Comparison of Efficacy of Teriparatide (Parathyroid Hormone 1-34) Alone and in Combination with Zoledronic Acid for Osteoporosis in Postmenopausal Women

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ABSTRACT

The purpose of this study was to compare the efficacy of teriparatide (parathyroid hormone 1-34) alone and in combination with zoledronic acid (ZA) for the treatment of osteoporosis in postmenopausal women. Ninety-six patients were randomly equally divided into Groups A (n=48) and B (n=48). Group A was given parathyroid hormone 1-34 alone. Group B was treated with parathyroid hormone 1-34 plus ZA. Visual analogue scale (VAS) score, bone mineral density(BMD), serum osteopontin (OPN), and C-terminal cross-linking telopeptide of type I collagen (S-CTX) etc. were compared. After 6 months of treatment, VAS score, serum OPN and S-CTX levels in Group B were significantly lower than those in Group A ($p=0.001$, $p<0.001$ and $p<0.001$, respectively); and BMD values of lumbar vertebrae L_{2-4}, femoral neck and total hip bone in Group B were higher than those of Group A ($p=0.002$, $p=0.028$ and $p<0.001$, respectively). In conclusion, parathyroid hormone 1-34 plus ZA is more effective than parathyroid hormone 1-34 alone in treating post postmenopausal osteoporosis.

Key Words: *Teriparatide (parathyroid hormone 1-34, Zoledronic acid (ZA), Postmenopausal, Osteoporosis, Bone mineral density (BMD).*

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Osteoporosis is a systemic disease with reduced bone strength and fracture.[1] Postmenopausal women are susceptible to osteoporosis due to decreased estrogen, accelerated bone loss and other factors. There is currently no definite cure for this progressive disease of osteoporosis in postmenopausal women. Traditional clinical treatment of osteoporosis in postmenopausal women mainly includes administration calcium, vitamin D, etc. Though curative effect of estrogen replacement therapy is good, its long-term use may induce adverse reactions such as breast pain, vaginal bleeding, and even the risk of endometrial cancer.[2] One study has revealed that teriparatide (parathyroid hormone 1-34) can not only inhibit bone apoptosis, but also stimulate the activity and proliferation of osteoblasts through the cyclic adenosine monophosphate system, so that bone growth is regulated through bone formation and resorption.[3] Reid *et al*. showed that zoledronic acid (ZA) can inhibit loss of bone mass and increase the bone mineral density (BMD).[4]

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However, there are few reports on the comparative study of parathyroid hormone 1-34 used alone and in combination with ZA in the treatment of osteoporosis in postmenopausal women.

The purpose of this study was to compare efficacy of parathyroid hormone 1-34 used alone and in combination with ZA for osteoporosis in postmenopausal women.

After approved by the Hospital's Ethics Committee, the experimental study was carried out in Changzhou Traditional Chinese Medicine Hospital, Nanjing University of Chinese Medicine, China, from January 2018 to March 2019. Ninety-six postmenopausal women with osteoporosis were selected as research subjects. Inclusion criteria were that patients diagnosed as osteoporosis, patients with natural menopause >1 year, no fractures in radiographs of the thoracolumbar spine, pelvis, hip joints and other joints, with locomotor activity; and postmenopausal women. Exclusion criteria were that patients with secondary and idiopathic osteoporosis; patients with multiple myeloma; patients who had used drugs affecting bone metabolism within one year; patients with a history of long-term use of glucocorticoids; patients with malignant tumors, nutritional metabolic diseases, trauma, rheumatoid arthritis or other autoimmune diseases; patients with thyroid or parathyroid dysfunction, etc.; and patients who withdrew from the trial.

Table I: Comparison of related indices.

Indices	Time	Group A (n=48)	Group B (n=48)	p-value
VAS	Before treatment	6.53±0.68	6.45±0.69	0.551
	After 6 months of treatment	4.06±0.45	3.78±0.34	0.001
BMD values of lumbar vertebrae L_{2-4} (g/cm^2)	Before treatment	0.773±0.045	0.767±0.053	0.576
	After 6 months of treatment	0.794±0.036	0.815±0.029	0.002
BMD values of femoral neck (g/cm^2)	Before treatment	0.654±0.047	0.648±0.040	0.480
	After 6 months of treatment	0.672±0.042	0.694±0.052	0.028
BMD values of total hip bone (g/cm^2)	Before treatment	0.594±0.011	0.592±0.023	0.687
	After 6 months of treatment	0.637±0.004	0.709±0.044	<0.001
Serum OPN (μg/*L*)	Before treatment	58.74±1.72	59.28±1.80	0.137
	After 6 months of treatment	44.82±1.45	40.27±1.02	<0.001
Serum S-CTX (ng/mL)	Before treatment	0.494±0.028	0.496±0.037	0.784
	After 6 months of treatment	0.414±0.017	0.384±0.011	<0.001

Ninety-six patients were randomly divided into Group A and Group B, with 48 cases in each group.

Both groups were given conventional treatment, *i.e.,* oral administration of calcium carbonate (1 time per day, each 600 mg) and vitamin D (1 time per day, each 125 IU) for 6 months. Patients in Group A were given teriparatide (parathyroid hormone 1-34), 1 time per day, each 20 μg, for six months. Patients in Group B were treated with parathyroid hormone 1-34 in combination with ZA, namely they were treated with parathyroid hormone 1-34 with reference to Group A, and ZA injection was diluted with 100 mL of saline and injected intravenously, one time per day, each 5 mg, for six months.

Visual analogue scale (VAS) was used to observe the degree of osteoporosis pain before and after six months of treatment. The scale is composed of 0 (no pain at all) to 10 (the worst imaginable pain). BMD of lumbar vertebrae (L_{2-4}), femoral neck, and total hip bone was detected by DEXA. Serum osteopontin (OPN) and C-terminal cross-linking telopeptide of type I collagen (S-CTX) were detected by ELISA. During treatment, both groups were observed and recorded for the presence of fresh fractures and adverse reactions.

Data were analysed using SPSS 25.0 statistical software. Qualitative data were represented by n (%), and analysed by Chi-square test. Qualitative data were expressed as mean ± standard deviation, and analysed by independent sample t test. The $p < 0.05$ was considered as statistically significant.

Among the 96 patients, all were females, aged 52-75 years, with the mean of 64.31±2.56 years. Their menopause duration was 1-21 years, with mean value of 9.56±1.22 years.

Before treatment, VAS score, BMD values of lumbar vertebrae L_{2-4}, femoral neck and total hip bone, serum OPN and S-CTX levels were no difference (p=0.551, 0.576, 0.480, 0.687, 0.137 and 0.784, respectively, Table I). After six months of treatment, VAS score, serum OPN and S-CTX levels in Group B were lower than those in Group A (p=0.001, p<0.001 and p <0.001, respectively); and BMD values of lumbar vertebrae L_{2-4}, femoral neck and total hip bone in Group B were higher than those of Group A (p=0.002, p=0.028 and p<0.001, respectively, Table I).

During treatment, 2 cases (4.17%) of osteoporotic fracture occurred in Group A and 1 case (2.08%) occurred in Group B. The frequency of fracture between two groups was not stalishcally significant (p=0.557). The frequency of adverse reactions in Group A was 6.25% (3 cases), with one case (2.08%) each of headache, dizziness and bone and joint pain. The incidence of adverse reactions in Group B was 4.17% (2 cases), with one case (2.08%) each of dizziness and bone and joint pain. The frequency of adverse reactions between two groups was not significantly difference (p=0.646).

This study results revealed that compared with Group A, the treatment of Group B could increase the BMD, as well as the patient's VAS score more effectively. OPN is a secreted glycosylated phosphoprotein and closely related to osteoporosis.[5] S-CTX is an important biochemical indicator reflecting bone resorption.[6] This study found that after treatment, serum OPN and S-CTX levels were lower in Group B than those in Group A. It suggested that there was inhibition of OPN expression and thereby the bone resorption process was a possible mechanism for parathyroid hormone 1-34 used in combination with ZA to improve osteoporosis in postmenopausal women.

In conclusion, parathyroid hormone 1-34 combined with ZA is more effective than parathyroid hormone 1-34 alone for osteoporosis in postmenopausal women.

Limitations of this study were the small sample size and short treatment and follow-up time. Increased sample size as well as extended treatment time and follow-up time will provide more guiding significance for clinical application.

CONFLICT OF INTEREST:

Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

KW: Conception or design of the work, analysis and interpretation of data for the work and drafting the work.
YQ: Analysis and interpretation of data for the work.

YG: Revising it critically for important intellectual content.
YM: Revising it critically for important intellectual content and final approval of the version to be published.

REFERENCES

1. Lecanda F, Warlow PM, Halstead LR, Steinberg TH, Civitelli R. Impaired intramembranous bone formation in connexin43 null mice. *Bone* 1998; **23**:S149-653. doi: 10.1083/jcb.151.4.931.
2. Higuchi T, Tanaka K, Mizunuma H. Estrogen replacement therapy for osteoporosis in post-menopausal women. *Clin Calcium* 2003; **13(11)**: 1450-6.
3. Ahlström M, Lamberg-Allardt C. Rapid protein kinase A-mediated activation of cyclic AMP-phospho-diesterase by parathyroid hormone in UMR-106 osteoblast-like cells. *J Bone Miner Res* 1997; **12(2):**172-8. doi: 10.1359/ jbmr.1997.12.2.172.
4. Reid DM, Devogelaer JP, Saag K, Roux C, Lau CS, Reginster JY, *et al*. Zoledronic acid and risedronate in the prevention and treatment of glucocorticoid-induced osteoporosis (HORIZON): A multicentre, double-blind, double-dummy, randomised controlled trial. *Lancet* 2009; **373(9671)**:1253-63. doi: 10.1016/S0140-6736(09)60250-6.
5. Fodor D, Bondor C, Albu A, Simon SP, Craciun A, Muntean L. The value of osteopontin in the assessment of bone mineral density status in postmenopausal women. *J Investig Med* 2013; **61(1)**:15-21. doi: 10.2310/JIM.0b013e3182761264.
6. Hindi SM, Vittinghoff E, Schafer AL, Silverman S, Bauer DC. Commercial laboratory reproducibility of serum ctx in clinical practice. *JBMR Plus* 2019; **3(10)**:10225. doi: 10.1002/jbm4.10225.