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Original article

Effect of alendronate on muscle mass: Investigation in patients with osteoporosis

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Abstract

Objectives: Many osteoporosis drugs reliably increase bone mass in the elderly; if these drugs also had a positive effect on muscle, their benefit would be even greater. We examined the effect of alendronate monotherapy on muscle mass in patients with osteoporosis.
Methods: In this retrospective cohort, case-control study, patients from an osteoporosis database were divided into 2 groups: alendronate-treated patients (group A; n = 199) and a control group receiving no drug treatment (group C; n = 233). Appendicular skeletal muscle mass (ASM) and skeletal muscle mass index (SMI) measured by dual-energy X-ray absorptiometry were assessed at approximately 1 year. The change in muscle mass was compared between the groups.
Results: At baseline, group A included more women and had lower height, weight, bone mineral content, and muscle mass than group C. A comparison of changes after 1 year—adjusted for age, sex, observation period, body mass index and initial values—revealed that the muscle mass in group A showed increases by 0.137 kg/m^2 in SMI, 514 g in ASM, and 319 g in lower limb muscle mass (LLM). Group C showed no changes in muscle mass. A significant difference in the amount of change in ASM and LLM was found between the groups after adjustment: 2.5 times and 4.4 times higher, respectively, in groups A and C. However, the difference in SMI disappeared after adjustment.
Conclusions: This is the first study to show that alendronate may have a positive effect not only on bone, but on muscle as well.
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Keywords: Alendronate; Drug treatment; Muscle mass; Osteoporosis; Sarcopenia

1. Introduction

Muscle decline with age is a well-known cause of decreased walking ability and is a major factor in restricted activities of daily living in the elderly. Sarcopenia, defined as a syndrome that causes physical disability because of decreased muscle mass and strength, leads to reduced quality of life and death [1,2]. The international agreement by the European Working Group on Sarcopenia in Older People states that sarcopenia should be diagnosed using walking ability, muscle strength, and muscle mass, and that judgments on the need for intervention can be made from walking ability and muscle mass levels [3]. The most basic underlying criterion for diagnosis is muscle mass, however [3,4].

Despite the importance placed on muscle mass, reports on drugs that have an effect on muscle mass are limited to testosterone [5–7], angiotensin-converting enzyme inhibitors [8], statins [9,10], and a few others [11]. Moreover, most of these drugs have problems in terms of effect and safety reliability, and there are no drugs that can be used regularly in

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clinical practice [11]. Many osteoporosis drugs reliably increase bone mass and contribute to reducing the risk of fracture in the elderly [12]. If these osteoporosis drugs were also to have a positive effect on muscle mass, their benefit would be even greater and would be of more value to patients. Vitamin D preparations may increase both bone and muscle mass [13,14], but a consistent assessment of their efficacy on muscle mass has not been reported [11]. To our knowledge, the effect of bisphosphonates has not been investigated; therefore, we examined the effect of alendronate monotherapy on muscle mass in osteoporosis patients.

2. Materials and methods

The study design was a case-control study with a retrospective cohort. In our hospital, dual-energy X-ray absorptiometry (DXA) bone density measurements of the lumbar spine, hip, and total body have been done since the hospital acquired a DXA machine (DXP-NT; GE Medical Systems Lunar, Madison, WI, USA). Using total body bone measurements in addition to total bone mineral content (BMC) and total fat mass (FM), the appendicular skeletal muscle mass (ASM), which correlates most closely with muscle mass, and skeletal muscle mass index (SMI), a corrected value for physique based on the individual's height, can be calculated [15]. Lower limb muscle mass (LLM) can also be obtained.

Between April 1992 and May 2011, body composition was measured by DXA in 5999 patients and osteoporosis drugs were prescribed to 33,734 patients, of whom 1283 were diagnosed with osteoporosis and included in a database. After excluding those patients who used other drugs, those who received combination therapy, and those assessed by DXA for less than 6 months or more than 1.5 years, 199 patients treated with alendronate monotherapy (35 mg or 5 mg, both doses approved by the Ministry of Health, Labour and Welfare in Japan) for 1 year and evaluated by DXA (group A) and a control group of 233 patients who received no drug therapy for 1 year also observed with DXA only (group C) were selected (Fig. 1). These 2 groups are the subjects of this analysis.

Sarcopenia was judged based on SMI only because full data on walking ability and muscle strength were not available. Patients with levels below the Japanese criteria (men 6.87 kg/m^2, women 5.46 kg/m^2) [16] were diagnosed as having sarcopenia and patients with levels above those values were not. The main outcome variables were skeletal muscle mass (ASM, SMI and LLM).

Statistical analysis was determined using SAS, version 9.2 (SAS Institute Inc.); $p < 0.05$ indicated significance. The amount of change in response variables was compared between the 2 groups. Differences in the amount of change after 1 year were determined using a general linear model with correction for age, sex, observation period, body mass index (BMI), and initial value for each item. Secondary analyses included the correlation between the amount of change in muscle and other body components after 1 year and the difference in the amount of change in muscle in patients receiving 35 mg and 5 mg of alendronate.

This study was approved by the Institutional Review Board. Its approval number is No. 687-2.

3. Results

A comparison of patient baseline characteristics showed no difference in mean age (72.4 years) between the groups. Group

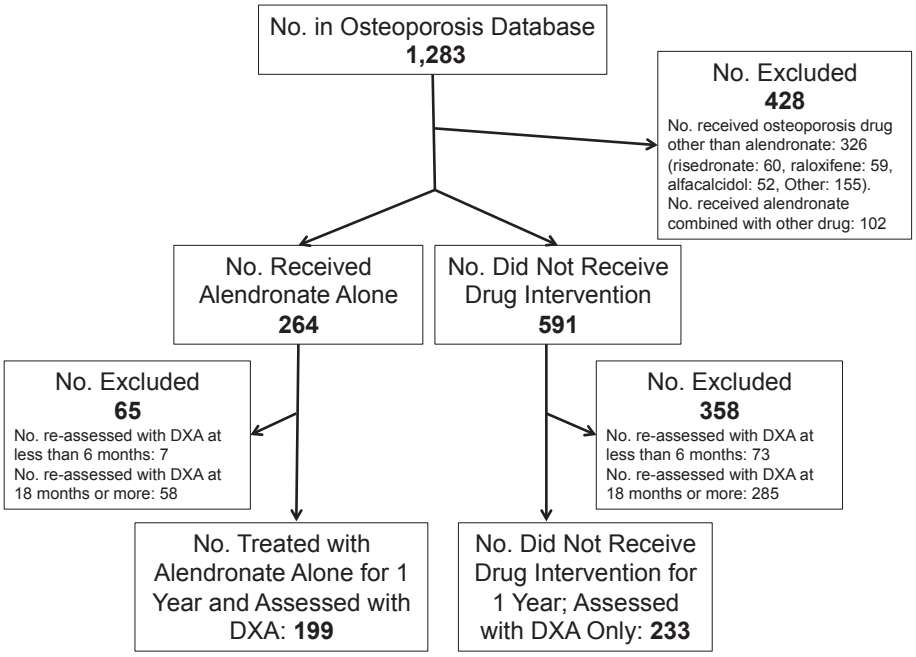

Fig. 1. Flow diagram of subject selection. Patients receiving alendronate monotherapy and those who were untreated and in whom changes in muscle-related items could be measured with total body DXA for 1 year were extracted from an osteoporosis database. DXA: dual-energy X-ray absorptiometry; no.: number.

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