Prolonged latency after preterm premature rupture of membranes: an independent risk factor for neonatal sepsis?

Elsa Lorthe, Mathilde Quere, Gilles Kayem

Title: Prolonged latency after preterm premature rupture of membranes: an independent risk factor for neonatal sepsis?

Ms Elsa LORTHE,[1,2] RM, MSc, Ms Mathilde QUERE,[1] MSc, Prof. Gilles KAYEM,[1,2,3] MD, PhD

1 Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team (Epopé), Center for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in pregnancy, Paris Descartes University

[2] Sorbonne Universités, UPMC Univ Paris 06, IFD, 4 Place Jussieu, 75252 PARIS cedex 05, Paris, France

[3] Department of Obstetrics and Gynecology, Trousseau Hospital, APHP, Paris, France

Disclosure statement: The authors report no conflict of interest.

Corresponding author: Elsa LORTHE, INSERM U1153, Bâtiment Recherche, Hôpital Tenon, 4 rue de la Chine, 75020 Paris, France. Phone +33 1 56 01 83 67, fax +33 1 56 01 71 88. Email: elsa.lorthe@gmail.com

Word count: 253

Dear editor,

We read with great interest the article by Drassinower et al who investigated the impact of prolonged latency after preterm premature rupture of membranes (PPROM) on neonatal sepsis.(1) The main finding highlights that, for a given gestational age at PPROM, prolonged latency does not increase the risk of neonatal sepsis, except for latencies over 4 weeks associated with reduced risk of sepsis. As rightly underlined by the authors, this result makes sense as the most stable cases of PPROM with the longest latency durations are probably those with the lowest risks of choriomnionitis and neonatal sepsis.

However we would like to raise some key points. First, the primary outcome included both early and late-onset sepsis. This definition seems inappropriate as late-onset sepsis mostly result from pathogens horizontally transmitted after birth,(2) thus do not reflect intra-uterine inflammation. Second, cases of stillbirths and neonatal deaths were not taken into consideration while potentially linked to severe prenatal or postnatal infection. This can lead to underestimate adverse effects of prolonged latency, especially for ruptures at 22 to 24 weeks of gestation that were included in the trial.(3) Third, in the multivariable model, adjustment for both latency and time-dependant covariates (e.g. multiple courses of steroids), may have introduced overadjustment bias.(4) We would also have appreciated to be able to interpret global p-values for each covariate included in the multivariable model.

Such results are likely to greatly impact daily practice, obstetric management and counselling of women with PPROM. Further analyses addressing the previous issues are therefore needed.

References:

1. Drassinower D, Friedman AM, Običan SG, Levin H, Gyamfi-Bannerman C. Prolonged latency of preterm premature rupture of membranes and risk of neonatal sepsis. Am J Obstet Gynecol. 2016 Jun;214(6):743.e1-743.e6.

2. Shah BA, Padbury JF. Neonatal sepsis. Virulence. 2014 Jan 1;5(1):170–8.

3. Rouse DJ, Hirtz DG, Thom E, Varner MW, Spong CY, Mercer BM, et al. A Randomized, Controlled Trial of Magnesium Sulfate for the Prevention of Cerebral Palsy. N Engl J Med. 2008 Aug 28;359(9):895–905.

4. VanderWeele TJ. On the Relative Nature of Overadjustment and Unnecessary Adjustment: Epidemiology. 2009 Jul;20(4):496–9.