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## **Osteoporosis and Traditional Chinese Medicine: an Animal Experiment**

**Huayue Chen, Shizuko Shoumura**

*Department of Anatomy, Gifu University Graduate School of Medicine, 1-1 Yanagido, Gifu, 501-1194, Japan*

Osteoporosis is a major public health problem in all developed countries. Despite numerous investigations, the pathogenesis, treatment and prevention of the osteoporosis remain unsolved problems. Several agents such as estrogens and selective estrogen receptor modulators, bisphosphonates, calcitonin and parathyroid hormone (PTH) have been used clinically in the treatment of the disease. Traditional Chinese medicine (TCM) has developed during a period of 3000 years its own unique system and is being reevaluated in the clinical field. TCM is known to have low toxicity and are suitable for long-term administration as compared to chemically synthesized medicines. In this symposium, we will report on osteoporosis and TCM using the animal experiments.

Senescence-accelerated mouse P6 (SAMP6) has been reported to be the first spontaneous experimental model for senile osteoporosis. As compared with the normal strain SAMR1, the body hair showed rough and the hair loss was conspicuous in SAMP6. The bone mineral density (BMD) of the whole body was significantly decreased in SAMP6 as early as 2 months of age. The trabecular bone of SAMP6 exhibited many features that were analogous to that of aging humans. The amount of trabecular bone in lumbar vertebra and distal metaphysis of the femur was significantly diminished. The number of osteoblasts in trabecular bones was also decreased. There was a greater proportion of resting surface and less forming surface in the femoral endosteal surface of SAMP6. The number of mast cells in bone marrow was significantly increased in SAMP6. The serum PTH level was increased, while the serum estradiol level was decreased in SAMP6. These findings indicated that the lower bone mass in SAMP6 was due to the reduction in the bone formation. We speculate that PTH, estradiol and mast cells in the bone marrow play a role in the pathogenesis of senile osteoporosis.

Hachimi-jio-gan (Ba-Wei-Di-Huang-Wan), consisting of 8 ingredients, has been used for treatment of various disorders attributed to aging, such as lower back pain. Juzen-taiho-to (Shi-Quan-Da-Bu-Tang) is consisting of 10 ingredients. It has traditionally been used to increase the vital energy and strengthen the immunity. It may have also improved the general condition of cancer patients who were weakened by conventional therapy such as chemotherapy and radiation therapy. Unkei-to (Wen-Jing-Tang) has been claimed to be effective for various gynecological diseases. Dried

extract powders of Hachimi-jio-gan, Juzen-taiho-to and Unkei-to were supplied by Tsumura & Co. (Tokyo, Japan).

Two-month-old female SAMR1 and SAMP6 were used in this experiment. Both strains were divided into 4 groups respectively. The control group had the tap water as the only drinking fluid available. The other 3 groups were given 0.05% solution of Hachimi-jio-gan, Juzen-taiho-to or Unkei-to as the only drinking fluid for 3 months. The daily solution intake of a mouse averaged 5.0 ml. Three months later, the serum PTH and estradiol levels were measured. The BMD of the whole body was determined. The femur, tibia and lumbar vertebra were processed for microscopic examination and histomorphometric analysis.

As compared with SAMP6 controls, the serum estradiol level was significantly increased in Unkei-to group. However, we did not find any significant changes of the bone morphology. In Hachimi-jio-gan and Juzen-taiho-to groups, the BMD and the femoral weight tended to increase. The amount of trabecular bone both in femur and lumbar vertebra was greater in Hachimi-jio-gan and Juzen-taiho-to groups. In the endosteal surface of the femoral diaphysis, we found that the percentage area occupied by the forming surface was higher in Hachimi-jio-gan and Juzen-taiho-to groups. Ultrastructurally, many osteocytes and osteoblasts showed degenerative changes in SAMP6 controls. While most of the osteocytes and osteoblasts in Hachimi-jio-gan and Juzen-taiho-to groups appeared almost normal. The number of mast cells in bone marrow was significantly decreased in Hachimi-jio-gan group. The serum PTH level was declined in Juzen-taiho-to group.

We consider that Hachimi-jio-gan and Juzen-taiho-to are effective in preventing the bone loss in SAMP6, while Unkei-to can only improve the ovary function. We speculate that PTH and mast cells play a role in the pathogenesis of the senile osteoporosis by different actions.