Journal of Hainan Medical University

http://www.hnykdxxb.com

Effect of different surgical methods on traumatic response degree and osteoblast−osteoclast balance in patients with distal tibial fracture

Yun−Qiang Fan✉

Department of Orthopedics, Shehong County Hospital of TCM of Sichuan Province, Shehong 629200, China

ARTICLE INFO

Article history:
Received 7 Jul 2016
Received in revised form 17 Jul 2016
Accepted 12 Jul 2016
Available online 24 Jul 2016

Keywords:
Distal tibial fracture
Delayed surgery
Stress response
Osteoblast
Osteoclast

ABSTRACT

Objective: To study the effect of different surgical methods on trauma response degree and osteoblast-osteoclast balance in patients with distal tibial fracture. **Methods:** 58 cases of patients with distal tibial fracture who received open reduction and internal fixation in Orthopedics Department of our hospital from May 2013 to October 2015 were selected as research subjects and divided into delayed group (n = 29) and routine group (n = 29) according to different timing of surgery. Delayed group received open reduction and internal fixation 7–15 d after trauma and routine group received open reduction and internal fixation within 24 h after trauma. Levels of serum stress response indicators and osteoblast-osteoclast markers were compared between two groups. **Results:** On the day after operation, serum adrenocorticotropic hormone, cortisol, renin, angiotensin II, epinephrine and norepinephrine levels of delayed group were significantly lower than those of control group ($P<0.05$); on the 7th day after operation, serum osteocalcin, procollagen type I carboxyl-terminal peptide and bone alkaline phosphatase of delayed group were significantly higher than those of control group ($P<0.05$) while cross-linked carboxyl-terminal telopeptide of type I collagen and tartrate-resistant acid phosphatase isoform 5b levels were significantly lower than those of control group ($P<0.05$). **Conclusions:** Delayed open reduction and internal fixation treatment of distal tibial fracture can reduce the trauma caused by surgical procedures, increase osteoblast viability and inhibit osteoclast viability, which are conducive to fracture healing.

1. Introduction

Middle and distal tibial fracture is more complex clinical type of fracture that is mostly caused by external violent injuries and can involve weight-bearing articular surface and metaphysis at the same time and be accompanied by more severe soft tissue injuries. The blood supply of the middle and distal tibia bone mainly comes from nourishing blood vessels, and serious soft tissue injuries can damage bone blood supply, which increases the risk of nonunion after internal fixation and brings larger difficulty to the clinical treatment[1,2]. Larger local soft tissue injuries and poor blood supply conditions are the main factors influencing the middle and distal tibial fracture healing, and emergency open reduction and internal fixation would further damage soft tissue and is not conducive to fracture healing. Fractional delayed open reduction and internal fixation is a new concept of fracture treatment put forward in recent years[3,4]. Studies have reported that it can achieve better clinical effect by improving local soft tissue conditions through a period of traction and external fixation and then conducting delayed open reduction and internal fixation[5,6]. In the following study, the clinical value of fractional delayed open reduction and internal fixation for distal tibial fracture was analyzed from the aspects of trauma response degree and osteoblast-osteoclast balance.

2. Materials and methods

2.1. Research subjects

✉Corresponding author: Yun-Qiang Fan, Department of Orthopedics, Shehong County Hospital of TCM, Middle Section of Meifeng Road, Shehong 629200, China.
Tel: 13419370973
Fund project: Research Projects of Sichuan Provincial Health Department (No.: 130819).

58 cases of patients with distal tibial fracture who received open reduction and internal fixation in Orthopedics Department of our hospital from May 2013 to October 2015 were selected for research subjects, and all patients were with clear history of trauma, were diagnosed with distal tibial fracture and Ruedi-Allgower II type or III type by imageological examination after admission, and met the surgical indications of open reduction and internal fixation. Patients complicated with fracture of other parts, heart, liver and kidney dysfunction and past history of fracture and osteoporosis were excluded. According to different timing of surgery, 58 cases of patients were randomly divided into delayed group and routine group, 29 cases in each group. Delayed group included 18 male cases and 11 female cases who were (40±6) years old; routine group included 17 male cases and 12 female cases who were (42±7) years old. Comparison of general information between two groups showed no significant differences ($P>0.05$).

2.2. Surgical methods

Both groups of patients received conventional symptomatic treatment after admission and received the routine use of antibiotics 1 d before surgery, and operation method of routine group is as follows: beginning open reduction and internal fixation surgery within 24 h after injury, and finishing fibula reconstruction, tibia facet reconstruction, manual reduction, bone graft filling in remaining cavity and internal fixation with anatomical plate in turn. Operation method of delayed group is as follows: calcaneal traction and plaster external fixation were conducted at first after admission, open reduction surgery was conducted after soft tissue swelling subsided and local condition recovery was better, surgery time was usually 7–15 d after injury, and the operation procedures were the same as those of routine group. Patients received antibiotics for anti-infection as well as plaster slab for fixation.

2.3. Methods of trauma degree evaluation

On the day of end of surgery, 6–8 mL of peripheral blood was collected from both patients and centrifuged to get serum, and enzyme-linked immunosorbent kit was used to determine adrenocorticotropic hormone, cortisol, renin, angiotensin II, epinephrine and norepinephrine levels.

2.4. Methods of osteoblast-osteoclast balance evaluation

On the 7th day after the operation, 6–8 mL of peripheral blood was collected from both patients and centrifuged to get serum, and enzyme-linked immunosorbent kit was used to determine osteocalcin (BGP), procollagen type I carboxyl-terminal peptide (PICP), bone alkaline phosphatase (BALP), cross-linked carboxyl-terminal telopeptide of type I collagen (CTX) and tartrate-resistant acid phosphatase isoform 5b levels (TRACP5b).

2.5. Statistical analysis

SPSS20.0 software was used to input and analyze data, measurement data ($\bar{x}\pm s$) analyzed by t test and differences were considered to be statistically significant at the level of $P<0.05$.

3. Results

3.1. Healing of two groups after internal fixation

Postoperative imaging complete healing time of delayed group was (125.4±16.9) d, time of full weight-bearing ambulation was (168.7±22.4) d, and score of ankle function was (91.34±11.45) points; postoperative imaging complete healing time of routine group was (162.1±19.3) d, time of full weight-bearing ambulation was (212.4±29.7) d, and score of ankle function was (82.51±10.22) points.

3.2. Serum stress response indicators

Analysis of stress response indicators serum adrenocorticotropic hormone, cortisol, renin, angiotensin II, epinephrine and norepinephrine levels of two groups on the day after operation is as follows: serum adrenocorticotropic hormone, cortisol, renin, angiotensin II, epinephrine and norepinephrine levels of delayed group were significantly lower than those of control group, and differences between two groups were statistically significant

Table 1

Postoperative serum stress response indicators of two groups (n = 29,$\bar{x}\pm s$).

Group	ACTH (pg/mL)	Cortisol (nmol/L)	Renin (pg/mL)	Ang II(pg/mL)	Norepinephrine (ng/mL)	Epinephrine (ng/mL)
Delayed group	14.91±3.52	231.3±34.6	2.61±0.42	26.52±3.62	104.5±15.6	76.9±10.3
Control group	22.35±4.48	562.5±75.4	5.58±0.81	44.27±7.85	184.7±27.2	193.1±25.6
t	7.813	13.944	11.251	9.385	8.681	14.417
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

ACTH: adrenocorticotropic hormone; Ang II: angiotensin II.

(P<0.05) (Table 1).

3.3. Osteoblast markers

Analysis of serum osteoblast markers BGP, carboxy terminal peptide of type I procollagen and BALP levels of two groups 1 week after operation is as follows: serum BGP level, procollagen type I carboxyl-terminal peptide level and BALP level of delayed group were significantly higher than those of control group, and differences between two groups were statistically significant (P<0.05) (Table 2).

Table 2

Postoperative serum osteoblast marker levels of two groups (n = 29, $\bar{x}$±s).

Group	BGP (μg/L)	PICP (μg/L)	BALP (U/L)
Delayed group	5.23±0.72	164.23±23.68	384.51±54.65
Control group	4.05±0.66	125.26±20.14	221.57±31.69
t	6.182	6.812	7.449
P	<0.05	<0.05	<0.05

BGP: osteocalcin; PICP: procollagen type I carboxyl-terminal peptide; BALP: bone alkaline phosphatase.

3.4. Osteoclast markers

Analysis of serum osteoclast markers CTX and TRACP5b of two groups 1 week after operation was as follows: serum CTX level and tartrate-resistant acid phosphatase isoform 5b level of delayed group were significantly lower than those of control group, and differences between two groups were statistically significant (P<0.05) (Table 3).

Table 3

Postoperative serum osteoclast marker levels of two groups (n = 29, $\bar{x}$±s).

Group	CTX (ng/mL)	TRACP5b (U/L)
Delayed group	3.05±0.57	6.46±0.82
Control group	4.89±0.78	10.35±1.51
t	7.182	8.685
P	<0.05	<0.05

CTX: Cross-linked carboxyl-terminal telopeptide of type I collagen; TRACP5b: tartrate-resistant acid phosphatase isoform 5b.

4. Discussion

Study has shown that fractional delayed surgical treatment of distal tibial fracture is helpful to the recovery of local soft tissue swelling, local soft tissue condition is better in the process of internal fixation surgery, postoperative limb swelling time is shorter and the limb function recovery is more ideal[7]. In this study, the value of different surgical methods for treatment of distal tibial fracture was further analyzed from the aspect of surgical trauma caused by surgery. Operation procedure trauma to local soft tissue is the intense stressor, on the one hand, it will activate the HPA axis and cause the enhancement of adrenal cortex function and the massive release of adrenocorticotropic hormone and cortisol[8,9], and it will also increase the secretion of renin and angiotensin II[10]; on the other hand, it can activate the sympathetic nervous system and cause the enhancement of adrenal medulla function and massive release of epinephrine and norepinephrine[11]. In the study, analysis of serum stress molecules levels of two groups on the day after operation confirmed that serum adrenocorticotropic hormone, cortisol, renin, angiotensin II, epinephrine and norepinephrine levels of delayed group were significantly lower than those of control group. Thus it indicated that fractional delayed surgical treatment of distal tibial fracture caused less extent of trauma.

Fracture healing process depends on the balance between osteoblast and osteoclast function, and under the regulation of complex neurohumoral factors in the body, the function of osteoblasts is in the dominant position while the function of osteoclasts is in inhibited state, which is conducive to the formation of bone tissue and the healing of fracture[12]. Osteoblast-osteoclast balance in bone fracture is closely related to the conditions of local soft tissue, and poor soft tissue condition of distal tibial fractures and surgical procedure damage to soft tissue will further aggravate the poor condition of local soft tissue and is not conducive to the regulation of osteoblast and osteoclast balance[13]. As mentioned earlier, the biggest value of fractional delayed surgery is to improve local soft tissue condition and create local environment conducive to fracture healing. But current studies about fractional delayed surgical treatment of distal tibial fracture are mainly focused on fracture healing and functional recovery, and the balance of osteoblast and osteoclast still needs to be studied.

BGP, PICP and BALP are commonly used markers reflecting osteogenetic process[14,15]. BGP is the colloid protein synthesized by osteoblasts, and can promote osteogenesis and reflect osteoblast function; PICP is a kind of specific fiber collagen derived from the pyrolysis process of collagen fiber, and its content is related to the activity of osteoblasts; BALP is synthesized and secreted by osteoblasts in ossified parts, and can promote calcium phosphate deposition in bone collagen matrix. CTX and TRACP5b are commonly used markers reflecting bone-resorbing process[16,17]. CTX is produced in bone-resorbing process, TRACP5b can promote bone resorption, and both are closely related to the osteoclast viability. In the research, analysis of postoperative osteoblast-osteoclast markers confirmed that serum BGP, PICP and BALP of delayed group were significantly higher than those of control group (P<0.05) while CTX and TRACP5b levels were significantly lower than those of control group (P<0.05). This meant that fractional delayed surgical treatment of distal tibial fracture surgery was with higher postopeartive osteoblast viability and lower osteoclast viability, which were conducive to fracture healing.

To sum up, delayed open reduction and internal fixation treatment of distal tibial fracture can reduce the trauma caused by surgical

procedures, increase osteoblast viability and inhibit osteoclast viability, and is conducive to fracture healing.

References

[1] Lomax A, Singh A, N Jane M, et al. Complications and early results after operative fixation of 68 pilon fractures of the distal tibia. *Scott Med J* 2015; **60**(2): 79-84.

[2] Danoff JR, Saifi C, Goodspeed DC, et al. Outcome of 28 open pilon fractures with injury severity-based fixation. *Eur J Orthop Surg Traumatol* 2015; **25**(3): 569-575.

[3] Tang X, Liu L, Tu CQ, et al. Comparison of early and delayed open reduction and internal fixation for treating closed tibial pilon fractures. *Foot Ankle Int* 2014; **35**(7): 657-664.

[4] He X, Hu Y, Ye P, et al. The operative treatment of complex pilon fractures: a strategy of soft tissue control. *Indian J Orthop* 2013; **47**(5): 487-492.

[5] Liporace FA, Mehta S, Rhorer AS, et al. Staged treatment and associated complications of pilon fractures. *Instr Course Lect* 2012; **61**: 53-70.

[6] Ballal A, Rai HR, Shetty SM, et al. A prospective study on functional outcome of internal fixation of tibial pilon fractures with locking plate using minimally invasive plate osteosynthesis technique. *J Clin Diagn Res* 2016; **10**(1): RC01-4.

[7] Zhou W, Ren D, Wei XL. Comparative study of fractional delay operation and early incision internal fixation operation in treatment of high energy Pilon fracture. *China J Modern Med* 2014; **24**(21): 73-76.

[8] Filardi V. The healing stages of an intramedullary implanted tibia: a stress strain comparative analysis of the calcification process. *J Orthop* 2015; **12**(Suppl 1): 51-61.

[9] Hall RJ, Watne LO, Robertson I, et al. Cerebrospinal fluid cortisol and cytokines in delirium after hip fracture. *Psychoneuroendocrinology* 2015; **61**: 49.

[10] Aoki M, Kawahata H, Sotobayashi D, et al. Effect of angiotensin II receptor blocker, olmesartan, on turnover of bone metabolism in bedridden elderly hypertensive women with disuse syndrome. *Geriatr Gerontol Int* 2015; **15**(8): 1064-1072.

[11] Lanteigne A, Sheu YH, Stürmer T, et al. Serotonin-norepinephrine reuptake inhibitor and selective serotonin reuptake inhibitor use and risk of fractures: a new-user cohort study among US adults aged 50 years and older. *CNS Drugs* 2015; **29**(3): 245-252.

[12] Vidovic D, Matejcic A, Ivica M, et al. Minimally-invasive plate osteosynthesis in distal tibial fractures: results and complications. *Injury* 2015; **46**(Suppl 6): 96-99.

[13] Rosenblat JD, Gregory JM, Carvalho AF, et al. Depression and disturbed bone metabolism: a narrative review of the epidemiological findings and postulated mechanisms. *Curr Mol Med* 2016; **16**(2): 165-178.

[14] Matuszewska A, Szechinski J. Evaluation of selected bone metabolism markers in rheumatoid arthritis patients. *Adv Clin Exp Med* 2013; **22**(2): 193-202.

[15] Terpos E, Christoulas D, Kastritis E, et al. The combination of lenalidomide and dexamethasone reduces bone resorption in responding patients with relapsed/refractory multiple myeloma but has no effect on bone formation: final results on 205 patients of the Greek myeloma study group. *Am J Hematol* 2014; **89**(1): 34-40.

[16] Yamamoto T, Taketsuna M, Guo X, et al. The safety and effectiveness profile of daily teriparatide in a prospective observational study in Japanese patients with osteoporosis at high risk for fracture: interim report. *J Bone Miner Metab* 2014; **32**(6): 699-708.

[17] Mohamed Y, Haifa H, Datel O, et al. The role of biochemical markers of bone turnover in the diagnosis of osteoporosis and predicting fracture risk. *Tunis Med* 2014; **92**(5): 304-310.