is also not a generally favored approach. It brings down the number of patients required for the trial but makes the results less reliable.

What are the results?
Keeping the problems with the validity aside, the results provided are statistically significant. With an absolute risk difference of 1.6%, the number needed to prevent the primary outcome (NNT) is 62.5 is a reasonable number for us to apply the results to clinical practice, keeping in mind the increased side effects in the intensive group.

Can I apply the results to my patients?
The BP measurement technique followed in the study (patient sitting quietly for 5 minutes in a separate room) is not how exactly BP is measured in a physician’s clinic. The patients are older, non diabetics, with no history of stroke but nevertheless have a risk for cardiovascular disease. Given the problems in the validity and the side effects and the smaller group of patients for whom the results are applicable, and the fact that a major study (ACCORD) did not find the approach useful in diabetics, it may be prudent for us to wait for more evidence than rush and apply the results to patients in our practice.

Expectant management in preterm pre-mature rupture of membranes:
Findings from the PPROMT trial

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Clinical question: Is it better to try immediate delivery or wait (expectant management) in cases of premature rupture of membranes?

Authors’ conclusion: In the absence of maternal or fetal compromise the authors recommend expectant management for preterm PROM.

Background
Guidelines for premature rupture of membranes (PROM) at term (>37 weeks of gestation), recommend immediate delivery based on evidences of reduced incidence of maternal infections without increasing the risks of perinatal morbidity[1]. On the other hand, cases of PROM at extreme preterm (23-30 weeks of gestation) are managed expectantly (in the absence of maternal or fetal indications for immediate delivery) to reduce neonatal complications. However, management guidelines in cases of preterm PROM (between 30-34 weeks) are not clear. The above study by Morris et al is one of the first large scale studies to compare immediate delivery with expectant management in cases of preterm PROM.

Methods
The PPROMT trial was a multi-centric randomized control trial involving 65 centres in 11 countries. Women with a singleton pregnancy and PROM between 34-36 weeks and 6 days of gestation (maternal age>16 years without contraindications to continuing pregnancy) were recruited for the study. Participants were randomly assigned to immediate birth group (n=924) or expectant management group (N=915). Women assigned to immediate birth group had their deliveries < 24h of recruitment. Women in the expectant management group were delivered after onset of labor at term, according to obstetric indications. In both groups, antibiotics deemed best according to local guidelines were given. Incidence of neonatal sepsis was the primary outcome of the study; other neonatal and maternal outcomes were also compared between the groups.
Results
Baseline characteristics of the participants in both arms were similar. Comparison of neonatal outcomes between the groups showed no difference in APGAR score, incidence of neonatal sepsis, pneumonia, circulatory compromise and perinatal or infant mortality. However, there was a significant decrease in the incidence of respiratory distress syndrome, use of mechanical ventilation, decreased hospital/ICU stay in the expectant management group. When the maternal outcomes were compared, mothers in the expectant management group had a marginally higher risk for antepartum/intrapartum hemorrhage, fever and longer hospital stay. The risks for postpartum hemorrhage and cord prolapse were similar in both groups.

Discussion
In cases of preterm PROM, expectant management is associated with better neonatal outcome without increasing risks of adverse events. There is a marginal trade-off in the risks of maternal outcomes specifically, the incidence of antepartum/intrapartum hemorrhage, fever and prolonged stay in hospital. The result of the primary outcome (risk of neonatal sepsis) of the PPROMT trial is similar to the smaller PPROMEXIL-2 trial in this area[2]. Major strengths of the study include the large sample size and minimal dropout rates of participants.

References

Expert opinion
Dr. Manisha Beck, Associate professor, Department of Obstetrics & Gynaecology, CMC Vellore

Preterm premature rupture of membranes (PPROM) accounts for nearly 40% of all preterm births. While there are clear cut guidelines on how to manage pregnant women with ruptured membranes at term, this is not so in the case of PPROM. Recommendations from American college and Royal College of Obstetricians and Gynecologists, UK (ACOG and RCOG) recommend planned delivery if a pregnant woman presents with leaking per vaginum after 34 weeks.

Expectant management (which means waiting for spontaneous onset of labour) may be associated with complications such as maternal and neonatal sepsis, abruption and cord prolapse. Immediate delivery following PPROM, on the other hand, leads to iatrogenic prematurity and its associated risks like intraventricular haemorrhage, hyaline membrane disease, necrotising enterocolitis etc. The benefits and risks of each approach, therefore, have to be clearly weighed.

The PPROMT trial, is the largest trial till date, which has tried to find out answers for the existing clinical dilemma. Being a multicentric, multicountry trial, the validity of results can be relied upon with confidence. The study design was good and the loss to follow up minimal, which are some of the salient features of a good clinical trial.

The results of the trial showed that immediate delivery does not curtail the risk of neonatal and maternal sepsis in comparison to expectant management. Interestingly, the results were similar even in mothers who had Group B streptococcal (GBS) infection, since GBS infection in mother is known to cause early onset neonatal sepsis. Moreover, the risk of respiratory distress was significantly more in the immediate delivery group (p value 0.02). This is likely to be secondary to prematurity.

The only drawback of the trial is that the researchers have excluded twin pregnancies from the study. Hence, we still don’t know whether the findings from the study can be extrapolated to twin pregnancies. Another clinical trial would be needed to find out the optimal management of PPROM in cases of twin pregnancies.

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