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Evaluation of the bone metabolism balance and traumatic reaction of minimally invasive mippo intramedullary nail internal fixation treatment of femoral shaft fractures

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ABSTRACT

Objective: To evaluate the bone metabolism balance and traumatic reaction of minimally invasive mippo intramedullary nail internal fixation treatment of femoral shaft fractures. **Methods:** 80 patients with femoral shaft fractures who were treated in our hospital between May 2011 and December 2016 were collected and divided into control group (n=40) and observation group (n=40) according to random number table, control group received conventional steel plate internal fixation treatment, and observation group received minimally invasive mippo intramedullary nail internal fixation treatment. Differences in serum levels of bone formation indexes, bone resorption indexes, inflammatory factors, and pain mediators and so on were compared between two groups of patients before operation and 1 week after treatment. **Results:** Before operation, differences in serum levels of bone formation indexes, bone resorption indexes, inflammatory factors and pain mediators were not statistically significant between two groups of patients. After operation, serum bone formation indexes P Ⅰ CP, BGP, BALP and ALP levels in observation group were higher than those in control group; serum bone resorption indexes β-CTX and OPG levels were lower than those in control group; serum inflammatory factors IL-1β, IL-6, IL-8 and CRP levels were lower than those in control group; serum pain mediators SP, PGE2 and 5-HT levels were lower than those in control group. **Conclusion:** Minimally invasive mippo intramedullary nail internal fixation treatment of femoral shaft fractures can promote the bone formation, relatively inhibit bone resorption and cause less traumatic reaction.

1. Introduction

Femoral shaft fracture is a clinical severe fracture type that is mostly caused by violence, and requires rational internal fixation to promote fracture end healing and furthest restore limb function[1,2]. Current research shows that the probability of poor healing, extended healing time and so on are high in patients with femoral shaft fractures after routine plate internal fixation, and poor postoperative limb function can appear in some patients, so looking for more efficient and reasonable treatment is the focus of clinical research. mippo technology is a kind of minimally invasive fracture reduction plate internal fixation technology, which has the advantages such as protecting fracture end blood supply and promoting the soft tissue healing around the fracture, and is thus recommended by many scholars for clinical treatment of femoral shaft fractures[3,4]. In order to clarify the best way to treat femoral shaft fracture, the patients with femoral shaft fractures who accepted conventional plate internal fixation and minimal invasive mippo intramedullary nail internal fixation were selected in this study, and the differences in bone metabolism and wound response were specifically studied after two kinds of treatments.

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2. Information and methods

2.1 Case information

A total of 80 patients with femoral shaft fractures who were treated in our hospital between May 2011 and December 2016 were selected, and patients themselves signed informed consent. According to the random number table method, the enrolled patients were divided into two groups, each with 40 cases, and the inclusion criteria included: (1) the X-ray examination confirmed femoral shaft fractures; (2) without history of femoral shaft fracture; (3) not taking glucocorticoids and other drugs that might affect bone metabolism; (4) cooperating with the treatment and inspection all the time. Exclusion criteria: (1) with pathological fracture; (2) associated with systemic infectious diseases; (3) associated with severe heart, liver and kidney insufficiency, and unable to tolerate surgical trauma; (4) dropping out of treatment, and with clinical data missing. Control group included 18 men and 22 women that were 24-78 years old; observation group included 19 men and 21 women that were 26-75 years old. The gender and age distribution of the two groups were not statistically different (P>0.05).

2.2 Therapy

Control group of patients received open reduction and plate internal fixation treatment, which was as follows: after epidural anesthesia, patients were put in supine position, a longitudinal incision (about 15-25 cm long) was made according to the length of top and bottom fracture end and used to cut open the tissue structure, lateral femoral circumflex artery branch was ligatured, and the periosteum was cut open to expose femoral shaft fracture end. The fracture end reduction was done gently, kirschner wire was used for temporary fixation, and the steel plate was attached to the outside of the femur and fixed with screws. The incision was flushed, catheter was embedded for drainage and then the incision was sutured

Observation group of patients received MIPPO intramedullary nail internal fixation to treat femoral shaft fractures, specifically as follows: after epidural anesthesia, the affected-side thigh was padded, fracture end traction reduction was conducted, and measurement was conducted to make affected-side thigh length equal to that of the healthy-side. Anteroposterior and lateral X-ray film was satisfactory, arc shaping of steel plate was conducted according to the fracture condition, then an incision about 3-5 cm long was made in distal fracture end and lateral femur, and periosteal detacher was used to make subcutaneous tunnel (extra periosteal), cross throught the fracture end and reach the contralateral (tunnel length was approximately equal to the steel plate). The steel plate was inserted through the tunnel along the incision, and the X-ray fluoroscopy was performed to confirm that the plate and the facies ossea fit well and the fracture end alignment and positioning were satisfactory. The plate exposed in the incision was drilled and fixed with screws. Same way was used to make a 3-5 cm long incision in the far side of steel plate, and the contralateral plate was drilled and fixed. After fixation, the incision was flushed and the skin was sutured.

2.3 Observation indexes

2.3.1 Bone formation and bone resorption indexes

Before operation and 1 week after operation, 2-3mL of fasting cubital venous blood was extracted from two groups of patients, anti-coagulated and then centrifuged at low speed to take upper serum, and RIA kit (Roche company in the United States) instructions were followed to determine the levels of bone formation indexes C-terminal propeptide of procollagen type I (PICP), bone gla protein (BGP), bone alkaline phosphatase (BALP) and alkaline phosphatase (ALP) as well as bone resorption indexes β isomer of C-terminal telopeptide of type I collagen (β -CTX) and osteoprotegerin (OPG).

2.3.2 Wound response indexes

Before operation and 1 week after operation, serum was obtained from two groups of patients in the same way, and ELISA kit (Roche company in the United States) was used to determine the contents of inflammatory factors and pain mediators, including inflammatory factors interleukin-1 β (IL-1 β), interleukin-6 (IL-6), interleukin-8 (IL-8) and C-reactive protein (CRP) as well as pain mediators substance P (SP), prostaglandin E2 (PGE2) and 5-hydroxytryptamine (5-HT).

2.4 Statistical processing

Data in the study were recorded and calculated by professional statisticians (1-2), and statistical software was SPSS 21.0. Bone formation indexes, bone resorption indexes, inflammatory factors, pain mediators and other measurement data were in terms of mean ± standard deviation, and the comparison was by paired t test. Statistics P<0.05 was the standard of statistical significance in differences.

3. Results

3.1 Bone formation indexes

Before operation and 1 week after operation, comparison of serum bone formation indexes P Ⅰ CP (μg/L), BGP (μg/L), BALP (U/L) and ALP (U/L) levels between two groups of patients was as follows: before operation, serum P Ⅰ CP, BGP, BALP and ALP levels were not significantly different between two groups of patients (P>0.05); compared with those before operation, serum P Ⅰ CP, BGP, BALP and ALP levels in both groups increased significantly 1 week after operation; compared with those in control group, serum P Ⅰ CP, BGP, BALP and ALP levels in observation group increased significantly 1 week after operation (P<0.05), shown in Table 1.

Table 1.

Comparison of serum bone formation index levels between two groups of patients before and after operation.

Groups	n	Time	P Ⅰ CP	BGP	BALP	ALP
Observation group	40	Before operation	98.34±10.19	2.38±0.31	70.17±8.54	60.28±7.19
		After operation	152.48±18.92$^{*\#}$	4.57±0.53$^{*\#}$	87.18±9.63$^{*\#}$	79.55±8.64$^{*\#}$
Control group	40	Before operation	98.72±10.53	2.41±0.34	70.23±8.62	60.17±7.05
		After operation	123.46±14.85*	3.21±0.35*	75.66±8.39*	68.73±8.19*

Note: compared with same group before operation, $^{*}P$<0.05; compared with control group after operation, $^{\#}P$<0.05.

3.2 Bone resorption indexes

Before operation and 1 week after operation, comparison of serum bone resorption indexes β-CTX and OPG levels between two groups of patients was as follows: before operation, serum β-CTX and OPG levels were not significantly different between two groups of patients (P>0.05); compared with those before operation, serum β-CTX and OPG levels in both groups decreased significantly 1 week after operation; compared with those in control group, serum β-CTX and OPG levels in observation group decreased significantly 1 week after operation (P<0.05), shown in Table 2.

Table 2.

Comparison of serum bone resorption index levels between two groups of patients before and after operation (pg/mL).

Groups	n	Time	β-CTX	OPG
Observation group	40	Before operation	503.82±59.12	2 927.00±374.19
		After operation	205.76±28.51*#	1 743.28±200.95*#
Control group	40	Before operation	502.17±56.35	2 934.16±384.25
		After operation	374.28±41.66*	2 403.47±311.84*

Note: compared with same group before operation, *P<0.05; compared with control group after operation, #P<0.05.

3.3 Inflammatory factors

Before operation and 1 week after operation, comparison of serum inflammatory factors IL-1β (ng/mL), IL-6 (pg/mL), IL-8 (pg/mL) and CRP (mg/L) levels between two groups of patients was as follows: before operation, serum IL-1β, IL-6, IL-8 and CRP levels were not significantly different between two groups of patients (P>0.05); compared with those before operation, serum IL-1β, IL-6, IL-8 and CRP levels in both groups increased significantly 1 week after operation; compared with those in control group, serum IL-1β, IL-6, IL-8 and CRP levels in observation group decreased significantly 1 week after operation (P<0.05), shown in Table 3.

3.4 Pain mediators

Comparison of serum pain mediators SP (ng/L), PGE2 (μg/L) and 5-HT (μmol/L) levels between two groups of patients before and after operation was as follows: before operation, serum SP, PGE2 and 5-HT levels were not significantly different between two groups of patients (P>0.05); compared with those before operation, serum SP, PGE2 and 5-HT levels in both groups decreased significantly 1 week after operation; compared with those in control group, serum SP, PGE2 and 5-HT levels in observation group decreased significantly 1 week after operation (P<0.05), shown in Table 4.

4. Discussion

Femoral shaft fractures are caused by strong violence, they cause huge damage and easily leave behind limb dysfunction, and the surgical method needs to be chosen carefully[5,6]. Early femoral shaft fractures are mostly treated by fracture-end open reduction and intramedullary nail, but follow-up shows that some patients are with poor fracture end healing, and high incidence of postoperative complications. mippo is the result of the recent progress in the concept of biological fixation, this internal fixation combines inner support principle and minimally invasive supraperiosteal dissection technique, and compared with the traditional plate internal fixation method, it has the following advantages: (1) minimally invasive surgery can reduce the scope of intraoperative fracture end exposure and protect the fracture end blood supply; (2) it effectively combines fixed screw, steel plate and bone, and is with higher internal fixation strength and structural stability; (3) it has uniform distribution of stress, and not subjects to the tension band principle; (4) the elastic fixation allows small activity between the fractures and is conducive to the callus growth and the fracture healing[7,8]. Based on the above advantages of mippo technology, its applications are gradually popular in patients with fractures, but there is not much research about the efficacy of minimally invasive mippo intramedullary nail internal fixation for the treatment of femoral shaft fractures at present, the efficacy and trauma of conventional plate internal fixation and mippo treatment of femoral shaft fractures were compared in the study, and specifically elaborated in the following paragraphs.

Bone metabolism balance can directly affect the healing of fracture end, there will be compensatory bone formation increase and bone resorption inhibition in the body after internal fixation of fracture

Table 3.

Comparison of serum inflammatory factor levels between two groups of patients before and after operation.

Groups	n	Time	IL-1β	IL-6	IL-8	CRP
Observation group	40	Before operation	76.19±8.67	70.63±8.93	40.27±5.93	2.09±0.31
		After operation	89.73±10.27*#	84.36±9.18*#	56.28±8.63*#	4.27±0.54*#
Control group	40	Before operation	75.38±8.91	70.17±8.54	40.18±5.27	2.18±0.34
		After operation	124.38±17.32*	103.27±14.18*	83.26±9.16*	9.28±1.05*

Note: compared with same group before operation, *P<0.05; compared with control group after operation, #P<0.05.

Table 4.

Comparison of serum pain mediator levels between two groups of patients before and after operation.

Groups	n	Time	SP	PGE2	5-HT
Observation group	40	Before operation	30.65±5.43	40.76±5.08	1.12±0.17
		After operation	6.08±0.79*#	10.86±1.97*#	0.45±0.06*#
Control group	40	Before operation	30.48±5.19	40.38±5.19	1.09±0.15
		After operation	13.29±2.11*	25.71±3.48*	0.82±0.09*

Note: compared with same group before operation, *P<0.05; compared with control group after operation, #P<0.05.

end, the intensity of bone formation is positively correlated with the degree of fracture healing, and negatively correlated with healing time, and the degree of bone resorption is positively correlated with the incidence of poor fracture healing[9,10]. PICP, BGP, BALP and ALP are the factors closely associated with osteoblasts, PICP is the specific collagen in the bone, BGP is the noncollagen specifically synthesized by osteoblasts, BALP and ALP are the markers that reflect the activity of osteoblasts, and to detect their serum levels can reflect the activity of the osteogenetic process[11,12]. In the study, serum levels of above bone formation indexes were compared between the two groups of patients before and after operation, and it was found that serum PICP, BGP, BALP and ALP levels in both groups after operation were higher than those before operation, and serum levels of above indexes in observation group were higher after operation, indicating that minimally invasive mippo intramedullary nail internal fixation treatment can be more effective to stimulate the osteogenetic activity of fracture end and help to improve fracture healing quality. β-CTX and OPG are markers that are secreted by osteoclasts and their levels are consistent with the osteoclast activity in fracture end[13]. It was found in the study that serum β-CTX and OPG levels in both groups after operation were lower than those before operation, suggesting that postoperative fracture ends show compensatory osteoclast activity inhibition; serum β-CTX and OPG levels in observation group were lower than those in control group after operation. It shows that minimally invasive mippo intramedullary nail internal fixation therapy can effectively inhibit osteoblast activity, and further promote osteoblast/osteoclast balance to shift to osteoblast.

Surgical trauma is an important part that affects the final outcome of the patients with femoral shaft fractures, and huge surgical trauma can mostly affect the fracture end healing speed and even cause severe postoperative complications. Surgery is an important cause of postoperative inflammatory reaction, IL-1β, IL-6, IL-8 and CRP are the most common inflammatory factors associated with surgical trauma in clinical research, and they are secreted into the blood early after operation, and quickly and objectively reflect the wound size[14,15]. It was found in the study that serum IL-1β, IL-6, IL-8 and CRP levels in both groups after operation were higher than those before operation, and serum IL-1β, IL-6, IL-8 and CRP levels in observation group were lower than those in control group after operation, it indicates that the both kinds of operation modes can cause damage to patients, but minimally invasive mippo intramedullary nail internal fixation causes less damage. Pain is the main subjective feeling in patients after fracture, surgical operation can also cause postoperative pain, and severe pain is one of the important factors that accelerate the secretion of inflammatory factors, and also a reliable sign of poor fracture healing in patients[16,17]. It was found in the study that serum pain mediators SP, PGE2 and 5-HT levels in both groups after operation were lower than those in control group, suggesting that effective internal fixation can reduce the acute pain from fracture dislocation; serum SP, PGE2 and 5-HT levels in observation group were lower than those in control group after operation, which further confirms the minimal invasiveness of the minimally invasive mippo intramedullary nail internal fixation treatment.

Minimally invasive mippo intramedullary nail internal fixation treatment of femoral shaft fractures can effectively promote the healing of fracture end and optimize osteoblast/osteoclast balance, also causes less postoperative inflammatory and painful injury, has the advantages such as efficiency and minimal invasiveness, and is worthy of popularization and application in clinical practice in the future.

References

[1] Pires RE, Santana EO Jr, Labronici PJ, Almeida Filho IA. Subtrochanteric and distal femur fractures in a patient with femoral shaft fracture malunion and knee disarticulation: a rare and challenging case report. *Ann Med Health Sci Res* 2016; **6**(5): 328-331.

[2] Jarmuzek T, Mendel T, Schenk P, Hofmann G, Ullrich BW. The complicated course of a femoral shaft fracture in childhood. *Unfallchirurg* 2017; **120**(5): 432-436.

[3] Wang Jin-feng, Yuan Jin-feng, Lin Yong-liang, Du Hong-wei, Cong Qiang, Xia Chuan-long, et al. Comparison of efficacy between anterior approach minimally invasive percutaneous plate osteosynthesis and intramedullary nailing internal fixation in treatment for humeral shaft fractures. *Chin J Bone Joint Injury* 2016; **31**(1): 51-54.

[4] Yu Hua-wei, Jia Xu-feng, Zhang Ge. Clinical efficacy and effects on postoperative quality of life of mippo in treatment of adult tibial shaft fracture. *Hebei Med* 2017; **23**(1): 69-72.

[5] Yang SD, Ning SH, Zhang LH, Zhang YZ, Ding WY, Yang DL. The effect of lower limb rehabilitation gymnastics on postoperative rehabilitation in elderly patients with femoral shaft fracture: A retrospective case-control study. *Med (Baltimore)* 2016; **95**(33): e4548.

[6] Fu Bei-gang, Wang Xiu-hui, Cai Pan, Xia Sheng-li. Comparative study on curative effect of closed reduction and open reduction with interlocking intramedullary nail in treatment of femoral shaft fractures. *Chin J Bone Joint Injury* 2015; **30**(2): 151-154.

[7] Asif N, Ahmad S, Qureshi OA, Jilani LZ, Hamesh T, Jameel T. Unstable intertrochanteric fracture fixation-is proximal femoral locked compression plate better than dynamic hip screw. *J Clin Diagn Res* 2016; **10**(1): RC09-RC13.

[8] Chen Tong-lin, Bai Hong-tao, Chen Xu-hui, Jia Wei-dou. Efficacy observation of MIPPO in complex femoral shaft fractures. *Chin J Coal Industry Med* 2015; **18**(1): 67-70.

[9] Yagishita K. Calcium and bone metabolism across women's life stages. Stress fracture in female athletes. *Clin Calcium* 2017; **27**(5): 699-706.

[10] Haffner-Luntzer M, Liedert A, Ignatius A. Mechanobiology and bone metabolism: Clinical relevance for fracture treatment. *Unfallchirurg* 2015; **118**(12): 1000-1006.

[11] Huang Jian-li. Influence of ossotide injection for the bone metabolism and inflammatory state of patients with limb fractures. *J Hainan Med Univ* 2014; **20**(9): 1234-1237.

[12] Xu Weifeng, Ye Jian, Wu Lianguo. Effect of Qianggu Yin on serum bone metabolism indexes and bone density after total hip ar-throplasty in patients with osteoporotic femoral neck fractures. *J Tradit Chin Orthopedics Traumatol* 2015; **27**(2): 12-15.

[13] Forslund JM, Archdeacon MT. The pathobiology of diabetes mellitus in bone metabolism, fracture healing, and complications. *Am J Orthop (Belle Mead NJ)* 2015; **44**(10): 453-457.

[14] Mao Jin-hua, Tu Gang-cheng, Qiu Jing, Sun Ping. Effects of taohong siwu decoction on inflammatory factors and hemorheology in patients with femoral shaft fracture after surgery. *J Nanjing Univ Tradit Chin Med* 2016; **32**(5): 419-422.

[15] Wang L, Guo TZ, Wei T, Li WW, Shi X, Clark JD, et al. Bisphosphonates inhibit pain, bone loss, and inflammation in a rat tibia fracture model of complex regional pain syndrome. *Anesth Analg* 2016; **123**(4): 1033-1045.

[16] Chen Ran, Liu Yuan-hui, Yan Yan, Luo De-xing. Effect of hydromorphone hydrochloride combined with ropivacaine for orthopedic postopera-tive PCEA on serum pain mediators and stress response. *J Hainan Med Univ* 2016; **22**(21): 2613-2616.

[17] Shangguan Wenji, Li Zhanchun, Cheng Guangqi, Tang Lumin, Li He. Effect of osteopractic total flavone on pain mediators and pain response in postmenopausal osteoporosis rats. *J Liaoning Univ Tradit Chin Med* 2017; **19**(3): 10-13.