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Effect of mid−frequency pulse therapy combined with external fixation on bone metabolism, inflammatory response and oxidative stress in patients with osteoporotic distal radial fractures

Bao−Ning Luo✉, Guo−Xin Wang

Orthopedics Department, the Second People's Hospital of Liangshan Yi Autonomous Prefecture Sichuan Province, Liangshan Prefecture, Sichuan Province, 615000

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ABSTRACT

Objective: To study the effect of mid-frequency pulse therapy combined with external fixation on bone metabolism, inflammatory response and oxidative stress in patients with osteoporotic distal radial fractures. **Methods:** A total of 72 patients with osteoporotic distal radial fractures who were treated in the hospital between September 2015 and January 2017 were collected and divided into control group (n=36) and observation group (n=36) according to the random number table method. Control group received routine external fixation, and observation group received mid-frequency pulse therapy combined with external fixation. The differences in serum levels of bone metabolism indexes, inflammatory factors and oxidative stress indexes were compared between two groups of patients before and after treatment. **Results:** Before treatment, differences in serum levels of bone metabolism indexes, inflammatory factors and oxidative stress indexes were not statistically significant between the two groups. After 1 month of treatment, serum BGP, TAC and SOD levels of both groups of patients were higher than those before treatment while β-CTX, AKP, TRAP, CRP, IL-1β, IL-6 and MDA levels were lower than those before treatment, and serum BGP, TAC and SOD levels of observation group were higher than those of control group while β-CTX, AKP, TRAP, CRP, IL-1β, IL-6 and MDA levels were lower than those of control group. **Conclusion:** Mid-frequency pulse therapy combined with external fixation can promote fracture healing and reduce postoperative inflammatory response and oxidative stress response in patients with osteoporotic distal radial fracture.

1. Introduction

Elderly people, especially elderly women, have decreased estrogen secretion after menopause, which can affect bone formation/bone resorption balance, and result in osteoporosis[1,2]. Distal radial fracture is common clinical type of fracture, external fixation can prompt the fracture end healing and the limb function recovery, but the fracture healing of patients with osteoporotic distal radial fracture is more difficult than that of other population, and some cases show that patients with external fixation alone are with the risk of poor fracture end healing[3,4]. Mid-frequency pulse therapy, also known as the non-invasive pulse therapy, applies pulse current with frequency less than 1 000 Hz to treat diseases and has been successfully applied in treatment of patients with chronic hepatitis, and some scholars recommend it as a supplementary means for the treatment of patients with fracture[5,6]. In the research, mid-frequency pulse therapy combined with external fixation was used for the treatment of patients with osteoporotic distal radial fracture, and its application value was explored from three aspects of bone metabolism, inflammation and oxidative stress, now reported as follows.

✉Corresponding author: Bao-Ning Luo, Orthopedics Department, the Second People's Hospital of Liangshan Yi Autonomous Prefecture Sichuan Province, Liangshan Prefecture, Sichuan Province, 615000.
Tel: 15283436337
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2. Information and methods

2.1 Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosed with osteoporosis by bone density test; (2) with distal radial fracture confirmed by the X-ray film; (3) with osteoporotic fracture for the first time; (4) cooperating with the treatment and inspection throughout the whole process, and without any stopover.

Exclusion criteria: (1) with pathological fracture; (2) combined with systemic infectious diseases; (3) with long-term application of glucocorticoids; (4) combined with pheochromocytoma, hyperthyroidism and other diseases that caused abnormal basal metabolism.

2.2 Case information

A total of 72 patients with osteoporotic distal radial fractures who were treated in the hospital between September 2015 and January 2017 were selected, and the patients themselves/their families signed informed consent. According to the random number table method, the patients were divided into control group and observation group, 36 cases in each group. Control group included 16 men and 20 women that were 63-79 years old; observation group included 15 men and 21 women that were 60-78 years old. The differences in the gender and age distribution were not significant between the two groups, the follow-up data were comparable, and the hospital ethics committee approved the study.

2.3 Therapy

Control group received routine external fixation, which was as follows: the distance from 10cm above elbow to metacarpophalangeal joint was used to fold the plaster into 12 layers. The patients were in horizontal position, the elbow joint was bent to about 90 , those with fracture displacement to the dorsal put the palm downward, and those with fracture displacement to the palm put the palm upward. The affected carpometacarpal part and elbow were held and pulled hard continuously until the fracture end was separated, the affected carpal bone was bend downward to 60 and the ulnar deviation was conducted at full tilt. The joint position after reduction was kept, the gypsum was soaked and placed on the dorsal side of the wrist joint, the lower end reached the metacarpophalangeal joint, the upper end reached the above elbow joint, and the X-ray was conducted to confirm the reduction was good.

Observation group, based on external fixation, received mid-frequency pulse therapy, specifically as follows: external fixation was the same as that of control group, mid-frequency pulse electrotherapeutic apparatus was used for treatment from the 2 d after reduction, the electrodes were placed on the distal and proximal ends of fractures, current intensity is better when patients can tolerate it, and a single treatment lasted for 30 min, 2 times/d, for 30 d in a row.

2.4 Observation indexes

Before treatment and after 1 month of treatment, proper amount of cubital venous blood (3-5 mL) was extracted from two groups of patients at the same point in time, anti-coagulated and centrifuged at low speed to get the upper serum and store it in the cryogenic environment. RIA method was used to determine serum levels of bone metabolism indexes bone gla protein (BGP), β isomer of C-terminal telopeptide of type I collagen (β-CTX), bone alkaline phosphatase (AKP), tartrate-resistant acid phosphatase (TRAP), enzyme-linked immunosorbent assay (ELISA) was used to determine serum levels of inflammatory cytokines C-reactive protein (CRP), interleukin-1 β (IL-1 β) and interleukin 6 (IL-6), and ELISA was used to determine serum levels of oxidative stress indicators malondialdehyde (MDA), total antioxidant capacity (TAC) and superoxide dismutase (SOD).

2.5 Statistical processing

Statistical software was SPSS 24.0. Bone metabolism indexes, inflammatory factors and oxidative stress indicators were in terms of mean ± standard deviation and compared by t test. Statistics $P<0.05$ was the standard of statistical significance in differences.

3. Results

3.1 Serum BGP, β-CTX, AKP and TRAP levels

Before treatment and after 1 month of treatment, comparison of serum bone metabolism indexes BGP (μg/L), β-CTX (ng/mL), AKP (pg/mL) and TRAP (pg/mL) levels was as follows: before treatment, serum BGP, β-CTX, AKP and TRAP levels were not statistically different between the two groups; after 1 month of treatment, serum BGP levels of both groups of patients were significantly higher than those before treatment while β-CTX, AKP and TRAP levels were significantly lower than those before treatment, and serum BGP level of observation group was significantly higher than that of control group while β-CTX, AKP and TRAP levels were significantly lower than those of control group.

Table 1.

Comparison of serum BGP, β-CTX, AKP and TRAP.

Groups	*n*	BGP		β-CTX		AKP		TRAP	
		Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment
Control group	36	2.08±0.27	2.75±0.31*	0.39±0.05	0.28±0.03*	64.83±7.19	50.17±5.83*	5.93±0.74	3.52±0.39*
Observation group	36	2.05±0.28	4.11±0.48*	0.38±0.04	0.21±0.03*	64.37±7.05	32.48±4.52*	5.91±0.72	2.16±0.25*
t		0.173	9.282	0.215	6.213	0.198	14.382	0.263	7.287
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: comparison of corresponding indexes within group before and after treatment, *$P<0.05$.

Table 2.

Comparison of serum CRP, IL-1 β and IL-6 levels.

Groups	*n*	CRP		IL-1 β		IL-6	
		Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment
Control group	36	9.72±1.53	3.27±0.42*	12.47±1.63	4.28±0.53*	7.83±0.92	2.04±0.35*
Observation group	36	9.68±1.62	1.19±0.16*	12.51±1.59	1.17±0.19*	7.81±0.94	0.76±0.09*
t		0.183	8.215	0.264	9.093	0.169	8.273
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: comparison of corresponding indexes within group before and after treatment, *$P<0.05$.

Table 3.

Comparison of serum MDA, TAC and SOD levels.

Groups	*n*	MDA		TAC		SOD	
		Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment	Before treatment	After 1 month of treatment
Control group	36	7.38±0.82	3.11±0.36*	9.26±0.98	11.53±1.74*	71.24±8.63	83.19±9.45*
Observation group	36	7.34±0.86	1.75±0.28*	9.23±0.97	14.09±1.93*	71.35±8.47	92.64±10.38*
t		0.173	8.982	0.206	10.612	0.154	15.482
P		>0.05	<0.05	>0.05	<0.05	>0.05	<0.05

Note: comparison of corresponding indexes within group before and after treatment, *$P<0.05$.

3.2 Serum CRP, IL-1 β and IL-6 levels

Before treatment and after 1 month of treatment, comparison of serum inflammatory factors CRP (mg/L), IL-1 β (pg/mL) and IL-6 (pg/mL) levels was as follows: before treatment, serum CRP, IL-1 β and IL-6 levels were not statistically different between the two groups; after 1 month of treatment, serum CRP, IL-1 β and IL-6 levels of both groups of patients were significantly lower than those before treatment, and serum CRP, IL-1 β and IL-6 levels of observation group were significantly lower than those of control group.

3.3 Serum MDA, TAC and SOD contents

Before treatment and after 1 month of treatment, comparison of serum oxidative stress indexes MDA (μmol/L), TAC (kU/L) and SOD (nU/mL) levels was as follows: before treatment, serum MDA, TAC and SOD levels were not statistically different between the two groups; after 1 month of treatment, serum MDA levels of both groups of patients were significantly lower than those before treatment while TAC and SOD levels were significantly higher than those before treatment, and serum MDA level of observation group was significantly lower than that of control group while TAC and SOD levels were significantly higher than those of control group.

4. Discussion

The incidence of osteoporosis is high in the elderly, severe osteoporosis can lead to fracture, and the distal radial fracture is the more common type in clinic. For the distal radial fracture not complicated by comminuted fracture, plaster external fixation after manual reduction can effectively make the fracture end reach reduction standard, but some patients still have delayed fracture end healing and even nonunion after external fixation alone[7,8]. The fracture end healing of patients with osteoporotic distal radial fracture is more difficult than that of other people, so it is feasible to use adjuvant therapy at the same time of external fixation. Mid-frequency pulse therapy is a quite common clinical physical therapy, it adopts pulse current with frequency of 1-100 kHz to stimulate the lesions and prompt local functional restoration, it is believed to be a feasible adjuvant therapy for fractures, and its specific mechanisms may be as follows: (1) the skeletal muscle contraction and the opening up of physiologically closed capillaries after electrical stimulation increase the blood circulation around the bone and cartilage tissue, and accelerate callus formation; (2) pulse electricity stimulates muscle soft tissue, fixes muscle contraction frequency, and enhances calcium and phosphorus deposition of bone tissue[9-11]. In the research, mid-frequency pulse therapy was added in clinical treatment of patients with osteoporotic distal radial fracture, and its effect and possible mechanisms were explored from the bone metabolism, inflammation and oxidative stress.

The basic pathological change of osteoporosis is osteoblast/osteoclast balance shifting to osteoclast, the osteoblast activity decreases, osteoclast activity increases, bone mineralization and bone deposition reduce, and eventually the bone mineral density decreases[12,13]. After fracture in patients with osteoporosis, the healing is more difficult than that of patients with non-osteoporosis, and mid-frequency pulse therapy stimulates fracture healing by increasing the blood supply around the fracture end, stimulating bone calcium phosphate deposit and other forms[14,15]. Bone metabolism index levels can objectively reflect the fracture healing process, and it was found in the study that compared with those before treatment, osteoblast index BGP levels of both groups of patients increased while osteoclast indexes β-CTX, AKP and TRAP levels decreased, indicating that the patients are in fracture healing process after both therapies; further compared with those of control group, serum BGP level of observation group was higher while β-CTX, AKP and TRAP levels were lower after 1 month of treatment, indicating that mid-frequency pulse therapy combined with external fixation can more effectively promote osteoblast activity and also inhibit osteoclast activity appropriately to make the overall fracture process evolve to bone deposition, and objectively confirming the feasibility and effectiveness of the mid-frequency pulse therapy.

Fracture itself is the process of severe trauma, it can cause further damage to the surrounding soft tissues, nerves, blood vessels and so on when it occurs, it can directly cause defensive inflammatory

reaction of the body, and a variety of inflammatory cytokines increase in secretion and are released into the bloodstream[16,17]. With treatment process and fracture healing, the systemic inflammatory response of the body is gradually weakened, but it is found that the serum levels of a variety of pro-inflammatory factors are high in patients with poor healing of fracture, indicating that the degree of inflammatory response is closely linked with the fracture healing process[18,19]. In this study, the serum levels of inflammatory cytokines were compared between the two groups of patients, and it was found that compared with those before treatment, serum inflammatory cytokines CRP, IL-1 β and IL-6 levels of both groups of patients decreased after 1 month of treatment, showing that both treatments can reduce the body's inflammatory response degree; further compared with those of control group, serum CRP, IL-1 β and IL-6 levels of observation group were lower after 1 month of treatment, indicating that mid-frequency pulse therapy can induce the alleviation of inflammatory response around the fracture end and in the whole body, which may be one of the internal mechanisms for it to promote the fracture healing and optimize the bone metabolism. Similar to the mechanism of inflammation, the patients suffer from both psychological and physiological effects after acute fracture, and systemic oxidative stress reaction occurs[20,21]. The release of large amount of oxygen free radicals and the appearance of oxidative metabolites in the fracture end are not conducive to the revascularization and bone deposition. Mid-frequency pulse therapy helps open the capillaries around the fracture end and stimulate calcium phosphate deposit, it is still unknown at present whether the process is associated with regulating oxidative stress, so serum contents of oxidative stress indexes were further compared between the two groups of patients before and after treatment, and it was found that compared with those before treatment, serum MDA levels of both groups of patients decreased while TAC and SOD levels increased after 1 month of treatment; further compared with those of control group, serum MDA level of observation group was lower while TAC and SOD levels were higher after 1 month of treatment, proving that the achievement of the curative effect of mid-frequency pulse therapy is closely related to its effect on inhibiting the systemic oxidative stress response.

Mid-frequency pulse therapy combined with external fixation can effectively optimize the bone metabolism and promote the fracture healing in patients with osteoporotic distal radial fracture, and the specific mechanisms are closely related to its effect on inhibiting systemic inflammatory, oxidative stress reaction and so on.

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