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Ambivalent effects of genistein on the male reproductive systems of mice

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Genistein, a soybean-originated isoflavone, is an anticancer agent preventing various cancers including prostate, uterus, and mammary gland cancers. However, recently, genistein has been classified into a potential endocrine disruptor, because it binds to estrogen receptors and causes reproductive disturbances in some animals. Therefore, the objective of the present study was to evaluate whether genistein has a detrimental effect on the reproductive systems of immature and mature male mice. Experiments with immature mice were divided into 2 groups; one was fed with a soybean-based diet (GI-1 group), the other was fed with an AIN-76 diet (soybean-free; GI-2 group) from the embryonic to the preweaning period (3 weeks old) for 6 weeks. Thereafter, both groups were administered with genistein (2.5 mg/kg or 5.0 mg/kg) orally daily for 5 weeks under the AIN-76 diet only. Also, 6 month-old mice fed with the soybean-based diet only were treated with genistein (2.5 mg/kg) orally daily for 5 weeks (GII group). In addition, 17β-estradiol (7.5 μg/kg) or corn oil was administered with the same treatment methods to mice as a positive or negative control.

Relative organ weights in all genistein-treated groups were not significant change compared to those in the corn oil-treated groups. Sperm counts in testis and epididymis of the GI-1 and GII groups were increased by genistein administration while those in the GI-2 group were somewhat decreased compared to those in the corn oil-treated group. Sperm motile parameters were slightly increased in all genistein-treated groups, but were remarkably decreased in estradiol-treated groups. The testosterone and estrogen levels in the genistein and estradiol administration groups were somewhat higher than those of the corn oil-treated group. The PHGPx (an antioxidant) mRNA levels in testis, epididymis and prostate of the genistein- and estradiol-treated groups were higher than those of the corn oil-treated group. In histopathological findings, no lesions were observed in GI-1 and GII groups. However, degeneration and apoptosis of germ cells, appearance of immature germ cells in lumens of seminiferous tubules, and hyperplasia of Leydig cell were observed in the GI-2 group and estradiol-treated group. Depletion and degeneration of epithelium, appearance of abnormal spermatogenic cells in epididymal ducts, were also

observed in both groups.

From these results, it appears that a constant intake of genistein may activate sperm viability without spermatogenic disturbances. However, unexpected exposure to excessive genistein before puberty may have a detrimental effect on normal spermatogenesis. Therefore, genistein may be a necessary substance to maintain normal biological condition during preadult period.