

General materials

142 patients who received a total hip replacement in our hospital from January 2019 to December 2019 were divided into SG (n=80) and CG (n=62) according to the methods of anesthesia.

Inclusion criteria: (1) Identification of hip fracture or traumatic arthritis through imaging diagnosis, and establishment of the necessity for hip replacement [10]; (2) Unilateral hip replacement; (3) Clear consciousness to cooperate with the study; (4) Complete clinical medical records; (5) ASA grades I to III; (6) Approval from the ethics committee of the hospital; (7) Informed consent from the patients or their family members.

Exclusion criteria: (1) Complications such as mental disorders, active infection, malignant tumors, coagulation disorders, diseases of the autoimmune system, and spinal diseases affecting the movement of lower limbs; (2) Allergic to the drug studied; (3) Long-term use of corticosteroids.

Removal criteria: (1) Died during the study; (2) Withdrew initiatively during the study.

Methods

The preoperative nursing services provided to the two groups were the same and consisted of collecting medical history, evaluating conditions and informing patients and their family members of the possible risks in anesthesia. Patients stopped eating and drinking at 8 h before the operation. A venous channel was formed in the upper limb for intravenous drip of lactated Ringer's solution. During the operation, patients were monitored for electrocardiogram, blood oxygen, arterial pressure and bispectral index (BIS), and supplied with oxygen through a mask.

Lying on the left, patients in the CG received epidural puncture at the space between the third and the fourth lumbar vertebrae. A spinal needle was then placed to draw about 1 ml of clear cerebrospinal fluid (CSF). Ropivacaine was added into the fluid at 1:1 and injected at a dose of 2 ml through the spinal needle. Afterward, the spinal needle was retreated and an epidural catheter was placed. Patients were positioned to lie on their back so that the anesthesia plane was beneath the tenth dorsal vertebra.

Patients in the SG were also anesthetized in a conventional manner as applied to these in CG. But, at 15 min before the operation, intravenous drip of dexmedetomidine hydrochloride injection (manufacturer: Jiangxi Hengrui Medicine Co., Ltd., specification: 200 μg/injection, approval document No.: GYZZ No. H200902-48) at the dose of 1.0 μg/kg was applied. The drug was diluted by normal saline to 10 ml and intravenously dripped in 15 min. At a rate of 0.1-0.6 μg/kg/h, intravenous pumping continued until 15 min before the operation ended. To minimize the error, normal saline was administered to patients in the CG with the same dose/volume adopted for SG.

Observation indicators and evaluation criteria changes in hemodynamics over time

MBP and HR were recorded at T0, T1, T2, T3, T4 and T5, and compared between the two groups.

Changes in laboratory indicators over time

Before anesthesia, at the end of and 24 h after the operation, 5 ml of peripheral venous blood was collected from all patients, stored in a biochemical tube, and delivered to the laboratory for testing after the operation. The sample was centrifuged at a rate of 3000 r/min for 15 min, and the serum was stored under -80°C. An ELISA was performed in strict accordance with the instructions of the kits to measure the lev-

Table 1. Intergroup comparison of general clinical materials ($\bar{x}$ ± sd)/[n (%)]

General clinical materials		SG (n=80)	CG (n=62)	t/X^2	*P*
Gender	Male	43	32	0.064	0.8
	Female	37	30		
Average age (y)		55.19±3.41	55.21±3.51	0.034	0.973
Average weight (kg)		65.10±5.98	65.08±6.01	0.02	0.984
Average BMI (kg/m^2)		23.10±3.43	23.08±3.41	0.035	0.972
Diagnosis	ONFH	23	20	0.123	0.718
	Coxarthria	28	22		
	Transcervical fracture	29	20		
Educational background	Illiteracy	6	3	0.223	0.701
	Elementary school	9	4		
	Junior middle school	27	23		
	Senior high school, college and university	36	32		
Marital status	Married	73	59	0.816	0.366
	Unmarried	7	3		
Hypertension	Yes	13	11	0.055	0.814
	No	67	51		
Diabetes	Yes	12	13	0.858	0.354
	No	68	49		

els of Cor, NE and E. Each indicator was measured three times and the mean value was taken as the final.

Differences in indicators of recovery from anesthesia after the operation

The scores of VAS, RSS and SAS at 24 h after the operation and the time to recover from anesthesia were measured. VAS is a 10 cm ruler to evaluate the pain intensity. On the ruler, each patient was required to choose a number subjectively. 0 indicates no pain and 10 the worst pain. RSS, a scoring system monitoring postoperative sedation degree, uses 1 to 6 points to suggest "restless", "tranquil and cooperative", "sedative", "deeply sedative", "anesthetized" and "deeply insensible". A higher point indicates deeper degree of sedation.

SAS, a common means to evaluate anxiety, included 20 items, each valuing 1 to 4 points. By totaling up the points assigned to each item, the final score was obtained. A higher score indicated more severe anxiety [11].

Intergroup comparison of incidences of anesthesia-associated adverse reactions after the operation

The incidences of anesthesia-associated adverse reactions, such as hypopiesia, sychnosphygmia, bradyarrhythmia, nausea and vomiting, were calculated and compared between the two groups.

Statistical analysis

Statistical analysis was performed with SPSS22.0. In case of numerical data expressed as mean ± standard deviation, intergroup differences were checked by Student's t tests; in case of nominal data expressed as [n (%)], comparison studies were carried out through X^2 test for intergroup comparison. F test was used for data difference analysis among groups. For all statistical comparisons, significance was defined as $P<0.05$ [12].

Results

Intergroup comparison of general clinical materials

The general materials, such as gender, age, average weight, educational background, and history of underlying diseases, were not significantly different ($P>0.05$) but comparable between the two groups (**Table 1**).

Changes in hemodynamics at different time points

The MBP and HR at T0 were not statistically different between the two groups ($P>0.05$). From

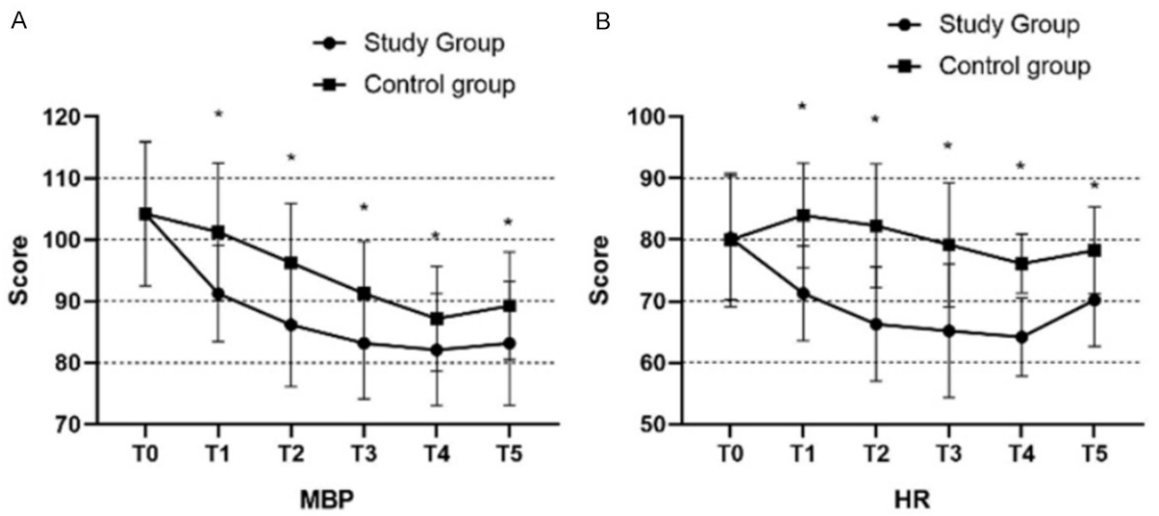

Figure 1. Intergroup comparison of changes in hemodynamics over time. For MBP and HR, no significant difference was found between the two groups at T0 (P>0.05), but from T1 to T5, the indicators were far lower in the SG (P<0.05) (A for MBP and B for HR); *P<0.05 vs CG for the same indicator at the same time point.

Table 2. Intergroup comparison of changes in laboratory indicators over time ($\bar{x}$ ± sd)

Indicator	Group	n	Before anesthesia	At the end of the operation	At 24 h after the operation
Cor (mmol/L)	SG	80	381.28±20.19	335.18±8.19	378.18±20.19
	CG	62	383.18±18.29	409.18±7.21	431.11±19.28
	t	-	0.579	56.228	15.8
	P	-	0.564	<0.001	<0.001
NE (μg/L)	SG	80	65.19±10.21	76.21±8.28	66.28±7.98
	CG	62	65.21±10.01	104.18±10.21	98.18±6.77
	t	-	0.012	18.025	25.215
	P	-	0.99	<0.001	<0.001
E (μg/L)	SG	80	61.28±13.10	93.11±12.11	50.19±9.88
	CG	62	60.98±14.11	123.17±10.28	87.17±7.18
	t	-	0.131	15.654	24.819
	P	-	0.896	<0.001	<0.001

T1 to T5, SG had far lower MBP and HR as compared with the CG (P<0.05) (**Figure 1**).

Changes in laboratory indicators over time

Cor, NE and E levels were not significantly different between the two groups before anesthesia (P>0.05), but were sharply lower in the SG at the end of and 24 h after the operation (P<0.05) (**Table 2**).

Differences in indicators of recovery from anesthesia after the operation

At 24 h after the operation, VAS and SAS scores were lower, RSS score was higher and the time to recover from anesthesia was longer in SG as compared with these of the CG (P<0.05) (**Figure 2**).

Intergroup comparison of incidences of anesthesia-associated adverse reactions after the operation

According to statistical analysis, the case numbers of hypopiesia, sychnosphygmia, bradyarrhythmia, nausea and vomiting were 2, 1, 1, and 1 in the SG (6.25%) and 3, 2, 2, 2 and 6 in the OG (19.35%) (P<0.05) (**Table 3**).

Discussion

Total hip replacement is a commonly adopted surgical method against osteoarthritis, rheu-

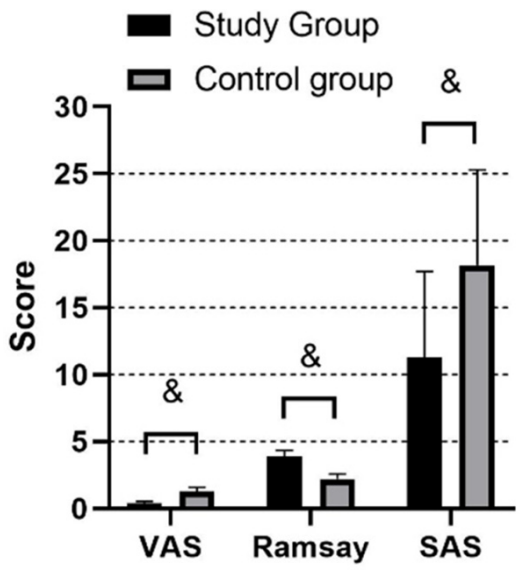

Figure 2. Intergroup comparison of recovery indicators at 24 h after the operation. The scores of VAS and SAS were lower, and the score of RSS was higher in the SG at 24 h after the operation ($P<0.05$). &$P<0.05$ vs CG for the same indicator at the same time point.

matoid arthritis, traumatic arthritis, osteonecrosis of the femeral head (ONFH), congenital hip dysplasia and transcervical fracture. Its application rate is next only to that of the cholecystectomy in western countries, and shows arising tendency in the wave of global aging [13, 14]. As revealed by data, hip replacement gained its popularity in China at the beginning of 1990s. After years of development, it has become one of the major orthopaedic operations in China. Each year, patients receiving the operation total up to 200,000 with a success rate of more than 90%. It has achieved remarkable results in improving the quality of life of the elderly and reducing the social burden [15].

According to clinical studies, total hip replacement is a major time-consuming orthopedic operation involving multiple steps and high blood loss. The surgeon has to saw off the diseased femoral head, reshape the femur and the acetabulum, and embed an artificial acetabulum. Close to the femoral head, the important neurovascular vessels may be subject to strong stimulation during the operation. Consequently, inflammatory factors are released largely, and hemodynamic indicators fluctuate strongly, leading to the possibility of hyoxemia and endangering patients' life and health [16]. An investigation of 228 patients receiving total hip replacement showed that their average age was above 60. In this operation, the elderly faced a higher risk as compared with the young population because of one or more underlying diseases and low tolerance to ischemia and hypoxia, which may trigger various cardiovascular and cerebrovascular events and affect the prognosis [17]. Many clinical studies have noted the significant influence of anesthetics on hemodynamics. A qualified anesthetic shall be effective, capable of maintaining the hemodynamic indicators and significantly reducing the incidence of anesthesia associated complications after the operation [18]. Traditionally, general anesthesia and intravertebral anesthesia are selected for total hip replacement. However, in the first case, opioids are used at high doses, resulting in high risks of nausea and vomiting. According to investigations, high doses of opioids also account for an increased incidence of pulmonary infection. In the second case, in addition to many contraindications, complications such as hypopiesia and urinary retention often have an impact on postoperative recovery. Therefore, the idea of combined anesthesia is proposed and popularized.

Dexmedetomidine is an α2 adrenergic receptor agonist and has good effects on both central and peripheral receptors, including sedation, analgesia, anti-anxiety and sympathetic nerve inhibition. According to clinical practice, the combination of this drug and local anesthetics could significantly shorten the onset time of local anesthetics and prolong the duration of action of local anesthetics, which provided a new idea for intraoperative anesthesia and postoperative analgesia in the total hip replacement [19]. Referring to previous studies, dexmedetomidine could stabilize the hemodynamic indicators in the elderly after an arthroscopic knee surgery, mitigate pains related to C-sect, and relieve anxiety arising from brachial plexus block, offering a theatrical foundation for anaesthetizing patients with dexmedetomidine in the total hip replacement [20].

By dividing patients into the SG and the OG, this study analyzed the effects of dexmedetomidine combined with CSEA on the hemodynamics and SAS score of patients undergoing total hip replacement. The results were lower MBP and HR in SG from T1 to T5. According to

Table 3. Intergroup comparison of incidences of complications after the operation [n (%)]

Group	n	Hypopiesia	Sychnosphygmia	Bradyarrhythmia	Nausea and vomiting	Total incidence
SG	80	2 (2.50)	1 (1.25)	1 (1.25)	1 (1.25)	5 (6.25)
CG	62	3 (4.84)	2 (3.23)	2 (3.23)	6 (9.68)	12 (19.35)
t	-	-	-	-	-	5.692
P	-	-	-	-	-	0.017

the curves, these indicators reduced significantly in the SG after anesthesia but maintained relatively stable during the operation. Some studies have demonstrated that the significant stress during a total hip replacement resulted in sharp changes in peripheral blood circulation, and increased release of catecholamine and risk of myocardial ischemia. The dexmedetomidine is known for inhibiting the sympathetic nervous system, stabilizing the blood pressure and heart rate in the operation as well as the peripheral circulation [21]. By interpreting the curves, the authors believed that maintaining MBP and HR at a lower level after anesthesia was conducive to reducing oxygen consumption and thus actively preventing ischemia and hypoxia. In the meanwhile, dexmedetomidine is a highly selective adrenergic receptor agonist, which can act on the nervous system after entering the body, inhibit the overstress in the body and improve myocardial ischemic symptoms, showing a positive significance for the patient's prognosis [22].

Changes in Cor, NE and E at different time of operation were also analyzed for both groups. According to the results, the three indicators were not significantly different between the two groups before anesthesia, but were significantly lower in the SG at the end of and 24 h after the operation. Cor, NE and E are clinical indicators reflecting the stress response of the body. The comparison of the above hormone levels between the two groups in this study further confirmed the effects of dexmedetomidine in inhibiting the stress response of the body. Studies have pointed out that for patients undergoing cardiovascular operations, dexmedetomidine can significantly reduce the incidence of myocardial infarction and sudden death without increasing the incidence of hypopiesia and bradyarrhythmia, suggesting the feasibility of dexmedetomidine application [23].

The pain intensity, sedation and anxiety at 24 h after the operation were also compared between the two groups. After the operation, the scores of VAS and SAS were lower, and the RSS score was higher in the SG, suggesting that the combination with dexmedetomidine can effectively reduce the postoperative pain intensity, mitigate anxiety and sedate patients favorably. As mentioned before, when dexmedetomidine is used with a local anesthetic, the local anesthetic's action time can be markedly prolonged with better sedation effects in the SG. A lot of studies have been designed centering on the analgesic effects of dexmedetomidine after an operation. Investigations have shown that by spinal anesthesia with dexmedetomidine and bupivacaine, the postoperative pain intensity of a patient undergoing C-sect and the dose of analgesics used were remarkably reduced. The possible reason is that dexmedetomidine could act on the α2-receptors in the postsynaptic membranes of spinal dorsal horn neurons to reduce the release of neurofibre transmitters and thus effectively inhibit the postoperative pain [24]. The difference in SAS score shall be attributed to the fact that dexmedetomidine has good lipid solubility, and can be combined with the nucleus ceruleus in the central nervous system to produce sedative effects and relieve patients from anxiety. Furthermore, its analgesic effect is another major reason of inhibiting anxiety [25]. The comparison of incidences of complications suggested that dexmedetomidine was a highly safe drug. It cut down the dose of anesthetics and therefore the incidences of complications associated with anesthesia.

In conclusion, for patients undergoing total hip replacement, dexmedetomidine combined with CSEA has demonstrated good anesthesia and sedation effects, reflected as stable hemodynamics, regulated hormone level, mitigated anxiety and reduced incidences of anesthesia associated complications. But, this study has following shortages: (1) Limited number of samples results in biased results; (2) Failure to develop long-term follow-up on patients. In view of these shortages, future studies shall be

based on a larger sample size and a longer follow-up time, in order to establish a more accurate and detailed theoretical basis for treating patients with total hip replacement.

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Disclosure of conflict of interest

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Address correspondence to: Jun Yang, Department of Anesthesiology, Shangrao People's Hospital, No. 72 Shuyuan Road, Xinzhou District, Shangrao 330046, Jiangxi, China. Tel: +86-0793-8100437; E-mail: yangjunya0@163.com

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