https://doi.org/10.31925/farmacia.2022.5.21 **ORIGINAL ARTICLE**

EFFECTS OF ORAL ATORVASTATIN ON INFLAMMATORY MARKERS AND POSTOPERATIVE DELIRIUM IN ELDERLY PATIENTS WITH HIP FRACTURE SURGERY

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Abstract

The aim of this study was to evaluate the therapeutic effect of dexmedetomidine anaesthesia assisted in elderly patients with osteoporotic hip fracture combined with postoperative oral atorvastatin, alendronate and calcium intake. A total of 60 elderly patients with osteoporotic hip fractures requiring surgical treatment were selected as the research subjects. They were randomly divided into group I (conventional surgery combined with postoperative alendronate), group II (dexmedetomidine-assisted surgery combined with postoperative alendronate and calcium intake) and group III (dexmedetomidine-assisted surgery combined with postoperative alendronate, calcium and atorvastatin intake), 20 patients *per* group. Serum inflammatory cytokine levels, cognitive function, sedation, pain, delirium, fracture healing rate and incidence of adverse reactions were analysed in each group. The results showed that compared with group I, postoperative serum interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), tumour necrosis factor α (TNF-α) and c-reactive protein (CRP) levels in groups II and III significantly decreased, while IL-10 significantly increased. Compared with group I, the Mini-Cog score and Ramsay score of group II and group III increased, while the visual analogue scale (VAS) score significantly decreased in groups II and III and the effect was superior in group III. The total delirium rates in groups I, II and III were 15.0%, 5.0% and 5.0%, respectively, the fracture healing rates were 90.0%, 90.0% and 100.0%, respectively, while the adverse reaction rates were 55.0%, 40.0% and 35.0%, respectively. Dexmedetomidine anaesthesia combined with postoperative alendronate, calcium and atorvastatin administration can reduce inflammation, delirium and adverse reaction rates and can be considered for clinical application.

Rezumat

Studiul actual a avut scopul de a evalua efectul terapeutic al anesteziei cu dexmedetomidină asistată la pacienții vârstnici cu fractură osteoporotică de șold, asociată cu atorvastatină administrată oral postoperator, alendronat și aport de calciu. Un total de 60 de pacienți vârstnici cu fracturi de șold osteoporotice, care necesită tratament chirurgical, au fost selectați drept subiecți de cercetare. Ei au fost împărțiți aleatoriu în grupul I (chirurgie convențională în asociere cu alendronat postoperator), grupul II (chirurgie asistată cu dexmedetomidină, în asociere cu alendronat postoperator și aport de calciu) și grupul III (chirurgie asistată cu dexmedetomidină, în asociere cu alendronat postoperator, calciu și atorvastatină), 20 de pacienți *per* grup. Nivelurile serice de citokine inflamatorii, funcția cognitivă, sedarea, durerea, delirul, rata de vindecare a fracturilor și incidența reacțiilor adverse au fost analizate în fiecare grup. Rezultatele au evidențiat că, în comparație cu grupul I, nivelurile serice postoperatorii de interleukină-1β (IL-1β), interleukină-6 (IL-6), interleukină-8 (IL-8), factor de necroză tumorală α (TNF-α) și proteină C reactivă (CRP) din grupurile II și III au scăzut semnificativ, în timp ce nivelul IL-10 a crescut semnificativ. Comparativ cu grupul I, scorul Mini-Cog și scorul Ramsay aferente grupului II și grupului III au crescut, în timp ce scorul la scara vizuală analogică (VAS) a scăzut semnificativ în grupurile II și III, iar efectul a fost superior în grupul III. Ratele totale de delir în grupurile I, II și III au fost de 15,0%, 5,0% și 5,0%, ratele de vindecare a fracturilor au fost de 90,0%, 90,0% și, respectiv, 100,0%, în timp ce ratele de reacții adverse au fost de 55,0%, 40,0% și, respectiv, 35,0%. Anestezia cu dexmedetomidină asociată cu administrarea postoperatorie de alendronat, calciu și atorvastatină poate reduce inflamația, delirul și ratele de reacții adverse și poate fi luată în considerare pentru folosire clinică.

Keywords: osteoporosis, hip fracture, dexmedetomidine, atorvastatin, inflammation, delirium

Introduction

Osteoporosis is a very common clinical orthopaedic disease, which occurs mostly in the elderly, and these patients are prone to fractures, thus seriously affecting the quality of life and health of patients [1]. A hip fracture refers to a femoral intertrochanteric fracture and a femoral neck fracture, which is one of the serious complications in elderly patients with osteoporosis. Hip fractures in the elderly are characterized by multiple comorbidities, high complication rates and difficulty in healing [2]. Because the physiological reserve capacity, stress resistance capacity and immune defence function of the elderly population are weakened to varying degrees, complications are

also very likely to occur after surgical treatment. The incidence of hip fracture in elderly patients with medical diseases is as high as 75%, which has seriously affected the treatment effect and prognosis of patients [3]. Alendronate is the main drug for the treatment of osteoporosis, which can be used for the postoperative treatment of elderly hip surgery patients with internal fixation. However, some studies have confirmed that patients taking alendronate will lead to destruction of the osteoclast-osteogenic coupling process, which affects the effect of bone healing [4]. Recent studies have shown that statins can stimulate the differentiation of osteoblasts and promote bone formation, improve bone density, and be used for the treatment of osteoporosis [5]. Atorvastatin is often used in the prevention and treatment of cardiovascular diseases such as atherosclerosis. In recent years, studies have also confirmed that it can be used in the treatment of osteoporosis and can also achieve excellent results [6].

The main complications of elderly hip fracture patients during the perioperative period include infection, deep vein thrombosis, delirium, pulmonary embolism and renal dysfunction. In severe cases, it can also lead to negative emotions such as depression in patients [7]. Postoperative delirium is a type of acute encephalopathy syndrome, which often occurs 3 to 5 days after surgery, and is mainly manifested as attention deficit and postoperative functional decline. Postoperative delirium will increase the risk of complications, increase postoperative morbidity and mortality, and ultimately lead to patients being unable to take care of themselves. Current studies have confirmed that age, own state, use of anaesthetics and postoperative pain control are closely related to the occurrence of postoperative delirium [8, 9]. Dexmedetomidine is a highly selective and specific alpha-2 adrenergic receptor (α2AR) agonist, which can act on the pons and medulla oblongata and participate in the transmission of sympathetic nerve signals. Dexmedetomidine has neuroprotective properties, and studies have demonstrated that dexmedetomidine can be used in the prevention of delirium in patients in the intensive care unit [10]. However, the effect of dexmedetomidine-assisted surgery combined with postoperative atorvastatin on the efficacy and safety of elderly patients with osteoporotic hip surgery is still unclear.

Therefore, this work included elderly patients with osteoporotic hip fractures as the research objects and explored the assisted surgical treatment of dexmedetomidine anaesthesia. After taking alendronate and atorvastatin calcium tablets in combination, it had effects on the cognitive function, postoperative delirium and inflammatory response of patients. It aimed to provide a reference for improving the clinical treatment effect and prognosis of elderly patients with osteoporotic hip fractures.

Materials and Methods

General data of patients

A total of 60 elderly patients with osteoporotic hip fractures who were treated at the Beijing Luhe Hospital, Capital Medical University, Beijing, China, from March 2019 to December 2021 were selected as the research subjects, including 39 females and 21 males. The patients were randomly divided into group I, group II and group III, with 20 cases in each group. Patients in group I were treated with conventional anaesthesia and sodium alendronate, patients in group II were treated with dexmedetomidine-assisted surgery and alendronate, and patients in group III were treated with dexmedetomidine-assisted surgery and alendronate combined with atorvastatin. This experiment has been approved by the ethics committee of the hospital, and the included patients and their families had signed the informed consent.

Inclusion criteria were: those with clear consciousness before surgery; those who meet the diagnostic criteria for osteoporotic hip fracture and receive inpatient surgery; those who can cooperate with surgical treatment and complete clinical observation; and those aged 60. Exclusion criteria were defined as follows: patients with haematological diseases, malignant tumours, or other serious organic diseases; patients with severe liver and kidney dysfunction; patients with long-term use of sedation drugs and mental diseases; those with abnormal recovery from anaesthesia and surgery; those with a history of a severe allergy to drugs; those younger than 60 years old or with fractures in other parts; and those who had not completed the treatment.

Anaesthesia method

All patients received no treatment before surgery, and the veins of the patient's right upper extremities were routinely opened after admission. The patient's heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), bispectral index (BIS), pulse oxygen saturation (SpO_2), partial pressure of CO_2 at the end of the exhalation ($PetCO_2$) and electrocardiogram (ECG) was monitored in real-time. After local anaesthesia, invasive blood pressure was monitored after cannulation of the left radial artery, followed by induction of anaesthesia. All patients were anesthetized by intravenous infusion of 0.4 μg/kg sufentanil, 1.5 mg/kg propofol, 0.02 mg/kg midazolam and 0.1 mg/kg vecuronium bromide. At the same time, 3 mg/mL propofol plasma, 0.3 μg/kg

remifentanil and 2 mg/kg vecuronium bromide target-controlled infusion were administered to maintain anaesthesia. Patients in group I received an appropriate amount of 0.9% normal saline injection for intravenous infusion before induction of anaesthesia. The patients in group II and group III received 0.04 mg/mL dexmedetomidine before anaesthesia induction, 15 minutes after the infusion, and maintained infusion at a rate of 0.4 μg/(kg·h) during anaesthesia induction. All the medicines were from Jiangsu Hengrui Medicine Co, Ltd, Jiangsu, China.

Treatment method

All patients were treated with Gamma nail surgery. After the patient was anaesthetized, a 10 - 12 cm incision was made on the lateral side of the hip joint. The greater trochanter was used as the effective centre area, and the rectus femoris space and the lateral femoral muscle were gradually separated to fully expose the patient's fracture position. Then, a pear-shaped slot was made in the greater trochanter of the femur, the Gamma main screw was inserted after effective diffusion, and the fracture site of the patient was reduced by the professional operator using the traction method. The guide sight was connected to the end of the Gamma main pin and drilled down the femoral neck and drive the guide pin. It should confirm the length and position under the X-ray of the C-arm, then insert the locking pin and control the length, fix the fracture end to form a "V" shape, connect the sight to the distal end of the Gamma main pin, and fix the locking pin after horizontal drilling. Real-time understanding of the patient's haemoglobin changes during the operation, and maintaining the patient's haemoglobin level above 85 g/L. After surgery, all patients received conventional anti-infection, deep vein thrombosis prophylaxis and other treatments.

The patients in groups I and II received 1 tablet of calcium carbonate D3 (contains 600 mg calcium and 400 UI cholecalciferol, Jiangsu Hengrui Medicine Co, Ltd, Jiangsu, China) twice *per* day and 1 tablet of alendronate (70 mg, Jiangsu Hengrui Medicine Co, Ltd, Jiangsu, China) *per* week. The patients in group III received the same treatment that the patients in groups I and II plus 40 mg oral atorvastatin (20 mg atorvastatin *per* tablet, Jiangsu Hengrui Medicine Co, Ltd, Jiangsu, China). All patients received continuous treatment for 6 months after surgery.

Observation indicators and detection methods

Vital signs and surgery-related indicators. During the surgery, HR, SBP, DBP, BIS, SpO_2 and $PETCO_2$ of patients were monitored at the time of entering the room (T0), after the anaesthesia experiment drug pumping (T1), the beginning of the operation (T2), the end of the operation (T3) and the time of leaving the operating room (T4). During the surgery, the intraoperative urine volume, extubation time and anaesthetic consumption of the patients were recorded.

Detection of serum inflammatory markers. Before the surgery and 3 days after surgery, 5 mL of fasting venous blood was collected from patients in the early morning, and the serum was separated after anticoagulation with sodium citrate. Serum was collected, and enzyme-linked immunosorbent assay kits were used to detect the inflammatory indexes interleukin-1β (IL-1β), interleukin-6 (IL-6), interleukin-8 (IL-8), tumour necrosis factor α (TNF-α) and c-reactive protein (CRP) levels. Enzyme-linked immunosorbent assay kits for detection were provided by Shanghai Enzyme-Linked Biological Company and the analyses were done according to the manufacturer instructions. Briefly, serum samples were incubated in the predefined ELISA wells for 1 h at room temperature. After incubation 100 μL of corresponding biotinylated detection antibody was added to each well and incubated for 1 h at room temperature. Then 100 μL of horseradish peroxidase-labelled streptavidin conjugate was added and incubated for 30 minutes at room temperature. After incubation 50 μL of stop solution was added and the absorbance of each well was measured.

Evaluation of cognitive function. The cognitive function of patients was assessed using the Mini-Cog. All patients were required to listen carefully and remember 3 unrelated words and repeat. The patient was required to draw the shape of a clock on a blank piece of paper, mark the number of the clock and ask the patient to mark a certain point in time. Upon completion, it should describe the 3 words previously remembered by the patient. When the patient failed to remember any word, it was scored as 0, that is, dementia; the patient can remember 1 ~ 2 words but failed to complete the clock drawing test, it was scored as 1, that is, cognitive function defect; the patient can remember 1 ~ 2 words and complete the clock drawing test, which was scored as 2 points, that is, the cognitive function was normal; and the patient can remember 3 words and complete the clock drawing test, which was scored as 3 points, that is, no dementia.

Evaluation of the degree of sedation. The Ramsay sedation scale was used to evaluate the degree of postoperative sedation in patients. Restlessness scored 1 point; quiet cooperation scored 2 points; drowsiness, rapid response to calls but blurred pronunciation during sleep, scored 3 points; light sleep state, and can be awakened during sleep, scored 4 points; moderate sleep state and slow response to calls during sleep, scored 5 points; deep

sleep state and no response to calls during sleep, scored 6 points.

Evaluation of pain level. The visual analogue scale (VAS) was used to evaluate the postoperative pain degree of patients, and the scale score ranged from 0 to 10 points. The pain level was marked by the patient on the horizontal line according to their feelings, 0 - 4 points represented mild pain, 5 - 7 points represented moderate pain and 8 - 10 points represented severe pain. It was considered that no pain was felt when coughing, which was scored as 0; the pain was unbearable when it was quiet, which was scored as 10.

Evaluation of delirium. The degree of delirium was evaluated by the method of disturbance of consciousness assessment at 1, 3 and 5 days after the surgery. The main symptoms included (1) acute onset and fluctuating condition; (2) the patient's attention inattentive or inattentive; (3) the patient's thinking is irregular; (4) the patient's level of consciousness changed. Patients were considered to have delirium when they were considered to have both (1) and (2) symptoms, and one of (3) or (4) was present.

Evaluation of fracture healing rate. X-ray films were used to observe the position of the hip internal fixator and fracture healing at 7 days, 15 days, 30 days, 90 days and 180 days after treatment. The patient was considered to be healed when there is no pain on the fracture site, no longitudinal percussion pain and other abnormal phenomena. If the X-ray showed that the patient's fracture site was blurred and there is a continuous callus at the fracture line, it indicated that the patient's fracture healing effect was not good. After removing the external fixation, the patient continued to lift 1 kg for 1 minute and can walk continuously for 30 minutes without crutches, with more than 30 steps. The morphological changes in the fracture site of the patients were continuously observed.

Evaluation of adverse reactions. The probability of adverse reactions such as heart rate disorder, hypoxemia, unstable blood pressure, nausea and vomiting and chills after surgery was evaluated. At the same time, the probability of adverse reactions such as headache, constipation and nausea in patients after treatment was evaluated.

Statistical analysis

Statistical analysis of the data was performed using SPSS 19.0 (IBM, New York, United States). Enumeration data were expressed by frequency (percentage), and differences between groups were compared using the chi-square (χ^2 test) or F test. Measurement data were expressed as mean ± standard deviation ($\bar{x} \pm s$), and differences between groups were compared using a one-way analysis of variance. When $p < 0.05$, the difference between groups was considered statistically significant.

Results and Discussion

Comparison of general data of three groups of patients

The differences in the general data of the three groups of patients were compared, and the results were shown in Table I. There was no significant difference in gender ratio, age, course of the disease, body temperature and BMI among groups I, II and III ($p > 0.05$).

Table I

Comparison of general data of patients at the beginning of the study

Indicator	Group I	Group II	Group III	*p* value	*p*
n	20	20	20		
Gender (n/%)				0.433	0.129
Male	7/35.0	8/40.0	6/30.0		
Female	13/65.0	12/60.0	14/70.0		
Age (years old)	68.92 ± 4.26	69.17 ± 5.05	68.84 ± 4.43	0.395	0.132
Disease duration (h)	23.31 ± 4.18	22.59 ± 4.80	23.07 ± 5.12	0.171	0.098
Body temperature (°C)	38.20 ± 0.17	37.75 ± 0.22	38.13 ± 0.16	0.250	0.117
BMI (kg/m^2)	22.35 ± 3.35	22.24 ± 3.51	22.63 ± 2.89	0.129	0.130

BMI referred to body mass index

Changes in vital signs in three groups of patients during the perioperative period

The differences in vital sign indexes HR, SBP, DBP, BIS, SpO_2 and $PETCO_2$ of patients in groups I, II and III at each time point in the perioperative period were compared, and the results were shown in Figure 1. It was found that HR, SBP and DBP first increased and then decreased in group I, BIS first decreased and then increased, and SpO_2 and $PETCO_2$ did not suffer any change. After comparison, there was no significant difference in BIS, SpO_2 and $PETCO_2$ between groups I, II and III patients at T0, T1, T2, T3 and T4 ($p > 0.05$). Compared with group II and group III, the HRs at T1, T2 and T3 time points in group I patients were significantly higher ($p < 0.05$), and the SBP and DBP at T2 and T3 in group I patients were significantly higher ($p < 0.05$).

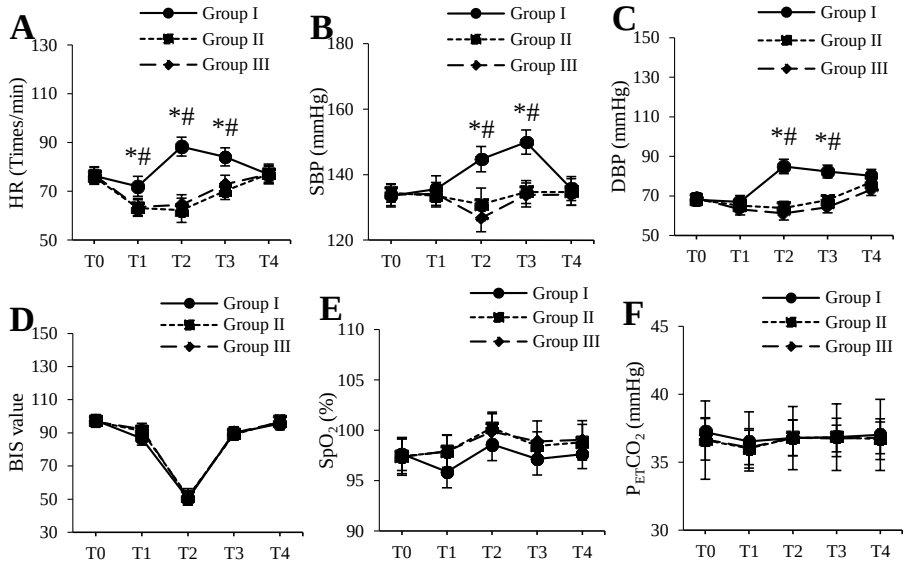

Figure 1.

Comparison of vital signs of patients at different time points

(A): HR; (B): SBP; (C): DBP; (D): BIS; (E): SpO_2; (F): $PETCO_2$; * and # suggested $p < 0.05$ compared with group II and group III, respectively

Comparison of surgery-related indicators among the three groups of patients

The differences between the operation-related indicators of urine volume, extubation time and the amount of anaesthetics used in patients in groups I, II and III were compared, and the results were shown in Figure 2. There was no significant difference between groups I, II and III in the operation-related indicators of urine volume and extubation time ($p > 0.05$). Compared with group I, the consumption of anaesthetics in group II and group III was significantly reduced ($p < 0.05$).

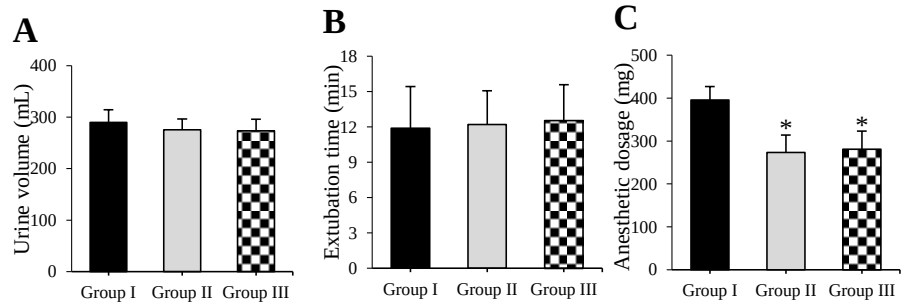

Figure 2.

Comparison of perioperative urine volume, extubation time and anaesthetic drug usage

(A): urine volume; (B): extubation time; (C): anaesthetic drug usage. * compared with group I, $p < 0.05$

Comparison of serum inflammatory cytokine levels in three groups of patients

The differences in serum levels of inflammatory cytokines IL-1β, IL-6, IL-8, IL-10, TNF-α and CRP among groups I, II and III patients before and after surgery were compared, and the results were shown in Figure 3. There was no significant difference in serum IL-1β, IL-6, IL-8, IL-10, TNF-α and CRP levels among groups I, II and III before surgery ($p > 0.05$). Compared with the levels before surgery, the serum levels of IL-1β, IL-6, IL-8, IL-10, TNF-α and CRP were significantly increased in groups I, II and III after surgery ($p < 0.05$). Intergroup comparison showed that the levels of serum IL-1β, IL-6, IL-8, TNF-α and CRP in group II and group III after surgery were significantly decreased compared with group I levels, while the level of IL-10 was significantly increased ($p < 0.05$). There was no significant difference in postoperative serum IL-1β, IL-6, IL-8, IL-10, TNF-α and CRP levels between groups II and III ($p > 0.05$).

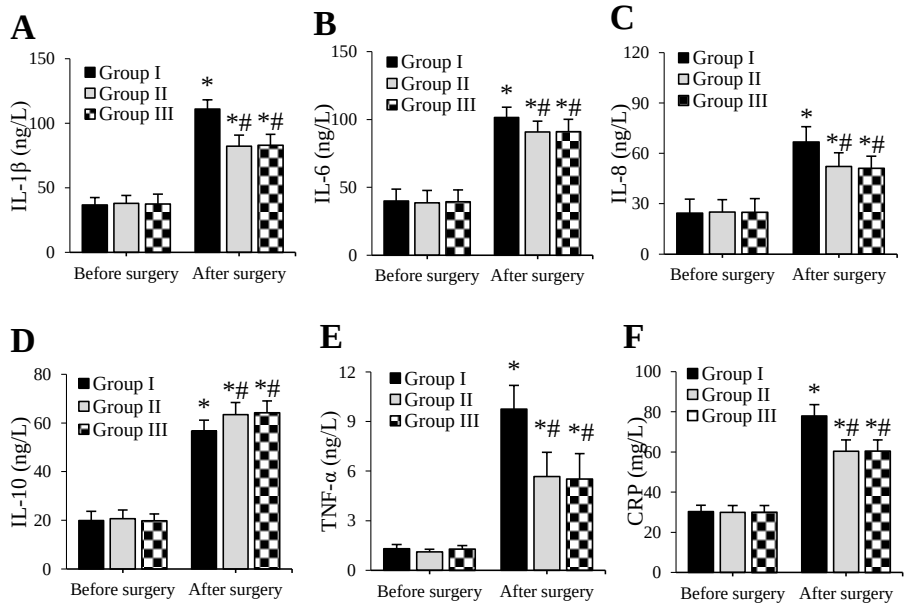

Figure 3.

Comparison of serum inflammatory cytokines IL-1β, IL-6, IL-8, IL-10, TNF-α and CRP levels before and after surgery

(A): IL-1β; (B): IL-6; (C): IL-8; (D): IL-10; (E): TNF-α; (F): CRP; * $p < 0.05$ compared with the value in same group before surgery; # $p < 0.05$ compared with the post-surgery levels in group I

Evaluation of cognitive function, sedation and pain in three groups of patients

The differences in cognitive function Mini-Cog score, Ramsay sedation score and VAS pain score were compared among groups I, II and III after treatment, and the results were shown in Figure 4. Compared with group I, Mini-Cog scores and Ramsay sedation scores of patients in groups II and III were significantly increased, while VAS pain scores were significantly decreased ($p < 0.05$). Compared with group II, the Mini-Cog score and Ramsay sedation score of group III patients were significantly increased, while the VAS pain score was significantly decreased ($p < 0.05$).

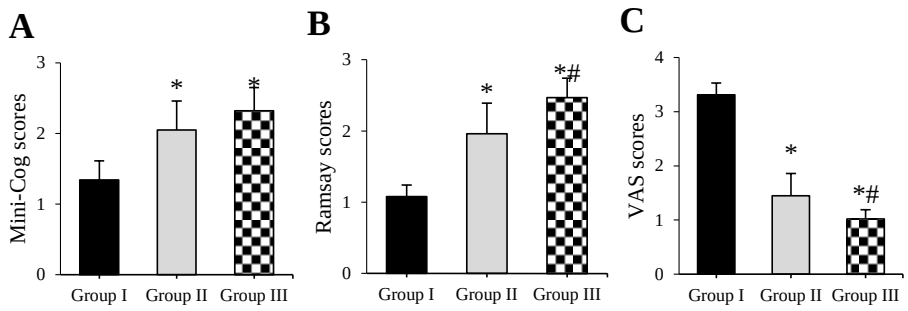

Figure 4.

Comparison of scores of various scales after treatment

(A): cognitive function Mini-Cog score; (B): Ramsay sedation score; (C): VAS pain score; * $p < 0.05$ compared with group I; # $p < 0.05$ compared with group II

Comparison of the incidence of delirium among the three groups of patients after treatment

The differences in the probability of occurrence of delirium at day 1, day 3 and day 5 in group I, group II and group III after treatment were compared, and the results were shown in Figure 5. One day after treatment, there were 0 patients (0.0%) with delirium in the three groups. Three days after treatment, 2 cases (10.0%), 1 case (5.0%) and repspectively 0 cases (0.0%) of delirium was recorded in group I, group II and group III, while 5 days after treatment there were 1 case (5.0%), 0 case (0.0%) and 1 case (5.0%) of patients with delirium in group I, group II and group III respectively. During the treatment, the total delirium rates of patients in groups I, II and III were 15.0%, 5.0% and 5.0%, respectively. Compared with group I, the incidence of delirium in group II and group III patients was significantly lower ($p < 0.05$).

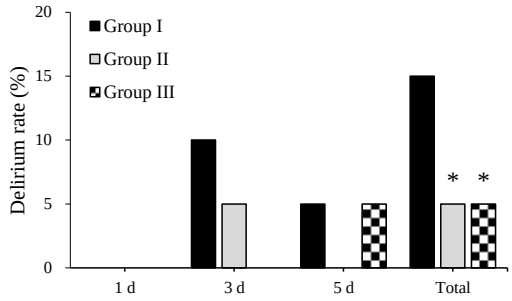

Figure 5.
Comparison of the incidence of delirium at each time point after treatment
* $p < 0.05$ compared with group I

Comparison of fracture healing rate in three groups of patients after treatment

The differences in the fracture healing rate of patients in group I, group II and group III at day 7, day 15, day 30, day 90 and day 180 of treatment were compared, and the results were shown in Figure 6. It was found that after 7 days of treatment, fracture healing occurred in 0 cases (0.0%), 2 cases (10.0%) and 4 cases (20.0%) in groups I, II and III, respectively. Fractures healed in 5 cases (25.0%), 5 cases (25.0%) and 11 cases (55.0%) in each group 15 days of treatment, respectively. After 30 days of treatment there were 13 cases (65.0%), 14 cases (70.0%) and 18 cases (90.0%) of fractures healed in group I, II and III respectively. After 90 days of treatment, fractures healed in 15 cases (75.0%), 17 cases (85.0%) and 20 cases (100.0%) in group I, II and III, respectively. 180 days after treatment, fractures healed in 18 cases (90.0%), 18 cases (90.0%) and 20 cases (100.0%) in group I, II and III, respectively.

Compared with the group I, the fracture healing rate of patients in group III increased significantly at day 7, 15, 30, 90 and 180 after treatment ($p < 0.05$). Compared with group II, the fracture healing rate of patients in group III increased significantly at day 15, 30, 90 and 180 after treatment ($p < 0.05$).

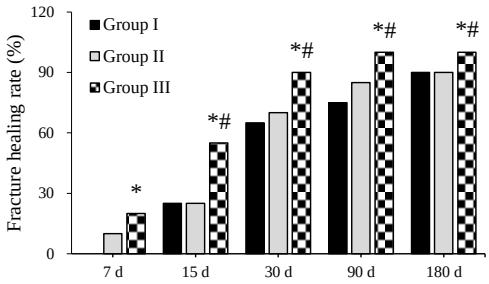

Figure 6.
Comparison of fracture healing rate of patients at various time points after treatment
*$p < 0.05$ compared with group I; # $p < 0.05$ compared with group II

Comparison of adverse reactions rate after treatment in three groups of patients

The differences in the incidence of adverse reactions such as arrhythmia, hypoxemia, blood pressure disorder, vomiting, chills, constipation, headache and malignant tumours, were compared among groups I, II and III during the treatment period. The results were shown in Figure 7. The numbers of patients with above adverse reactions in group I were 7 cases (35.0%), 2 cases (10.0%), 3 cases (15.0%), 5 cases (25.0%), 4 cases (20.0%), 3 cases (15.0%), 6 cases (30.0%) and 7 cases (35.0%), respectively. The numbers of patients with above adverse reactions were 4 cases (20.0%), 1 case (5.0%), 3 cases (15.0%), 2 cases (10.0%), 2 cases (10.0%), 4 cases (20.0%), 2 cases (10.0%) and 4 cases (20.0%), respectively. The numbers of patients with above adverse reactions were 3 patients (15.0%), 0 (0.0%), 2 (10.0%), 1 (5.0%), 3 (15.0%), 5 (25.0%), 2 cases (10.0%) and 5 cases (25.0%) in the group III, respectively. The total adverse reaction rates of patients in groups I, II and III were 55.0%, 40.0% and 35.0%, respectively. Compared with the group I, the total adverse reactions rate of patients in group II and group III was significantly lower ($p < 0.05$). Compared with group II, the total adverse reaction rate of patients in group III was significantly lower ($p < 0.05$).

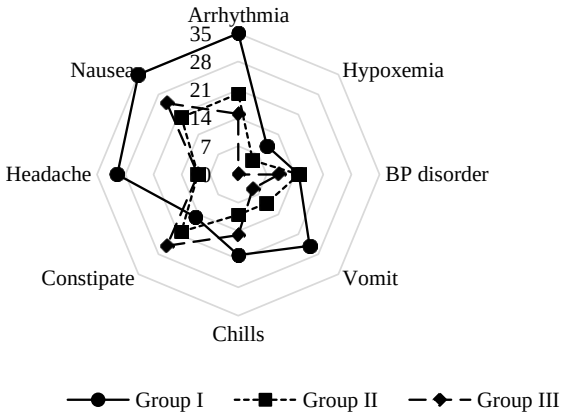

Figure 7.
Comparison of incidence of adverse reactions in patients after treatment
BP referred to blood pressure

Osteoporosis is a common disease in elderly patients, and its incidence is increasing year by year. The incidence of osteoporosis in men over the age of 60 in China is about 30%, while the incidence of osteoporosis in women is as high as 50% - 70% [11]. Osteoporosis can lead to fragility fractures in patients, often manifesting as spinal compression fractures, distal radius fractures, upper humerus fractures and hip fractures caused by minor trauma. Hip fractures caused by osteoporosis have the highest morbidity and mortality rates, and

patients have a relatively high postoperative complication rate [12]. Delirium is a clinical acute brain syndrome, mainly caused by organic brain diseases, and its main clinical manifestations are mental disorders, unconsciousness and memory loss [13]. If the occurrence of delirium cannot be effectively controlled, it can cause intracerebral haemorrhage in severe cases and lead to death. Postoperative delirium causes death in about 20% to 75% of patients, and age, mechanical ventilation and postoperative pain all contribute to the occurrence of delirium [14]. Complications such as perioperative hypoxemia increase the incidence of delirium. Therefore, the use of effective sedation measures after surgery is the key point in preventing delirium.

Dexmedetomidine is a class of sedation drugs widely used in clinical anaesthesia, which can effectively predict the occurrence of postoperative delirium and improve the prognosis of patients [15]. The results of this study showed that perioperative use of dexmedetomidine can significantly reduce the use of postoperative anaesthetics in elderly patients with osteoporotic hip fracture surgery. The use of anticholinergic drugs can cause cognitive function impairment and postoperative delirium in patients, and prolong the hospitalization time of patients [16]. Secondly, the results of this study suggested that perioperative use of dexmedetomidine can significantly improve the cognitive function, Mini-Cog score and Ramsay sedation score in elderly patients with osteoporotic hip fracture surgery. The Mini-Cog scale is often used in the evaluation of cognitive function disorders in patients. Subsequently, this work found that perioperative use of dexmedetomidine could significantly reduce the incidence of postoperative delirium in elderly patients with osteoporotic hip fracture surgery. Dexmedetomidine is an α2AR agonist with sedation, sleep aid and anxiolytic effects, which can reduce the use of postoperative sedation drugs [17].

After traumatic surgery, the patient's body is often accompanied by an acute inflammatory response, so the expression of inflammatory cytokines plays an important role. IL-1β, IL-6, IL-8 and TNF-α are typical pro-inflammatory cytokines, while IL-10 is an anti-inflammatory cytokine. CRP can be used to monitor the inflammatory state of the patient's body. IL-1β is a key pro-inflammatory cytokine, which is involved in a variety of autoimmune inflammatory responses and cell biological processes, including cell proliferation, differentiation and apoptosis [18]. IL-6 is a strong inflammatory response mediator, which can act together with TNF-α in acute inflammatory response, and is an important indicator for evaluating the degree of inflammatory response and tissue damage in the body [19]. IL-8 is a chemotactic cytokine, which can promote the chemotaxis and cell proliferation of inflammatory cells [20]. IL-10 is an anti-inflammatory cytokine in traditional Chinese medicine, which can inhibit the synthesis and secretion of TNF-α, reduce the degree of tissue damage and enhance the body's anti-infection ability [21]. In this study, the changes of inflammatory cytokine levels in serum of patients were detected, and it was found that all inflammatory cytokine levels were increased in patients after surgery. Perioperative use of dexmedetomidine can significantly reduce serum pro-inflammatory cytokines IL-1β, IL-6, IL-8, TNF-α and CRP levels, and increase anti-inflammatory cytokines in elderly patients with osteoporotic hip fracture surgery IL-10 levels. It shows that hip fracture can initiate inflammatory response to a certain extent, and dexmedetomidine can effectively maintain the balance of pro-inflammatory and anti-inflammatory responses in postoperative patients, which is beneficial to patients' postoperative recovery.

Alendronate is the main drug for the treatment of osteoporosis. It can destroy the body's osteoclasts by combining with hydroxyapatite, promote the apoptosis of osteoclasts, and then inhibit the process of osteoporosis. Other studies have confirmed that alendronate can increase the stability of femoral implants in patients with hip fractures treated with internal fixation and promote bone healing in patients [22]. Statins are often used in the treatment of hyperlipidaemia, atherosclerosis and other diseases, and can also promote callus growth [23]. Bass *et al*. [24] confirmed that statins combined with alendronate have a synergistic effect to promote the healing effect of patients with osteoporotic fractures. To this end, this work investigated the safety of alendronate alone and alendronate combined with atorvastatin after surgical treatment. The results showed that after taking alendronate and atorvastatin, the fracture healing rate of the patients was significantly increased, and the incidence of adverse reactions after treatment was lower. It shows that alendronate combined with atorvastatin is beneficial to promote postoperative bone healing in elderly patients with hip fracture.

Conclusions

The use of dexmedetomidine in elderly patients with osteoporotic hip fracture can significantly reduce the postoperative inflammatory response and the incidence of delirium, and can also improve the cognitive function and pain level of patients. The postoperative use of alendronate, calcium and atorvastatin can promote the bone healing effect of

patients, improve the clinical symptoms of osteoporosis and have higher safety. This work only used clinical data to explore the therapeutic effect of drugs, and it was necessary to explore the efficacy and safety of different doses of drugs in the treatment of elderly osteoporotic hip fractures. In conclusion, the results of this work can provide parameters for the selection of clinical treatment methods for elderly osteoporotic hip fractures and improve the prognosis of patients.

Conflict of interest

The authors declare no conflict of interest.

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