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Re: Pregnancy outcomes in women with mechanical prosthetic heart valves – a prospective descriptive population-based study using the United Kingdom Obstetric Surveillance System (UKOSS) data collection system

Sir,

We read with interest the study by Vause and colleagues¹ on the reported outcomes of pregnant women with mechanical heart valves *in situ* in the UK over a 2-year period. We agree with the accompanying editorials to this paper that the poor maternal and fetal outcomes are disheartening and that, given the low number of women with mechanical heart valves, their management should be undertaken in units where women can receive expert care.

In Vause's study, 41 women (71%) were managed with low molecular weight heparin throughout pregnancy, with the authors reporting large variation in the frequency of monitoring and the target levels aimed for. The gravid state has a significant impact on the pharmacokinetics of LMWH. It is well recognised that the glomerular filtration rate increases by ~50% by the end of the first trimester and is maintained throughout the remainder of pregnancy, and that the intravascular plasma volume increases by up to 60% during the gravid state. These changes will directly impact on the clearance and volume of distribution of LMWH due to their significant renal excretion and their distribution being largely confined to the intravascular space. Therefore, one would predict a significantly higher

clearance of LMWH during the first trimester of pregnancy, where clearance changes dominate; however, as changes in the volume of distribution begin to take hold, this will begin to rebalance over the course of pregnancy, and the elimination half-life of LMWH will begin to be prolonged, having been reduced earlier on in pregnancy.

We have developed a pharmacokinetic model for enoxaparin during the antenatal period.² This demonstrates that as pregnancy progresses, if a woman is given the same dose of LMWH throughout pregnancy, a gradual increase in the trough concentration is observed during pregnancy, illustrating the prolongation of the half-life of enoxaparin. Others have reported similar findings.^{3,4} Given this and those from outcomes papers like Vause and colleagues, there is a clear need to be aggressive with LMWH dosing during the first trimester to ensure therapeutic anticoagulation, and a careful evaluation of dosing in the third trimester to prevent bleeding. Although not routinely recommended by international societies, we are of the opinion that trough anti-Xa monitoring has a role in this setting. Trough anti-Xa levels will provide clinicians with an indication of how quickly the LMWH is being cleared and arguably is more informative than a peak level.

Vause and colleagues' paper highlights the real challenge clinicians are faced with when women with mechanical heart valves present at the clinic. The lack of consensus has led to wide variation on how women are managed. We call on international societies from the cardiology, obstetric and

haematology disciplines to provide unified guidelines for this patient population, with clearer guidance on dosing and monitoring of LMWH, with real consideration of the role of trough anti-Xa monitoring, so this high-risk group receives optimal and standardised management, and informative evaluation studies can be performed. ■

References

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