Prolonged exposure to acetaminophen during pregnancy reduces testosterone production by the human fetal testis

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Congenital anomalies are a major cause of infant morbidity and mortality, and a significant proportion of these anomalies involve urogenital malformations (1). As fetal testosterone has crucial importance in the development of the male reproductive system, any disruption in its production can result in disorders such as hypospadias, cryptorchidism or testicular cancer (2).

The risk of congenital malformation, including urogenital abnormalities, is increased by the administration of medical treatments during pregnancy (3). Weak analgesics, particularly acetaminophen containing over-the-counter drugs, are widely used among pregnant women in Europe and North America (4). However, recent studies have demonstrated that these analgesics may impair fetal testicular hormone production (5,6) and increase the risk of cryptorchidism in the offspring (7). Moreover, some have reported that this risk is even further promoted by the combination of acetaminophen-containing medications with other analgesics (5).

In an elegant study, van den Driesche *et al*. (8) demonstrated that protracted exposure of xenografted human testes to a therapeutic dose of acetaminophen decreased the plasma levels of testosterone, as well as decreased the weight of seminal vesicles in castrated host mice. After recording a significant reduction in both Cyp11a1 and Cyp17a1 mRNA expression after the final dose of acetaminophen administration via reverse transcription polymerase chain reaction, the authors concluded that the acetaminophen-induced testosterone reduction may result from the reduced quantities of these key steroidogenic enzymes (8).

With these important findings, the study of van den Driesche *et al*. (8) sheds light to the unknown aspects of the impact of endocrine disrupting compounds on fetal testosterone production. The detrimental effect of widely used acetaminophen containing analgesics on testosterone production must be taken into consideration by policy makers in order to heighten public awareness regarding the potential teratogenic effects of these over-the-counter analgesics. Meanwhile, researchers should corroborate the findings of this study in order to develop further preventive measures, if necessary.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Dolk H, Loane M, Garne E. The prevalence of congenital anomalies in Europe. Adv Exp Med Biol 2010;686:349-64.

2. Virtanen HE, Rajpert-De Meyts E, Main KM, et al. Testicular dysgenesis syndrome and the development and occurrence of male reproductive disorders. Toxicol Appl Pharmacol 2005;207:501-5.
3. Jentink J, Loane MA, Dolk H, et al. Valproic acid monotherapy in pregnancy and major congenital malformations. N Engl J Med 2010;362:2185-93.
4. Headley J, Northstone K, Simmons H, et al. Medication use during pregnancy: data from the Avon Longitudinal Study of Parents and Children. Eur J Clin Pharmacol 2004;60:355-61.
5. Kristensen DM, Lesné L, Le Fol V, et al. Paracetamol (acetaminophen), aspirin (acetylsalicylic acid) and indomethacin are anti-androgenic in the rat foetal testis. Int J Androl 2012;35:377-84.
6. Snijder CA, Kortenkamp A, Steegers EA, et al. Intrauterine exposure to mild analgesics during pregnancy and the occurrence of cryptorchidism and hypospadia in the offspring: the Generation R Study. Hum Reprod 2012;27:1191-201.
7. Jensen MS, Rebordosa C, Thulstrup AM, et al. Maternal use of acetaminophen, ibuprofen, and acetylsalicylic acid during pregnancy and risk of cryptorchidism. Epidemiology 2010;21:779-85.
8. van den Driesche S, Macdonald J, Anderson RA, et al. Prolonged exposure to acetaminophen reduces testosterone production by the human fetal testis in a xenograft model. Sci Transl Med 2015;7:288ra80.

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