Original Article

Bone-strengthening supplement (BSP) promotes bone and cartilage repair, for the treatment of Osteonecrosis of Femoral Head: an MRI-based study

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Abstract: Currently, no effective drug treatment is available for bone and joint disease, a disorder of the bone and cartilage cells. Osteonecrosis of the femoral head (ONFH) is an example of bone and joint disease. It is progressive, with femoral head collapse resulting from the death of osteocytes and the bone marrow, leading to a poor quality of life and surgical interventions. However, the mechanism of this disease is still unknown, and the effects of current therapy are not satisfactory. In our previous study, we showed, using an ONFH rat model, that a new Chinese medicine, “bone-strengthening supplement” (BSP), enhances bone growth, promotes bone density, and restores blood circulation in the femoral head, and can significantly relieve pain, improve hip joint function, and reduce claudication. In the present study, we evaluated the curative effect of BSP in patients with ONFH using MRI with a double-blind randomized protocol. BSP significantly relieved pain unlike the control treatment; in addition, this treatment could improve MRI signal in ONFH patients. These results suggest that, overall; BSP can restore blood circulation and promote bone and cartilage growth during restoration of bone necrosis and the treatment of bone and joint disease.

Keywords: Bone and joint disease, osteonecrosis of the femoral head, bone-strengthening supplement, BSP, MRI

Introduction

Bone and joint disease is a disorder of bone and cartilage cells, for which currently no effective drug treatment is available [1, 2]. Osteonecrosis of the femoral head (ONFH) is a typical example of bone and joint disease involving bone cell necrosis [3-5]. It is a progressive form with osteocyte and bone marrow death, resulting in collapse of the femoral head [6-8]. ONFH may lead to permanent deformation of the femoral head, severely compromising hip-joint durability, and lead to premature end-stage osteoarthritis [9-11]. Glucocorticoids were used for the treatment of many diseases such as inflammatory and autoimmune disorders [12, 13]. However, glucocorticoids decrease skeletal vascularity, hydration, and angiogenesis, reducing blood flow to the femoral head, and have vasoconstrictive effects on the lateral epiphyseal arteries, leading to ischemia and subsequent necrosis of the femoral head [14-17]. ONFH may result in a poor quality of life and debilitation and requires surgical intervention [10, 18]. Eighty percent of ONFH cases require total hip arthroplasty (THA) [19, 20]. However, there is no effective conservative treatment or drug for ONFH.

The Chinese medicine “bone-strengthening supplement” (BSP), also called bone-strengthening pill and Jiangusheng Wan, which is comprised of pearl, angelica, pheretima, and pseu-
do-ginseng, is an empirical recipe, which has been used for the treatment of early- and middle-stage ONFH for several years [21, 22].

Pearl can improve the function of the kidneys and bone marrow; in addition, it can promote blood circulation, resolve thrombosis, drain collaterals, and promote the production of blood and bone [23]. Angelica promotes hematopoiesis and is commonly used for the treatment of many diseases such as coagulopathies, arthralgia, and traumatic injury [24]. The Chinese medical text Bielu notes the following: “Angelica can relieve pain, treat blood clots, improve blood flow to internal organs, and promote muscle generation”. The Chinese medical text Bencaocongxin notes that angelica can clear abnormal blood cells and promote the generation of fresh blood [22]. The main ingredients of angelica [Angelica sinensis (Oliv.) Diels are ferulic acid, nicotinic acid, succinic acid, vanillic acid, lignoceric acid, and palmitic acid; it is also rich in amino acids and essential inorganic nutrients [15]. In recent years, many studies have indicated that angelica can promote hematopoiesis; decrease platelet aggregation; protect the liver, kidneys, and brain from ischemic injury; reduce inflammation; provide analgesia; and promote bone repair [25].

Pheretima (an earthworm genus) has the effect of regulating meridian obstruction. Earthworm contains different kinds of bioactive materials, such as amino acids, antipyretic alkalim, earthworm element, earthworm toxin, hyaluronic acid, choline, guanidine, substances that promote bone marrow proliferation, and platelet activating factor (PAF) [26, 27]. Earthworm extracts have been reported to contain highly active components that promote osteoblast proliferation and differentiation as well as matrix mineralization; in addition, the extracts inhibit bone resorption and promote bone repair and bone reconstruction [28].

These medications can also increase blood circulation to the femoral head to promote the resorption of necrotic bone, bone regeneration, and the repair of ONFH, improve the pathological status of the femoral head, reverse ONFH necrosis and collapse of the femoral head, reduce osteoarthritis and the development of necrosis, and promote the recovery of necrotic bone [22].

Magnetic resonance imaging (MRI) has been shown to be useful in evaluating the development of ONFH. Therefore, in this study, we evaluated the curative effect of BSP in patients with ONFH by using MRI.

Materials and methods

Patients

All patients provided their written informed consent. This prospective study was approved by the Ethics Committee of the Peking Union Medical College Hospital and Beijing Jianxing Traditional Chinese Medicine Hospital. A total of 434 patients were included from January 2014 to February 2016. Patients were eligible for inclusion if they had a diagnosis of ONFH at stages I or II, and had not yet received any intervention. Exclusion criteria were the presence of congenital heart disease or pulmonary disease, such as asthma or bronchiectasis. All patients underwent full radiographic assessment of their ONFH.

MRI evaluation

Using MRI, experienced orthopedic surgeons and radiologists diagnosed all patients. MRI was diagnostic for osteonecrosis if crescentic subchondral areas demarcated by a band or ring of decreased signal intensity on T1-weighted images and of increased signal intensity on the corresponding STIR images were observed.

Statistical analysis

All results are reported as mean ± standard deviation (SD). Student’s t-test and one-way analysis of variance (ANOVA) were used to analyze the statistical significance using SPSS 18.0 software (SPSS Inc., Chicago, IL, USA). P<0.05 indicated statistically significance.

Results

Four hundred and thirty-four patients, 220 females and 214 males, aged 18 to 70 years, were included in the study. There were 306 patients in the BSP group and 128 patients in the control group. All these patients had their MRI taken before the experiment, at six months and at one year after therapy. There were no significant differences in demographics (sex, age, slides, and cause) between the BSP group and the control group. At the first MRI scan, in the control group, 52 patients were diagnosed as being at stage I and 76 patients at stage II.
However, there were 81 patients at stage I and 225 patients at stage II in the BSP group (Table 1).

In the control group, ONFH was trauma-induced in 36 patients and non-trauma-induced in 92. In the BSP group, 69 patients had trauma-induced and 237 patients had non-trauma-induced ONFH. Sixty-four hips were affected on the left side and 64 hips on the right side in the control group. In the BSP group, left-sided ONFH occurred in 151 hips, and in 155 hips it was right-sided.

At follow-up, after six months, 47 of the 128 patients (36.7%) in the control group showed some discomfort reduction, while 81 (63.3%) showed no discomfort reduction. Significance of the difference in experienced discomfort: *P<0.05; **P<0.001.

According to the baseline MRI scans, 113 patients (88.2%) showed no change and 15 (11.8%) showed some improvement in the control group. Among the 306 subjects in the BSP group, 169 patients (55.2%) showed remarkable improvement; 109 (35.6%) showed some improvement and 28 patients (9.1%) showed no change. Significance of the difference in improvement: *P<0.05; **P<0.001.

Four representative MRI scans are shown in Figures 3-5.

**Discussion**

Currently, an effective drug treatment for bone and joint disease is lacking. ONFH is a typical bone and joint disease involving necrosis of bone cells; it is a debilitating and painful, and influences both young and middle-aged patients [29, 30]. The etiology and pathogenesis of ONFH is complex and no factors have been accrued yet that can explain exactly how the blood supply to the femoral head becomes damaged, resulting in damage to bone cells, hematopoietic cells, and adipocytes [31, 32]. So far, several surgical therapies such as grafting vascularized bone, core decompression, rotational osteotomy, and stem cell transplantation have been performed to cure early-stage ONFH [33, 34]. Most ONFH patients eventually require hip arthroplasty [35]. Although many studies have explored the mechanism of ONFH, an effective medical therapy for these patients is still lacking. Our previous study showed that a new Chinese medicine, BSP, can prevent prednisone-induced fat accumulation and resto-
**Figure 3.** Representative case of osteonecrosis of the femoral head (ONFH) evaluated by magnetic resonance imaging (MRI). A 47-year-old alcoholic (250 ml of alcohol per day) male patient. A-C. There were signal abnormalities on the right-side indicative of osteochondritis of the femoral head and an extensive area of signal abnormalities under the perichondrium. D-F. After treatment with the bone-strengthening pill (BSP) for six months, the signal abnormalities disappeared and the patient resumed normal work. G-I. The MRI image displayed no abnormalities at one-year follow-up.

**Figure 4.** Representative case of osteonecrosis of the femoral head (ONFH) evaluated by magnetic resonance imaging (MRI). A 56-year-old female patient who was administered steroids five years previously. A-C. There were signal abnormalities on the right-side indicative of osteochondritis of the femoral head and an extensive area of double line signal abnormalities under the perichondrium. D-F. After treatment with bone-strengthening pills (BSP) for six months, the signal abnormalities disappeared and the patient resumed normal work. G-I. The MRI image displayed no abnormalities at one-year follow-up.
Figure 5. Representative case of osteonecrosis of the femoral head (ONFH) evaluated by magnetic resonance imaging (MRI). A 52-year-old female patient who was administered steroids four years previously. A-C. There were signal abnormalities on the right side indicative of osteochondritis of the femoral head and an extensive area of signal abnormalities under the perichondrium. D-F. After treatment with the bone-strengthening pills (BSP) for six months, the signal abnormalities disappeared and the patient resumed normal work. G-I. The MRI image displayed no abnormalities at one-year follow-up.

re the disruption of bone microcirculation and microstructures in rats. In this study, we performed a RCT to study the functional role of BSP in the treatment of ONFH using MRI. We showed that BSP can significantly relieve the pain compared to the control treatment. Further, we demonstrated that the MRI signal in ONFH patients is improved as a result of treatment with BSP. These observations imply that BSP acts comprehensively to restore blood circulation and promotes bone and cartilage growth to repair bone necrosis and treat bone and joint disease.

In summary, we have shown that BSP is safe and can act comprehensively to restore blood circulation and promote the growth of bone and cartilage to repair bone necrosis and treat bone and joint disease.

Disclosure of conflict of interest
None.

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