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CLINICAL STUDY

Effects of Yishengukang decoction on expression of bone-specific alkaline phosphatase, carboxyterminal propeptide of type Ⅰ procollagen, and carboxyterminal cross-linked telepeptide of type Ⅰ collagen in malignant tumor patients with bone metastasis

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Abstract

OBJECTIVE: To investigate the effect of Yishengukang decoction on the expression of the metabolic bone markers, bone-specific alkaline phosphatase (BAP), carboxyterminal propeptide of type Ⅰ procollagen (PICP), and carboxyterminal cross-linked telepeptide of type Ⅰ collagen (ICTP), in cancer patients with bone metastasis.

METHODS: Patients (n = 180) were divided into three groups: (a) bone metastasis patients treated with Yishengukang and pamidronate disodium injection (treatment group, n = 60); (b) bone metastasis patients treated with pamidronate disodium injection alone (control group, n = 60); (c) cancer patients without metastatic bone lesion (non-bone metastasis group, n = 60). Serum levels of the metabolic markers BAP, PICP, and ICTP were detected by enzyme-linked immunosorbent assay pre- and post-therapy.

RESULTS: A significant decrease in serum BAP level was observed in the treatment group compared with the control group. However there were no significant differences in serum levels of PICP and ICTP before or after treatment compared with the control group.

CONCLUSION: Yishengukang decoction combined with pamidronate disodium injection reduced serum BAP level to a greater extent that pamidronate disodium injection alone. Furthermore, the combined therapy was more beneficial in regulating imbalanced bone metabolism after bone metastasis, and may represent the molecular mechanism underpinning the effects of Yishengukang decoction.

Key words: Malignant tumor; Neoplasm metastasis; Alkaline phosphatase; Collagen type Ⅰ

INTRODUCTION

Bone is the most affected tissue-type and common site for metastasis in patients with advanced malignant tumors. Furthermore, after liver and lung, bone is the third metastasized organ, occurring in almost two-thirds of advance malignant tumor cases. Bone metastasis can occur from any malignant tumor type, especially in cases of breast cancer and prostate cancer where bone metastasis is observed in up to 80% of cases.[1] Skeletal-related events caused by bone metastasis are directly responsible for poor quality of life and low life expectancy in patients. Biochemical markers play an important role in the assessment and differential diagnosis of bone metastasis, with relatively high sensibility, specificity and accuracy.[2]

Used in Traditional Chinese Medicine (TCM) practice, Yishengukang decoction is effective in treating malignant tumors with bone metastasis. Based on the theory that the kidney governs the bone and generates the bone marrow, Chinese herbs that positively affect kidney tonifying and bone marrow generation, toxin resolving, and stasis dissolving are selected in Yishengukang decoction.[3-5] This study aimed to determine the molecular mechanisms by which Yishengukang decoction acts in treatment of malignant tumor patients with bone metastasis. We used an enzyme-linked immunosorbent assay (ELISA) to determine the influence of Yishengukang decoction on the expression of the serum markers, bone-specific alkaline phosphatase (BAP), procollagen I C-terminal propeptide (PICP), and cross-linked carboxyterminal telopeptide region of type I collagen (ICTP), in cancer patients.

MATERIALS AND METHODS

Patients and groups

Patients (n = 120) diagnosed as having malignant tumors with bone metastasis were evenly and randomly divided into the treatment group (Yishengukang decoction plus pamidronate disodium injection) and control group (pamidronate disodium injection only) (n = 60/group). A third group comprising malignant tumor cases without bone metastasis was included (n = 60). All participants were recruited from The Department of Oncology, Wangjing Hospital, China Academy of Chinese Medical Sciences, from January 2007 to June 2013. There were no statistically significant differences in gender, age, pathological pattern, tumor stage, or course of treatment in chemotherapy and radiotherapy before therapy among the three groups (P > 0.05).

Diagnostic criteria

Both Western and TCM diagnosis criteria were used for patient selection. Western Medicine diagnosis criteria comprised cytological diagnosis, pathological diagnosis and imageological diagnosis. Clinical diagnosis via X-ray, computed tomography (CT), magnetic resonance imaging (MRI), or emission computerized tomography (ECT) for bone metastasis, were also taken in account alongside operation specimens, biopsy specimens by fiber-optic bronchoscopy, gastroscopy or colonoscopy, and metastatic biopsy samples.

In TCM diagnosis criteria, patients diagnosed with kidney-yin-deficiency pattern, blood stasis pattern, or yin-deficiency and heat toxin pattern, were recruited with reference to Guiding Principle of Clinical Research on New Drugs of TCM (first edition) published by China Medical Science Press in May, 2002 and Diagnostics of Traditional Chinese Medicine published in 1984.

Inclusion criteria

Inclusion criteria included meeting the diagnostic criteria of Western medicine and the patterns in TCM. Participants whose predicted life expectancy was over 3 months were given the whole course of treatment. Patients previously treated by chemothreapy and radiotherapy were not recruited until the therapy had been completed for over one month. In the study, only conservative treatment was provided without chemothreapy or radiotherapy. All participants had given informed consent to join the study. All samples were collected with prior approval from the Ethical Committee of Wangjing Hospital (approval No. WJEC-KT-2012-002-P002).

Drugs, reagents, and instruments

The main herbs in Yishengukang decoction include prepared Dihuang (*Radix Rehmanniae*) 15 g, Gusuibu (*Rhizoma Drynariae*) 9 g, Baihuasheshecao (*Herba Hedyotdis*) 10 g, Banzhilian (*Herba Scutellariae Barbatae*) 10 g, Shanyao (*Rhizoma Dioscoreae Oppositae*) 15 g, Shanzhuyu (*Fructus Macrocarpii*) 12 g, Mudanpi (*Cortex Moutan Radicis*) 10 g, Zexie (*Rhizoma Alismatis*) 10 g, and Fuling (*Poria*) 10 g. The prescription was decocted by the Pharmacy Department, Wangjing Hospital, China Academy of Chinese Medical Sciences (Beijing, China). One package per day, twice in the morning and evening with 100 mL each time, was required. One course of treatment lasted one month, and three consecutive courses of treatment were carried out in the study.

Pamidronate disodium injection (15 mg/bottle) was manufactured by Zhejiang Aotuokang Pharmaceutical Group Company LTD (Zhejiang, China: medical permanent No. H19991037; batch No. 070103).

BAP was produced by Immunodiagnostic Systems Limited (IDS Ltd., UK; batch No. 57582). PICP was from Bionewtrans Pharmaciutical Biotechnology (BPB Ltd., USA; batch No. 70621S). ICTP was from Orion Diagnostica (the Netherlands; batch No. 2531201). The ELISA instrument was a BIO RAD Model 550 (USA).