Authors' reply Antidepressants in pregnancy and postpartum haemorrhage

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Abstract – Not Required

Main Text

Sir,

We thank Dr Kawada for their interest and comment on our article: "Antidepressant use in late gestation and risk of postpartum haemorrhage: a retrospective cohort study".[1]

While we only reported on outcomes following exposure to any antidepressant type overall, we did collect data on the type of antidepressant exposure. Out of the 558 women exposed to antidepressants, 435 were exposed to Selective Serotonin Re-Uptake Inhibitors (SSRIs), 64 to Serotonin Norepinephrine Re-Uptake Inhibitors (SNRIs), and the remainder (n=59) to other antidepressants.[1] When classified according to serotonin re-uptake inhibition, 542 women were exposed to Serotonin Re-Uptake Inhibitors (SRIs) and just 16 to Non-SRIs. Compared to women with a non-medicated psychiatric illness, the unadjusted risk of postpartum haemorrhage was increased following use of SSRIs (RR 1.46; 1.12-1.91) and SNRIs (RR 1.88; 1.13-3.11), as well as SRI (RR 1.46; 1.20-1.77) and Non-SRI (RR 2.23; 0.97-5.30) antidepressants.

Dr Kawada highlights the apparent inconsistent findings with respect to different types of antidepressants and the risk of postpartum haemorrhage, suggesting that this may weaken the case for a causal relationship. We do not necessarily agree with this assertion. The association between antidepressant use in late pregnancy and risk of postpartum haemorrhage has been analysed in a recent meta-analysis. This found an overall significantly increased risk of PPH associated with the use of any antidepressant use (OR 1.32; 95% CI 1.17-1.48), with sub-group analyses identifying a greater risk for SNRIs (OR 1.62; 95%CI 1.41-1.85) then SSRIs

(OR 1.20; 95%CI 1.04-1.38).[2] While on face-value these findings may appear counterintuitive, given the known differences in pharmacological activity within and between antidepressant types, together with differences in use in clinical practice (e.g. in terms of dose or indications), expecting all antidepressants to be associated with the same level of risk is highly improbable. In contrast, while accounting for potential confounding by underlying maternal illness remains a challenge, the case for a causal relationship between antidepressant use and risk of PPH is strengthened by the identification of an increased risk associated with current antidepressant use (RR = 1.37, 95% CI = 1.09-1.71) but not past users (RR = 1.08, 95% CI = 0.88-1.31). These findings suggest that the association not be restricted to SSRs alone.

A further finding of the recent meta-analysis was an increased risk of PPH for women exposed to non-SRIs (OR 1.31; 95%CI 1.10-1.56) as well as SRIs (OR 1.23; 95%CI 1.06-1.44). This finding may not be entirely unexpected as while Non-SRIs do not impact on serotonin reuptake, they may still have impacts on serotonergic activity. For example, in our study[1], the main Non-SRI used was mirtazapine (13/16; 81%) which is a 5-HT2A receptor antagonist. This is of importance as 5-HT2A is recognised to be involved in platelet response and aggregation[3] and uterine contractility[4].

Taken together, the growing body of evidence supports Dr Kawada's sentiments for the requirement for continual research on this association to determine causative factors. Future studies should focus on examining underlying biological mechanisms underpinning this association and must include attempts to better account for potential confounding by underling maternal illness.

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References

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