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Congenital anomaly linked to paracetamol

Danish data show small rise in risk with prolonged use of painkiller in pregnancy



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Expectant mothers who take the painkiller paracetamol (acetaminophen) frequently during certain periods of pregnancy may face a small rise in the risk of giving birth to a boy with a genital problem, according to research published online in the November issue of *Epidemiology*.

The study is the first to link exposure to the drug with cryptorchidism, a common condition where a testis is obscure or completely hidden, which affects at least 3% of boys in the UK and the USA.

In Denmark, where the prevalence ranges from 2–3%, a team of epidemiologists led by Morten Søndergaard Jensen used national data to estimate a 30% increase in the probability of a boy being born with cryptorchidism if the mother took paracetamol in both the first and second trimester, or for more than four weeks. This included periods when the foetus is thought to be vulnerable to the condition.

Jensen points out that the actual difference in risk is small — with a 2% prevalence of the condition in babies unexposed to the drug rising to 2.6% in those who were exposed. He also calls for the study to be replicated, to rule out the possibility that the association is a false-positive result. But he believes the finding warrants cautioning women to limit their use of the painkiller during pregnancy.

"We do not want to 'scare' pregnant women to use other analgesics," says Jensen in an email to EHTF News, pointing out that the alternatives are no safer. "But it may be an idea to recommend pregnant women to restrict the use of acetaminophen / paracetamol when possible."

The cause of cryptorchidism is unknown, but scientists believe the risk rises with maternal exposures related to lifestyle, such as smoking, and environmental contaminants. Previous studies suggest that certain drugs — acetaminophen, ibuprofen, and acetylsalicylic acid — can disrupt the production of androgenic hormones that have a key role in the normal development of testes.

Jensen and colleagues saw that no research had looked into the effect of these drugs in pregnancy, and probed the link after an earlier study into congenital abnormalities as a group revealed a significant association with exposure to acetaminophen in the first trimester.

The team used two national databases, extracting data about diagnosis of the condition, and exposure to all three drugs for nearly 1000 boys born to women who were pregnant between 1996 and 2002.

To measure exposure, the researchers found out which painkillers the expectant mothers used, at which point in their pregnancy, and how often. The women gave this information in a questionnaire when they enrolled in the birth registry, and then again on two separate occasions: in two telephone interviews during pregnancy, and an additional interview six months after they gave birth.

Accounting for other risk factors for cryptorchidism, including the mother's age and any treatment for infertility, the analysis shows that the risk of having the condition was significantly higher in the group exposed to acetaminophen, but neither of the other painkillers.

Nearly half the women included in the national database reported having used acetaminophen at least once during pregnancy. Use of ibuprofen and acetylsalicylic acid was uncommon.

"Our study indicates that cumulative acetaminophen exposure of more than 4 weeks' duration, especially during the first and second trimesters, may moderately increase the occurrence of cryptorchidism," write Jensen and colleagues.

The authors didn't have enough data to examine the risk specifically for exposures that occurred from 8–14 gestational weeks, when male sexual characteristics develop in the womb. But they note that the association with cumulative doses of the drug was valid for exposures in that period.

Reference and link

1. Jensen MS, Rebordosa C, Thulstrup AM, Toft G, Sørensen HT, Bonde JP, et al. Maternal use of acetaminophen, ibuprofen, and acetylsalicylic acid during pregnancy and risk of cryptorchidism. *Epidemiology* 2010; 21:779–85. doi: [10.1097/EDE.0b013e3181f20bed](https://doi.org/10.1097/EDE.0b013e3181f20bed)

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