

## Correspondence

### Contractility of the myometrium; the rationale for pharmacological intervention in preterm labour

Dear Sir,

Thank you for asking us to comment on the issues raised by Professors Åkerlund and Maršál. We would like to thank them for their interest and comments. We agree that in some cases of preterm labour, tocolysis is contraindicated. In particular, if there is significant fetal distress it would be unwise to delay delivery. Since preterm labour is multifactorial, there are a range of precipitating causes which could result in fetal compromise to a greater or lesser extent. At one extreme tocolysis will be harmful (major abruption or fetal infection) and at the other it may be beneficial (uncomplicated preterm labour). We agree that a delay in delivery at very early gestational ages is likely to shift the balance in favour of an improved fetal outcome. Nevertheless, this remains to be demonstrated in a randomised trial. Since tocolysis could be harmful in certain situations, it is important to undertake a risk–benefit analysis for each individual patient.

As tocolysis may be associated with fetal benefit or harm, our view is that a placebo-controlled study or well-designed comparator study without rescue tocolysis is ethical. The documented benefits of steroids mandate that all patients, whether receiving active treatment or comparator should be given steroids. It is important (since indication for tocolysis is to improve neonatal outcome) that a benefit on neonatal morbidity or mortality is demonstrated. This is preferable to secondary outcome measures, such as delay in delivery. We accept that in practice the numbers of patients required may make this unrealistic. Once the benefits of tocolysis have been demonstrated, the challenge will be to tailor the appropriate tocolytic to the cause of preterm labour.

With regard to the mechanism of action of atosiban, our recent work suggests that oxytocin and its receptor have a fundamental role in the onset of term human parturition. It is less likely that the vasopressin  $V_{1a}$  receptor has an important role, so a high affinity oxytocin receptor antagonist may provide the more effective tocolysis. Although this requires documentation, we have recently demonstrated (Wilson *et al.* 2001; *British Journal of Obstetrics and Gynaecology* **108**, 960–966) that in human myometrial contractility studies, a specific and high affinity oxytocin receptor antagonist is more effective at reducing contractility than a non-specific oxytocin– $V_{1a}$  antagonist. We are encouraged that this is in keeping with the studies of Professors Åkerlund and Maršál.

Finally, we agree that atosiban seems to be as effective as

$\beta$ -sympathomimetics (The Worldwide Atosiban *versus* the Beta-agonist Study Group, 2001; *British Journal of Obstetrics and Gynaecology* **108**, 133–142) and has a markedly improved safety profile. We also agree that this a reasonable drug to use in clinical practice, although our hope for the future is that we will eventually have even more effective, high affinity oxytocin receptor antagonists.

Yours sincerely

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