Unexpected outcome (positive or negative) including adverse drug reactions

The use of fetal fibronectin testing in the management of a triplet pregnancy with a short cervix

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Correspondence to Alexandra Karin Morriss, alexandra.morriss@kcl.ac.uk**Summary**

Following in vitro fertilisation treatment, a 40-year-old woman was expecting trichorionic, triamniotic triplets. Her cervix shortened from 34 mm at 16⁺⁵ weeks to 16 mm at 20⁺⁵ weeks, a risk reported with 100% delivery before 28 weeks gestation. She was admitted to hospital and at 24⁺¹ weeks was given corticosteroids. From 21⁺⁵ weeks her cervical length remained below 16 mm. However, weekly fetal fibronectin (fFN) tests were negative from 22⁺⁵ weeks to delivery at 35⁺⁵ weeks. This, along with an absence of symptoms, gave her doctors confidence to manage her as an outpatient from 28 weeks. At 33⁺⁵ weeks she was diagnosed as having pre-eclampsia and three live births were delivered by prelabour caesarean section. Prior to delivery her cervical length was 10 mm and fFN test remained negative. There are no reports of outcome following a negative fFN with a short cervix in triplet pregnancies but fFN could be a useful tool, in conjunction with cervical length measurement, in the management of triplets.

BACKGROUND

This patient, expecting triplets, was managed as an outpatient on the basis of negative fFN tests despite her alarmingly short cervical length.

This case history presents a new way of guiding the management of triplet pregnancies, when the cervix is short. In singleton pregnancies, fFN has a high negative prediction in asymptomatic high-risk women, even when the cervix is short.¹ This has never been reported in triplet pregnancies.

The mean gestational age for triplets is 32.6 ± 2.7 weeks which puts all such pregnancies at risk of the consequences of early preterm labour.² The medical and social costs

arising from preterm birth (PTB) are vast, particularly in triplets.³

The management of triplets often involves admission, corticosteroids and in utero transfer. These interventions improve outcome by saving lives but are difficult to time appropriately and resources are often misspent. As well as being financially costly, inpatient admission is often socially inconvenient and psychologically distressing.

The use of reliable tests to predict the risk of preterm delivery and guide the timing of interventions would be of high value in terms of obstetric decision-making and patient counselling.

Figure 1 A graph demonstrating the patient's cervical length measurements (mm) throughout the course of her pregnancy. The gestation of her corresponding negative fFN results are depicted by the red triangles.

Figure 2 Transvaginal ultrasound at 32⁺⁵ weeks gestation. This revealed a further shortening of the patient's cervical length to 5 mm (see arrow).

This promising area requires further evaluation and research.

CASE PRESENTATION

A 40-year-old primiparous, Asian woman, with a 3-year history of infertility and a BMI of 32, received in vitro fertilisation (IVF) treatment at Guy's Hospital, London in 2010. Three embryos were transferred and an ultrasound scan at 5 weeks gestation showed she was expecting trichorionic, triamniotic triplets.

At 17⁺⁶ weeks she was diagnosed as having gestational diabetes which was well controlled on insulin. Otherwise the patient remained well and regular ultrasound scans showed normal fetal growth, dopplers and fluid.

The patient was referred to the Preterm Surveillance Clinic at St. Thomas' Hospital, London as her triplet pregnancy placed her at high risk of PTB; here she received regular transvaginal ultrasound scanning to measure her cervical length, and fetal fibronectin (fFN) testing to assess her risk of going into preterm labour.

Her cervical length shortened from 34 mm at 16⁺⁵ weeks to 16 mm at 20⁺⁵ weeks. A cervical length ≤ 25 mm between 15 and 20 weeks gestation in triplet pregnancies has previously been reported to have both a specificity and a positive predictive value of 100% for delivery at <28 weeks gestation.⁴ The patient was at high risk of spontaneous abortion and at 21⁺⁵ weeks she was admitted to St Thomas' Hospital and placed on bed rest. At 24⁺¹ weeks she was given two doses of corticosteroids for fetal lung maturation.

Despite her short cervical length, her fFN tests were negative at 22⁺⁵, 23⁺⁵, 24⁺⁵, 26⁺⁵ and 27⁺⁵ weeks gestation (figure 1). These negative results were treated with caution due to the absence of literature supporting fFN testing

in triplets. However, the consistently negative results gave her physicians growing confidence that inpatient management was unnecessary and, in spite of her short cervix, it was considered safe to discharge her at 28⁺⁰ weeks on the basis of her negative fFN tests.

From 28⁺⁵ weeks to 31⁺⁵ weeks her cervical length remained below 16 mm. However, due to her weekly fFN tests remaining negative and her absence of symptoms, her management continued as an outpatient.

At 32⁺⁵ weeks her cervix measured 5 mm (figure 2).

At the same gestation, her fFN test was negative. On the basis of her negative fFN result it was considered appropriate to continue outpatient management, in spite of her short cervix.

At 33⁺⁵ weeks she was diagnosed as having pre-eclampsia and three live births were delivered by prelabour caesarean section, as the induction of labour was thought to be inappropriate in a triplet pregnancy. Prior to delivery her cervical length was 10 mm and her fFN test was negative.

INVESTIGATIONS

Cervical length measurement and fFN testing.

OUTCOME AND FOLLOW-UP

fFN testing was used in conjunction with cervical length measurement in the management of a triplet pregnancy. Despite the extremely short length of her cervix, this patient was managed as an outpatient on the basis of negative fFN tests which were performed weekly from 22⁺⁵ weeks until delivery at 35⁺⁵ weeks by prelabour caesarean section which was indicated for pre-eclampsia; she did not ever go into spontaneous labour. At delivery her cervix measured 10 mm and her fFN test was negative.

DISCUSSION

The incidence of PTB is rising, with considerable implications in terms of morbidity, mortality and health costs.³ The overall proportion of preterm deliveries increased by 22% between 1995 and 2004 and multiple birth and primiparity were the most important contributing factors.³ The recent increase in multiple births has largely been driven by the rise in assisted conception.³

In March 2004, the Human Fertilisation and Embryology Authority (HFEA) announced its decision to restrict the number of embryos that may be transferred in a single IVF treatment cycle to two for women under the age of 40 years, regardless of the circumstances.⁵ Nevertheless, it is still considered acceptable by the HFEA for women aged 40 and over to receive a maximum of three embryos, as occurred in this case.⁵

fFN is a glycoprotein, acting as a 'glue' between the fetal membranes and the uterine endometrium.⁶ It is considered to be the most powerful biochemical indicator of PTB.⁶ Normally cervicovaginal secretions will contain fFN until approximately 20 weeks gestation and then again as term approaches.⁶ Its presence between 20 and 37 weeks is suggestive of mechanical or inflammatory damage, disrupting the attachment of the pregnancy to the uterus.⁶

Testing for the presence of fFN involves a swab taken from the posterior fornix of the vagina.⁶ It has proved a sensitive predictor of PTB in singleton and twin pregnancies between 22 and 35 weeks gestation and is used in both symptomatic and asymptomatic, high-risk women to facilitate management decisions.⁶

The cervix acts as both a biochemical and physical barrier. Lack of fFN may indicate a competent cervix, that is, little chance of ascending infection, known to be a potent cause of labour. A short cervix can be consistent with a long gestation, as long as it is 'closed'.

In asymptomatic, high-risk women the predictive power of fFN at 24 weeks was greatest for delivery <30 weeks, with a likelihood ratio of 15 for a positive test (6/13 positive women delivered before 30 weeks).⁷

Although the combined use of fFN and cervical length have been reported in 29 triplet pregnancies, there are no reports of a negative test with a short cervix.⁸

This case also illustrates the potential for fFN testing to reduce unnecessary admissions and the associated costs; here, trusting in negative fFN results saved the NHS the cost of >5 weeks hospital admission costs, as well as having psychological and practical benefits.

Learning points

- ▶ Triplet pregnancies that are deemed very high risk of PTB when associated with a short cervix can have further stratification by the addition of cervicovaginal fFN.
- ▶ A negative fFN test with a short cervix in triplets can be associated with good outcome.
- ▶ The management of triplet pregnancies may be altered by the fFN result independent of cervical length.

Competing interests The authors have no direct financial interest in the sale of fetal fibronectin kits. Professor Shennan has received expenses for talking at educational meetings arranged by Hologic, the manufacturers of fetal fibronectin kits.

Patient consent Obtained.

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