



PIC QUESTION OF THE WEEK: 10/15/07

Q: Can any medications produce oligospermia?

A. Four different mechanisms have been associated with drug-induced male infertility: direct gonadotoxic effects, alteration of the hypothalamic-pituitary gonadal (HPG) axis, impairment in erectile function and ejaculation, and a decrease in libido. The first two mechanisms can produce oligospermia, a subnormal sperm count in the ejaculate. Other factors that negatively affect spermatogenesis include increased temperature as well as urologic, endocrine, and genetic disorders. Medications implicated as causing oligospermia include the 5-aminosalicylates sulfasalazine and mesalamine, 5-alpha-reductase inhibitors, anabolic steroids, ketoconazole, and chemotherapeutic agents. One of the medications classically associated with oligospermia is sulfasalazine, a compound used to treat inflammatory bowel disease (IBD) and rheumatoid arthritis. The sulfapyridine metabolite of sulfasalazine is most likely responsible for the associated oligospermia. This adverse effect may be related to a decrease in spermatogenesis caused by the drug's anti-folate activity. The incidence of oligospermia associated with sulfasalazine may be as high as 70%. It appears to be fully reversible with complete spermatogenesis returning approximately 3 months following discontinuation of therapy. Because of the recurrent nature of IBD, it may be difficult to discontinue sulfasalazine. Limited data suggests that treatment with mesalamine is less likely to affect spermatogenesis; however, this precaution is still included in the labeling for mesalamine products. Oligospermia associated with 5-alpha reductase inhibitors (dutasteride and finasteride) is attributed to reduction of spermatogenesis due to decreased serum dihydrotestosterone levels. In one study, both drugs produced a significant but *transient* (~ 26 weeks) decrease in sperm count compared to placebo. Anabolic steroids affect fertility by interfering with the HPG axis through feedback inhibition. Ketoconazole doses greater than 400 mg daily may produce oligospermia by reducing testosterone secretion. Finally, chemotherapeutic agents can cause oligospermia through damage to germinal epithelium and Sertoli cells and subsequent effects on the HPG axis. Chemotherapeutic agents vary in gonadotoxicity and regimens can be tailored to be less toxic and allow for greater spermatogenetic recovery. Excluding chemotherapeutic and hormonal agents, sulfasalazine appears to be the most frequently implicated drug-induced cause of oligospermia.

References:

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The PIC Question of the Week is a publication of the Pharmaceutical Information Center, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA 15282 (412.396.4600).