

Emerging Therapeutic Importance of Ashwagandha in Stress and Male Reproductive System Via Modulation in Estrogen Receptor

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Abstract

The paper reviews the literature regarding therapeutic use of *Withania somnifera* (Ashwagandha) in stress and infertility in males. It has recently gained recognition as a treatment for infertility as well as stress. Stress may cause infertility and loss of libido in men by inhibiting testosterone. A certain minimum amount of reactive oxygen species is certainly needed for the physiological function of the spermatozoa. The mechanisms of action for the anti-stress and antioxidant properties are not fully understood. Further, the paper reviews the involvement of estrogen receptor and anti-oxidant enzymes in modulating the reproductive potential. The expression of ER α plays a predominant role in mediating estrogen action in response to stress. The results demonstrate that pretreatment with estradiol modulates the response of HPA and HPG axis mediated by reduction in the expression of ER α as a consequence of stress triggered action. Studies have found various constituents of Ashwagandha exhibit a variety of therapeutic effects with little or no associated toxicity. These results are very encouraging and indicate this herb should be studied more extensively to confirm these results and reveal other potential therapeutic effects.

Keywords: *Ashwagandha; Estrogen Receptor Alpha; Infertility; Stress*

Background

Ashwagandha is best known for its stress-lowering effects. The medicinal herb appears to help lower levels of cortisol, a hormone produced by adrenal glands in response to stress. The prevalence of infertility has notably increased over the last decades. Taking into consideration the rising incidence of male factor infertility; researchers have attributed diet, lifestyle and environment factors for the deteriorating semen parameters and reproductive potential [1,2]. Stress is one of the most important contributing factors for effecting reproductive potential. Many studies have reported the cumulative chronic exposure to stress has surged and are being found to have a dramatic impact on individual health. With the background of all these intricacies put together, there are many loop holes and levels at which chronic stress may cause male subfertility. The possible mechanisms of stress affecting fertility may be the hormonal changes due to endocrine disruptor action, generation of oxidative stress or epigenetic modifications. Some studies have suggested that the stress hormone cortisol and the sex hormone testosterone work against each other. Stress may cause infertility and loss of libido in men by inhibiting testosterone. A certain minimum amount of reactive oxygen species is certainly needed for the physiological function of the spermatozoa [3]. However, unfortunately an excess of ROS may cause a catastrophe. Stress of any kind is capable of generating them. At physiological concentrations, reactive oxygen species (ROS) are known to function as key signaling molecules mediating various aspects of sperm function viz., capacitation, acrosome reaction, membrane fluidity and fertilization ability [4]. In addition, it was observed that long-standing exposure to excess ROS compromised sperm chemotactic response, which could be substantially recovered upon treatment with antioxidant [5]. Epigenetic alterations have been reported to cause failure in spermatogenesis. ROS-induces epigenetic

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deregulation of the molecular mechanism(s) involved in spermatogenesis. Aggregation of chromatins and epigenetic modifications play a vital role in spermatogenesis via regulation of molecular pathways to maintain testicular homeostasis [6]. These epigenetic mechanisms consist of histone modification, chromatin remodelling, DNA methylation and miRNA, etc., which reportedly are critical players in spermatogenesis. One such mechanism involves regulation of oxidative stress in the male reproductive system. Traditionally, testosterone and estrogen have been considered to be male and female sex hormones, respectively. However, estradiol, the predominant form of estrogen, also plays a critical role in male sexual function. Estradiol in men is essential for modulating libido, erectile function, and spermatogenesis [7]. Fluctuating hormone levels, such as estradiol might underlie the difference in the prevalence of disorders in men. Estradiol exerts its effects primarily through binding on the two classical estrogen receptor subtypes, alpha (ER α) and beta (ER β). Both receptors have been role in the development of reproductive as well as non-reproductive functions, however, most of the current literature is limited to their role in females. We investigated the role of estrogen receptors on stress-responsiveness in both males and females. The expression of estrogen receptor ER α can be modulated by both stress and estrogen [8]. Administration of estradiol in stress decreases corticosterone induced sensitivity mediated by an increased expression of ER α in brain, ovary and shell gland in avian model. Abundant expression of ER α has been observed in the shell gland of egg laying birds while stress and estrogen antagonist tamoxifen down-regulates its expression [9]. Thus, the expression of ER α plays a predominant role in mediating estrogen action in response to stress and tamoxifen. Ashwagandha administered in male chicks increases the expression of estrogen receptor alpha when stress had decreased it. The quality of sperms affected due to stress is improved by administering Ashwagandha. The treatment with *W. somnifera* effectively reduced oxidative stress, as assessed by decreased levels of various oxidants and improved level of diverse antioxidants. Moreover, the levels of T, LH, FSH and PRL, good indicators of semen quality, were also reversed in infertile subjects after treatment with the herbal preparation [10]. Stress induced ROS generation, DNA damage and their adverse effect on sperm is a latest knowledge in research, however their utility in clinical evaluation and effect of this damage at protein level is still unexplored. Therefore, a proteomic study may act as an excellent tool for understanding the molecular mechanisms that regulate sperm functions.

Conclusion

Our findings indicate an involvement of estrogen receptor alpha in the development of stress-mediated behaviors as well as estrogen activation responses suggesting that these receptors might act as potential treatment targets in a specific manner. In a nut shell, stress has an unfavorable impact on the male gametogenesis. The quality of sperms at both at the genetic and epigenetic end are affected; along with the deteriorating sperm quantity. All these factors assembled together form a poor quality embryo with a decreased survivability to a term pregnancy. The study adds to the evidence on the therapeutic value of Ashwagandha (*Withania somnifera*), as attributed in Ayurveda for the treatment of infertility. The research findings of Ashwagandha will definitely benefit the field of reproductive biology, as it might improve our understanding of underlying processes in infertility and narrow down the number of cases diagnosed.

Bibliography

1. Kumar N and Singh A. "Trends of male factor infertility, an important cause of infertility: A review of literature". *Journal of Human Reproductive Sciences* 8.4 (2015): 191.
2. Jungwirth A, et al. "European Association of Urology Guidelines on Male Infertility: The 2012 Update". *European Urology* 62.2 (2012): 324-332.
3. Agarwal A and Allamaneni SS. "Free radicals and male reproduction". *Journal of the Indian Medical Association* 109 (2011): 184-187.
4. Bansal AK and Bilaspuri GS. "Impacts of oxidative stress and antioxidants on semen functions". *Veterinary Medicine International* (2011): 1-7.
5. Sánchez R, et al. "Human sperm chemotaxis depends on critical levels of reactive oxygen species". *Fertility and Sterility* 93 (2010): 150-153.

6. Sharma P, *et al.* "Epigenetics and oxidative stress: A twin-edged sword in spermatogenesis". *Andrologia* 51.11 (2019): e13432.
7. Schulster M., *et al.* "The role of estradiol in male reproductive function". *Asian Journal of Andrology* 18 (2016): 435-440.
8. Niranjan MK and Srivastava R. "Expression of estrogen receptor alpha in developing brain, ovary and shell gland of Gallus gallus domesticus: Impact of stress and estrogen". *Steroids* 146 (2019): 21-33.
9. Niranjan MK, *et al.* "Expression of estrogen receptor alpha in response to stress and estrogen antagonist tamoxifen in the shell gland of Gallus gallus domesticus: involvement of anti-oxidant system and estrogen". *Stress* (2020).
10. Ahmad MK, *et al.* "Withania somnifera improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males". *Fertility and Sterility* 94.3 (2010): 989-996.

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