Late preterm rupture of membranes: it pays to wait

In contrast to previous assumptions, there is increasing evidence that being born in the late preterm period—between 34 and 36 weeks gestation—is associated with important long-term adverse effects. Several adverse outcomes have been reported, including cerebral palsy, more hospital admissions in early childhood, lower childhood height, asthma, limiting long-term illness, and poorer educational attainment. Findings from studies show a gradient of health outcomes with decreasing gestation. An estimated 4–5% of infants are born at 34–36 weeks, and 30% of preterm births follow pre-labour rupture of the membranes. Because of the potential risks of fetal and neonatal infection—although with limited evidence to support this assumption—present guidance favours planned early delivery in women presenting with ruptured membranes. With the emerging evidence of differences in long-term outcomes between late preterm and term infants, robust assessment of the risks and benefits of this strategy is essential, because a small increase in gestation at birth is likely to be beneficial to the infant.

In The Lancet, Jonathan Morris and colleagues present the results of a pragmatic randomised controlled trial of planned immediate delivery versus expectant management in women presenting with pre-labour ruptured membranes at 34–36 weeks. Findings from this trial advance substantially the evidence on the optimum management strategy in these women. 1839 women in whom there was no indication for urgent delivery were randomly assigned to immediate delivery (n=924) or expectant management (n=915). There was no difference in the primary outcome of definite or probable neonatal sepsis between neonates in the immediate birth and expectant management groups (23 [2%] of 923 vs 29 [3%] of 912; relative risk [RR] 0·8, 95% CI 0·5–1·3). Additionally, there was no difference between groups in a secondary composite neonatal outcome of sepsis, ventilation for 24 h or more, or death (73 [8%] of 923 in the immediate delivery group vs 61 [7%] of 911 in the expectant management group; RR 1·2, 95% CI 0·9–1·6).

Infants of women assigned to planned immediate delivery had a significantly higher risk of respiratory distress syndrome (76 [8%] of 919 vs 47 [5%] of 910; RR 1·6, 95% CI 1·1–2·3) and mechanical ventilation (114 [12%] of 923 vs 83 [9%] of 912; 1·4, 1·0–1·8) compared with those whose mothers were assigned to expectant management. These infants also had a significantly longer stay in a special care nursery or neonatal intensive care unit (median 4·0 days, IQR 0·0–10·0 vs 2·0 days, 0·0–7·0) and a longer total hospital stay (6·0 days, 3·0–10·0 vs 4·0 days, 3·0–8·0). However, in contrast to their infants, mothers in the expectant management group had a longer hospital stay than mothers who were assigned to planned immediate delivery (median 6·0 days, IQR 4·0–9·0 vs 5·0 days, 3·0–7·0), owing to the fact that most women in the expectant group were managed in hospital and were not discharged home to await the onset of labour. Almost 90% of women randomly assigned to expectant management received antibiotics before delivery, but this was not universal despite clear evidence of benefit. Also, a planned subgroup analysis of women who had group B streptococcus cultured from a vaginal swab showed no difference in the primary outcome of neonatal sepsis between the groups (RR 0·9, 95% CI 0·2–4·5).

The main strength of Morris and colleagues’ study is its size; previous meta-analyses included a total of only 1230 infants. However, a concern associated with the present study is the time taken to recruit sufficient women—10 years. Patterns of obstetric care are unlikely to have changed sufficiently over that time to have a major effect on the study’s results, but preferences for antibiotic
use will have changed in view of the findings of the ORACLE II trial and the association identified between maternal co-amoxiclav and necrotising enterocolitis. Morris and colleagues’ trial adopted a pragmatic approach to management within the expectant group, allowing women to be cared for according to the usual practice of the recruiting centre. Therefore, management was varied, as shown by the fact that some women were treated at home, and laboratory testing and antibiotic prescription were not universal. This variation might have affected outcomes, but one could argue that it enhanced the generalisability of the results. However, women were recruited at 65 centres in 11 countries, and major differences in the respective maternity care systems should be considered when interpreting the results for practice in individual countries. What then do we still need to know? The investigators speculate that their findings will be associated with economic as well as health benefits, but in view of the reciprocity of length of stay data between mothers and infants in the two groups, this clearly needs formal assessment. Any economic benefit will be affected by variation in home versus hospital expectant management, the relative risks and benefits of which are unclear. The prolongation of pregnancy achieved with expectant delivery was small—will this translate into longer-term health and educational benefits for infants? Even small differences are likely to be important on a population basis, but still should be robustly examined. Additionally, to enhance the safety of expectant management, research must continue to be done to understand the effects of the inflammatory process on the fetal brain and on improving the detection of chorioamnionitis.

The prevailing orthodoxy in obstetric practice, despite the emerging evidence on long-term outcomes, is to have a low threshold for delivery in the face of obstetric problems between 34 and 36 weeks, on the basis that neonatal outcome is uncompromised. Morris and colleagues’ trial fundamentally challenges this thinking in the area of late preterm pre-labour rupture of membranes, and, even with the caveats noted, this new evidence suggests an urgent need for reassessment of present recommendations regarding immediate delivery of women with ruptured membranes close to term.

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7 Morris JM, Roberts CL, Bowen JR, et al, on behalf of the PPROMT Collaboration. Immediate delivery compared with expectant management after preterm pre-labour rupture of the membranes close to term (PPROMT trial): a randomised controlled trial. Lancet 2015; published online Nov 9; http://dx.doi.org/10.1016/S0140-6736(15)00724-4.