

Should One Consider Abandoning Intake of Soy Based Products in Women Wanting Pregnancy - A Controversial Issue

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In soy plant, agents known as phytoestrogens have been found, although their actions regarding reproductive health action as well as safety remains controversial. Lot of studies point to their advantages with regard to health like decrease in breast as well as other cancers, fibroids, menopausal symptoms cardiovascular disease (CVD) inflammation along with metabolic syndrome (MetS) as well as obesity [1].

But lot of studies indicate a harmful action because of the endocrine-interfering actions of phytoestrogens in male as well as female reproductive tissues. Most of the research was done in nonhuman animals, mostly via subcutaneous injections, but human data has not corroborated the nonhuman observations. Moreover, trying to extrapolate findings from nonhuman animals or *in vitro* (*ex-vivo*) data and trying to use it for humans adds lot of hurdles, problems and mostly conclusions that create confusion. Any relationship made by population or large human clinical studies might convey mixed reports with no capacity to interpret a cause action association in view of person to person variations, complicated medical conditions and superimposed environmental exposures. Like many non-human as well as basic research studies point to a stimulatory and probably aetiological effect of phytoestrogens on breast cancer cells. But it is a little tedious to override the *JAMA* published study demonstrating > 5000 Shanghai breast cancer survivors in a time span of 4yrs and observed that those who ate regular quantities of soy got a 32% decrease in recurrence as well as 29% in death as compared to those who took little or none [2]. These findings were observed irrespective of estrogen receptor status or use of tamoxifen.

Correlations among phytoestrogens exposure as well as fertility remain nonconclusive be it positive or negative. Certain studies in humans as well as other mammals showed no variations in menstrual cycles or fertility, while others pointed that certain lengthening of cycles and decreases in gonadotrophins on intake of quantities of isoflavones (> 100 mg). Usually both prospective as well as retrospective studies in couples undergoing infertility or artificial reproductive therapy (ART) therapies did not demonstrate any correlation with soy intake and any side effects, with some pointing advantages. Usually others point to problems with other endocrine disruptors like phthalates, PCB's as well as digoxins.

Salsano., *et al.* studied soy phytoestrogens as they are chemically identical to 17 β -estradiol [3]. The 2 major soy isoflavones, genisteins and daidzein bind primarily to estrogen receptor (ER) β but are very weak estrogens as compared to endogenous E2. Results are there regarding their action via hormonal as well as non-hormonal paths that are arresting or changing cellular growth via kinases or epigenetics also [4].

Salsano., *et al.* [3] did the complicated environmental research in fertility that is disputed with concentration on human tissues. Their observations were that the maximum amounts of genisteins and daidzein exposure decreased endometrial cell proliferation as well as decidualization as compared to lowest or nil exposure in *in vitro* assays. These assays were done from endometrial biopsies (EB's) taken

from oocyte donors on the day of oocyte pick up (OPU). We presume oocyte donors are similar but that might not be true in all cases. Very scanty data is reported regarding the subjects or what gonadotrophins stimulations, GnRH agonist or antagonist exposure smoking status or dietary supplement utilised. If any had developed premature progesterone (P) escalation on the day of trigger, that occurs in many women at time of moderate or aggressive stimulation of donor, since it could change the endometrial receptors as well as decidualization. Additionally, the quantities of isoflavone exposure they utilized would be equivalent to very huge soy exposure that would not usually be observed with typical diet input. But the results are interesting emphasizing on requirement of future research. ERs have their importance in the luteal phase, i.e. a time when ER β might be maximum hence it is good that the authors looked at that as well. Moreover, utilization of easily available supplements is commoner these days as compared to earlier hence excessive intake needs to be taken in history regarding dietary as well as herbal use or any other supplement at each visit.

Most dilemma arises from the definition of soy intake. Is it that processed food like tempeh, edamame as well as miso better as compared to markedly processed soy powders? In certain Asian countries adults might take 50 mg or isoflavones in a day mostly like soy products as compared to Western ones [5]. Still most phytoestrogens in the Western diet are availed from legumes, whole grains as well as seeds out of fruits and vegetables. What is the way of knowing the variations? Population variations like polymorphisms in the genome as well as gut microbiome might explain this. For most people it is difficult to comprehend how much isoflavone intake is. Like as per United States (US) Department of Agriculture (USDA), presuming that half a cup serving, most vegetables possess < 1 mg, miso soup- 1 - 2 mg, cooked edamame 15 - 20 mg, raw pistachios 1 - 3 mg, most soymilks 1 - 10 mg with some high soy containing cereals 20 - 100 mg [6]. Meats the so called “meatless” meats have very little to high quantities of isoflavone based on the way they are formed. Most of the amount of all soy products is based on processing, if alcohol or water is extracted as well as the crop variety. Thus, it is highly complex.

Hence there is definitely requirement of further work. But one should not recommend that women who want pregnancy should omit soy intake on the basis of current literature. In US one of the biggest manufacturing units of soy in world, soy is seen in processed foods that are cereal, chips and umpteen other foods where one doesn't expect it. Actually, processing might need attention than the soy topic itself. Thus dietary “clean eating” of foods having low amounts of phytoestrogens might actually have a total health advantage [7]. Hence there must be a report that benefits have advantages over risk. Just this single study cannot let us think that phytoestrogens from soy are equivalent to other endocrine disruptors like phthalates, PCB's as well as digoxin although sketchy reports on phytoestrogens affecting ER- β are there considering the other benefits that soy isoflavones, genisteins and daidzein possess.

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