Two-dose vs single-dose methotrexate for treatment of ectopic pregnancy

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TO THE EDITORS: Dr Alur-Gupta et al[1] published a systematic review and metaanalysis concerning 2-dose vs single-dose methotrexate for treatment of ectopic pregnancy. However, their statistical analyses are confounded by several potential biases.

First, their systematic review should have been registered with an International Prospective Register of Systematic Reviews (PROSPERO, https://www.crd.york.ac.uk/) or other international databases of prospective registration to avoid duplication and reduce the opportunity for reporting bias by enabling comparison of the completed systematic review with what was planned in the protocol.

Second, the primary outcomes, treatment success, were 87.2% and 78.9% for 2-dose and 1-dose groups, respectively; however, their metaanalysis used of the odds ratio to estimate pooled treatment effects. It seems that they have not followed the Cochrane Handbook,[2] which stated that odds ratios are more difficult to interpret than risk ratio and can overestimate and magnify risk when events are not rare.[3]

Third, publication bias was assessed via funnel plots in their study. That is incorrect. The use of funnel plots to analyze publication bias went to the 1980s and 1990s. However, over time, researchers realized that there could be numerous causes for asymmetry of funnel plots. Asymmetry in a funnel plot does not tell whether there is publication bias. Therefore, the term *publication bias* has been replaced largely with the term *small study effects* in the analysis of funnel plots.[2] ■

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REFERENCES

1. Alur-Gupta S, Cooney LG, Senapati S, Sammel MD, Barnhart KT. Two-dose versus single-dose methotrexate for treatment of ectopic pregnancy: a meta-analysis. Am J Obstet Gynecol 2019;221:95–108.e2.
2. Higgins JPT, Green S, eds. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available at: www.handbook.cochrane.org.
3. Sinclair JC, Bracken MB. Clinically useful measures of effect in binary analyses of randomized trials. J Clin Epidemiol 1994;47:881–9.

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Artificial placenta: Miles to go before I sleep…

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TO THE EDITORS: First of all, we would like to congratulate the authors for this adventurous novel piece of research.[1] With advancement in technology and better medical care the survival of premature infants has improved drastically over the last few decades. However, the survival of micro preemies in the periviable period (22−25 weeks) and the associated long-term morbidities have not changed meaningfully. Hence, prevention of spontaneous prematurity is a real challenge and requires scientific breakthrough in the form of artificial placenta. The development of artificial placenta has been a subject of investigation over the last 50 years with limited success. Definitely, this technology has potential to do miracles in intact survival of neonates born at periviable period (22−25 weeks); if found successful, its use is likely to be expanded to cover much wider gestation.

As compared with a recent invention in this field, the authors rightly have improvised the technique towards a more real-life human fetus scenario.[2] Salient points are the use of more immature ewe fetuses (95 days; weight 600−700 g, which is equivalent to a human fetus at 20−24 weeks gestation), the sole use of umbilical catheterization for vascular access instead of carotid artery and jugular vein cannulation, prostaglandin E1 infusion for patency of umbilical vessel, and, last but not the least, a lower concentration of heparin (12.5 units/kg/hr) in the circuit to prevent intracranial hemorrhage in these premature fetuses.

The study has a few concerns that need to be clarified by authors for the easy comprehension of readers and for future applicability:

1. The duration of use of the artificial womb in the current study was nearly 5 days, which is much shorter compared with the usual period of ventilation and nutrition support in human fetuses who are born in the periviable period.
2. To prevent infection, the authors have used prevention measures like empiric antibiotics (meropenem) and antifungal (fluconazole). However, because of the potential risk of adverse effects (such as thrombocytopenia) with these antibiotics, it may not be advisable to use them as empiric therapy in human fetuses. Despite this, the authors have demonstrated infection in 1 of the fetus in experimental arm.