

Effects of selective serotonin reuptake inhibitors on sperm and male fertility

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Abstract

Question Some of my male patients who are taking antidepressants are planning to become fathers. Do selective serotonin reuptake inhibitors (SSRIs) affect sperm, causing either decreased fertility or increased risk of congenital anomalies?

Answer There is limited evidence regarding paternal SSRI use before conception and its effects on reproductive outcomes; however, there might be some increased risk of subfertility based on animal studies and sperm-quality studies. There are insufficient data at this time to change prescribing practices of SSRIs in men who are hoping to become fathers.

Effets des inhibiteurs sélectifs de la recapture de la sérotonine sur le sperme et sur la fertilité masculine

Résumé

Question Certains de mes patients qui prennent des antidépresseurs projettent d'avoir un enfant. Les inhibiteurs spécifiques de la recapture de la sérotonine (ISRS) affectent-ils le sperme et peuvent-ils causer soit une diminution de la fertilité ou encore une augmentation des risques d'anomalies congénitales?

Réponse Il existe peu de données probantes concernant l'utilisation d'ISRS avant la conception chez les hommes souhaitant procréer et leurs effets sur la reproduction; par contre, il pourrait y avoir une augmentation des risques d'hypofertilité selon des études effectuées sur des animaux et la qualité du sperme. Il n'y a pas suffisamment de données en ce moment qui justifieraient qu'on change les pratiques concernant la prescription d'ISRS chez les hommes qui souhaitent devenir pères.

Despite a large increase in the number of studies documenting the effects of maternal medication use on pregnancy outcomes, there remains a relatively large void in studies on paternal exposures and reproductive outcomes. A few studies of exposures in men have suggested that radiation increases the risk of pregnancy loss and stillbirths^{1,2}; organic solvents increase the rate of congenital malformations³ and neural tube defects,⁴ decrease the vitality and mobility of sperm,⁵ and lower the success rates of in vitro fertilization⁶; and chemotherapeutic agents increase chromatin damage in human sperm.⁷ Therefore, more research is needed to better understand the effects of paternal exposures on sperm and reproductive outcomes.

Paternal use of selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are very commonly prescribed. In fact, a Dutch database study found that 13.6 per 1000 fathers took SSRIs in the 6

months before conception.⁸ Given that spermatogenesis takes approximately 74 days, the fact that fathers taking SSRIs represent the fathers of more than 300 children in this study is reassuring.

Studies that specifically investigated the effects of paternal SSRI use on reproductive outcomes are very sparse. There have been a few animal studies⁹⁻¹¹ and 5 studies in humans¹²⁻¹⁶ that evaluated the effects of SSRIs on sperm. Only one of these, a case report, looked at reproductive outcomes other than semen parameters.¹³ There are no studies in humans that evaluate the effects of paternal SSRI use on the fetus.

In an animal study fluoxetine decreased spermatogenesis, sperm motility, and sperm density. It also decreased the weight of male reproductive organs and decreased testosterone and follicle-stimulating hormone levels. Finally, the study found that there was a decrease in the number of pregnancies and in the number of viable fetuses with paternal fluoxetine use.⁹ In another study evaluating fluoxetine in mice, there were increases

in sister chromatid exchanges and sperm abnormalities that were dose dependent. There was also a decrease in sperm count and sperm motility in the fluoxetine groups compared with control mice.¹⁰ Similarly, a study of citalopram in mice found that there was an increase in DNA strand breaks and oxidative DNA damage in sperm.¹¹ Neither of these studies specifically evaluated reproductive outcomes.

In humans, the first report to implicate SSRIs in reduced fertility was a case report with 2 cases: the first man was taking citalopram and had oligozoospermia and decreased motility but these parameters returned to the normal range 1 month after discontinuation of citalopram. The second man was taking sertraline and had decreased sperm concentration and motility, and again the parameters returned to normal 3 months after ceasing sertraline.¹³

A follow-up study of 35 healthy men found that there was an association between paroxetine use (for 5 weeks) and DNA fragmentation that would not have been detected with routine fertility screening. The authors suggested that changes to sperm DNA integrity might negatively affect men's fertility but did not measure this directly.¹²

Three additional studies on human sperm suggested reduced concentration and motility and altered morphology with escitalopram¹⁴ and any SSRI,¹⁵ and reduced motility with any SSRI.¹⁶ In each of the above studies and in subsequent reviews¹⁷ it was concluded that the abnormal semen parameters (decreased sperm concentration and motility, and damaged DNA) and quick recovery upon discontinuation could be due to SSRIs negatively affecting sperm transport. They also all stated that more studies are necessary before a clinical conclusion can be drawn.

Conclusion

At this time there is no evidence regarding paternal SSRI use and fetal outcomes, so this should be an area of future study. More studies are required to determine if changes in semen parameters result in decreased fertility. If a patient presents with decreased fertility and is taking an SSRI, reducing the dosage might have a benefit; however, we do not recommend refraining from providing men with necessary medical treatment, particularly if there are no fertility issues, based on this evidence alone.



Competing interests

None declared

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MOTHERISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in

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