The Fetal and Neonatal Outcomes of Rhesus D Antibody Affected Pregnancies in Northern Ireland

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Abstract

It has been suggested that routine antenatal prophylactic anti-D should be introduced for prevention of Rhesus D (RhD) haemolytic disease. Before making changes to the current prevention program it is important, therefore, to have up-to-date data on affected infants. Pregnant women with anti-D antibodies between September 1994 and February 1997 were identified by the Northern Ireland Blood Transfusion Service. The records of 124 women and 130 babies were examined. 26% of planned deliveries occurred in hospitals without paediatric cover. Rhesus isoimmunisation affected 78 babies. Fifty-nine infants were admitted to one of seven neonatal units. There were 2 stillbirths and 1 neonatal death. Two infants have severe neurodevelopmental delay. There is still significant morbidity associated with RhD haemolytic disease. Care for RhD affected pregnancies should be centralised to guarantee training opportunities and maintenance of expertise. The current management of these pregnancies should be re-examined before changing the Rhesus prevention program.

Introduction

The number of babies affected by Rhesus incompatibility declined rapidly in the late 1960's and early 1970's following the introduction of anti-D immunoglobulin. In England and Wales there were 106 deaths per 100,000 births due to Rhesus incompatibility in 1977; ten years later this figure had fallen to 27.1 In the Royal Maternity Hospital, Belfast the number of infants affected by Rhesus haemolytic disease declined from 190 in 1970 to 46 in 1977 (Royal Maternity Hospital, Belfast. Clinical Reports for 1970-72 and 1976-77).

There is a debate at present in the UK over whether a programme of routine antenatal prophylactic anti-D should be introduced or not. At a recent consensus conference on anti-D prophylaxis it was noted that there is little up-to-date information on the number of babies affected by Rhesus disease or their ultimate outcome. This data is required so that any decision on antenatal anti-D prophylaxis is evidence based. We therefore examined the current extent of Rhesus isoimmunisation and the outcome of affected infants in Northern Ireland.

Methods

Northern Ireland has a population of approximately 1.5 million and there are between 24,000 and 25,000 live births each year. Approximately 17% of pregnant women are Rhesus D (RhD) negative. The Northern Ireland Blood Transfusion Service (NIBTS) provides a centralised antibody testing service for all maternity hospitals and general practitioners in the Province, and maintains a computerised register of all results. This register was used to identify all pregnant women with anti-D antibodies between September 1994 and February 1997. Data was then obtained from the hospital records of these women and their infants.

Results

A total of 129 pregnant women with RhD antibodies were identified from the NIBTS register. The records of 124 women were examined; five sets of records were unobtainable. Twenty-one (17%) of these women were primigravidae and 103 were multigravidae, although in 60 of the multigravidae this was the first pregnancy during which RhD antibodies were detected. In two of the primigravidae antibodies were present at booking at around 18 weeks; five had antibodies detected later in second trimester and fourteen had the RhD antibodies detected during the third trimester.

In total the 124 women delivered 130 babies. There were 120 live births. Two pregnancies were terminated because of fetal abnormalities. There were five spontaneous abortions. In one of these a very high titre of anti-D antibody (1 in 2048) was found at booking and this pregnancy aborted at 16 weeks. In the other four spontaneously aborted pregnancies, anti-D antibodies were detected at low titres only, and the abortions occurred in the first trimester. There were two stillbirths following intrauterine blood transfusions and one stillbirth for which no cause was found (no signs of hydrops al post mortem). The deliveries took place in 15 different maternity units and 32 of the 120 live births (26%) occurred in hospitals which did not have on-site paediatric cover.

Rhesus isoimmunisation, defined as a positive direct Coombs’ test in cord blood or from the baby, occurred in 57.3% (71/124) of the pregnancies examined, although 17 of the 124 pregnancies were associated with Rhesus negative infants, and thus would not have been at risk of isoimmunisation. Seventy-eight babies (48 term and 30 preterm) were affected in total as there were 4 twin pregnancies and 1 quadruplet pregnancy. Seventy-six were live born; two intrauterine deaths followed fetal transfusions at 25 and 27 weeks gestation. The mean (SD) birth weight was 2786g (923g) (range 796g to 4760g) and median gestation was 37 weeks (range 25 to 41 weeks).

<table>
<thead>
<tr>
<th>No. of phototherapy days</th>
<th>No. of babies requiring phototherapy</th>
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<tbody>
<tr>
<td>280</td>
<td>55</td>
</tr>
<tr>
<td>No. of exchange transfusions</td>
<td>61</td>
</tr>
<tr>
<td>No. of babies requiring an exchange transfusion</td>
<td>29</td>
</tr>
<tr>
<td>No. of neonatal intensive care days</td>
<td>1263</td>
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<tr>
<td>No. of babies admitted to a neonatal unit</td>
<td>59</td>
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Table 1: The Neonatal Intensive Care Unit Workload Associated with Rhesus Isoimmunisation September 1994 to February 1997

<table>
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<tr>
<th>Total for Northern Ireland</th>
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<tr>
<td>No. of babies requiring phototherapy</td>
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<tr>
<td>No. of exchange transfusions</td>
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<tr>
<td>No. of babies requiring an exchange transfusion</td>
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<tr>
<td>No. of neonatal intensive care days</td>
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<td>No. of babies admitted to a neonatal unit</td>
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Fifty-nine of the 76 live born infants (77.6%) required admission to a neonatal unit. All infants required intravenous fluid and/or nutritional support along with the therapies summarised in Table 1. There was one neonatal death; an infant who was born at term with severe hydrops, and who died at seven days of age with multi-organ failure. Nine of the infants who required neonatal care were transferred from hospitals with no on-site paediatric cover. Two of the 9 were born to mothers who had been sensitised in a previous
pregnancy and had been induced at 38 weeks because of the presence of antibodies. Therefore in these two pregnancies and in one other, which was associated with rapidly rising antibody titres during late pregnancy, it could have been possible to predict that the infants would require paediatric care.

The group of infants who received intensive care have been followed up to the age of 18-24 months. Two infants have severe permanent neurodevelopmental delay. They were born at 26 and 29 weeks gestation, and in both cases intrauterine transfusions had been performed. Five infants have minor developmental problems such as myopia, squint, or delay in language and fine motor skills. Thus in total, five of the 78 immunised babies (6.4%) have had a poor outcome, defined as death or severe neurodevelopmental delay.

Discussion

There is still a significant morbidity and mortality associated with RhD haemolytic disease in Northern Ireland. This is consistent with a recent study in Scotland which showed that the mortality from RhD haemolytic disease is underreported and often unrecognised. Therefore, in view of the poor fetal and neonatal outcomes, it is important to re-examine the management of RhD affected pregnancies and determine if improvements are possible.

An unexpected finding during this study was the number of planned deliveries which occurred in hospitals without on-site paediatric cover. This degree of decentralisation is in contrast to the early 1970’s when all Rhesus infants in the Province were cared for in the Royal Maternity Hospital, Belfast. In 1970, there were 190 babies with RhD haemolytic disease who had a total of 300 exchange transfusions (Clinical Report for the Royal Maternity Hospital, Belfast 1970), whereas in this study, 59 babies were cared for in seven hospitals and only 29 required exchange transfusions. It is impossible to say whether decentralisation influenced the outcomes of the immunised pregnancies, although it is interesting to note that the infant who died at seven days of age was born in a hospital without on-site paediatricians and that for three of the nine transferred babies it could have been predicted that they would require neonatal care. However, it would appear that decentralisation does limit the opportunities for training in procedures such as exchange transfusions, as individual registrars have no guarantees of being “in the right place at the right time.” During the study period, a trainee paediatrician (approximately 20 registrars per year) would only have performed about one exchange transfusion per year. Furthermore, the medico-legal risks of such procedures being undertaken by inexperienced registrars cannot be understated as the infants are often acutely unwell and the side-effects of exchange transfusions can be life-threatening. The best way to guarantee sufficient volumes of work for training, the maintenance of expertise in the future and to minimise medico-legal risks, might be to re-centralise the care for RhD antibody affected pregnancies.

The current programme for prevention of Rhesus immunisation in Northern Ireland consists of administration of anti-D after birth and other potentially immunising events. There is evidence that within the UK this program is not being fully implemented or completely effective. Routine antenatal prophylaxis with anti-D has repeatedly been shown to significantly reduce the rate of maternal alloimmunisation, irrespective of whether it is given to primigravidae or multigravidae as a single dose of 300 mcg at 28-30 weeks of pregnancy or two doses of 500 IU at 28 and 34 weeks gestation. However, antenatal prophylaxis would greatly increase the amount of anti-D immunoglobulin required. There is already a global shortage of anti-D immunoglobulin and a sufficient supply of the immunoglobulin for an antenatal prophylaxis program may only be possible when human monoclonal anti-D is available. The overall extra cost of antenatal prophylaxis is small when compared to other areas of health care and has been shown to be most cost effective if given to just primigravidae, rather than all RhD negative women. 3-10

A study is now under way in the Province to determine whether the current guidelines are being adhered to and to identify when maternal alloimmunisation is occurring. Given that the current infant morbidity from RhD isoimmunisation is unacceptable, it should then be possible to determine if a programme of routine antenatal anti-D is an intervention which is likely to succeed in reducing the level of infant morbidity.

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References

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