EDITORIAL

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New findings suggest selenium supplementation to reduce the risks of PROM in pregnancy: a new overview concerning supplementation during pregnancy

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New analysis published in the *New England Journal of Medicine* [1] has identified six genomic regions conferring risk of premature delivery following preterm rupture of membranes (PROM), which is a major health problem worldwide. The information obtained may be useful in implementing new preventive strategies, some of which are simple and inexpensive, such as the use of selenium dietary supplements. The study conducted at the Cincinnati Children's Hospital Center (USA) as part of an international collaboration identified six genomic regions that affect the duration of pregnancy and time of delivery. The study, which involved more than 50,000 women, could have important consequences for the prevention of premature births and related complications. Premature births (those that occur before the 37th week of pregnancy) are an important public health problem globally: it is estimated that premature birth is the main cause of death among children under the age of five [2, 3].

Children who survive also sometimes face serious lifelong health problems which may be due to chronic kidney failure in disabilities resulting from imperfect neuro-cerebral development [4]. It has been known for a long time that preterm birth results from a combination of genetic and environmental factors, with some studies indicating that 30–40% of the risk is genetic. This new study is the first to provide solid information on the importance of genetic factors. In particular, one of the identified genomic areas suggests that a lack of selenium, a common mineral found in nuts, some green vegetables, liver and other meats, strongly influences premature delivery risk.

Pregnant women likely require dietary supplementation, and the recent *New England Journal of Medicine* article provides new details. However, it is not clear which nutrients the woman really needs and often inappropriate supplements with various ingredients are targeted at pregnant women for commercial reasons.

Diet during pregnancy and lactation is very important as it has a fundamental impact on the health of both the mother and her child. To optimize the woman's health and to reduce the risk of malformations or illness in the unborn child, it is crucial that the mother reaches an optimal nutritional state before and during gestation and during breastfeeding, when nutritional requirements are still high [5]. Pregnant and lactating women should always consume a varied diet meeting nutritional requirement as defined in national and international dietary guidelines. Pregnant women have an increased energy requirement, especially in the second and third trimesters, of about 300-400 kcal/day. During breastfeeding, the mother requires an extra 500 kcal/day. Increasing the amount of food usually consumed is normally sufficient to achieve the calorie requirement during pregnancy and lactation. Nevertheless, supplements may be needed if some nutrients are lacking. However, the pregnant women should be advised that exceeding recommended doses may be dangerous for her and her unborn child.

National and international guidelines suggest pregnant women should have a daily intake of 400 µg folic acid (double the normal recommended dose for women). The main sources of folate are broad-leaf plants, liver, citrus fruits, legumes and whole wheat bread. To prevent neural tube defects (spina bifida and anencephaly), which have been associated with folate deficiency, the pregnant woman should consume in addition to her normal diet, supplements or enriched foods containing folates. Similarly, a daily folate intake of 350 µg/day is advised during breastfeeding.

It should be noted that:

1. Supplementation must begin 3-4 weeks before conception.
2. Minimum daily intake should be 200 µg from food plus 400 µg from a supplement.
3. In at-risk women (previous pregnancy and/or a history of spina bifida, current chemotherapy or treatment with anticonvulsant drugs) 4–5 mg of folic acid should be consumed daily.
4. Folic acid supplementation also seems to reduce the risk of other complications in pregnancy (including pre-eclampsia and intrauterine growth delay), congenital malformations (particularly cardiovascular) and (perhaps) subsequent development of nerve tissue tumours.

Pregnant women should also be encouraged to consume iron-rich foods, such as lean meat, fish, poultry, nuts and enriched cereals. The bioavailability of iron from meat is higher when consumed with fruit rich in ascorbic acid. International guidelines recommend a daily intake of 30 mg iron during gestation, which should be recommended to women at the first gynaecological examination after conception.

As iron deficiency can have serious consequences while consumption is practically risk-free, a supplement containing enough iron for storage is normally recommended during pregnancy and after delivery. Supplementation with iron can be particularly useful in close pregnancies. Considering the average levels of iron intake in adulthood, a daily supplement containing 10–15 mg is reasonable. We highly recommend the simultaneous intake of vitamin C-rich foods and citric acid to increase iron absorption. Breastfeeding women do not seem to need more iron than women in the normal physiological state, but iron intake in vegetarians must be monitored depending on whether or not the diet contains eggs and milk. A varied and controlled vegetarian diet can usually supply the same amount of iron as a normal diet due to the increased intake of citric acid and vitamin C from fruits and fresh vegetables. However, the mother's iron status should be determined in case of other secondary deficits seen in vegans and vegetarians, primarily lack of zinc, vitamin D and vitamin B12.

Iron intake may reduce the bioavailability of zinc and copper, so iron supplementation should be accompanied by increased zinc and copper intake. All supplements intended for pregnant women contain these three minerals.

Although calcium absorption is increased during pregnancy and lactation, higher calcium intake from dairy products (more bioavailable) rather than supplements, is recommended because the developing baby needs calcium for bones and teeth and calcium is supplied in breast milk to the infant. Moreover, vitamin D supplementation may be particularly useful in women not exposed to the sun and in those who do not consume dairy products because they are allergic, intolerant or vegan.

Vitamin B12 intake from enriched foods or suitable dietary supplements is critical for women following a vegan diet (which supplied no animal or animal-derived foods). B6 supplementation in pregnancy could be important too, along with folate and vitamin B12, to reduce the risk of hyperhomocysteinemia. This last has been described to lead to neural tube defects and other congenital defects, spontaneous miscarriages, intrauterine growth retardation, preeclampsia and intrauterine fetal death.

Concerning n-3 polyunsaturated fatty acids, children born to vegan mothers have a lower level of plasma docosahexaenoic acid (DHA) than the children of omnivorous mothers. The significance of this difference is not clear, but as DHA is involved in cerebral and ocular maturation, it is advised that vegan women increase their DHA intake by consuming DHA-rich foods. Microalgae supply DHA but may have a high/excessive iodine content if they are of marine origin. Eicosapentaenoic acid (EPA)+DHA supplements are not recommended during pregnancy because of their effect on arachidonic acid, which is crucial for fetal growth. The beneficial effects of higher levels of DHA in the diet of pregnant and lactating women have been demonstrated by a recently published high-quality randomized clinical trial [6]. Since cigarette smoking lowers DHA levels in breast milk, perhaps because it inhibits synthesis [7], supplementation is particularly recommended in smokers, even if they have ceased tobacco use during pregnancy.

Although, as mentioned above, an appropriate diet largely supplies the nutrients needed during pregnancy and lactation, vitamin and mineral supplementation may be considered in women who abuse tobacco or alcohol, in vegetarians or those consuming an unbalanced diet, and in multiple pregnancies. However, food supplements must be taken with caution and with the advice of a doctor as apparently safe nutrients can be dangerous at the incorrect dose.

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