Evaluation of the effects of atosiban on breast feeding

Author's Reply

Sir,

We would like to thank Fallon and Fallon[1] for their interest in our study and for their acknowledgement that atosiban

(Tractocile®; Ferring Pharmaceuticals, Saint-Prex, Switzerland) is an effective tocolytic with an improved safety profile.

The discussed study was aimed to assess atosiban in a clinical practice setting rather than to determine potential adverse events postpartum, but we agree that the safety of a drug administered during pregnancy is of great importance for the fetus and neonate. We therefore appreciate the opportunity to comment on the effect of atosiban on breastfeeding.

Although atosiban is the only tocolytic currently available, which has been developed specifically for the treatment of spontaneous preterm labour and which is the most uterospecific tocolytic to date, it must be pointed out that there is no uterine specific oxytocin (OT) receptor antagonism. Therefore, theoretically OT antagonism in tissues that express OT receptors (such as breast) may lead to an inhibition of milk release.

Development of any tocolytic for worldwide registration requires extensive documentation of safety, and the development of atosiban has included a full programme of nonclinical safety studies, including general toxicology studies, as well as postnatal, cross-fostering and fetal toxicity studies in different animal species. But generally animal studies have to be interpreted with caution, and conclusions drawn should not be directly transferred into humans.

While an effect on lactation in rats and cows has been shown,[1] a recent large study in monkeys showed that different doses of a selective OT antagonist (barusiban) have no effect on maternal milk let-down and that maternal treatment has no effect on the development of the offspring.[2]

It can be assumed that atosiban would behave similar like barusiban, although two major differences between these compounds have to be taken into account. Atosiban has a much shorter half-life than barusiban.[3] Approximately 90 minutes after the last dose, about 97% of the drug will be eliminated. In addition, atosiban is a mixed V1A/OT antagonist and not a selective OT inhibitor, which might result in a less pronounced effect on peripheral OT receptors.

Although studies in humans have not been performed specifically to address the impact of atosiban on breastfeeding, safety data from numerous randomised controlled trials have not revealed any significant safety concerns for the mother, fetus or neonate and no effects on lactation was observed.[4]

This is supported by data from a number of clinical studies. In a study, in which none of the perinatal deaths was attributed to tocolytic therapy there was no excess mortality in the offspring of women assigned to receive atosiban.[5]

In a comparison with a calcium channel blocker, Al-Omari *et al.*[6] found similar neonatal complications and there were no statistically significant differences regarding the incidence of poor feeding.

In summary, the different receptor affinity, the short duration and readily reversible effect of atosiban due to its short half-life and the data from a number of clinical studies make the risk of an adverse effect on breastfeeding and the neonate unlikely. ■

References

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Accepted 22 April 2007.

DOI: 10.1111/j.1471-0528.2007.01404.x

