Effect of isoflavone on the prostate specific antigen level and risk of prostate cancer in men with benign prostate hyperplasia

Shiro Hinotsu[1], Naoto Miyanaga[2], Taiji Tsukamoto[3], Tomoaki Fujioka[4], Mikio Namiki[5], Shigeo Horie[6], Satoru Takahashi[7], Yoshihiko Hirao[8], Seiji Naito[9], Mitsuru Mori[10], Hideyuki Akaza[2]

[1]Department of Pharmacoepidemiology, Kyoto University, Japan, [2]Department of Urology, University of Tsukuba, [3]Department of Urology, Sapporo Medical University School of Medicine, [4]Department of Urology, Iwate Medical University School of Medicine, [5]Department of Integrative Cancer Therapy and Urology, Kanazawa University, [6]Department of Urology, Teikyo University School of Medicine, [7]Department of Urology, Nihon University School of Medicine, [8]Department of Urology, Nara Medical University, [9]Department of Urology, Kyushu University, [10]Department of Public Health, Sapporo Medical University School of Medicine

The age adjusted incidences of prostate cancer are high in the Western countries but low in Japan. One explanation is the high level of soy consumption in Japan. In some animal models, soy isoflavones reduce prostate tumor growth. One of the most abundant soy isoflavones, daidzein, is metabolized to equol and O-demethylangolensin (DMA) by gut microflora in humans. Equol and DMA have been shown to bind to human estrogen receptors with a greater affinity than the parent compound of daidzein. However, equol does not bind prostatic androgen receptor. From the results of animal experiments, equol can bind circulating dihydrotestosterone(DHT) and isolate it from the androgen receptor, then altering growth of prostate gland regulated by androgens.

Our previous case-control study (Akaza H. et al. Jpn J Clin Oncol. 2002; 32:296-300) revealed that equol itself or some unknown factor regulating the metabolism of daidzein is deeply involved in the biology of prostate cancer. And another case-control study (Sonoda T. et al. Cancer Sci 2004; 95: 238-242) concluded that the traditional Japanese diet, which is rich in soybean products and fish, might be protective against prostate cancer. Furthermore, the result of case-control studies of Isoflavones in Japanese, Korean and American residents suggest that the Japanese residents who are not able to degrade daidzein to equol have higher incidence of prostate cancer comparing those who are able to degrade daidzein. From these results of observational studies, there is substantial epidemiological evidence that soy isoflavones especially equol may prevent prostate cancer.

Moreover, it is essential to make clear that which bacteria and what enzyme play important role for metabolism of daidzein to equol.

Then, a multicenter, double-blind, placebo controlled randomized trial was designed to determine if soy isoflavone 60mg daily decrease the Prostate Specific Antigen (PSA) level and the risk of biopsy detectable prostate cancer supported by Ministry of Education, Science, Sports and Culture, Japan. A total of 158 men were randomized to receive soy isoflavone or placebo for one year. Primary endpoint was the change of PSA level. Secondary endpoints were the risk of biopsy detectable prostate cancer and pathological findings in the prostate cancer patients. Eligible men were 50 to 75 years old, had a serum PSA level of 2.5 to 10ng/ml (ages 50 to 60 years) or 3.0 to 10ng/ml (older than 60 years). Men had a negative 6 to 12 core biopsy within 12 months prior to randomization. Re-biopsy was taken at one year after randomization. Serum PSA, testosterone, DHT, sex hormone-biding globulin (SHBG), estradiol and isoflavone levels (genistein, daidzein and equol) were measured at the time points of 0, 3, 6, 9 and 12 months. Change in each values from 0 to 12 months were evaluated. We defined men of serum equol level higher than 0.5 ng/ml at the randomization as “equol producer” and the others as “equol non-producer”. Patients enrollment was finished at the end of August 2008. Most of patients already done re-biopsy, and some patients are planning to perform re-biopsy.

From the results of this randomized controlled study will make it clear the cancer prevention effect of soy isoflavone 60mg daily for benign prostate hypertrophy patients.