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The impact of supplements on fertility

Dr Farah Djeridi
General Practitioner, UK
Email: farahdjeridi@gmail.com

Dr Sidrah Ali
General Practitioner, UK.
Email: sidrah.ali@doctors.org.uk

Dr Sabana Shaikh
Family Medicine Consultant, Qatar.
Email: sabanashaikh1234@gmail.com

Abstract

The global decline in fertility has increased the demand for fertility treatments. The evidence for good nutrition including the use supplements such as folic acid is well established in pregnancy but the use of additional supplementation in the preconceptual period and during assisted reproductive techniques is less recognised. The purpose of this article is to review the current literature to ascertain the impact of supplements such as vitamins upon fertility.

Keywords: Infertility, pregnancy, supplements, vitamins, antioxidants.

ملخص البحث

وقد أدى الانخفاض العالمي في الخصوبة إلى زيادة الطلب على علاجات الخصوبة .الأدلة على التغذية الجيدة بما في ذلك استخدام ملاحق مثل حمض الفوليك راسخة جيدا في الحمل ولكن استخدام مكملات إضافية في الفترة قبل تصور وأثناء تقنيات المساعدة الإنجابية هو أقل المعترف بها .الغرض من هذه المقالة هو استعراض الأدبيات الحالية للتأكد من تأثير مكملات قبل الحمل.

الكلمات المفتاحية: العقم، الحمل ، المكملات الغذائية، الفيتامينات ،مضادات الأكسدة.

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1. Introduction

Infertility affects around 48.5 million couples worldwide[1] and it is defined as the inability to achieve pregnancy after 12 months of regular unprotected intercourse. Infertility can have a detrimental impact on the couple. Many couples suffer with a great deal of emotional stress surrounding infertility, which is often made worse by the physical and financial strains of assisted reproduction techniques.

There are definitive causes of infertility such as tubal factors, anovulation and male factor infertility. However a significant proportion of couples suffer with unexplained infertility (UI) which is diagnosed when there is no clear cause for the infertility. There are recognised lifestyle factors which can have an impact on fertility such as smoking, obesity, alcohol and caffeine intake. Advanced maternal age, which has a significant impact on oocyte quality, is also a recognised cause of infertility.

Micronutrients are essential vitamins and minerals that are needed in small quantities in a balanced diet and act at a cellular level. The evidence of good nutrition in pregnancy is well established but it is less well documented in matters of fertility. This article will review the mechanism of action of common supplements

2. Antioxidants

Aging is known to have an impact on female fertility due to the notable reduction in ovarian reserve as well as the declining oocyte quality. Although the molecular pathways that lead to these processes are not well understood, it is thought that a reduction in DNA repair could contribute to the problem of declining oocyte quality with age. [2] Oxidative imbalance has been linked to oocyte quality especially in women with advanced maternal age and endometriosis. [3]

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Normal metabolism leads to production of reactive oxygen species (ROS). Oxidative stress is the failure to convert ROS to an inactive state. The body's ability to detoxify these products is influenced by the presence of antioxidants. ROS can cause damage to lipid membranes and amino acids, which can lead to DNA damage and replication errors. Mitochondrial dysfunction is linked with higher levels of ROS which is associated with reproductive problems including reduced ovarian reserves, poor oocyte quality and chromosomal errors. [4]

There are many antioxidants that are recommended for those struggling to conceive, particularly those women who suffer with UI often have an abundance of ROS and reduced antioxidants which both contribute to oxidative stress. [5]

i. Co-enzyme Q10

Many aspects of reproduction require a significant amount of energy, including oocyte maturation, fertilization and implantation. During the transition of a primordial follicle into a primary follicle, the energy requirements and consequently the mitochondria markedly increase. [6] Therefore, all aspects of reproduction which require energy can be subject to influence by mitochondrial dysfunction. The potentially harmful effects of oxidative stress can be counteracted by antioxidants such as Co-enzyme Q10, which is a key component involved in the production of energy by oxidative phosphorylation.

Furthermore, co-enzyme Q10 increased the rates of ovulation in women with PCOS who were undergoing clomiphene stimulation.[7] In women having ART, those taking Co-enzyme Q10 had increased number of oocytes, higher fertilisation rate and better quality embryos. [8]

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ii. Melatonin

Melatonin is an antioxidant which can counteract oxidative stress. It has variable functions in the body including regulation of biological rhythms as well as various metabolic affects. Melatonin plays a role in reproduction and can be found in the ovary as well as the placenta. [9] The use of melatonin restored oxidative balance in the follicular fluid of those women having ART. There was an improvement of oocyte quality, consequently there were an increased number of transferable embryos leading to increased pregnancy rates. [10]

iii. Vitamin E

Vitamin E deficiency have been linked with female infertility, as well as pregnancy related complications such as premature delivery, eclampsia and intrauterine growth restriction.[11] Vitamin E supplementation had beneficial effects in women with UI undergoing IVF cycles, women had an improved endometrial thickness. There were higher implantation rates in those women taking vitamin E compared to controls, however the difference was not statistically significant. The impact of Vitamin E supplementation seems to be somewhat variable, there is some evidence that women having ovulation induction in PCOS the use of Vitamin E did not alter pregnancy outcome. [12]

3. Other supplements

i. Zinc, Copper and Selenium

Trace elements such as zinc, copper and selenium are deemed to be essential for health but they also play an important role in reproductive health. There is evidence to suggest roles for these trace elements in pregnancy, such as protein synthesis and cell proliferation.[13]

Copper is commonly found in meats, seafood, as well as nuts and seeds. It is important for energy metabolism and also plays an important role in iron transport.

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Animal studies have shown reduced fertility was associated with copper deficiency. In women undergoing IVF, those who had higher copper levels had more oocytes retrieved with better quality embryos.[14]

Selenium is an essential trace mineral found mainly in seafood, poultry and eggs. Selenium plays an important role in antioxidant defence. It is involved in the formation of thyroid hormones and DNA synthesis, which can have an impact on reproduction. The role of selenium in the preconceptual state has not been studied extensively, however there is some evidence to suggest that selenium is important in follicle growth and maturation. [15] Women with unexplained fertility have been found to have lower levels of selenium and there is evidence to suggest that low selenium levels can impact pregnancy outcomes. [16]

Zinc plays a role in many cellular processes including gene transcription and protein synthesis. Zinc deficiency is known to be related to problems with ovarian development and follicular growth. [17]

ii. Vitamin D

Vitamin D is mainly produced in the skin following sunlight exposure and its predominant role in the body is regulating bone health. There has been much interest in the extra-skeletal effects of vitamin D such as the link between vitamin D insufficiency and many other chronic diseases including diabetes and cardiovascular disease. The presence of Vitamin D receptors in ovarian tissue and the placenta imply its involvement in reproduction. [18] Research on human and animal studies show the impact of vitamin D levels and how different seasons can influence fertility. [19]

Polycystic ovarian syndrome (PCOS) is a common cause of infertility in women. There is increasing evidence to suggest that vitamin D is linked to insulin resistance and other features such as hyperandrogenism commonly found in PCOS. Studies have shown that vitamin D deficiency is closely linked to follicle growth as well as pregnancy outcomes in those suffering with anovulation and undergoing clomiphene stimulation. [20]

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Endometriosis is another common condition associated with infertility. Studies have shown an inverse relationship between vitamin D levels and endometriosis, as women with higher vitamin D levels had 24% lower risk of developing the condition. [21] In women undergoing IVF, those with sufficient vitamin D levels had higher pregnancy and implantation rates compared to those who were vitamin D deficient. [22]

iii. Dehydroepiandrosterone (DHEA)

DHEA is a steroid hormone produced by adrenal glands and ovaries. It is a precursor for hormones such as estradiol and testosterone. Follicles in the ovary have androgen receptors which play pivotal roles in follicular development and therefore fertility. DHEA is known to be involved in early follicular development by increasing FSH receptor expression and prevention of follicular atresia by reducing apoptosis. [23]

DHEA has also been linked with higher serum insulin-like growth factor which in turn has been linked with improved oocyte quality, embryo development and subsequent pregnancy outcomes.[24] Poor ovarian responders are those women who have suboptimal ovarian stimulation in response to gonadotrophins during IVF. DHEA is linked to improved ovarian stimulation in poor ovarian responders and there is evidence to suggest that DHEA supplementation can improve pregnancy and live births in this cohort.

4. Discussion

There is ample information linking supplements with the management of infertility. Considering the important role that supplements play in female reproduction it would be reasonable to assume that restoring micronutrient deficiencies would improve fertility outcomes. Micronutrient deficiencies can result in obstetric complications such as pre-eclampsia and can cause fetal complications including neural tube defects and low birth weight. Women with fertility problems who adopt a balanced diet do improve chances of pregnancy.[25]

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There are many studies promoting the use of antioxidants and various supplements for those struggling to conceive or undertaking assisted reproduction.

The physiological changes in response to some supplements, especially the improvement in oocyte quality is very encouraging. However, there is often lack of good quality evidence in the form of head to head randomised control trials to support this data. [26]

5. Conclusion and Recommendation

The global vitamin market is highly lucrative, generating significant revenue, however often these supplements are mostly unregulated. In the current era of information overload, where there is an abundance of accessible information, it can be a challenge to extract accurate data for health professionals and patients alike.

Infertility is often an incredibly emotive topic, in which couples are often highly motivated to explore alternative remedies and explore any possible options that would increase the chance of pregnancy. The lack of evidence-based research may not deter some couples from exploring any possibility of achieving pregnancy. There is a need for better quality evidence including well designed trials with clear outcome measures. Physicians need to be mindful of the ever-changing practices in fertility management.

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