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Short Communication

The use of pentoxifylline in male reproduction abnormalities

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Abstract

Pentoxifylline a derivative of methylxanthine and nonspecific inhibitor of the phosphodiesterase with vasodilatory properties and rheological properties on blood that made it useful in the treatment of intermittent claudication. Pentoxifylline also has an immunomodulatory effect which inhibits on the production inflammatory cytokines including tumor necrosis factor-alpha. The aim of this paper is to review the uses of pentoxifylline in male reproduction abnormalities.

The available research evidence suggests that the addition of pentoxifylline to the traditional treatment of erectile dysfunction can be helpful, it also beneficial in the treatment of oligo-asthenozoospermia, possibly through stimulation of sperm motility by increasing the intracellular levels of cAMP.

Keywords: pentoxifylline; male reproduction; methylxanthine

Introduction

Allenby and colleagues (1991) reported three impotent patients with claudication of the lower limbs whom were treated with pentoxifylline, and spontaneously reported improved sexual function [1].

Korenman and Viosca (1993) reported a controlled study which included males with mild to moderate penile vascular insufficiency causing impotence whom were treated with pentoxifylline 400 mg twice daily for 12 weeks. Pentoxifylline treatment regularly increased the penile-brachial pressure index frequently into the normal range, in comparison with patients who received placebo. In 9 of 12 patients, pentoxifylline treatment was associated with reestablishment of coital function [2].

Peşkircioğlu (1996) reported a study which included 36 patients with borderline arterial disease diagnosed with penile duplex ultrasonography. Twenty patients (Aged 40-66 years, mean age 54 years) were treated with oral 400 mg three times daily for 2 months. Sixteen patients (34-65, mean age 54 years) received a placebo. Pentoxifylline treatment increased peak systolic velocities on penile duplex ultrasonography in 12 of the 20 , and the mean change in peak systolic velocities caused by pentoxifylline treatment (6.25 cm/s) was considerably higher than the observed in the control patients (0.38 cm/s). Seven patients treated by pentoxifylline had successful coitus. Treatment was not associated with side effects [3].

Ozdal et al (2008) reported a study which included 68 patients with various degrees and types of vasculogenic erectile dysfunction who were treated initially with oral sildenafil (minimum two 50-mg tablets/week), 60 minutes before sexual intercourse for four weeks. Thereafter, pentoxifylline 400 mg three times daily was to the treatment for the next four weeks period. The mean international index of erectile function score was higher after sildenafil treatment than before treatment score. The mean international index of erectile function score was higher after the combination treatment compared to pre-treatment score. The increase in international index of erectile function score was 5.62+/-2.08 with sildenafil treatment, but the score increased 9.51+/-3.77 with the combination therapy. (P<0.001). Ozdal et al suggested the use of sildenafil citrate and pentoxifylline combined therapy in the treatment of patients with vasculogenic erectile dysfunction [4].

Kumar et al (2015) reported a study which included 237 patients having erectile dysfunction whom were treated with tadalafil or tadalafil + pentoxifylline for 8 weeks. 78.6% of the patients treated with tadalafil reported improvement. 86.6% of the patients treated with tadalafil + pentoxifylline reported improvement. There was no significant difference in between the two groups with regards to occurrence of side effects [5].

Aparicio and colleagues (1980) reported a study which included 15 infertile men (aged 22 to 44 years) with normogonadotropic asthenozoospermia who were treated with pentoxifylline 1200 mg daily for at least four months. Treatment was associated with marked improvement of the percentages of forwardly progressive spermatozoa and of live and motile spermatozoa. Five of the patients experienced

normalization of semen, and seven experienced improvement in comparison to pre-treatment values. Pregnancy was achieved in two patients [6].

Schill (1980) reported a study which included 25 males with idiopathic asthenozoospermia and 40 males with idiopathic normogonadotropic oligozoospermia whom were treated with oral pentoxifylline 1200 mg daily for three months. Treatment was associated with considerable increase of progressive sperm motility in patients with asthenozoospermia, and the conception rate was 37%. Patients with normogonadotropic experienced only a small transitory increase of the ejaculate volume and seminal plasma fructose level, and the conception rate 17%. Schill suggested that the mode of action of pentoxifylline involve an improvement of the microcirculation within the epididymis and the male accessory sexual glands which possibly resulted in improved epididymal sperm maturation [7].

Marrama et al (1985) reported a study which included 22 young males (mean age 28.4 years) with idiopathic oligo-asthenozoospermia whom were treated oral pentoxifylline 1200 mg daily for six months. Treatment was associated with marked increase in sperm count and motility. Sperm count increased a 1.5-fold (p less than 0.01) at the third month of treatment, increased a 2.0-fold (p less than 0.001) at the sixth month of treatment. Sperm motility increased by 1.8-fold (p less than 0.001) at the third month of treatment, and increased by 2.8-fold (p less than 0.001) at the sixth month of treatment. After treatment, fructose level in seminal fluid were considerably higher (p less than 0.001) than before. Sperm ATP level was markedly lower after treatment (p less than 0.05). Marrama et al suggested that pentoxifylline may have a beneficial effect on the cAMP metabolism, and can be useful in the treatment of idiopathic oligo-asthenozoospermia. [8].

Merino et al (1997) reported a controlled study which included 47 males with normogonadotropic men with idiopathic asthenozoospermic. Twenty-five patients were treated with pentoxifylline 1200 mg daily during 6 months, and 22 patients receive placebo. Pentoxifylline treatment increased sperm motility from 25.5 (21.0-30.0) to 35.5 (31.5-39.0) ($p < .00001$), and to 42.0 (38.0-46.0) ($p < .00001$) after 3 and 6 months respectively. Changes in the control patients were less significant. Additionally, pentoxifylline increased progressive motility from 2.5 (0.0-6.0) to 12.0 (6.0-19.5) ($p < .001$) at 3 months, and to 22.5 (17.0-26.0) at 6 months ($p < .00001$) [9].

Oliva et al (2009) reported the treatment of thirty-six males with varicocele-associated infertility with oral pentoxifylline with zinc and folic acid for 12 weeks. Treatment was associated with marked increase in the proportion of morphologically normal sperm cells [10].

Safarinejad (2011) reported a double-blind study which included 254 infertile males. 127 patients were treated with pentoxifylline 400 mg twice daily for six months, 127 received placebo. Treatment was associated with marked increase in sperm count, sperm motility, and sperm with normal morphology, while the controlled patients experience a subtle decrease in these parameters [11].

Azgomi et al (2018) reported a study which include 100 males with infertility of unknown cause whom were treated with either pentoxifylline 800 mg/daily or Withania somnifera herbal capsules (5 g/daily) for 90 days. Pentoxifylline increased mean semen volume (16.46%), progressive motility (25.97%) and improved sperm morphology (13.28%). Withania somnifera also increased mean sperm count (12.5%) and progressive motility (21.42%) and improved sperm morphology (25.56%) [12].

Conclusion

The available research evidence suggests that the addition of pentoxifylline to the traditional treatment of erectile dysfunction can be helpful, it also beneficial in the treatment of oligo-asthenozoospermia, possibly through stimulation of sperm motility by increasing the intracellular levels of cAMP.

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