Commentary: medication during pregnancy and negative impact on offspring

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Medication use during the pregnancy has potential negative impact on offspring because most medicines taken during pregnancy cross the placenta and reach the baby. Safety concerns about the common medicines such as of antibiotic medications, antidepressants and paracetamol have been raised in postmarketing studies.

A nested control study with 77 429 pregnancies including 7039 cases of spontaneous abortions and 70 390 controls within the Quebec Pregnancy Cohort was published recently in the British Journal of Clinical Pharmacology (BJCP) (1). They reported that trimethoprim–sulfamethoxazole (TMP-SMX) exposure during pregnancy was associated with an almost 3-time risk of spontaneous abortion (AOR 2.94, 95% confidence interval (CI) 1.89–4.57, 25 exposed cases). This strong association is unlikely to be biased by unmeasured confounding factors.

A study from France found that about a quarter of pregnant women took antidepressants (2) and this highlights the potential safety concern about offspring in these pregnant women. However, the decision for use of antidepressants during pregnancy is complex and requires balancing the risk and benefit of the medications on both mother and child. The association between antidepressants in pregnancy and risk of children' attention-deficit/hyperactivity disorder 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 and congenital malformations in infants (4). Fluoxetine use was associated with increased risks of major malformations (RR = 1.18, 95% CI = 1.08–1.29), cardiovascular malformations (RR = 1.36, 95% CI = 1.17–1.59), septal defects (RR = 1.38, 95% CI = 1.19–1.61), and non-septal defects (RR = 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, a commonly used medicine to treat pain and reduce a high temperature is linked with maternal intake and fetal ductus arteriosus constriction or closure. A 25 case series review article published in BJCP recently (5) 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 event and put the current findings into clinical perspective.

The public should recognize the potential risk to offspring when pregnant women take any medicines. Due to the observational nature of the observational studies, the results should be interpreted cautiously, especially the weak associations. Further well designed studies would be encouraged to explore the safety issues further within the limits of association.

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