Integrative Medicine Meeting

Abstract Presentation
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Soy Intake and Breast Cancer

Dr. Edy Virgili[1], L. Calza[2], E. Testa[3], R. Emili[3]

[1]*Department of Oncology, Urbino Hospital S.Maria, Porto Sant'Elpidio, Italy*

[2]*Outpatient Nutritionist, Porto Sant'Elpidio, Italy*

[3]*Outpatient Nutritionist, Fermo, Italy*

Introduction:

Each individual is colonized by several microbes composing the MICROBIOTA.

Its composition varies depending on different factors: age, sex, ethnicity, lifestyle and medication. The microbiota is diffused in all over the organism, about 90% of it is in the intestine, where the number of different species reaches 500 and the amount of cells per gram of the luminal content reaches 1011.

The microbial community and the host live in a condition of balance whose role is important to maintaining health. In the same way, the disruption of this balance, determined by different factors, is strictly correlated to many pathologies. In particular, diysbiosis can promote oncogenesis, tumor progression, therapy response and toxicity profiles of chemotherapeutic drugs. Although the microbiota stays in the intestine, it exerts both locally and in other further parts of the body; this is possible thanks to the involvement of hormone intermediates, metabolites and immune messengers.

In 2011, Plottel and Blaser were already about the ESTROBOLOME, such as the aggregate of enteric bacterial genes whose products are capable of metabolizing estrogens.

Estrogens are steroid hormones (C-18), and they originate from the gradual reduction of cholesterol (C-27). The main endogenous estrogens are estradiol (E1), estrone (E2) and estriol (E3). Estrogens E1 and E2 undergo a first passage in the liver, an irreversible hydroxylation in C-2, C-4 or C-16 positions of the steroid ring, whose metabolites vary in term of hormone potency and half-life. Always in the liver, estrogens and their metabolites are combined by glucuronization or sulfunation allowing the excretion in bile, urine and feces.

The estrobolome becomes activated during this step, because combined estrogens can be uncombined by enteric bacterial β-glucuronidase and β-glucosidase, determining their resorption in blood circulation.

In human microbiota, many different β-glucuronidase genes have been described, and they refer to different bacterial species existing in the intestine, even if these genes are particularly detected in bacteroidetes and firmircutes phyla.

The enzyme β-glucuronidase and β-glucosidase activity is induced by high pH values.

Another factor influencing the enzyme activity is the diet: an increase of the activity is reported in healthy subjects consuming diets high in fat or protein.

Estrogens are recognized as one of the causal elements in the onset of breast cancer, and they have an important role in neoplastic growth. The estrobolome is important because it is involved in the modulation of endogenuous estrogen production and their reabsorption. In this context, mammary glands suffer an “enhanced” estrogen stimulation determining the pathological malignancy expression.

The most common cancer among women is breast cancer. Probably genetics is not the main cause of breast cancer, but rather other crucial factors may have a bearing on the issue, such as age at first birth, age at the onset of menarche, age at the onset of menopause, and diet. Diet plays a fundamental role both in the incidence of this type of neoplasia.

The role of soy is highly discussed in this context. Soy and soy based foods are considered healthy, particularly in many Asia-Pacific countries.

Soy and soy-related products contain phytoestrogens that can affect breast cancer cells. There are many studies praising the positive properties of soy isoflavones, but there are also many others considering these molecules able to promote cancer development. In reality, we should try to understand the molecular mechanisms with which isoflavones modulate the risk of breast cancer, that is, how they manage to enter in synergy with estrogen receptors or, on the contrary, how they can act as antagonists for the receptors themselves. Then, there are mechanisms of hormonal signaling in which the isoflavones are involved independently from the estrogens which cannot be omitted in this context.

Phytoestrogens are plant compounds structurally similar to estrogens and they are categorized in 5 main classes: flavonoids, isoflavonoids, lignans, coumestani and stilbenes.

The amount of food isoflavonoids consumed per capita varies from 30 to 50 mg per day for the elderly people in Japan to less than 3 mg in the US and Europe. The traditional Asian diet is a poor diet, which relies on foods derived from the original first-generation soy (such as tofu, tempeh, miso and soy milk), while Western diets rely, in addition to soybeans, on several food sources such as meat, fish, dairy products, eggs and cereals. Moreover, in the Western diet second-generation soy is used, which is very different from the Asian one.

Soy isoflavones can bind to estrogen receptors and therefore can both inhibit and promote the expression of estrogen-sensitive genes. Many studies indicate that the onset of breast cancer is decidedly lower in the Asian populations because people regularly consume many food isoflavones from childhood onward. Early exposure to soy would seem to be a fundamental element for cancer prevention. Nevertheless, the interest in isoflavones is wide; in fact, they are successfully used also to alleviate menopausal disorders and are an alternative to hormone replacement therapy. In addition, isoflavones would seem to have the ability to activate the immune system and have antineoplastic properties such as inhibition of the enzymes necessary for DNA replication, for metastasis and for signal transduction. We know that estrogens cause breast cancer progress, ion and dietary and pharmacological interventions aiming at blocking or reducing estrogen production are associated with a favorable prognosis in patients with breast cancer. However, there are also many studies that demonstrate an inverse association between frequent consumption of soy isoflavones and breast cancer risk; other studies claim that soy isoflavones do not have any estrogenic effect in humans and conclude that a diet containing soy derivatives can be considered safe, even in patients with risk of relapse.

Still other studies confirm a chemo-protective and preventive effect on possible relapses in patients with breast cancer. Isoflavones, in general, are able to inhibit a key enzyme, 17 beta-hydroxysteroid dehydrogenase, necessary to convert the estrone into its active form: estradiol.

However, many of the antitumor effects of isoflavones occur through estrogen-independent signaling pathways. Unfortunately, these isoflavones are also phytoestrogens and, as we said before, estrogens can induce carcinogenesis. Indeed, these concerns are not groundless and there are many studies that demonstrate, contrary to those listed above, how soy isoflavones at different concentrations induces neoplastic growth in mice.

One of these studies highlights how dahydetic consumption of food stimulates the growth of breast carcinoma cells by binding to the estrogen receptor. Still other researchers declare the interference between isoflavones and tamoxifen, blocking its therapeutic effect, ecc…We are, therefore, facing a confused panorama, where the soy isoflavones have opposite effects.

We must always consider that in vitro experiments are far from what happens in a living human and that a mouse is not human being. Furthermore, there is not a standard isoflavone diet to take into account; on the contrary, there are many foods containing isoflavones, and this makes it difficult to compare and analyze data from various studies. Soy is different depending on the type of cultivation (genetically modified or not), on the phytochemical treatments (organic or not) and the foods deriving from soy differ according to the type of

Methods:

NA

Results:

NA

Conclusion:

NA