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Original article

Effect of a dietary supplement on peri-implant bone strength in a rat model of osteoporosis

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ABSTRACT

Purpose: Osteoporosis contributes to impaired bone regeneration and remodeling through an imbalance of osteoblastic and osteoclastic activity, and can delay peri-implant bone formation after dental implant surgery, resulting in a prolonged treatment period. It poses several difficulties for individuals with large edentulous areas, and decreases their quality of life. Consequently, prompt postoperative placement of the final prosthesis is very important clinically. Peri-implant bone formation may be enhanced by systemic approaches, such as the use of osteoporosis supplements, to promote bone metabolism. We aimed to confirm whether intake of synthetic bone mineral (SBM), a supplement developed for osteoporosis, could effectively accelerate peri-implant bone formation in a rat model of osteoporosis.
Methods: Thirty-six 7-week-old ovariectomized female Wistar rats were randomly assigned to receive a standardized diet with or without SBM (Diet with SBM group and Diet without SBM group, respectively; $n = 18$ for both). The rats underwent implant surgery at 9 weeks of age under general anesthesia. The main outcome measures, bone mineral density (BMD) and pull-out strength of the implant from the femur, were compared at 2 and 4 weeks after implantation using the Mann–Whitney U test.
Results: Pull-out strength and BMD in the Diet with SBM group were significantly greater than those in the Diet without SBM group at 2 and 4 weeks after implantation.
Conclusions: This study demonstrated that SBM could be effective in accelerating peri-implant bone formation in osteoporosis.

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1. Introduction

Japan is known for having the world's most rapidly aging population; individuals above the age of 65 years account for 25% of the total population, and number over 30 million [1]. The trend toward an increasingly elderly population is evident not only in Japan and other developed countries, but also in nations across the globe, attesting to ongoing improvements in health, welfare, diet, and other factors [2]. In an aging society, even elderly individuals are targeted for dental implant treatment to improve quality of life.

In one investigation, 80% of patients who received implant treatment reported that the treatment period was too long [3], suggesting that shortening of the treatment period is an important factor in improving this therapy. However, osseointegration between the implant and bone requires at least 3–6 months [4]. Furthermore, the elderly are at risk of osteoporosis, a condition characterized by a severe decrease in bone mineral density (BMD) that results in reduced bone strength and alterations in trabecular bone characteristics [5]. Osteoporosis also contributes to impaired bone regeneration and remodeling through an imbalance in osteoblastic and osteoclastic activity, and may delay peri-implant bone formation [6,7]. It poses several difficulties for individuals with large edentulous areas, and decreases their quality of life. Thus, it is very important to study approaches for accelerating bone formation around dental implants in patients with osteoporosis.

Several strategies to accelerate bone formation after implant placement have been reported, the simplest of which is immediate implant restoration with immediate implant placement [8,9]. However, few patients undergo this treatment, as only those with adequate bone strength and bone volume are candidates. Other approaches have involved improving the interface between the implant and the peri-implant bone tissue. Implant materials and/or implant surface treatments have been developed to augment cell adhesion and protein adsorption at the implant–bone tissue interface [10,11]. Ogawa [12] reported that titanium surfaces treated with ultraviolet light developed a unique electrostatic status and acted as direct cell attractants to effectively reduce the osseointegration period without the aid of ionic or organic bridges, which is a novel physicochemical characteristic of titanium [13]. Vibratory stimulation has also been reported to improve the bone-to-implant contact ratio [14].

In addition to these local approaches to improve osseointegration between the implant body and surrounding bone tissue, systemic approaches such as the use of osteoporosis medication to promote bone metabolism may improve peri-implant bone formation [15,16]. LeGeros developed synthetic bone mineral (SBM), a calcium-phosphate-based supplement incorporating magnesium (Mg), zinc (Zn), fluoride (F), and carbonate, to promote bone formation and inhibit bone resorption in osteoporosis [15]. On the basis of this background, we previously conducted studies revealing that SBM accelerates bone formation in normal rats both with and without implant placement [15,17].

As a next step in this research, the current study was conducted to assess whether SBM could effectively accelerate peri-implant bone formation in a rat model of osteoporosis.

Table 1 – Mineral compositions (wt%) of diets without and with SBM.

	Diet without SBM	Diet with SBM
Calcium (Ca)	0.51	0.74
Phosphate (P)	0.30	0.48
Magnesium (Mg)	0.05	0.35
Zinc (Zn)	0.003	0.036
Fluorine (F)	0	0.005
Carbonate (CO3)	0	0.12
Natrium (Na)	0.10	0.13
Kalium (K)	0.35	0.75
Chlorine (Cl)	0.16	0.17

SBM: synthetic bone mineral.

The null hypothesis was that bone formation evaluated by BMD and pull-out strength would not significantly differ between osteoporosis rats fed diets with and without an SBM supplement.

2. Materials and methods

2.1. Animal diet

AIN-93M, developed by the American Institute of Nutrition Committee and prepared by Oriental Yeast Co., Ltd. (Tokyo, Japan), was used as the control diet. The experimental diet consisted of AIN-93M and SBM. SBM was prepared according to LeGeros' protocol [18]. Briefly, a mixture of dicalcium phosphate dihydrate ($CaHPO_4 \cdot 2H_2O$) and magnesium and zinc chlorides ($MgCl_2$ and $ZnCl_2$, respectively) were hydrolyzed in double-distilled water containing dissolved potassium carbonate and sodium fluoride. Thereafter, SBM was added to AIN-93M, the mineral composition of which was adjusted using Mijares' method [19]. The compositions of the diets with and without SBM are shown in Table 1.

2.2. Animal experiments

The study protocol was approved by the Ethical Committee of Nihon University (AP14-MD018). Thirty-six 6-week-old female ovariectomized (OVX) Wistar rats (Sankyo Labo Service, Tokyo, Japan) were included. Seven-week-old rats were fed a diet without SBM for 1 week to acclimate them to environmental changes, then randomly allocated into one of two groups: a control group fed a diet without SBM (Diet without SBM group, $n = 18$) or an experimental group fed a diet with SBM (Diet with SBM group, $n = 18$). Rats were housed individually; food and water were given ad libitum, and temperature and relative humidity were maintained at 20 ± 1 °C and $50 \pm 1\%$, respectively.

All rats underwent implant surgery on their femurs at 9 weeks old while under general anesthesia administered via an intraperitoneal injection of medetomidine, midazolam and butorphanol. One operator prepared a hole in the femur 1.2 mm in diameter and 2.5 mm deep using a 1.2-mm-diameter drill. Cylindrical implants 1.2 mm in diameter and 4.0 mm long were prepared from pure titanium (CLINE Co., Ltd., Tokyo, Japan), sandblasted with 110-μm-diameter AlO_2, cleaned with an ultrasonic device, and autoclaved. The