

MATERNAL ANTECEDENTS AND OUTCOMES FOR RHD
ALLO-IMMUNIZATION: A STUDY OF A BRAZILIAN POPULATION

*ANTECEDENTES MATERNOS E EVOLUÇÃO NA ALOIMUNIZAÇÃO RHD:
ESTUDO DE UMA POPULAÇÃO BRASILEIRA*

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ABSTRACT

Objective

To evaluate the association between perinatal evolution and maternal antecedents of sensitizing events, in RhD immunized pregnancies in a local population.

Methods

Retrospective analysis of the medical records collected from RhD allo-immunized pregnant women attending the *Centro de Atenção Integral à Saúde da Mulher da Universidade Estadual de Campinas* for antenatal care, between January 1990 and May 1999. As maternal variables, previous blood transfusions and the lack of anti-D prophylaxis (non anti-D), were analyzed. As perinatal variables: gestational age at delivery, birthweight, fetal blood transfusion and/or fetal death.

Results

The lack of anti-D use was identified in 70% of these women. There were no statistical differences in the rates of fetal death or necessity for fetal blood

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transfusions between the previous blood transfusions and non-anti-D groups. The gestational ages and birthweight for the mothers with and without previous blood transfusions were respectively 35.7 and 37.9 weeks ($p=0.03$) and 2232g and 2784g ($p=0.04$).

Conclusion

The most frequent antecedent in maternal allo-immunization found in the current study population, was the lack of immuno-prophylaxis. The cause of maternal immunization did not influence the prognosis of pregnancy, except for a reduction in gestational age and birthweight from mothers who had suffered previous blood transfusions.

Indexing terms: blood transfusion, gestational age, Rh immunization, perinatal outcome, pregnancy.

RESUMO

Objetivo

Avaliar a associação entre a evolução perinatal e os antecedentes maternos de eventos sensibilizadores em gestações RhD aloimunizadas, em uma população local.

Métodos

Análise retrospectiva de prontuários médicos de um grupo de gestantes RhD imunizadas, atendidas no Centro de Atenção Integral à Saúde da Mulher da Universidade Estadual de Campinas entre janeiro de 1990 e maio de 1999. As variáveis maternas analisadas foram: passado de hemotransusão e falta de profilaxia anti-D. Variáveis perinatais: idade gestacional ao parto, peso ao nascimento, transfusão intra-uterina e/ou óbito fetal.

Resultados

A ausência de profilaxia anti-D foi identificada em 70% dos casos. Não houve diferença estatística nas taxas de óbito fetal e necessidade de transfusão intra-uterina entre os grupos de gestantes sem anti-D e o grupo com história de hemotransusão. A idade gestacional ao parto e o peso ao nascimento nos grupos com e sem hemotransusão foram, respectivamente, 35,7 e 37,9 semanas ($p=0,03$) e 2232g e 2784g ($p=0,04$).

Conclusão

O antecedente materno mais freqüente de causa de aloimunização encontrado na população deste estudo foi a falta de imunoprofilaxia anti-D. A causa da imunização materna não influenciou o prognóstico gestacional, exceto na redução da idade gestacional e no peso ao nascimento nas mulheres com passado de transfusão sangüínea.

Termos de Indexação: transfusão de sangue, idade gestacional, imunização Rh, evolução perinatal, gravidez.

INTRODUCTION

The etiology, physiopathology, diagnosis, treatment and prophylaxis of Hemolytic Disease of the Fetus and Newborn (HDFN) are well known¹. Despite this, Rh immunization still occurs for many reasons². These can be related to the failure to

administer the anti-D prophylaxis, occasions on which a woman does not receive postnatal anti-D following delivery of a RhD-positive or un-typed fetus, or following a clinical event that could be associated with feto-maternal hemorrhage during a continuing pregnancy, or on which anti-D administration was inadequate or delayed. Also, with recent advances

on the molecular basis of the Rh blood group, women with atypical D-structures ("D variants") were identified who had been treated as RhD-positive, although some of them could form anti-D if exposed to typical D-antigen³. Another form of maternal sensitization is the exposure to mismatched blood products.

Without treatment, 25% to 30% of the fetuses will have some degree of hemolytic anemia, and another 20% to 25% will develop severe hydropsis⁴. Of the affected fetuses, 50% will need intrauterine transfusion (IUT)⁵. In tertiary centers the mortality rate after IUT is 14% to 38% for hydropic fetuses and about 10% for non-hydropic ones⁶.

Thus, in order to achieve low rates for HDFN as seen in other countries, where the frequency has declined in the past decades^{7,8}, the main problems to be controlled are incompatible blood transfusion and the failure to administer anti-D prophylaxis.

The association between the severity of RhD sensitization and the form of sensitization is not clear in the literature. Reports from the 1950's^{9,10} showed that maternal immunization due to incompatible blood transfusion had a worse perinatal prognosis than pregnancy-induced immunization. The hypothesis was that the greater the antigenic load of the maternal sensitization mode, the worse the prognosis for HDFN. Considering the lack of more recent studies about this possible prognostic factor and the dramatic changes in obstetric technology and fetal treatment since these earlier reports, the present study examined the association between the maternal antecedents and perinatal evolution in women sensitized to the RhD antigen, treated in a Brazilian tertiary fetal medical center.

METHODS

Women showing RhD immunization, who attended the *Centro de Atenção Integral à Saúde da Mulher* of the *Universidade Estadual de Campinas* (Unicamp) for public antenatal care between January 1990 and May 1999, were included in this study. The women were confirmed as being RhD sensitized

and bearing RhD-positive fetuses. Those showing multiple pregnancies or fetal structural or chromosomal abnormalities were excluded.

The data was collected on a chart specially designed for this study, which contained patient identification, diagnosis, and follow up data from pregnancy to postpartum. Their records were reviewed for sensitizing events, fetal interventions and pregnancy evolution resulting from the RhD hemolytic disease. The need for intrauterine transfusions, gestational age at delivery by the Capurro method, birthweight and occurrence of fetal death in the current pregnancy, were compared between the two groups of mothers, distinguished according to the form of sensitization: blood transfusion or lack of anti-D prophylaxis.

A data bank in Epi Info 6.0 software was used to store and analyze the data. The variables were studied by comparison of the means and frequency distributions in relation to the maternal antecedent data. A "Chi-square" test was used for this analysis. Continuing variables were analyzed by a one-way analysis of variance. The statistical significance of p was considered for values lower than 0.05.

The University Ethics Committee approved the study.

RESULTS

In the period studied, 126 pregnancies were included: 24 women had no known previous history for Rh sensitizing events (19%); 14 women were identified as receiving blood transfusions (11%) and 4 of these presented blood transfusions as an isolated sensitizing event; ten cases presented both blood transfusion and lack of anti-D; 88 (70%) women presented "non anti-D". The maternal antecedents associated with Rh sensitization are presented in Table 1.

The maternal sensitization history (PBT or no anti-D prophylaxis) and the need for intrauterine transfusion or fetal death in index pregnancy are shown in Table 2.

Table 1. Maternal antecedents in pregnant women with the RhD disease.

Antecedents	n	Grouped by association
No antecedent identified	24	24
Isolated Previous Blood Transfusion	4	
PBT + no Anti-D prophylaxis	10	14
No Anti-D prophylaxis	88	88
Total	126	126

PBT = Previous Blood Transfusion.

Table 2. Maternal sensitization antecedent in relation to intrauterine transfusion and fetal death in the index pregnancy.

Maternal history	Fetal death in index pregnancy*		Intrauterine transfusion**		Total
	Absent	Present	Not performed	Performed	
No antecedent identified	20	4	18	6	24
With PBT	10	4	9	5	14
No Anti-D prophylaxis	74	14	61	27	88
Total	104	22	88	38	126

* $p=0,50$; ** $p=0,43$. PBT = Previous Blood Transfusion.

The mean gestational age at birth in the PBT history group was 35.7 ± 3.3 weeks and in the group without PBT it was 37.9 weeks ($p=0.03$). The mean birthweight in the PBT group was 2272 ± 713.9 g and in the group with no PBT it was 2784.2 ± 669.4 g ($p=0.04$).

DISCUSSION

In this particular group of women it was observed that the form of sensitization, either previous blood transfusion or non anti-D, did not identify fetuses at greater risk for death or invasive treatment in the index pregnancy. However, it was verified that there was a decrease in gestational age and birthweight in babies from women who had had previous blood transfusions, as compared to those without this antecedent. This study provided no explanation for these events, since there were not a great number of transfused fetuses in this group, which would tend to shorten the length of pregnancy and thus interfere with these aspects.

The data presented here regarding the form of sensitization has a potential bias to be considered when analyzing the influence of blood transfusion as a determining prognostic factor for Rh disease.

Unfortunately, the overlapping of both antecedents makes it impossible to have a completely error free evaluation, since at least one third of the women who received blood transfusions also failed to receive adequate anti-D prophylaxis.

Failure to perform adequate RhD sensitization prophylaxis was the most frequent event in maternal antecedent, even presenting an association with previous blood transfusions. The observation that only 3.2% of the patients studied had an isolated antecedent of blood transfusion and that the great majority of cases failed to receive anti-D prophylaxis, raised troubling questions as to why this simple and fairly inexpensive method of avoiding such an extremely dangerous health problem is still overlooked by health authorities in this country. This is a completely different situation from the one referred to by Portman et al.¹¹, in which they report the failure of prophylaxis despite adequate use, as the most frequent cause of sensitization.

It was also observed that there was no increase in the number of fetal deaths in index pregnancies or in the need for intrauterine transfusions in cases with a history of previous fetal death. This association of a history of previous fetal death and prognosis in index pregnancy is not the same as that identified by other authors^{1,2,9,12,13}.

One limiting factor in this study was that 19% of our sample had no identified antecedents for sensitization. Some of these non-identified causes of sensitization could be due to failed prophylaxis, despite its administration. Other causes could include atypical D-variants but, one cannot exclude an RhD blood mistyping of the mother, depending on the antiserum used.

Data from Walker & Murray¹⁰ showed a 70% chance of fetal death for woman with a previous fetal death, secondary to Rh sensitization. These data have of course, been dramatically changed by treatment of fetuses at risk of death during pregnancy, by intravascular intrauterine blood transfusion^{1,14}. It may be argued that this more aggressive treatment has been changing the natural history of the disease, and consequently, its prognosis. This effect can be shown by the number of fetal deaths in index pregnancies and reflects the effect of the intrauterine treatment on the final prognosis.

In conclusion, it was not possible to affirm that the cause of isoimmunization in this population was associated with the severity of the disease. However, maternal sensitization by blood transfusion was associated with prematurity and low birthweight. Future studies must be directed toward the identification of maternal antecedents as risk factors for the severity of the Hemolytic Disease of the Fetus and the Newborn, in order to direct available management tools.

A C K N O W L E D G E

Sponsored by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), process number 98/14737-3.

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Recebido para publicação em 16 de dezembro de 2004 e aceito em 12 de abril de 2005.

