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*CASE REPORT*

# Atosiban for the primary prevention of preterm labour

**T.A. Johnston*, A.D. Cameron**

## Case report

The patient was a 35 year old multipara with a poor past obstetric history. Her first pregnancy ended in an intrapartum stillbirth following spontaneous preterm labour at 26 weeks of gestation, and her second in a spontaneous miscarriage at 22 weeks of gestation. In her third pregnancy, a Mcdonald cervical suture was inserted at 14 weeks of gestation for a diagnosis of presumed cervical incompetence. However, she laboured spontaneously at 29 weeks and was delivered by emergency classical caesarean section on account of a transverse lie. The baby died at less than an hour of age. She was then referred to the Queen Mother's Hospital for pre-pregnancy counselling, when cervical resistance studies were performed. The diagnosis of cervical incompetence was confirmed and at the time of the investigation she was found to have very little vaginal cervix. She was advised that vaginal insertion of a cervical suture in a future pregnancy would be of little benefit and an abdominal suture was recommended. She conceived again and a transabdominal cervical suture was inserted at 14 weeks of gestation. Elective caesarean section was planned for 36 weeks of gestation, but she was admitted with abdominal pain just a few days prior to her planned admission. An intrauterine death was confirmed on ultrasound scan, and at laparatomy the classical uterine scar was found to have ruptured and the fetus was in the abdominal cavity. Repair of the uterus was performed. The couple were advised that any future pregnancy would carry a significant risk of further rupture, and that this may endanger her life. Just over two years later, she came to us with seven weeks amenorrhoea and a positive pregnancy test. An ultrasound scan confirmed a viable intrauterine twin pregnancy. We discussed the risks of preterm labour and uterine rupture, which were increased because of the twin gestation. The couple decided to continue with the pregnancy. Our plan was to admit her to hospital at 24 weeks of gestation for the remainder of her pregnancy and administer prophylactic tocolysis. The tocolytic used was atosiban (Tractocile Ferring Pharmaceuticals Ltd), a synthetic oxytocin antagonist. An intravenous infusion of 30 μg per minute of atosiban was started at 24 weeks of gestation, administered through a 5ml syringe driver infusion pump. However, this high concentration caused significant inflammation at the infusion site, requiring re-insertion of the intravenous cannula every 12 hours. The atosiban was diluted to the standard concentration of 10:1 with normal saline and administered through a 60ml syringe driver infusion pump. This improved the ease of administration significantly, and each intravenous cannula thereafter lasted four to five days. Steroids were administered each week to increase fetal lung maturity, and regular ultrasound assessments of the infants and of the cervix were performed.

The pregnancy progressed uneventfully until 32 weeks of gestation when she developed regular uterine contractions. Arrangements were made for immediate transfer to theatre and delivery. Meanwhile, the infusion rate of atosiban was doubled to 60 μg per minute, which was effective in decreasing the uterine contractions until delivery could be achieved. She was delivered by emergency lower uterine segment caesarean section of two boys weighing 2.03kg and 2.35kg. Both babies required minimal resuscitation and had uncomplicated postnatal courses in the neonatal unit. The previous classical uterine scar was found to be extremely thin but intact. The couple are now considering sterilisation.

## Discussion

Cervical incompetence is a significant contributor to preterm delivery and to perinatal morbidity and mortality. The diagnosis can be difficult to confirm objectively, but the cervical resistance index[1] can be calculated with a force monitor[2] and can be used to confirm the diagnosis[3], as was done in this case. It has been demonstrated that cervical cerclage can significantly reduce the risk of preterm delivery[4]. Transabdominal cervical cerclage is now an accepted method of treatment where the traditional vaginal aperation has failed or is not possible[5]. In

*Department of Fetal Medicine, The Queen Mother's Hospital, Glasgow, UK*

* **Correspondence**: Dr T. A. Johnston, Department of Fetal Maternal Medicine, St Mary's Hospital for Women and Children, Whitworth Park, Manchester M13 0JH, UK.


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our case both applied, as a vaginal cervical suture had failed and there was now insufficient vaginal cervix to insert another suture.

With her past obstetric history, the dangers to the mother and her baby in a further pregnancy were substantial. The risks of preterm labour and uterine rupture were significantly increased with a twin gestation and the couple were counselled accordingly. Despite the risks to the mother's life, the couple decided to proceed with the pregnancy. We felt that everything possible should be done to minimise the risk of preterm labour and also allow rapid access to theatre and delivery if uterine contractions started, and so she was admitted to hospital. Long term prophylactic tocolysis was considered. Most current tocolytics, such as beta-sympathomimetics, non-steroidal anti-inflammatory drugs, and calcium channel blockers, have significant maternal and fetal side effects, and none has been shown to be effective in the primary prevention of preterm labour. We thought that long term prophylaxis with standard tocalytic drugs could not be justified.

Atosiban is an oxytocin antagonist[6] which has been shown in clinical studies to be an effective tocolytic[7–10] with minimal side effects[10,11]. One study of long term maintenance therapy with atosiban following treatment of premature contractions showed that it was more effective than placebo at delaying recurrence of contractions. As this is the first case in which atosiban has been used for the primary prevention of preterm labour, as opposed to the treatment of premature contractions followed by prevention of their recurrence, it is difficult to be certain that atosiban prolonged pregnancy. However, when uterine activity developed at 32 weeks, increasing the infusion rate of atosiban decreased the strength and frequency of the contractions, although it is recognised that this assessment is somewhat subjective. Atosiban used for the primary prevention of preterm labour requires further study.

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