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Original Article

Effect of dexmedetomidine-assisted ultrasound-guided lower extremity nerve block on postoperative cognitive function in elderly patients undergoing hip surgery

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Abstract: Objective: To investigate the effect of dexmedetomidine (Dex)-assisted ultrasound-guided lower extremity nerve block on elderly patients undergoing total hip arthroplasty (THA). Methods: This retrospective study analyzed data of 60 elderly patients treated with unilateral artificial THA from January 2021 to February 2022. Among them, 30 patients anesthetized using Dex-assisted ultrasound-guided lower extremity nerve block were regarded as the research group (RG), and 30 patients anesthetized with the use of subarachnoid block were considered as the control group (CG). Serum interleukin 6 (IL-6) and interleukin 1β (IL-1β) levels were measured by enzyme linked immunosorbent assay (Elisa) in patients. Also, the heart rate (HR) and mean arterial pressure (MAP) were measured before, 10 min and 60 min after the anesthesia. The cognitive function was evaluated before anesthesia, as well as 2 h, 6 h and 36 h after anesthesia. The adverse reactions during hospitalization were recorded, and the incidence of adverse reactions was calculated. Results: IL-1β and IL-6 levels in both groups after operation were higher than those before operation (P>0.05), but those in the RG were lower than those in the CG (P<0.05). The HR and MAP at 10 min after anesthesia were lower than those before anesthesia (P<0.05). After anesthesia, the HR and MAP at 60 min in the RG were higher than those at 10 min in the CG, while the two in the RG were lower than those in the CG at 60 min (P<0.05). In addition, the postoperative pain score of the RG was lower than that of the CG, while the cognitive score of the RG was higher than that of the CG (P<0.05). There was no marked difference in the incidence of adverse reactions between the two groups (P>0.05). Conclusion: Dex-assisted ultrasound-guided lower extremity nerve block can effectively inhibit the postoperative inflammation, improve the cognitive function, and benefit the postoperative rehabilitation in elderly patients undergoing THA.

Keywords: Dexmedetomidine, ultrasound-guided lower extremity nerve block, hip arthroplasty in the elderly, cognitive function, inflammation

Introduction

With the rapid development of China's social economy and the continuous progress of medical technology, the average life expectancy of residents is increasing, and the process of population aging is also intensifying [1]. Due to the continuous decline of physical function and the loss of calcium in bone, the elderly have shown a high incidence in hip fracture, and the treatment of this disease is usually surgery [2]. Patient-controlled intravenous analgesia (PCIA) is a common analgesic protocol used clinically after hip replacement. However, there are numerous opioid-related side effects associated with PCIA in patients undergoing traditionally surgery, such as gastrointestinal reactions like nausea, vomiting and constipation, or even respiratory depression, cardiovascular accidents and drug dependence in some patients [3]. At this time, the advantage of peripheral nerve block becomes more and more obvious, because it can reduce the dose of opioids after PCIA, thereby greatly reducing the incidence of drug-related complications [4]. Concurrently, as ultrasound technology develops, ultrasound-guided nerve block has gradually become a mainstream way for clinical anesthesia [5].

Although the analgesic effect of peripheral nerve block is obvious, scholars have proposed a more optimized scheme, that is, dexmedetomidine (Dex)-assisted ultrasound-guided lower extremity nerve block [6]. To date, there have been a large number of studies on the application of Dex in elderly patients undergoing hip surgery. It has been pointed out that Dex can stabilize hemodynamic indexes and reduce adverse reactions [7, 8]. But, after referring to the previous data, we still find some limitations, such as the lack of research on the relationship between inflammation and postoperative dysfunction in elderly patients undergoing total hip arthroplasty (THA). Thus, this paper is making a detailed discussion on the effect and correlation of Dex-assisted ultrasound-guided lower extremity nerve block on the cognitive function of elderly patients undergoing hip surgery, so as to inspire a more effective anesthetic scheme for clinical treatment. In the meantime, we also try to provide some reference for improving the postoperative rehabilitation and reducing the incidence of adverse reactions.

Materials and methods

Patient data

A total of 60 elderly patients admitted from January 2021 to February 2022 and received unilateral artificial THA were included in this retrospective analysis. Among them, 30 patients anesthetized using Dex-assisted ultrasound-guided lower extremity nerve block were regarded as the research group (RG), and another 30 patients anesthetized using subarachnoid block were considered as the control group (CG). This study was approved by our medical ethics committee, with ethical approval number of 20210114 (A).

Inclusion and exclusion criteria

Inclusion criteria: (1) Patients with age over 60 years; (2) Patients with complete medical records; (3) Patients with normal communication skills; (4) Patients who met the indications of hip surgery; (5) Patients with normal vital signs before operation.

Exclusion criteria: (1) Patients with preoperative hemodynamic abnormality; (2) Patients with other cardiovascular diseases, cerebrovascular diseases, chronic diseases or autoimmune defects; (3) Patients with organ dysfunction or abnormality; (4) Patients who were transferred to another hospital during the treatment.

Methods

In the operating room, the upper extremity venous access of the patients was opened, and compound electrolyte solution 6-8 mL/kg was infused within 35 min. Routine inhalation of oxygen and monitoring of vital signs was performed. In the CG, patients were given subarachnoid anesthesia with 0.4% ropivacaine (Astra Zeneca, trade name: naropin) light specific gravity solution 5 mL (2 mL 1% ropivacaine hydrochloride in 3 mL sterile injection water). They were lying in a lateral horizontal position and punctured with a pen-pointed 25G lumbar puncture needle in the L3-4 space. The subarachnoid anesthetic solution was injected at an average rate of 0.5 mL/s, and a 3.5 cm epidural tube was placed in the head for backup. The upper boundary of the anesthesia plane was controlled at T8-T10. Patients remained in the original position until the end of the operation. The epidural was supplemented with 0.5% ropivacaine (Chengdu Tiantai Mountain Pharmaceutical Co., Ltd., SFDA Approval No. H20052666) as appropriate, and the anesthesia was continued until the end of the operation. In the RG, patients were placed in a lateral position. The skin of the puncture area was routinely disinfected, and the ultrasound machine was used to localize the lumbar plexus and sciatic nerve using SonoSite. SB8-HNS12 neurostimulator (Braun Medical, Germany), posterior thoracic 12 paravertebral, lumbar plexus, and sacral plexus nerve blocks with small doses of Dex (Yangtze River Pharmaceutlcal Group, SFDA Approval No. H20183220) compounded with ropivacaine (0.5 μg/kg Dex and 30 mL 0.33% ropivacaine mixture) 10 mL of thoracic paravertebral and 20 mL each of lumbar and sacral plexus were used. Dex sedation was pumped by intravenous micropump at a rate of 0.4 μg/(kg-h) with a continuous infusion and BIS values of 60 to 80.

Sample collection

Altogether 5 mL of fasting venous blood was drawn from patients 1 h before and 1 h after the surgery, respectively, and stored in a coagulation-promoting tube. The samples were left standing at room temperature for 30 min and

Table 1. Comparison of clinical baseline data

	Control group (n=30)	Research group (n=30)	t or χ^2	P
Age (year)	67.93±4.97	67.27±5.50	0.488	0.628
BMI (kg/cm^2)	21.15±2.69	21.71±2.99	0.763	0.449
Sex			0.318	0.573
Male/Female	22/8	20/10		
Educational level			0.067	0.796
Below high school/high school or above	14/16	15/15		
Place of residence			-	-
Urban/countryside	19/11	19/11		
Smoking			0.272	0.602
Yes/no	16/14	18/12		
Drinking			0.077	0.781
Yes/no	10/20	9/21		
History of surgery			0.577	0.448
Yes/no	3/27	5/25		

Note: BMI: Body Mass Index.

then centrifuged to obtain serum for subsequent detection.

Detection methods

Serum hypersensitive interleukin-6 (IL-6, Beyotime, PI330) and interleukin-1β (IL-1β, Beyotime, PI305) were tested by ELISA. Also, the heart rate (HR) and mean arterial pressure (MAP) were recorded before, 10 min, and 60 min after the anesthesia.

Evaluation criteria

The intraoperative pain score, motor block score and anesthetic muscle relaxation score were evaluated during operation. Cognitive function was assessed before, 2 h, 6 h and 36 h after anesthesia using the Mini-Mental State Examination (MMSE) [9]. The postoperative pain level was evaluated comprehensively using Visual Analogue Scale (VAS, 0-10 points) [10]. Higher scores indicate greater pain in patients. In addition, the adverse reactions during hospitalization were recorded, and the incidence of adverse reactions was calculated.

Statistical methods

SPSS 22.0 software was used for statistical analysis. The counting data were expressed by (%) and compared through chi-square test between groups. The measurement data were represented as ($\bar{x}$ ± sd) and compared through independent sample t-test. One-way ANOVA and LSD post-test were used for multi-group comparison. Multiple time point expressions were assessed using repeated measures ANOVA, expressed as F, with post hoc test using Bonferroni. The difference was statistically significant at $P<0.05$.

Results

Comparison of clinical baseline data

The clinical baseline data such as age and sex were compared between the groups, and there was no marked difference ($P>0.05$) (**Table 1**).

Comparison of inflammatory factors

IL-1β, IL-6 levels increased after operation in both groups ($P>0.05$), but the levels in the RG were lower than those in the CG ($P<0.05$) (**Figure 1**).

Comparison of vital signs

The HR and MAP at 10 min after anesthesia in both groups were lower than those before anesthesia ($P<0.05$), and the two in the CG at 60 min after anesthesia were higher than those at 10 min after anesthesia ($P<0.05$), but the differences were not significant in the RG between 10 min and 60 min after anesthesia ($P>0.05$). There was no obvious difference in HR and MAP between the groups before and 10

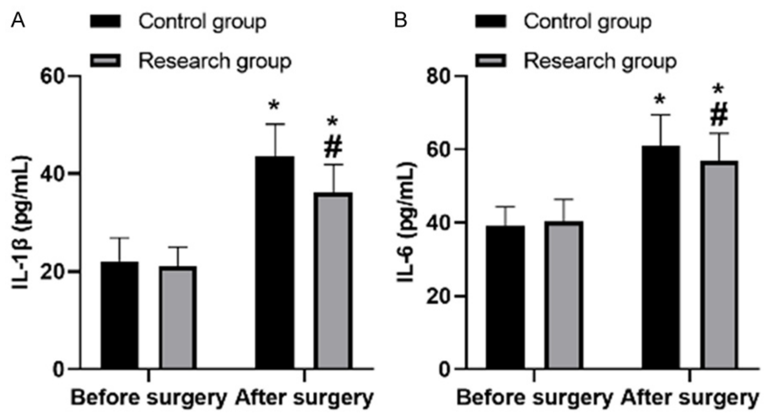

Figure 1. Comparison of inflammatory factors before and after operation. A. Comparison of IL-1β before and after operation. B. Comparison of IL-6 before and after operation. *P<0.05, comparison with before operation; #P<0.05, comparison with control group. IL-6: Interleukin-6; IL-1β: Interleukin-1β.

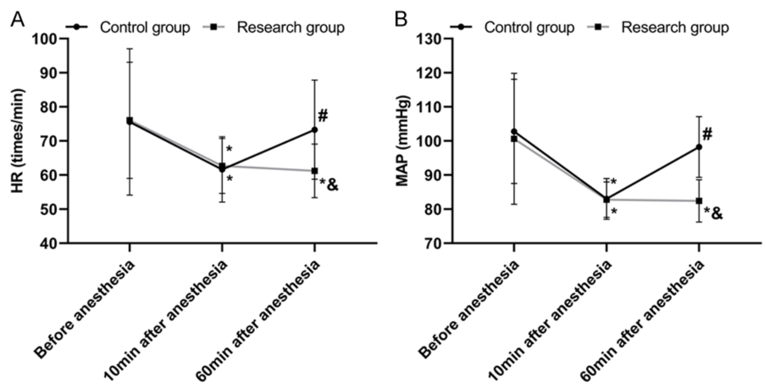

Figure 2. Vital signs of both groups. A. Comparison of HR. B. Comparison of MAP. *P<0.05, compared with before anesthesia; #P<0.05, compared with 10 min after anesthesia; &P<0.05, compared with the control group. HR: Heart Rate; MAP: Mean arterial pressure.

min after anesthesia (P>0.05), but the two in the RG were lower than those in the CG at 60 min after anesthesia (P<0.05) (**Figure 2**).

Comparison of pain

There was no marked difference in intraoperative pain score, motor block score and anesthetic muscle relaxation score between the groups (P>0.05), but the postoperative pain score in the RG was lower than that in the CG (P<0.05) (**Figure 3**).

Cognitive function comparison

There was no marked difference in cognitive function scores between the groups before the operation (P>0.05) The cognitive score at 2 h after operation in both groups was lower than that before operation, and the scores began to increase at 6 h after operation, and there was no difference between the groups at 36 h after operation (P>0.05), but the scores at 2 h and 6 h after operation in the RG were higher than those in the CG (P<0.05) (**Table 2**).

Comparison of adverse reactions

The incidence of postoperative adverse reactions in the RG was 13.33%, which is not markedly different from 23.33% in the CG (P>0.05) (**Table 3**).

Discussion

At present, ultrasound visualization technology has been mature and constantly used in surgery, so that ultrasound-guided peripheral nerve block has been further promoted and applied, and a good analgesic effect can be achieved while improving the accuracy of the puncture. It not only further reduces the damage of postoperative analgesia to local nerves and peripheral blood vessels, but also reduces the probability of serious postoperative complications [11]. At this time, the advantage of peripheral nerve block becomes more and more obvious, which is to dramatically reduce the dose of opioids needed by patients after PCIA, thereby greatly reducing the incidence of drug-related complications [12]. Both single or continuous femoral nerve block can reduce the perioperative dosage of opioids, improve the postoperative analgesic effect of patients undergoing THA, accelerate the recovery of postoperative hip joint function, decrease the incidence of postoperative adverse reactions, shorten the duration of hospitalization, improve the quality of life of patients, and help to recover the postoperative physical function [13]. Thus, this research has

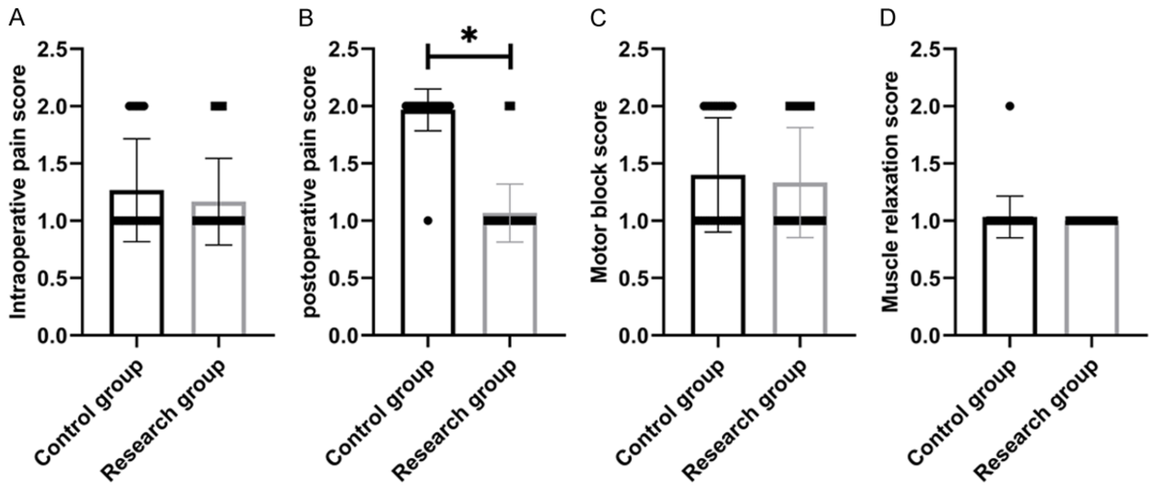

Figure 3. Comparison of pain between the two groups. A. Comparison of intraoperative pain score between the two groups. B. Comparison of postoperative pain score between the two groups. C. Comparison of motor block scores between the two groups. D. Comparison of anesthetic muscle relaxation scores between the two groups. *P<0.05, comparison between the two groups.

Table 2. Cognitive function score of the two groups

	Before operation	2 h after operation	6 h after operation	36 h after operation
Control group (n=30)	18.00±1.46	4.00±1.44*	11.17±1.17*,#	18.13±1.72#,&
Research group (n=30)	18.30±2.02	6.63±1.79*	13.93±2.16*,#	18.47±1.48#,&
t	0.659	6.270	6.154	0.415
P	0.512	<0.001	<0.001	0.821

Note: *P<0.05, compared with before operation; #P<0.05, compared with 2 h after operation; &P<0.05, compared with 6 h after operation.

Table 3. Incidence of postoperative adverse reactions

	Nausea and vomiting	Headache	Hypotension	Infection	Total incidence rate (%)
Control group (n=30)	3 (10.00)	2 (6.67)	1 (3.33)	1 (3.33)	23.33
Research group (n=30)	2 (6.67)	0 (0.0)	1 (3.33)	0 (0.0)	13.33
χ^2					1.002
P					0.317

crucial clinical significance by exploring the effect of Dex assisted ultrasound-guided lower extremity nerve block on elderly patients undergoing THA.

After surgery, due to mechanical invasion, trauma, stress response, etc., the peripheral immune system of elderly patients can be activated. In this case, immune cells release various inflammatory factors and then trigger the body inflammatory response. These factors are then involved in the pathophysiological process of central nervous system diseases, thus affecting the postoperative cognitive function of patients [14]. IL-6 and IL-1β, as important pro-inflammatory factors, are also sensitive and important indicators and mediators of the body's stress response [15]. In this experiment, we tested IL-1β and IL-6 in both groups, and the levels of these indexes increased in both groups after surgery, but the rising trend in the RG was lower than that in the CG, suggesting that the postoperative inflammation of patients in the RG was lower. This is because that Dex may have the effect of suppressing the inflammation in patients by activating postsynaptic α2 receptors, producing analgesia, sedation, and reducing sympathetic activity, thereby effectively suppressing the sympathetic nervous system excitation induced by surgical stimulation [16-18].

When the body has inflammation such as trauma and stress, the dynamic balance between Th17 cells and Treg cells in body fluid will be broken, inducing macrophages to be transferred to the brain, damaging the blood-brain barrier, neurons and nerve synapses, and resulting in postoperative cognitive dysfunction. Especially in the elderly with weak blood-brain barrier function, the nervous system is more vulnerable to injury [19, 20]. In a randomized controlled trial by Mei et al. [21], it was found that Dex intraoperative sedation reduced the incidence of delirium and may be beneficial in reducing the incidence of early postoperative cognitive dysfunction and providing better short-term recovery for elderly patients undergoing hip arthroplasty. Postoperative cognitive dysfunction is a kind of central nervous system functional impairment after operation, which is mainly characterized by memory loss and abnormal learning ability, and may even develop into permanent cognitive impairment, dementia and loss of independent living ability, which seriously affects the quality of life of patients [22]. As a highly selective α2-adrenoceptor agonist, Dex can promote the activation of α2-adrenoceptor in presynaptic membrane of locus ceruleus and reduce the excitability of postsynaptic membrane, which then inhibit the sensory-controlled arousal response of cerebral cortex [23]. When α2 receptor is activated and conjugated with G protein, it can reduce the concentration of intracellular cyclic phosphate, inhibit the phosphorylation of protein kinase A, and then reduce the excitability of cells, thus achieving sedation [24]. Moreover, Dex can also achieve analgesic effect by activating presynaptic membrane α2 receptors in spinal dorsal horn synaptic neurons and intermediate neurons to hyperpolarize cells and inhibit norepinephrine channels, reduce the release of P nerve presynaptic membrane and other harmful proteins, and directly block peripheral nerve C fibers and A fibers [25, 26]. Therefore, lower extremity nerve block guided by Dex-assisted ultrasound can effectively reduce the activation of postoperative inflammation and provide effective postoperative safety for patients. As demonstrated in a study by Liu et al. [27], iliac fascia compartment block combined with Dex reduced pain, improved sleep quality, and reduced serum inflammatory factor levels after total hip arthroplasty. When comparing the vital signs, cognitive function and pain between groups, we found that patients in the RG had a better postoperative state, which verified our above point of view, and once again showed that Dex-assisted ultrasound-guided lower extremity nerve block have a reliable postoperative safety for patients undergoing THA. This is mainly because that Dex, as a new selective α2 adrenergic agonist, can produce moderate sedative and analgesic effects, and control patients' blood glucose and adrenergic hormone levels, which effectively alleviate the adverse effects in the perioperative period, thus improving patients' cognitive function and postoperative pain.

There are still limitations in this study. There are lots of anesthetic schemes clinically, but we only took subarachnoid block as control, so we need to include more clinical comparative studies to further improve the representativeness of the results. Besides, due to the limited experimental conditions, the number of cases included is small, and the experimental period is short. Therefore, we will conduct in-depth analyses of the application of lower extremity nerve block guided by Dex-assisted ultrasound to provide more reliable reference and guidance for clinical practice.

To sum up, Dex-assisted ultrasound-guided lower extremity nerve block can effectively inhibit the postoperative inflammation, improve the cognitive function, and benefit the postoperative rehabilitation in elderly patients undergoing THA.

Disclosure of conflict of interest

None.

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