J. Phys. Ther. Sci. 28: 1791–1794, 2016

The Journal of Physical Therapy Science

Original Article

Effect of aerobic exercise and raloxifene combination therapy on senile osteoporosis

Chengjin Zhao[1, 2], Haibing Hou[2], Yutao Chen[2], Kai Lv[3]*

[1] *School of Medicine, Xi'an Jiaotong University, China*
[2] *Department of Orthopedic Surgery, Yan'an University Affiliated Hospital, China*
[3] *Yan'an Traditional Chinese Hospital of Shanxi Province: No.72 South Street, Yan'an 716000, Shanxi, China*

Abstract. [Purpose] This study assessed the effects of combined application of raloxifene and aerobic exercise on senile osteoporosis. [Subjects and Methods] A total of 70 elderly patients with osteoporosis, who treated at our hospital between April 2013 and August 2014, were divided into equal-sized observation and control groups. The control group was administered raloxifene, whereas the observation group received raloxifene treatment plus aerobic exercise. [Results] Outpatient outcomes were considered dependent variables. After treatment, the two groups differed significantly in terms of lumbar spine (L2–L4) and proximal femoral bone mineral density. The urine pyridine/creatinine ratio decreased significantly and serum calcitonin level increased significantly in the observation group. These differences were statistically significant. [Conclusion] Raloxifene combined with aerobic exercise therapy significantly improves bone density and promotes bone formation in patients with senile osteoporosis.
Key words: Raloxifene, Aerobic exercise, Elderly

(This article was submitted Jan. 5, 2016, and was accepted Mar. 12, 2016)

INTRODUCTION

Osteoporosis is a common metabolic disease in the elderly and is closely associated with patient age. Its main signs are overall bone tissue density loss and structural fiber changes. Recent studies have shown that an age-related decrease in intestinal calcium absorption is closely related to senile osteoporosis and bone loss[1]. A lack of exercise among the elderly is also an important factor in promoting osteoporosis[2]. Here we report on the beneficial effects of a combination of aerobic exercise and raloxifene therapy for patients with senile osteoporosis.

SUBJECTS AND METHODS

This study included 70 elderly patients with osteoporosis treated at our hospital between April 2013 and August 2014. Patients with renal disease, liver disease, and secondary osteoporosis; those who had not visited a doctor in 3 months; and those taking drugs known to affect bone metabolism were excluded. Patients were divided into observation and control groups according to the treatment received (n=35 for each group). The control group included 24 female and 11 male patients, with a mean age of 64.7 ± 3.2 years (range, 51–76 years). The control group included 12 female and 23 male patients, with a mean age of 65.3 ± 4.1 years (range, 50–78 years). The two groups did not differ significantly with regard to sex or age.

Both patient groups would normally be prescribed a chewable D2 calcium hydrogen phosphate tablet (Guangxi Wuzhou Pharmaceutical Group Co., Ltd.; approval H45021454, 2010-09-20) once per day. The control group patients were also prescribed 60 mg raloxifene hydrochloride (Spanish Eli Lilly Nederland B.V.; registration card number H20120499, 2012-11-29) once per day. Patients in the observation group received the drug plus aerobic exercise. Patients were offered choices

*Corresponding author. Kai Lv (E-mail: ruancailian@126.com)

among tai chi, walking, jogging, running, and sports. The exercise intensity was advised to be based on patient tolerance. With increasing patient fitness, the workout was gradually increased to a duration of approximately 30 minutes, distance of approximately 3 km, or tai chi duration of approximately 30 minutes[3].

All patients were involved in the study for 6 months. Data were collected before and after treatment. Data included: 1) bone mineral density measurements, including the lumbar spine (L2–L4 intervertebral) and proximal femur; 2) serum calcitonin levels measured using commercial bone gla protein (BGP) kits (Metra, USA) based on an enzyme-linked immunosorbent assay (ELISA) method; and 3) urine pyridine/creatinine ratios (U-Pyd/Cr), with urine pyridine and Cr measured using ELISA Pyd and a biochemical method, respectively (Metra, USA).

In this study, the data were collected and processed by personnel of a specialized data processing center to ensure authenticity and appropriate scientific technique[4]. Preliminary data were entered into Excel (2003 version; Microsoft Inc., Seattle, WA, USA) for logic check and analysis. IBM SPSS Statistics for Windows, version 22.0 (Armonk, NY, USA) was used to analyze bone mineral density, resorption, and formation data using Student's t-test; values of $p<0.05$ were considered statistically significant[5].

RESULTS

Patients in both groups showed varying degrees of improved bone mineral density after treatment (Table 1 and Fig. 1).

U-Pyd/Cr was significantly decreased and serum calcitonin level was significantly increased in the observation group (Table 2).

Table 1. Comparison of pre- and post-treatment bone density changes between the observation and control groups (n; g/m^2)

Group	Number of cases	L2–L4		Proximal femur	
		Before treatment	After treatment	Before treatment	After treatment
Observation	35	0.80 ± 0.09	0.92 ± 0.11*	0.61 ± 0.09	0.66 ± 0.10*
Control	35	0.78 ± 0.08	0.83 ± 0.10	0.60 ± 0.08	0.61 ± 0.09

*Differences were statistically significant ($p<0.05$).

Table 2. Comparison of the pre- versus post-treatment U-Pyd/Cr ratio and BGP level in the observation and control groups (n; nm/mm; ng/ml)

Group	n	U-Pyd/Cr		BGP	
		Before treatment	After treatment	Before treatment	After treatment
Observation	35	38.5 ± 3.9	23.1 ± 2.7*	1.8 ± 0.3	5.7 ± 0.4*
Control	35	37.5 ± 3.1	36.9 ± 3.1	1.8 ± 0.3	4.9 ± 0.4

U-Pyd/Cr: urine pyridine/creatinine ratios; BGP: bone gla protein.
*Differences were statistically significant ($p<0.01$).

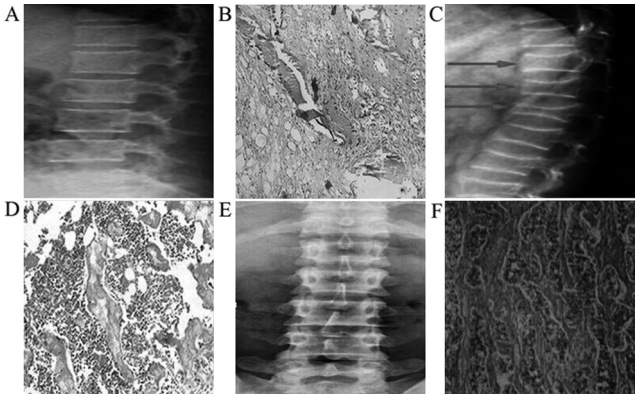

Fig. 1. (A) Normal lumbar X-ray film. (B) Hematoxylin and eosin (HE) staining of a sample of the normal lumbar spine (300 × 300); (C) Lumbar spine X-ray slice representative of the observation group (arrow, osteoporosis); (D) HE staining of a representative observation group sample (300 × 200); (E) Representative X-ray film of the lumbar spine of the control group; (F) HE-stained sample representative of the control group (300 × 400).

DISCUSSION

Osteoporosis is caused by a variety of factors related to bone strength, including bone mineral density and quality as well as microstructural damage. Increased osteopsathyrosis results in easy bone fracture[6–8]. Osteoporosis can be primary or secondary. Primary osteoporosis can be classified as postmenopausal (PMOP; type I), senile (type II), or idiopathic (also seen in teenagers). PMOP typically occurs 5–10 years after menopause; senile osteoporosis generally refers to osteoporosis in older men aged >70 years; and idiopathic osteoporosis, while known to occur mainly in adolescents, has unknown etiology. PMOP occurs mainly due to decreasing estrogen levels, which increases bone conversion and absorption, causes trabecular bone perforation and rupture, and increases osteopsathyrosis, with a loss of mainly cancellous bone[9]. Senile osteoporosis is associated with oxidative stress; it is characterized by increased rheological bone loss and reduced bone cell and osteoblast function. Bone loss and osteoblast function declines result in decreased bone formation. Because osteoclast function is normal or reduced, bone resorption may not be active; therefore, cortical bone loss is slightly greater than cancellous bone loss.

Senile osteoporosis has direct reference to the age of patients with primary osteoporosis, who may have various types of osteoporosis concurrently[10]. For example, a female osteoporosis patient who is 65 years of age may have idiopathic osteoporosis or PMOP based on age, previous treatment for postmenopausal osteoporosis, and bone transformation condition. If osteoporosis had previously been under control, senile osteoporosis would be the most likely diagnosis or at least given priority. Similarly, a single male patient >65 years with senile osteoporosis may have a history of cured idiopathic juvenile osteoporosis.

Osteoporosis is a common chronic disease, ranking sixth among causes of morbidity and mortality in the elderly[11–13]. Osteoporosis-related fracture outranked the incidence of stroke, heart attack, and all breast cancers from 2004 to 2006. A woman's lifetime risk of osteoporotic fracture is higher than that of breast cancer, endometrial cancer, and ovarian cancer combined. In men, the risk of osteoporotic fracture is greater than the risk of prostate cancer. As this is a common and dangerous disease in the elderly, clinicians should attach great importance to the diagnosis and treatment of osteoporosis. Additionally, poor treatment adherence over time is a universal problem. Therefore, clinicians should strive for early screening, prevention, diagnosis, and treatment.

The ultimate goals of osteoporosis prevention and treatment are to reduce the occurrence of osteoporosis fracture and improve quality of life in the elderly. However, doctor and patient awareness of osteoporosis degree are insufficient, as bone hydrophobic pine disease is underdiagnosed, treatment rates are low, and adequate treatment is often not completed. Additionally, osteoporosis fracture is correlated with no prior treatment for osteoporosis[14]. This is a common problem worldwide. A retrospective study in the United States reported 300 fractures in >50 women, more than half of whom did not receive anti-osteoporosis treatment. A women's community survey of another 60 patients with >165 recent hip fractures found that only 13% of patients received sufficient osteoporosis treatment in accordance with the guidelines of the International Osteoporosis Foundation: 47% of women were insufficiently treated and 40% received no treatment. Assessment of male osteoporosis patients after fracture revealed a lower probability of prior osteoporosis treatment.

Current clinical research on osteoporosis treatments tends to compare the curative effects of single drugs and observe the effects of drug treatments combined with aerobic exercise. The Diagnosis and Treatment of Primary Osteoporosis Guide (2011), from a branch of the Chinese Medical Association of Osteoporosis and Bone Mineral Salt Disease, advises against treating osteoporosis simultaneously with bone formation promoters and bone resorption inhibitors that use the same mechanism of action[15]. However, existing studies have shown that compared with the use of a single drug, a combination of two kinds of bone resorption inhibitors can significantly improve bone absorption, which in turn significantly increases bone mineral density[16]. A complementary decrease in fracture risk, however, is yet to be confirmed.

Raloxifene belongs to a category of selective estrogen regulators that interfere with some aspects of estrogen activity and thereby simulate other functions. Raloxifene is rapidly absorbed after oral ingestion. The minimum concentration is 60%; it has a bioavailability of 2% and a plasma half-life of approximately 27.7 hours[17]. A number of clinical studies have shown that raloxifene has an obvious preventive effect on postmenopausal osteoporosis since it can supplement estrogen levels in patients to improve bone density[18]. The current study shows that raloxifene treatment well before the bone mineral density in the treatment of patients with L2–L4 (0.78–0.08) for g/m^2, after treatment for (0.83 + 0.10 g/m^2, change obviously before and after treatment. Previous research has demonstrated the curative effects of raloxifene for the treatment of senile osteoporosis, which resulted in improved patient bone density. Always study, human bones but as sport and adaptability to changes[19]. Aerobic exercise, also referred to as green therapy, can achieve results beyond what drug treatment alone can achieve. Regular, systemic, and feasible aerobic exercise can maintain nerve cell integrity and accelerate lipid metabolism. Long-term regular aerobic exercise can reduce the incidence of viscera-related diseases and improve physical and mental health in the elderly[20].

In the current study, the observation and control groups differed significantly in lumbar spine and femoral bone mineral density levels after treatment ($p<0.05$). These results confirmed that combined treatment with raloxifene and aerobic exercise can significantly improve bone mineral density in patients with senile osteoporosis. As shown in Table 2, U-Pyd/Cr differed significantly between the two groups ($p<0.01$), while BGP measurements in the observation group were significantly higher than those in the control group ($p<0.01$). These findings confirmed that raloxifene and aerobic exercise combined can reduce

bone absorption rate and promote bone formation.

In conclusion, a combination of raloxifene and aerobic exercise in patients with senile osteoporosis can significantly improve bone mineral density and promote physical and mental health. This combination is worth further study and widespread use in clinical settings.

REFERENCES

1) Lampropoulos CE, Papaioannou I, D'Cruz DP: Osteoporosis—a risk factor for cardiovascular disease? Nat Rev Rheumatol, 2012, 8: 587–598. [Medline] [CrossRef]
2) Ko T, Han G, Cho B, et al.: Intrarater reliability and interrater reliability in spinal motion assessments. J Phys Ther Sci, 2010, 22: 301–306. [CrossRef]
3) Tsartsalis AN, Dokos C, Kaiafa GD, et al.: Statins, bone formation and osteoporosis: hope or hype? Hormones (Athens), 2012, 11: 126–139. [Medline] [CrossRef]
4) Horie J, Murata S, Inoue Y, et al.: A study of the influence of the pulmonary function on the angles of thoracic kyphosis and lumbar lordosis munity-dwelling elderly women. J Phys Ther Sci, 2009, 21: 169–172. [CrossRef]
5) Ogiwara S, Hayashi H: Burnout amongst physiotherapists in Ishikawa Prefecture. J Phys Ther Sci, 2002, 14: 7–13. [CrossRef]
6) Tremollieres F, Ribot C: Bone mineral density and prediction of non-osteoporotic disease. Maturitas, 2010, 65: 348–351. [Medline] [CrossRef]
7) Fragoso JM, Delgadillo H, Llorente L, et al.: Interleukin 1 receptor antagonist polymorphisms are associated with the risk of developing acute coronary syndrome in Mexicans. Immunol Lett, 2010, 133: 106–111. [Medline] [CrossRef]
8) Santos MC, Barros L, Carolino E: Occupational stress and in Ishikawa Prefecture. J Phys Ther Sci, 2002, 14: 7–13.
9) Kim KK, Horan ML, Gendler P, et al.: Development and evaluation of the Osteoporosis Health Belief Scale. Res Nurs Health, 1991, 14: 155–163. [Medline] [CrossRef]
10) Csuka M, McCarty DJ: Simple method for measurement of lower extremity muscle strength. Am J Med, 1985, 78: 77–81. [Medline] [CrossRef]
11) Pflugmacher R, Schroeder RJ, Klostermann CK: Incidence of adjacent vertebral fractures in patients treated with balloon kyphoplasty: two years' prospective follow-up. Acta Radiol, 2006, 47: 830–840. [Medline] [CrossRef]
12) Johnell O, Kanis JA: An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int, 2006, 17: 1726–1733. [Medline] [CrossRef]
13) Brixen K, Kassem M, Abrahamsen B: Prevention and treatment of osteoporosis in women: an update. Obstetrics, Gynaecol Reprod Med, 2009, 19: 157–163. [CrossRef]
14) Tatehara S, Miyamoto Y, Takechi M, et al.: Osteoporosis influences the early period of the healing after distraction osteogenesis in a rat osteoporotic model. J Craniomaxillofac Surg, 2011, 39: 2–9. [Medline] [CrossRef]
15) Kubo T, Shiga T, Hashimoto J, et al.: Osteoporosis influences the late period of fracture healing in a rat model prepared by ovariectomy and low calcium diet. J Steroid Biochem Mol Biol, 1999, 68: 197–202. [Medline] [CrossRef]
16) Nikolaou VS, Efstathopoulos N, Kontakis G, et al.: The influence of osteoporosis in femoral fracture healing time. Injury, 2009, 40: 663–668. [Medline] [CrossRef]
17) Anderson JJ, Klemmer PJ: Risk of high dietary calcium for arterial calcification in older adults. Nutrients, 2013, 5: 3964–3974. [Medline] [CrossRef]
18) Hermann AP, Abrahamsen B: The bisphosphonates: risks and benefits of long term use. Curr Opin Pharmacol, 2013, 13: 435–439. [Medline] [CrossRef]
19) Shiroshita T, Fukubayashi T: Comparison of towel-gathering exercise and toe exercises for the painful accessory navicular. J Phys Ther Sci, 2011, 23: 455–458. [CrossRef]
20) Myler RK, Ryan C, Dunlap R, et al.: Dyslipoproteinemias in atherosclerosis, thrombosis and restenosis after coronary angioplasty. J Invasive Cardiol, 1995, 7: 33–46. [Medline]