

SPOTLIGHT COMMENTARY

Spotlight Commentary: Medicines use during pregnancy and harmful effects on offspring

Medicines use during the pregnancy can have a potentially negative impact on offspring because most medicines taken during pregnancy cross the placenta and reach the foetus. Safety concerns about the common medicines such as antibiotics, antidepressants, and paracetamol have been raised in postmarketing studies.

A nested case-control study with 77 429 pregnancies which included 7039 spontaneous abortions and 70 390 controls in the Quebec Pregnancy Cohort was published recently in the *British Journal of Clinical Pharmacology*.¹ They reported that trimethoprim-sulfamethoxazole (TMP-SMX) exposure during pregnancy was associated with an increased risk of spontaneous abortion (adjusted odds ratio 2.94, 95% confidence interval (CI) 1.89–4.57, 25 exposed cases). This strong association was unlikely to be biased by unmeasured confounding factors.

A study conducted in France found that about a quarter of pregnant women took antidepressants² and this highlights the potential safety concern about the offspring of these pregnant women. However, decisions regarding the use of antidepressants during pregnancy are complex and requires balancing the risks and benefits of the medications on both mother and child. The association between antidepressants in pregnancy and risk of attention-deficit/hyperactivity disorder in children has been reported in the literature.³ Zhao and colleagues conducted a systematic review and meta-analysis of cohort studies on the association between maternal fluoxetine use during the first trimester of pregnancy and congenital malformations in infants.⁴ Fluoxetine use was associated with increased risks of major malformations (relative risk (RR) 1.18, 95% CI, 1.08–1.29), cardiovascular malformations (1.36, 95% CI, 1.17–1.59), septal defects (1.38, 95% CI, 1.19–1.61), and non-septal defects (1.39, 95% CI, 1.12–1.73) with low heterogeneity in infants. No significant observations of other system-specific malformations were found from this review articles.

Paracetamol is a commonly used medicine to treat pain and reduce a high temperature. A 25 case series review article⁵ reported that a causal relationship between maternal paracetamol intake and fetal ductus arteriosus constriction or closure is likely according to the World Health Organization Uppsala Monitoring Centre (WHO-UPC) causality tool (one case was classified as unlikely, nine as possible, 11 as probable and four as certain). The authors concluded that the findings suggest that pharmacovigilance studies on paracetamol safety

during pregnancy are warranted to quantify the risk of such event and put the current findings into clinical perspective.

The public should recognize the potential risk to offspring when pregnant women take any medicines should be highlighted to the general population. Due to the nature of observational studies, the results should be interpreted cautiously, especially any weak associations. More well designed studies are required to investigate the medicine safety issues in pregnant women.

COMPETING INTERESTS

There are no competing interests to declare.

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REFERENCES

1. Muanda FT, Sheehy O, Bérard A. Use of trimethoprim-sulfamethoxazole during pregnancy and risk of spontaneous abortion: a nested case control study. *Br J Clin Pharmacol*. 2018;84(6):1198–1205. <https://doi.org/10.1111/bcp.13542>
2. Bénard-Larivière A, Pambrun E, Sutter-Dallay AL, et al. Patterns of antidepressant use during pregnancy: a nationwide population-based cohort study. *Br J Clin Pharmacol*. 2018;84(8):1764–1775. <https://doi.org/10.1111/bcp.13608>
3. Man KKC, Chan EW, Ip P, et al. Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder in offspring: population based cohort study. *BMJ*. 2017;357:j2350. <https://doi.org/10.1136/bmj.j2350>
4. Gao SY, Wu QJ, Zhang TN, et al. Fluoxetine and congenital malformations: a systematic review and meta-analysis of cohort studies. *Br J Clin Pharmacol*. 2017;83(10):2134–2147. <https://doi.org/10.1111/bcp.13321>
5. Allegaert K, Mian P, Lapillonne A, et al. Maternal paracetamol intake and fetal ductus arteriosus constriction or closure: a case series analysis. *Br J Clin Pharmacol*. 2019;85(1):245–251. <https://doi.org/10.1111/bcp.13778>