MedicalXpress

Taking ibuprofen for long periods found to alter human testicular physiology

January 9 2018, by Bob Yirka

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A team of researchers from Denmark and France has found that taking regular doses of the pain reliever ibuprofen over a long period of time can lead to a disorder in men called compensated hypogonadism. In their

paper published in *Proceedings of the National Academy of Sciences*, the group describes their study, which involved giving the drug to volunteers and monitoring their hormones and sperm production.

To learn more about the possible impacts of the popular anti-inflammation drug Ibuprofen on male fertility when taken for long periods of time, the researchers asked 31 men between the ages of 18 and 35 to take 600 milligrams (three tablets) a day of the drug for six weeks. Other volunteers were given a placebo. Over the course of the study, the volunteers were tested to see what impact the drug had on their bodies.

The researchers report that just two weeks into the study, they found that all of the volunteers had an increase in luteinizing hormones, which the male body uses to regulate the production of testosterone. The increase indicated that the drug was causing problems in certain cells in the testicles, preventing them from producing testosterone, which is, of course, needed to produce sperm cells. They further report that the change caused the pituitary gland to respond by producing more of another hormone, which forced the body to produce more testosterone. The net result was that overall testosterone levels remained constant, but the body was overstressing to compensate for the detrimental impact of the Ibuprofen—a state called compensated hypogonadism.

The researchers note that while compensated hypogonadism can cause a temporary reduction in the production of sperm cells, reducing fertility, it is generally not cause for alarm. What is more of a concern, they note, is using the drug for longer periods of time. It has not been proven yet, but the researchers suspect such use, as is seen with some professional athletes or others with chronic pain issues, might lead to a condition called overt primary hypogonadism, in which the symptoms become worse—sufferers report a reduction in libido, muscle mass and changes in mood. Additional studies are required, they note, to find out if this is,

indeed, the case.

More information: David Møbjerg Kristensen et al. Ibuprofen alters human testicular physiology to produce a state of compensated hypogonadism, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1715035115

Abstract

Concern has been raised over increased male reproductive disorders in the Western world, and the disruption of male endocrinology has been suggested to play a central role. Several studies have shown that mild analgesics exposure during fetal life is associated with antiandrogenic effects and congenital malformations, but the effects on the adult man remain largely unknown. Through a clinical trial with young men exposed to ibuprofen, we show that the analgesic resulted in the clinical condition named "compensated hypogonadism," a condition prevalent among elderly men and associated with reproductive and physical disorders. In the men, luteinizing hormone (LH) and ibuprofen plasma levels were positively correlated, and the testosterone/LH ratio decreased. Using adult testis explants exposed or not exposed to ibuprofen, we demonstrate that the endocrine capabilities from testicular Leydig and Sertoli cells, including testosterone production, were suppressed through transcriptional repression. This effect was also observed in a human steroidogenic cell line. Our data demonstrate that ibuprofen alters the endocrine system via selective transcriptional repression in the human testes, thereby inducing compensated hypogonadism.

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