Can Soy Change Serum Estradiol Concentration in Neonate Ovariectomized Rat?

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Abstract: Problem statement: Phytoestrogens are plant derived compound found in a wide variety of foods, most notably soy. The purpose of this study was to assess the effect of soy isoflavones on circulating 17-β estradiol in neonate ovariectomized rat. Approach: Thirty, one day old rats were used. Blood sample were collected after two months. 17-β estradiol was assayed by radioimmuno assay method. Data were analyzed by one way ANOVA and Duncan as post-hoc test. The level of significance was considered p<0.05. Results: Our data showed that ovariectomy significantly (p<0.05) reduced serum 17-β estradiol. Application of soy in doses 0.75 and 1.5 mL kg\(^{-1}\) day\(^{-1}\) following ovariectomy had not significant effect relative to ovariectomy without application of soy, but application of soy in dose 3 mL kg\(^{-1}\) day\(^{-1}\) significantly (p<0.05) increased 17-β estradiol relative to ovariectomy without application of soy. There was no significant difference between dose 3 mL kg\(^{-1}\) day\(^{-1}\) and control and sham group. Conclusion/Recommendation: Our results indicated that soy milk isoflavone can compensate the 17-β estradiol decrease in ovariectomized rat.

Key words: Soy milk, 17-β estradiol, neonate ovariectomized, ovariectomized rat

INTRODUCTION

Soy isoflavones, Known as Phytoestrogens, have estrogenic and anti-estrogenic properties (Cohen et al., 2007), they have structural similarities with mammalian estrogens and may interact with pathways of estrogen activity in the body (Wood et al., 2007). Soy isoflavones have been characterized as natural selective estrogen receptor modulators (Wood et al., 2006). The three soy isoflavones are genistein, daidzein and glycitein.

These isoflavone are diphenolic compounds that bond to both Estrogen Receptors alpha (ER\(_{\alpha}\)) and beta (ER\(_{\beta}\)) and for this reason, are commonly referred to as phytoestrogens (Messina and Wood, 2008). Genistein, which is the main circulating and best studied isoflavone transactivates ER\(_{\alpha}\) and induces estrogenic effect with \(\sim\)10\(^{-3}\)-10\(^{-4}\) less potency than that 17-β estradiol (Messina and Wood, 2008).

Low estrogen level in menopause often result in vasomotor symptoms, atrophy of the vaginal epithelium and bone loss (Levis and Griebeler, 2010). Isoflavone are currently used extensively as an alternative to traditional hormone replacement therapy (Cohen et al., 2007). Between dietary phytoestrogens, isoflavones of soy seem to have the most beneficial effects (Chiechi et al., 2003). There is some evidence suggesting that soy or its isoflavones, while suppressing the rate of bone resorption, concomitantly enhance the rate of bone formation. Soy or its isoflavones enhance bone formation based on at least two lines of evidence: (1) Soy isoflavone stimulate osteoblastic activity through activation of estrogen receptor and (2) Soy isoflavone promote insulin-like growth factor-I Production (Arjmandi and Smith, 2002).

It seems that soy isoflavone can change the serum concentration of 17-β estradiol, so the aim of present investigation was to study of the effect of soy milk on the serum 17-β estradiol in neonate ovariectomized rat.

MATERIALS AND METHODS

Thirty neonate one day old rats were obtained from Shiraz University of medical. Animals were maintained on 12h light/dark cycles and standard temperature 20-24°C.

Animals were divided into 6 groups of five rats each. No operation was done on the first group (control), the rats in the group 2 were served as the
sham group which underwent laparotomy and abdominal manipulation. The rest of the rats were underwent ovariectomy operation. Group 3 received no treatment at all. The rats in group 4, 5 and 6 received soy in doses of 0.75, 1.5 and 3 mL kg\(^{-1}\) day\(^{-1}\) respectively. Blood sample were collected after two months. The soy milk contained 2.5% (2.5 g 100 mL\(^{-1}\)) of soy protein.

Ovariectomy was done on 7th day of birth. They were anesthetized by xylazine and ketamine combination. The rats restrained on their back, the abdominal wall was prepared for an aseptic surgery. The linea alba incised and both ovaries were located, excised and removed. The abdominal wall was closed routinely. Application of soy milk was done after ovariectomy for two months.

Data were analyzed by SPSS (version 18). The data was analysis by one way ANOVA and Duncan as post-hoc test and the level of significance was considered p<0.05. The Data were presented in Mean ± SEM.

RESULTS

The data in group 3 (negative ovariectomized rats) show that the serum 17-β estradiol concentration was significantly (p<0.05) lower than control and sham groups and the three positive ovariectomized group (Fig. 1). In positive ovariectomized groups with soy milk doses of 0.75 and 1.5 mL kg\(^{-1}\) day\(^{-1}\) the serum 17-β estradiol was significantly (p<0.05) lower than control and sham groups; but in positive ovariectomized group which received soy milk dose 3 mL kg\(^{-1}\) day\(^{-1}\), 17-β estradiol significantly (p<0.05) increased relative to negative ovariectomized and positive ovariectomized (0.75 and 1.5 mL kg\(^{-1}\) day\(^{-1}\)). There was no significant difference between positive ovariectomized group (3 mL kg\(^{-1}\) day\(^{-1}\)) compared to control and sham groups (Fig. 1).

DISCUSSION

Phytoestrogens are plant substances that have effects similar to those of estrogens. Since the first discovery of the estrogenic activity of plant compounds, over 300 plants have been found to have phytoestrogenic activity. Preparations vary from enriched foods such as bread or drinks (soy milk) to more concentrated tablets (Panay and Rees, 2005). Soy products have been actively sought by menopausal women because of their isoflavone content (Levis et al., 2010).

In the present investigation soy milk in low doses of 0.75 and 1.5 mL kg\(^{-1}\) day\(^{-1}\) during two months had no effect on ovariectomized reduced of 17-β estradiol rats. Chiechi et al. (2002a) reported that soy rich diet, containing high levels of active phytoestrogens, can provide some protection against postmenopausal osteoporosis. They also found that diet is not as effective as hormone replacement therapy (Chiechi et al., 2002a). Imhof et al. (2008) findings showed safety improvement of the conventional hormonal replacement therapy by boosting the clinical combination of estrogens and soy isoflavones, especially regarding the risk of breast cancer (Imhof et al., 2008). Wood et al. (2007) reported that diet containing isoflavones lead to reduction of catabolism of estradiol by 21-26%, since the estrogens circulate predominately as inactive sulfate which are deconjugated within peripheral tissues, selectively catabolized and excreted. As estrogen-like phytochemicals, soy isoflavonoids are metabolized in similar enzymatic pathways. They suggest that exposure to certain isoflavones may modulate pathway of estrogen catabolism (Wood et al., 2007).

Nahas et al. (2007) showed that regular consumption of soy isoflavone extract (100 mg) produces a significantly higher reduction in the number of hot flushes than placebo. Chiechi et al. (2003) reported that dietary phytoestrogens may modulate the consequences of the postmenopausal estrogen deficiency state (Chiechi et al., 2002b). Pop et al. (2008) suggested that unconjugated soy isoflavones are safe and well tolerated in healthy postmenopausal women at dose of 900 mg day\(^{-1}\). Very few adverse events occurred and the only drug-related adverse events were mild in severity (Pop et al., 2008).

CONCLUSION

Present investigation proved that soy milk in high dose 3 mL kg\(^{-1}\) day\(^{-1}\) can compensated the low estradiol following ovariectomy. It may be due to diminished catabolism of β estradiol (Wood et al., 2007), or by the
increasing the levels of 17-ß estradiol production in other sites. Also, in the present study by determining the level of the 17-ß estradiol in soy milk samples proved that the 17-ß estradiol was \( \sim 143.1 \) pg mL\(^{-1}\). Therefore, it seems that soy isoflavone are 17-ß estradiol agonist (Messina and Wood, 2008) and in high dose can compensate the absence of ovarian hormone.

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**REFERENCES**

Arjmandi, B.H. and B.J. Smith, 2002. Soy isoflavones' osteoprotective role in postmenopausal women: Mechanism of action. J. Nutr. Biochem., 13: 130-137. PMID: 11893477

Chiechi, L.M., G. Secreto, M. D'amore, M. Fanelli and E. Venturelli et al., 2002a. Efficacy of a soy rich diet in preventing postmenopausal osteoporosis: The Menfis randomized trial. Maturitas, 42: 295-300. PMID: 12191852

Chiechi, L.M., G. Secreto, A. Vimercati, P. Greco and E. Venturelli et al., 2002b. The effects of a soy rich diet on serum lipids: The Menfis randomized trial. Maturitas, 41: 97-104. PMID: 11836040

Chiechi, L.M., G. Putignano, V. Guerra, M.P. Schiavelli and A.M. Cisternino et al., 2003. The effect of a soy rich diet on the vaginal epithelium in postmenopause: A randomized double blind trial. Maturitas, 45: 241-246. PMID: 12927310

Cohen, L.A., J.S. Crespin, C. Wolper, E.A. Zang and B. Pittman et al., 2007. Soy isoflavone intake and estrogen excretion patterns in young women: Effect of probiotic administration. In Vivo, 21: 507-512. PMID: 17591361

Imhof, M., S. Molzer and M. Imhof, 2008. Effects of soy isoflavones on 17ß-estradiol-induced proliferation of MCF-7 breast cancer cells. Toxicol Vitro, 22: 1452-1460. DOI: 10.1016/j.tiv.2008.04.018

Levis, S. and M.L. Griebeler, 2010. The role of soy foods in the treatment of menopausal symptoms. J. Nutr., 140: 2318S-2321S. DOI: 10.3945/jn.110.124388

Levis, S., N. Strickman-Stein, D.R. Doerge and J. Krischer, 2010. Design and baseline characteristics of the Soy Phytoestrogens As Replacement Estrogen (SPARE) study--a clinical trial of the effects of soy isoflavones in menopausal women. Contemp Clin. Trials, 31: 293-302. PMID: 20230914

Messina, M.J. and C.E. Wood, 2008. Soy isoflavones, estrogen therapy and breast cancer risk: Analysis and commentary. Nutr. J., 7: 17-17. PMID: 18522734

Nahas, E.A., J. Nahas-Neto, F.L. Orsatti, E.P. Carvalho and M.L. Oliveira et al., 2007. Efficacy and safety of a soy isoflavone extract in postmenopausal women: A randomized, double-blind and placebo-controlled study. Maturitas, 58: 249-258. PMID: 17913408

Panay, N. and M. Rees, 2005. Alternatives to hormone replacement therapy for management of menopause symptoms. Curr. Obstetrics Gynaecol., 15: 259-266. DOI: 10.1016/j.curobgyn.2005.05.004

Pop, E.A., L.M. Fischer, A.D. Coan, M. Gitzinger and J. Nakamura et al., 2008. Effects of a high daily dose of soy isoflavones on DNA damage, apoptosis and estrogenic outcomes in healthy postmenopausal women: A phase I clinical trial. Menopause, 15: 684-692. DOI: 10.1097/gme.0b013e318167b8f2

Wood, C.E., T.C. Register, A.A. Franke, M.S. Anthony and J.M. Cline, 2006. Dietary soy isoflavones inhibit estrogen effects in the postmenopausal breast. Cancer Res., 66: 1241-1249. DOI: 10.1158/0008-5472.CAN-05-2067

Wood, C.E., T.C. Register and J.M. Cline, 2007. Soy isoflavonoid effects on endogenous estrogen metabolism in postmenopausal female monkeys. Carcinogenesis, 28: 801-808. DOI: 10.1093/carcin/bgl1163