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Fetal thrombocytopenia : preventive strategies.

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Chapter 5

Vaginal delivery for fetuses at risk of alloimmune thrombocytopenia?

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ABSTRACT

Objectives To evaluate the safety of vaginal delivery in pregnancies with fetal and neonatal alloimmune thrombocytopenia (FNAIT).

Design Prospective data collection.

Setting Leiden University Medical Centre, the national centre for management of severe red cell and platelet alloimmunisation.

Population Thirty-two pregnancies with FNAIT, with a sibling with thrombocytopenia but without an intracranial haemorrhage (ICH).

Methods The mode of delivery, platelet count in cord blood and neonatal outcome were analysed. All women received weekly intravenous immunoglobulin from 32 to 38 weeks of gestation. Head ultrasound scan was performed in all neonates.

Main outcome measures Signs of ICH or other bleeding in the neonates.

Results Twenty-three women delivered vaginally. Nine caesarean sections were performed, all for obstetric reasons. Median platelet count at birth was $142 \times 10^9/l$ (range, $4-252 \times 10^9/l$), with severe thrombocytopenia ($< 50 \times 10^9/l$) in four neonates, of which three were born vaginally. None of the neonates showed signs of ICH or other bleeding.

Conclusions In pregnancies with FNAIT and a thrombocytopenic sibling without ICH, vaginal delivery was not associated with neonatal intracranial bleeding. These initial results support our noninvasive management of these pregnancies with FNAIT.



INTRODUCTION

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) is a rare but potentially devastating disease. It is the most common cause of thrombocytopenia in term neonates. In contrast to haemolytic disease due to rhesus D antibodies, the index pregnancy is often affected. Consequently, treatment is only possible in the next pregnancy. Many controversies still exist about the management, including mode of delivery.

The recurrence rate of severe thrombocytopenia and the risk to develop an intracranial haemorrhage (ICH) in the absence of ICH in a previous child is not known. Radder *et al.*¹ estimated the ICH risk to be 7% in a subsequent untreated pregnancy after a previous child with thrombocytopenia but without ICH.

Moreover, in 80% of neonates with ICH, this bleeding would occur before labour,² implying that, during labour or postpartum, the chance to develop ICH is approximately 1.4% in this group. In these milder FNAIT cases, the estimated 2.8% risk of complications associated with fetal blood sampling (FBS) and the 1.6% risk of fetal loss per procedure may not be justified when balanced against the risk of ICH.¹ Caesarean section is often routinely employed for delivery in these cases. Practice guidelines advise vaginal delivery as an option in case of a platelet count $> 50 \times 10^9/l$ established by FBS, with or without an intrauterine platelet transfusion.³⁻⁵

However, there is no evidence that a vaginal delivery poses the fetus with a platelet count $< 50 \times 10^9/l$ at higher risk for ICH than caesarean section. We report our experience with the safety of vaginal delivery in FNAIT pregnancies without ICH in a previous child.

METHODS

The Department of Obstetrics at the Leiden University Medical Centre is the national referral centre for pregnancies complicated by FNAIT in the Netherlands.

Our less invasive treatment strategy in women who are at risk for FNAIT and who have an index child with severe thrombocytopenia ($< 50 \times 10^9/l$) but without an ICH has been described previously.⁶ We prospectively collected all data from pregnancies complicated by FNAIT referred to us between March 1989 and August 2004. For this study, we selected all women with an index child with thrombocytopenia due to FNAIT but without an ICH. All women received weekly 1 g/kg bodyweight of intravenous immunoglobulins (IVIG) from 32 to 38



weeks followed by induction of labour. Head ultrasound scan was performed in all fetuses before starting the IVIG treatment and after birth. No diagnostic FBSs were performed. Assisted vaginal delivery was considered contraindicated. Caesarean section was only performed for obstetric reasons. The mode of delivery, the platelet count in cord blood and neonatal outcome were analysed.

RESULTS

Between March 1989 and August 2004, 29 women with 32 pregnancies met the inclusion criteria. The characteristics of the study group are given in Table 1. Twenty-three neonates from the 29 untreated siblings had a platelet count $< 50 \times 10^9/l$. Four neonates were delivered by assisted vaginal delivery, having a platelet count of 11, 14, 21 and $30 \times 10^9/l$, respectively.

In Table 2, the characteristics of the neonates are given. Twenty-three deliveries were by vaginal route. Nine caesarean sections were performed, four because of breech presentation, one for transverse presentation and two because of an earlier caesarean section. Two secondary caesarean sections were performed for failure to progress, one breech and one vertex presentation.

Median platelet count in cord blood at birth was $145 \times 10^9/l$ (range, $4-252 \times 10^9/l$). Median platelet count in the caesarean section group was $144 \times 10^9/l$ (range, $4-231 \times 10^9/l$), with severe thrombocytopenia ($4 \times 10^9/l$) in one neonate. Median platelet count in the vaginal group was $146 \times 10^9/l$ (range, $12-252 \times 10^9/l$), with three neonates being severely thrombocytopenic (12, 40 and $41 \times 10^9/l$, respectively). Nine neonates needed treatment for thrombocytopenia; three received platelet transfusions combined with IVIG. Three others needed only platelet transfusions and three neonates received only IVIG after birth. None of the neonates had signs of ICH at ultrasound examination. In Figure 1, the relationship between the platelet count at birth in the index group and the platelet count at birth in the treated group is shown.



Table 1: Characteristics of the study group

Mothers (n=29)	
Median age (range)	33 (29-40)
Children involved, <i>n</i>	32
Previous pregnancy (n=29)	
Median platelet count (range)	30 x 10 ⁹ /l (4-134)
Platelet count < 50 x 10 ⁹ /l, <i>n</i>	23/29 (79%)
Delivery mode; Caesarean section	4/29 (14%)
Delivery mode; Instrumental delivery	4/29 (14%)
Current pregnancy (n=32)	
HPA-1a, <i>n</i>	28
Mean IVIG (weeks), <i>n</i> (range)	5 (3-7)
Preterm, <i>n</i>	1 [#]

Delivered at 35+4 weeks

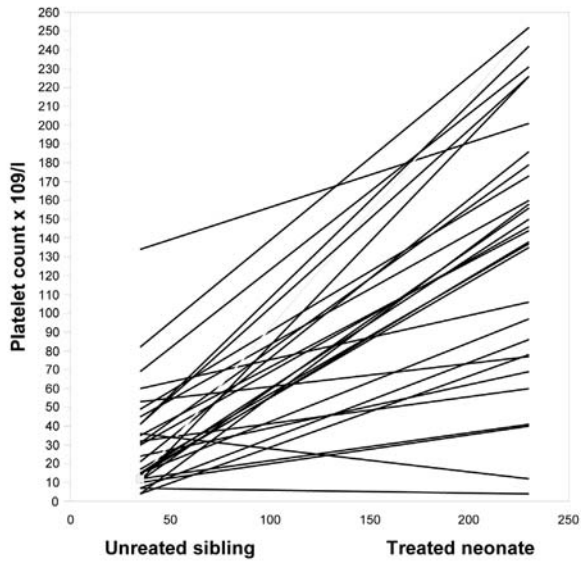
Table 2: Data on delivery, neonatal outcome and treatment

	Spontaneous vaginal delivery (n=23)	Caesarean section (n=9)
Intracranial haemorrhage, <i>n</i>	0	0
Median platelet count (range)	146 x 10 ⁹ /l (12-252)	144 x 10 ⁹ /l (4-231)
Platelet count < 50 x 10 ⁹ /l, <i>n</i>	3	1
Neonatal treatment	6	3
IVIG only, <i>n</i>	3	0
Platelet transfusion only, <i>n</i>	0	3
Combination of IVIG and donor platelet transfusion, <i>n</i>	3	0

There were no significant differences between the two groups for all parameters.



Figure 1: Relationship between the platelet count at birth in the index group and the platelet count in the treated group.



DISCUSSION AND CONCLUSION

In our study group of pregnancies complicated by FNAIT, we achieved a 72% vaginal delivery rate. None of the 32 neonates developed an ICH, although in four neonates, the platelet count was less than $50 \times 10^9/l$. Three of these four children were safely born vaginally. The relatively high number of malpresentations could be explained by contraindication to external cephalic version in this group.

For the mother, the benefits of a vaginal delivery against a caesarean section are obvious. Although a caesarean section is safer than ever before, risks are not negligible. Maternal mortality, even with a planned section, is three times higher than with a vaginal birth⁷ and maternal morbidity - thrombosis, hysterectomy, infections, extended hospital stay and chance of rehospitalisation - is also higher.^{8,9} Uterine scar is also associated with increased risks in future pregnancies.^{10,11}

Predelivery FBS is not without risk, especially for fetuses with thrombocytopenia. Mortality associated with FBS performed in a low-risk population is estimated to be 1.5% per procedure.^{12,13} Based on a review in the literature, the complication rate of FBS in FNAIT pregnancies was calculated as 1.6% fetal loss and 2.8% other complications.¹

In the group of FNAIT pregnancies with a sibling without ICH, not treated with IVIG, the risk to develop ICH is estimated to be 7%.¹ IVIG strongly reduces ICH in pregnancies with a sibling with ICH, but not completely, and at least four cases of recurrent ICH have been reported despite maternal IVIG treatment.¹⁴⁻¹⁷ There is only one case report of an ICH after maternal IVIG treatment in a pregnancy in which the previous child had a platelet count of $8 \times 10^9/l$ but no ICH.¹⁸ We can therefore assume that the risk to develop an ICH after optimal IVIG treatment in the group without a previous ICH is low, even in fetuses or neonates without an adequate response to IVIG.

Although our study group of 32 pregnancies is relatively large for such a rare disease, the number of patients is still too low to sustain our results statistically. In the vaginal delivery group of 23 children, only three children had severe thrombocytopenia ($<50 \times 10^9/l$). The fact that none of these three children had an ICH may be due to chance. Nevertheless, our experience supports that the mode of delivery in FNAIT without a history of ICH should be further investigated.

To achieve this, an international registry (www.noich.org) has been developed, in which all FNAIT cases from participating centres will be collected both retrospectively and prospectively. We expect to find more conclusive evidence through



this data collection to optimise management of pregnancies with FNAIT.

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FETAL THROMBOCYTOPENIA: PREVENTIVE STRATEGIES

