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Review

Effects of black seeds (*Nigella sativa*) on male infertility: A systematic review

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ABSTRACT

Following an increase in free radicals, DNA damage and lipid peroxidation in human sperm may occur. Antioxidant components in medicinal herbs such as *Nigella sativa* (NS) have been indicated to improve spermatogenesis and steroidogenesis. The aim of the present study was to conduct a systemic review summarizing the effects of NS on male infertility. A number of electronic databases were searched namely Pubmed, Science Direct, Google scholar and Springer from the period January 2000 until June 2014. Searching was limited to articles in the English language. Patents and abstracts from symposiums and congress were excluded because they contained insufficient information for evaluation and comparison with other studies. The outcome of this study indicated that NS can positively influence sperm parameters, semen, Leydig cells, reproductive organs and sexual hormones. The main potential mechanism is through the antioxidant properties of NS. Thymoquinone (TQ) and unsaturated fatty acids are the main antioxidant components of NS. NS and TQ derived from NS can improve male fertility parameters through promoting antioxidant defence. Although the findings of this review suggest that NS is a good candidate for male infertility treatment, there is insufficient evidence to make recommendations for its use as an adjunct therapy in infertile men. More clinical trials are recommended to demonstrate the efficacy of NS on male infertility.

Contents

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1. Introduction

Infertility is defined as an inability of a couple to achieve a pregnancy after 12 months of intercourse without contraception (Gurunath et al., 2011). Infertility among men is more prevalent than among women. It affects almost one in 20 men and male infertility is a factor in about 50% of infertile couples. The remaining 50% is due to female problems, both male and female problems and unknown causes of infertiity (Gurunath et al., 2011). The main aetiologies of male infertility include anatomical abnormalities, some conditions such as varicocele, renal failure and liver cirrhosis, side effects of medications, lifestyle and environmental factors, which may act alone or in combination (Krausz, 2011). About 60% of reasons for infertility are related to sperm dysfunction. Therefore, increasing spermatozoa counts, functionality and sperm quality can improve fertility status (Wright et al., 2014; Agarwal et al., 2014).

The sperm cell membrane includes a large amount of polyunsaturated fatty acids and phospholipids which are vulnerable to oxidative stress (Aitken et al., 2014; Gharagozloo and Aitken, 2011). Oxidative stress has deleterious effects on the structure, function, motility and survival of sperm. Smoking, alcohol ingestion, infection, exposure to environmental toxins or radiation can trigger rising mitochondrial production of reactive oxygen species (ROS) and oxidative stress. Following a rise in free radicals, DNA damage, lipid peroxidation, protein and biomembrane damage in sperm may occur (Aitken et al., 2014; Agarwal et al., 2014). Ingredients with antioxidant properties can transfer electrons to oxidizing agents and inhibit free radical production and sperm damage (Adedara et al., 2014). Antioxidant components have been indicated to improve spermatogenesis and steroidogenesis (Menezo et al., 2014a, 2014b). Current evidence demonstrates that some medicinal herbs can scavenge free radicals and prevent the deleterious consequences of oxidative stress (Sen et al., 2010; Atanassova et al., 2011; Awah et al., 2012). One of the medicinal plants with antioxidant characteristics is *Nigella sativa* (Ismail et al., 2010; Ashraf et al., 2011).

N. sativa (NS), or 'black seeds', is a plant of the Ranunculaceae family. It grows widely in many Middle Eastern countries. Its seed is black in colour and bitter in taste (Randhawa and Alghamdi, 2011). *N. sativa* has many different chemical ingredients including thymoquinone (TQ) (30–48%) (Ahmad et al., 2013), flavonoids, anthocyanins, alkaloids and essential fatty acids, particularly linoleic and oleic acid. It has been traditionally used for the treatment of different diseases such as respiratory and digestive disorders, kidney and liver dysfunction and rheumatism (Ahmad et al., 2013) in different forms (powder, oil and extract) (Paarakh, 2010). Previous studies have indicated many medical properties of black seeds, including immunomodulatory activities as well as anti-inflammatory, antimicrobial and antioxidative effects (Paarakh, 2010; Tembhurne et al., 2014). No toxic effects of NS were observed in animal models (Ahmad et al., 2013) and no serious side effects have been observed in clinical trials (Paarakh, 2010). The aim of the present study was to review the existing literature and assess the effects of NS on male infertility.

2. Materials and methods

The authors searched a number of electronic databases, namely Pubmed, Science Direct, Google scholar and Springer from the period January 2000 until June 2014. The following keywords were selected based on Mesh terms: *N. sativa*, black seeds, infertility, oxidative stress, free radicals, sperm and semen. These keywords were searched individually and in combination. Two reviewers extracted data independently, and then the titles and abstracts of each article were assessed to delete duplication of data. Searching was limited to articles in the English language. Patents and abstracts from symposiums and congress were excluded because they contained insufficient information for evaluation and comparison with other studies. Based on the above criteria, 24 articles were excluded and 13 eligible articles were evaluated in this study (Fig. 1). Characteristics of the evaluated studies have been summarized in Table 1.

3. Results and discussion

Apparently only one clinical trial has evaluated the effects of NS in childless men. Kolahdooz et al., in a randomized double-blind placebo-controlled clinical trial, indicated that 5 mL of NS oil improved sperm count and motility, semen volume, semen pH and its round cells after 2 months treatment in infertile men. The inclusion criteria were as follows: men with abnormal sperm morphology (<30%) or sperm count (less than 20×10^6/mL) or type A and B motility (below 25% and 50%, respectively) who had not received drug or hormone therapy in the past 3 months. The authors reported that the antioxidant properties of NS may neutralize free radicals in semen and improve sperm parameters. Furthermore, the authors noted that NS oil included some unsaturated fatty acids such as linoleic acid (about 60%) and oleic acid (about 20%) which can improve sperm parameters such as sperm count and sperm motility and also reduced abnormal sperms (Kolahdooz et al., 2014).

Based on El-Tohamy et al., a combination of 50% black seeds and 50% common meal (soy protein) fed to rabbits improved reaction time, latency period, semen volume and sperm quality (total sperm, motile sperm, sperm concentration and total functioning sperm fraction) after 29 weeks compared to a diet of mixed seeds and soy protein. In addition, in rabbits fed NS, free radicals, malondialdehyde (MDA), reactive nitrogen species and peroxynitrite in the seminal plasma were lower than in other groups (El-Tohamy et al., 2010). Flavonoids, anthocyanins, carotene, isothiocyanates and carotenoids are antioxidant components of NS which can contribute to antioxidant defence and scavenge ROS (Alenzi et al., 2013). As reported in Mohammad et al.'s study, 300 mg/kg body weight of NS seeds taken for 60 days increased the weight of the reproductive organs, the number of mature Leydig cells, number of spermatocytes, total sperm count and motility in male albino rats. They suggested that the effects of NS on the pituitary gland triggered a rise in spermatogenesis hormones, and that the increase in the weight of reproductive organs proved this fact. Also, the authors found that NS can