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Therapeutic Medications and Male Fertility

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Abstract

While many studies have evaluated the effect of medications on semen quality, there is little guidance as to what is the true impact of many medications on male fertility. Further well designed studies are required to elucidate the precise associations between certain therapeutic medications and their effect on male fertility.

Keywords: Semen; Medications; Infertility

Text

Male factor infertility (MFI) is a common cause of infertility. Only recently has more attention been given to the underlying causes of MFI including the association between semen parameters and certain medications. Establishing clear relationship between medications and MFI, however, is challenging on several levels. Consequently, there are few recommendations regarding which pharmaceuticals may have a deleterious effect on male fertility and how to modify the administration of potentially problematic medications in male infertility patient to maximize pregnancy outcomes.

The number of couples seeking counsel for problems with infertility has steadily increased over the past decade, affecting 10-15% of the sexually active population [1,2]. MFI contributes to approximately 50% of all infertility [2-4]. MFI is generally diagnosed through an abnormal semen analysis (SA). While the SA has multiple measured parameters, the most important are abnormalities in sperm count, ranging from fewer than normal sperm (oligospermia) to no detected sperm (azoospermia), sperm motility, a condition known as asthenospermia, and sperm morphology [5,6]. The relative importance of each of these parameters, among other measures of semen quality, is constantly a subject of debate within the fertility community [5,7]. Further complicating matters is the poor reproducibility of the SA as an assessment of sperm quality and quantity. Indeed, data has shown that, the within-subject, inter-ejaculate coefficients of variation for sperm concentration and motility are estimated to be as high as 44% and 15% respectively [8]. Intra sample variability is commonly reported among all men who provide multiple sequential semen analyses.

Furthermore, the number of days a man abstains from ejaculating prior to the semen analysis may affect the results of the evaluation in terms of sperm concentration and sperm quality [9,10]. A myriad of other factors may also affect semen parameters including aging, stress, and even seasonal variation [11-13]. Therefore many of the trials that evaluate this topic are inherently limited by these variations and would require relatively large sample sizes to minimize their impact. The majority of these studies, however, used relatively small sample sizes and, with few exceptions, failed to give specific details regarding the days of abstinence, age of subjects, and other factors that could certainly impact semen quality and quantity.

Another variable that can be modified by researchers to a large extent is time. The entire process of spermatogenesis can last anywhere between 45 and 60 days. However, the most crucial final stage between the transitions of spermatids to motile spermatozoa requires about 2 weeks for completion [14]. With this knowledge in mind, it is important that any effect of medications on semen quality can be measured after significant time has elapsed since administration. Therefore, it is possible that events, even several months prior to the ejaculate, could affect the semen quality and quantity. Additionally, many studies evaluating the effect of medications on semen quality do not evaluate different doses of medications tested, precluding the ability to determine if there is a dose depended relationship between the drug in question and the SA parameters. These factors confound the ability to establish a firm cause and effect relationship between a suboptimal SA and exposures to specific medications.

A further limitation of many of these studies is the lack of determining if an alteration documented in semen quality or quantity translates into a tangible deleterious effect on the ability to achieve pregnancy or is correlated to possible birth defects in the offspring produced. Rather, the vast majority of the studies reviewed focused solely on the semen parameters as the endpoint. Without establishing if these medications confer a decreased fertility rate, labeling a medication as having an effect on MFI *per se* seems premature.

Another drawback from many clinical trials is the absence of a placebo medication or a control group. Most often, researchers compared collected samples to normal WHO criteria for healthy males. Even though the WHO criteria likely serves as a fair representation for normal male characteristics, the absence of a control group increases the likelihood of ignoring an important confounding variable in a certain trial. As such, to eliminate any chance of bias and provide more certainty to the results, researchers should seek to limit confounding variables to the best of their capabilities.

Despite these design limitations, the literature does suggest that certain medications may, in fact, prove detrimental to male reproductive potential. Specifically, there is good data that selective serotonin reuptake inhibitors (SSRIs), calcium-channel blockers (CCBs), certain alpha-adrenergic blockers (AABs), and highly active antiretroviral therapy (HAART) medications certainly could contribute to MFI [15-21]. However, many men still father healthy children even while taking medications. Therefore, as the detrimental effects of these medications

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were never universally observed, counseling men taking these medications should include discussing the risk that the medications may, but also may not, pose to their reproductive health. In many instances, the detrimental aspects of these drugs on semen parameters is likely outweighed by the significant medical benefit conferred to taking the medications, especially in life-extending treatments such as HAART.

The association between MFI and exposure to pharmaceutical compounds has also recently been explored and is surely a subject to generate more research and discussion in the years to come. In addition to the semen analysis parameters, whether sperm function is potentially compromised by taking or exposing pharmaceutical agents or compounds is an extended open field for investigation. Indeed, SA certainly does not evaluate many of the parameters of sperm that may impact MFI such as an intact acrosome reaction [8]. Future exploration into this field must relate the effect that medications may or may not have, not only on semen parameters, but also on the ability to actually father a child.

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