Efecto del calcitriol combinado con calcio D sobre el metabolismo óseo y el efecto terapéutico en la osteoporosis posmenopáusica

Effect of Calcitriol Combined with Calcic D on Bone Metabolism and Therapeutic Effect in Postmenopausal Osteoporosis

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Resumen
En este trabajo, se estudió el efecto del calcitriol combinado con calq-d sobre el metabolismo óseo y el efecto terapéutico en la osteoporosis posmenopáusica. El proceso de recambio óseo o metabolismo óseo es en realidad el proceso de osteoclastos que absorben hueso y osteoblastos para la síntesis de hueso nuevo. Los índices metabólicos relacionados con la formación de hueso incluyen ALP, osteocalcina, etc., y el calcio / creatinina (Ca / Cr) urinario, la hidroxiproline / creatinina urinaria, etc. relacionados con la absorción ósea. El grupo de control se trató con calq-d solo, y el grupo de estudio se trató con calq-d combinado con calcitriol para observar y comparar el nivel de metabolismo óseo, el grado de dolor y la calidad de vida antes y después del tratamiento. Los resultados mostraron que antes del tratamiento, no hubo diferencias significativas en los índices de metabolismo óseo entre los grupos. Después del tratamiento con diferentes métodos, los índices del grupo de estudio fueron superiores a los del grupo de control, con significación estadística (P <0.05); después del tratamiento, la puntuación VAS del grupo de estudio fue menor que la del grupo control; después del tratamiento, las puntuaciones de los índices de calidad de vida del grupo de estudio fueron más altas que las del grupo de control, con significación estadística (P <0.05). La combinación de D cálcico y calcitriol puede mejorar la calidad de vida de las mujeres posmenopáusicas.

Palabras clave: Calcic D; Calcitriol; Mujeres posmenopáusicas; Osteoporosis

Abstract
In this paper, the effect of calcitriol combined with calq-d on bone metabolism and therapeutic effect in postmenopausal osteoporosis was studied. The process of bone turnover or bone metabolism is actually the process of osteoclasts absorbing bone and osteoblasts for new bone synthesis. The metabolic indexes related to bone formation include ALP, osteocalcin, etc., and the urinary calcium / creatinine (Ca / Cr), urinary hydroxyproline / creatinine, etc. related to bone absorption. The control group was treated with calq-d alone, and the study group was treated with calq-d combined with calcitriol to observe and compare the bone metabolism level, pain degree and quality of life before and after treatment. The results showed that before treatment, there was no significant difference in bone metabolism indexes among the groups. After treatment with different methods, the indexes of the study group were superior to those of the control group, with statistical significance (P < 0.05); after treatment, the VAS score of the study group was lower than that of the control group; after treatment, the scores of the indexes of the quality of life of the study group were higher than that of the control group, with statistical significance (P < 0.05). The combination of calcic D cálcico and calcitriol can improve the quality of life of postmenopausal women.

Key words: Calcic D; Calcitriol; Postmenopausal women; Osteoporosis

1. Introduction

Osteoporosis (OP) is a kind of systemic osteopathy, which can reduce bone density and quality, destroy bone microstructure, increase bone brittleness, and then fracture. In recent years, with the aggravation of aging, the number of people suffering from osteoporosis is increasing, and the number of people suffering from osteoporosis in the world is up to more than 200 million. In general, it can be divided into primary and secondary[1]. Among them, the elderly men and postmenopausal women are the high incidence population of osteoporosis, especially postmenopausal women. In the first 10 years after menopause, bone loss is serious, especially in the 3-5 years after menopause, and osteoporosis is easy to occur. Bone strength index is an important index to evaluate the bone condition from the perspective of biomechanics[2-3]. It can comprehensively measure the biomechanical characteristics of bone, which is more significant than using bone
mass or bone density alone to predict the bone condition, and has more advantages in predicting the risk of osteoporotic fracture[4]. However, studies have shown that in addition to bone mass and bone density, bone strength is also closely related to body composition, which is affected by gender, race and body composition distribution[5]. At the same time, there are also studies at home and abroad found that after menopause, the body composition changes such as the increase of bone loss, the decrease of muscle mass and the increase of fat tissue quality will occur in women, which will inevitably affect the bone strength and the relationship between bone strength and body composition[6-7]. Postmenopausal osteoporosis (PMO) is characterized by hunchback, brittle fracture, decreased respiratory function and lumbar pain, which seriously harms women’s physical and mental health and reduces their quality of life[8]. Therefore, if the clinical diagnosis of postmenopausal osteoporosis, it is recommended to treat the disease as early as possible to avoid serious consequences. In this study, we investigated the effect of calcitriol combined with calcin-d on the treatment of postmenopausal osteoporosis and bone metabolism.

2. Materials and methods

2.1 General information

From March 2017 to September 2018, 100 postmenopausal osteoporosis patients were selected and divided into observation group and control group according to the order of admission, each group has 50 cases. All patients met the diagnostic criteria of osteoporosis issued by the World Health Organization in 2004. There was no significant difference in age, menopause time, bone pain and other general data between the two groups (P > 0.05), which was comparable, as shown in Table 1. Inclusion criteria: (1)Patients over 45 years old; (2)Postmenopausal time more than 1 year, spontaneous low back pain or weight-bearing pain; (3) BMD in at least one part of the upper femur or lumbar L2-4 was lower than 25 SD of BMD peak in young people of the same sex; (4) The anatomical structure of the lumbar spine was more suitable for BMD measurement with dual energy X-ray, no obvious scoliosis of the spine, or more than one lumbar spine (5) The patients belong to natural menopause. Exclusion criteria: (1) Patients who do not meet the diagnostic criteria of osteoporosis; (2) Patients with high and low blood calcium; (3) Patients with osteogenesis, hyperthyroidism and chronic gastrointestinal diseases; (4) Patients with alcoholism, liver and kidney functional damage and other diseases that may affect bone metabolism; (5) Patients who have not taken estrogen replacement therapy in the past year; (6) Patients with mental disease or dementia; (7) Patients with cardiovascular and cerebrovascular diseases and hematopoietic system diseases Patients. All patients participated in the study treatment knowingly and voluntarily.

Table 1. Comparison of general data between two groups of patients

<table>
<thead>
<tr>
<th>Normal information</th>
<th>Observation group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Age / year</td>
<td>64.29 ± 5.44</td>
<td>64.38 ± 5.37</td>
</tr>
<tr>
<td>Menopause time / year</td>
<td>13.75 ± 6.44</td>
<td>15.11 ± 6.31</td>
</tr>
<tr>
<td>BMI / ( kg / m²)</td>
<td>22.63 ± 2.65</td>
<td>23.37 ± 2.59</td>
</tr>
<tr>
<td>L2 ~ 4BMD ( g / cm²)</td>
<td>0.74 ± 0.06</td>
<td>0.73 ± 0.05</td>
</tr>
<tr>
<td>Bone pain</td>
<td>47</td>
<td>45</td>
</tr>
<tr>
<td>Lumbar spine BMD / ( g/cm²)</td>
<td>0.92 ± 0.11</td>
<td>0.93 ± 0.15</td>
</tr>
<tr>
<td>Femoral neck BMD / ( g/cm²)</td>
<td>0.68 ± 0.10</td>
<td>0.69 ± 0.12</td>
</tr>
</tbody>
</table>

2.2 Method

The observation group was treated with calcium Erqi D combined with calcitriol, and the patients took calcium d 1 tablets (developed and produced by Wyeth pharmaceutical company of the United States; production batch number: h10900013; calcium content of each tablet is 600mg). 1 tablet / D, and 0.25 μ g of calcitriol (produced and developed by Huihai pharmaceutical industry of Guangdong Province; production batch number: h20080225; specification: 0.25 μ g), once a day. The patients in the control group were treated with a simple d-tablet. The two groups of patients were treated for 6 months. The therapeutic effects of the two groups were compared before and after treatment, and the changes of ALP, Ca and P were observed.

2.3 Observation indicators

(1) The BMD metabolism of the two groups before and after treatment was compared, including three indexes, namely, blood calcium (CA), β - CTX and type I procollagen amino terminal pro peptide (PINP); (2) The pain degree of the two groups before and after treatment was evaluated by visual analog scale / score (VAS), 0-10 points, the higher the final score, the more obvious the pain; (3) According to the life of the World Health Organization Quality brief table (WHOQOL-BREF) was used to evaluate the quality of life of two groups of patients before and after treatment, including four indicators of physiology, psychology, society and environment. The full score of each indicator was 100. The higher the score, the higher the quality of life. (4)
The patient's bone pain was divided into 4 grades, 0 points for no pain; 1 point for mild pain: the patient felt mild pain, and the pain occasionally occurred; 2 points for moderate pain: the patient felt light and heavy pain, which had no serious impact on work and life; 2 points for severe pain: the patient's pain continued, which brought a burden on normal life, 3 points. According to the patient's pain after treatment, the curative effect was judged as follows: significant effect: the patient's pain improved, and the score decreased by more than 2 / 3; effective: the patient's pain decreased, and the score decreased by 1 / 3 - 2 / 3; ineffective: the patient's pain did not improve significantly, and the score decreased by less than 1 / 3. ALP, Ca and P were detected before and after treatment, and the changes of ALP, Ca and P were analyzed.

2.4 Statistical analysis
SPSS17.0 was selected for data statistics. The data was expressed by mean ± standard deviation. The comparison of measurement data was t-test. The comparison of count data was χ² test. The comparison of grade data was conducted by rank sum test (Wilcoxon two sample comparison method). When p < 0.05, the difference was statistically significant.

3. Results

3.1 Bone metabolism
The results showed that the levels of t-pin, -CTX and Ca2 + in the study group and the control group decreased, and the difference between the study group and the control group was statistically significant (P < 0.05). See Table 2.

Table 2. Bone metabolism before and after treatment (x ± S)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Time</th>
<th>T−PINP</th>
<th>β−CTX</th>
<th>Ca²⁺</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>Before treatment</td>
<td>63.94±8.91</td>
<td>513.93±108.47</td>
<td>2.54±0.14</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>19.25±7.24</td>
<td>114.58±32.49</td>
<td>2.21±0.32</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>62.37±9.01</td>
<td>514.87±119.34</td>
<td>2.65±0.45</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>28.35±5.67</td>
<td>201.47±58.25</td>
<td>2.41±0.29</td>
</tr>
</tbody>
</table>

3.2 Pain in the two groups
There was no significant difference in VAS score between the two groups before treatment (P > 0.05). After treatment in different ways, the VAS score of the study group was significantly lower than that of the control group. There was significant difference between the two groups (P < 0.05). See Table 3.

Table 3. Pain in two groups (x ± S, min)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Before treatment</th>
<th>After treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>6.89±1.82</td>
<td>3.48±1.13</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>7.01±1.56</td>
<td>5.13±1.09</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>0.598</td>
<td>5.624</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>0.413</td>
<td>0.000</td>
</tr>
</tbody>
</table>

3.3 Quality of life
Before treatment, there was no significant difference between the two groups (P > 0.05). After treatment, the scores of each index in the study group were higher than those in the control group, the difference was statistically significant (P < 0.05). See Table 4.

Table 4. Observe and compare the quality of life of patients (x ± S, min)

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of cases</th>
<th>Time</th>
<th>Physiological aspects</th>
<th>Psychological aspect</th>
<th>Social aspect</th>
<th>Environmental aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>Before treatment</td>
<td>45.92±4.12</td>
<td>56.28±5.13</td>
<td>60.14±5.78</td>
<td>49.52±4.51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>90.14±6.72</td>
<td>87.45±4.89</td>
<td>85.62±4.51</td>
<td>82.35±5.61</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>Before treatment</td>
<td>44.46±7.11</td>
<td>55.62±4.13</td>
<td>59.09±7.83</td>
<td>50.62±7.83</td>
</tr>
<tr>
<td></td>
<td></td>
<td>After treatment</td>
<td>79.32±4.92</td>
<td>76.63±5.69</td>
<td>72.35±6.49</td>
<td>71.97±6.79</td>
</tr>
</tbody>
</table>

3.4 Bone metabolism index and curative effect of postmenopausal osteoporosis
ALP, Ca and P in the serum of the two groups were significantly higher than those before treatment (P < 0.05), and ALP, Ca and P in the observation group were significantly higher than those in the control group (P < 0.05). See Table 5. In the observation group, 27 cases were effective, 20 cases were effective, 3 cases were ineffective, the total effective rate was 94%; in the control group, 15 cases were effective, 26 cases were
4. Discussion

4.1 Analysis of experimental results

OP is a systemic bone disease, and its greatest risk lies in the increase of bone fragility, which is easy to lead to fracture. Prevention and reduction of bone loss, further improvement of bone mass and reduction of fracture risk are the main objectives of clinical treatment of Op. There are many drugs to prevent op. according to the mechanism of action of drugs, they can be divided into drugs to inhibit bone absorption and drugs to promote bone formation[9-10].

The process of bone turnover or bone metabolism is actually the process of osteoclasts absorbing bone and osteoblasts for new bone synthesis. The metabolic indexes related to bone formation include ALP, osteocalcin, etc., and the urinary calcium / creatinine (CA / Cr), urinary hydroxyproline / creatinine, etc. related to bone absorption. In recent years, some studies showed that ALP decreased sharply and Ca / Cr increased in bone formation index of postmenopausal patients[11]. The results showed that ALP of PMO patients treated with calcitriol and Ca increased from (61.22 ± 5.97) U / L to (75.72 ± 6.23) U / L, which was significantly higher than that treated with Ca alone (70.25 ± 4.11) U / L. With the increase of patients' age, 1,25 (OH) 2D3 in serum will decrease, the activity and quantity of vitamin D receptor (VDR) in intestines will also decrease, calcium absorption will decrease, bone absorption will increase, etc., calcitriol will induce the activity and quantity of VDR receptor to increase, and it does not need the hydroxylation of kidney and liver, so it has quick effect and high efficiency[12-13]. In addition, calcitriol supplementation for postmenopausal women can increase intestinal calcium absorption, inhibit bone absorption, enhance patients' muscle strength, regulate the central nervous system, increase body coordination, reduce the incidence of falls, and reduce the risk of fractures. When calcium enters the patient's body, it mostly accumulates in the bone tissue in the form of phosphate, which is the basis of ensuring the hardness of bone tissue. However, calcitriol can promote the synthesis of intestinal calcium transporter, increase the calcium transport ability of intestinal epithelial cells, and promote the absorption of intestinal calcium[14]. The results showed that the CA of the patients increased to (2.67 ± 0.11) mmol / L after treatment, which was significantly higher than that of the patients treated with calcium alone (2.32 ± 0.08) mmol / L. In addition, calcitriol can stimulate the synthesis of bone matrix protein and collagen, which is conducive to the deposition of blood calcium in bone calcium and the promotion of bone mineralization. Calcium and vitamin supplementation in postmenopausal women can prevent osteoporosis and improve bone metabolism[15-16]. This study showed that P in the observation group increased from (1.05 ± 0.06) mmol / L before treatment to (1.32 ± 0.11) mmol / L, which was significantly higher than that in the calcium D group (1.26 ± 0.09) mmol / L.

4.2 Before and after menopause, bone strength, bone condition and body composition characteristics of women

The function of estrogen secretion in postmenopausal women’s ovaries decreased, and the body lacked the inhibition of estrogen on osteoclasts and the stimulation of osteoblasts. At the same time, the sensitivity of osteoclasts to parathyroid hormone is increased, the proliferation of osteoclasts is promoted, osteoclasts are inhibited, bone resorption is increased, the synthesis of bone cells and glia is less, bone loss is accelerated and bone mass is reduced[17]. The results show that the bone strength of postmenopausal women is significantly lower than that of premenopausal women. Some studies have also shown that estrogen can reverse the Notch signaling pathway activity of bone marrow mesenchymal stem cells in postmenopausal osteoporosis patients, and promote the differentiation of bone marrow mesenchymal stem cells into osteoblasts through Notch signaling pathway[18-19].

Research shows that postmenopausal women are more likely to have osteoporosis; the bone mass of postmenopausal women decreases at a rate of 2% - 3% per year, and the incidence of osteoporosis in women who have been menopausal for more than 5 years is significantly increased. The research shows that the incidence of osteoporosis in the general population, premenopausal and postmenopausal women is 6.4%, 2.9% and 9.9%, and the incidence of postmenopausal osteoporosis is significantly increased, which is consistent with the results of fan, Ma Weihong, Li Yan and other studies, which shows that menopause is an important factor in
the occurrence of osteoporosis in women, and further explains the osteoprotective effect of estrogen in postmenopausal women. Weakening is an important cause of postmenopausal osteoporosis.[20].

Studies at home and abroad show that the changes of body composition in postmenopausal women are characterized by the decrease of bone mass, muscle mass and the increase of fat mass, which is consistent with the above conclusions[21-22]. The results showed that the body composition of muscle tissue in postmenopausal women was lower than that in premenopausal women, while the body composition of fat tissue was higher than that in premenopausal women. It has been proved that estrogen can reduce lipolysis by inhibiting the activity of lipoprotein lipase[23]. It can be seen that the body composition characteristics of postmenopausal women are closely related to the decrease of estrogen secretion. In addition, the changes of life state (such as physical activity, eating habits, etc.) before and after menopause are also the important reasons for the differences of body composition before and after menopause.

4.3 Self care ability and health behavior education strategy of postmenopausal women with osteoporosis

Postmenopausal female osteoporosis is a common degenerative orthopedic disease. Although targeted treatment can improve the clinical symptoms to a certain extent, its treatment effect is closely related to the disease awareness, healthy behavior and self-care ability of the patients. Most patients have limited awareness of the disease, and the treatment effect is often poor. Health education is an important part of nursing work, and its application effect in postmenopausal women osteoporosis has been paid more and more attention. But in the past, traditional health education is usually based on one-way knowledge transmission, with a single form, less targeted content, poor interaction, and poor education effect. In addition to the routine oral education, we should also use the combination of graphics and text, PPT, video, telephone, wechat and door-to-door visit to guide health, effectively avoid the boring and blindness of traditional education, strengthen patients' understanding of disease, and improve the effect of health education.

4.3.1 Establish diversified health education team

Set up a diversified health education team, which includes the chief orthopedic physician, head nurse, responsible nurse and family members, with clear division of labor and each performing its own duties. The attending physician is responsible for the diagnosis and treatment of the patient's diseases and the follow-up work; the responsible nurse is responsible for collecting the patient's health information, carrying out health information education and follow-up care for the patient; the head nurse is responsible for coordinating the work of all members; the family members are responsible for cooperating with the responsible nurse's work, supervising the patient's compliance behavior, etc. A 3-month health education plan was developed by comprehensively assessing the health status and disease awareness of patients.

4.3.2 Form of health education

In addition to the routine oral and written health education during hospitalization, on the second day after the patient's admission, the attending physician and the specialist nurse will introduce the pathogenesis, hazards, treatment methods and preventive nursing measures of osteoporosis to the patient in detail through the combination of graphics and text, PPT and video. After the patient leaves the hospital, the health education will be extended to the family, making full use of wechat platform Follow up education was carried out for the patients, and they were instructed to conduct online consultation through wechat in case of daily doubt. After discharge, they were followed up by telephone once every two weeks, and after three months, the responsible nurses were arranged to visit the patients on site to assess the health behaviors of the patients at home.

4.3.3 Contents of health education

(1) Diet guidance: tell the patients the importance of regular diet for disease recovery, instruct the patients to eat high calcium food more than 3 times a week, and add more green vegetables; for the patients who like to drink coffee or strong tea, timely inform the harm of strong tea to bone metabolism, let the patients replace it with light flower tea; for the patients who smoke and drink, let them quit smoking and alcohol, so as not to affect calcium synthesis. (2) Exercise guidance: according to the rehabilitation situation of the patients, make personalized exercise plan, guide the patients to take a walk, Taijiquan and other aerobic exercises as the main, exercise more than 3 times a week, about half an hour each time. (3) Medication guidance: tell the patients in detail about the use mode, dosage and possible adverse reactions of conventional calcium supplement drugs, and the importance of regular medication. For patients with poor memory, set the medication alarm clock to avoid forgetting to take the medicine. (4) Sunlight: instruct the patients to receive more than 3 times of sunlight every week for more than 15 minutes to promote the absorption of calcium.

5. Conclusion
To sum up, the treatment of postmenopausal osteoporosis with calcitriol combined with calcin-d can effectively improve the bone metabolism index and improve the treatment effect, which is worthy of clinical application.

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References