Review paper

Use of diet supplements, synthetic drugs and herbal remedies with immunotropic activity during pregnancy. I. *Echinacea*

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Abstract

This mini-review summarizes some experimental and clinical data about safety of Echinacea treatment during pregnancy. There is evidence from human studies that Echinacea is not teratogenic. However, in pregnant mice Echinacea purpurea reduced the number of viable fetuses, interfered with embrional angiogenesis and negatively influenced maternal lympho- and hemopoiesis.

Key words: *Echinacea, pregnancy, mice, human studies.*

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Fetus is a kind of semiallogeneic graft, its tissues contain histocompatibility antigens of maternal and paternal origin. The lack of rejection of fetus by the maternal immune system is the result of delicate interplay between many factors at the maternal-fetal interface. Among them, a family of pregnancy-specific glycoproteins (PSGs) and some cytokines (IL-10, IL-6, TGFb1) play immunomodulatory roles during pregnancy and has also some role in placental vascular morphogenesis. There is evidence that PSGs can modulate the secretion of important pro-angiogenic factors , TGFb1 and VEGFA, by different cell types involved in the development of the placenta. Abnormally low levels of PSG1s in maternal serum may lead to complications, including spontaneous abortion. It was reported, that the levels of PSG1 and pregnancy-associated plasma protein A (PAPP-A) in first-trimester maternal serum are influenced by smoking [1-5].

Many women use herbal remedies during pregnancy. However, data regarding safety of this kind of treatment is sparse and very limited . Moreover, women often do not inform their doctors about the use of herbal remedies during pregnancy and lactation. A survey of 578 pregnant women in the eastern United States reported that 45% of them had used herbal drugs. In Australia, 36% of 588 pregnant women used herbal medicines. In Nigeria, 67.5% of 595 women had used herbal remedies during pregnancy. In Norway study 57.8% of pregnant responders used herbal medicines. In Switzerland, pilot study was performed on small group of 139 women. During pregnancy 96%, and within the lactation period 84% of the women consumed at least 1 natural remedy [6-10].

Laws regulating production and distribution of herbal medicines, especially in developing countries, are poor. Access to herbal remedies is easy and unrestricted, because they are often introduced to the market as food supplements. Medical herbs are often regarded as gentle and safe. However, there are no rigorous studies of their safety during pregnancy [11].

Plant-based immune stimulation provides an alternative to conventional therapy of infections, especially in immunocompromised patients. Conventional chemotherapy may often result in undesirable effects. Animal and human studies revealed a modulatory effect of various antibiotics on humoral and cellular immune response. For example, ampicillin and other antibiotics from this group suppress some parameters of cellular, and enhance some parameters of humoral immunity [12-16]. Furthermore, treatment of pregnant mice with ampicillin resulted in abnormalities in immunological response to antigens of 30-day old offspring of these mice. A lowering of cellular immunity, accompanied by a decrease in T lymphocyte percentage in lymph nodes, and an increase of humoral immune response were observed [17-19].

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Echinacea

Echinacea purpurea and *Echinacea angustifolia* are some of the most significant medicinal herbs. Native to the North American prairies they are now cultivated in many countries. *Echinacea* extracts contain many compounds with proved immunomodulatory, antioxidant and anti-inflammatory activities. They may be used both internally and externally to treat respiratory infections, skin burns and skin infections [20]. Scientific evidence for the safe use of this herb during pregnancy and lactation was not available for a long time. Only one prospective study suggested that gestational use of *Echinacea* during organogenesis is not associated with an increased risk for major malformations [21]. In 2006 Perri searched 7 electronic databases, compiled data according to the grade of evidence found, and concluded, that there is a good scientific evidence from a prospective cohort study that *Echinacea* is non-teratogenic when used during pregnancy. Low-level evidence based on expert opinion showed safety of *Echinacea* consumption during lactation [22]. However, there are no formal studies which may exclude the possibility, that the absence of malformations in the living births resulted from the fact that consuming *Echinacea* may promote spontaneous abortions.

Animal studies of this problem are scarce. However, in 2006 Chow reported unwanted effects of *Echinacea* feeding in pregnant mice. Pregnancy-induced elevation in splenic lymphocytes and hemopoietic cells was eliminated by feeding pregnant mice *Echinacea*. Moreover, the number of viable fetuses was reduced [23].

In an experiment on mice Barcz *et al.* found that two *Echinacea* drugs lowered the number of embryos in litter and significantly diminished the vascular endothelial growth factor (VEGF) and the basic fibroblast growth factor (bFGF) content of embryos tissue. These studies showed that the most important mechanism influencing fetal development in case of *Echinacea sp.* intake is its influence on angiogenic activity of developing tissues [24].

Vascular endothelial growth factor and bFGF are known as the most potential angiogenesis promoters. Vascular endothelial growth factor plays a crucial role in organogenesis (liver and pancreas induction, kidney glomerulus, bone and nervous system development). Moreover, VEGF and bFGF take part in placentation and cytotrophoblast proliferation during pregnancy [25-27].

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