Title:

Misinterpretation of blood group and antibody screen leading to serious errors in RhD Immunglobulin administration: a report on first 2 years of data from Serious Transfusion Incident Reporting program

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Misinterpretation of blood group and antibody screen leading to serious errors in RhD Immunglobulin administration: a report on first 2 years of data from Serious Transfusion Incident Reporting program

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Abstract:

The Serious Transfusion Incident Reporting program (STIR) commenced haemovigilance in relation to RhD Immunoglobulin (Ig) administration in 2015.

During two years of reporting 21 reports relating to RhD Ig administration were received. Thirty-three percent (7/21) were related to omission of RhD Ig, putting women at risk of RhD alloimmunisation and adverse consequences in future pregnancies. A recent case reported to STIR highlights poor communication and misinterpretation of pathology results leading to significant morbidity from haemolysis in the Fetus.

STIR makes recommendations related to education of staff and communication between clinical and laboratory staff to improve the safety of patient care.

In Australia, approximately 15% of pregnant Caucasian women will be RhD negative[1]. In the event these women become pregnant with an RhD positive baby, there is a risk of maternal sensitisation to RhD and development of Haemolytic Disease of the Fetus and Newborn

(HDFN).[1] Until the late 1960s, HDFN due to RhD incompatibility was an important cause of fetal and neonatal morbidity and mortality. The immunisation rate can be reduced to ≤0.2% by the administration of RhD immunoglobulin (RhD Ig) during pregnancy, at 28 weeks, 34 weeks, following sensitising events and after delivery, making mortality as a result of HDFN uncommon.[2, 3]

In 2015, the Serious Transfusion Incident Reporting program (STIR) commenced haemovigilance in relation to RhD Ig. STIR is a voluntary, central reporting system for serious adverse events, managed by the Blood Matters program (a collaboration between the Victorian Department of Health and Human Services and the Australian Red Cross Blood Service). STIR receives reports from public and private health services in Victoria, Tasmania, the Australian Capital Territory and the Northern Territory. STIR's aim is to report the number and types of adverse events associated with transfusion for the purpose of developing recommendations for practice improvement.

In the first 2 years of RhD reporting, STIR received 21 reports relating to RhD Ig (Table 1). These events related to all areas of RhD Ig administration. A single report could represent two or more problems on two or more occasions; for example, a woman who has missed both routine prophylaxis and post-natal RhD Ig.

Table 1. RhD reporting to STIR (Jan 2015-Dec 2016)

Inappropriate administration includes anti-D given to four RhD positive women, two RhD negative women with RhD negative babies who received anti-D postnatally, and one woman with RhD alloimmunisation. All of these women were unnecessarily exposed to a blood product.

Inappropriate administration occurred following a postnatal home visit with misinterpretation of the positive feto-maternal haemorrhage (FMH) result as meaning the patient required RhD Ig, even though the woman had given birth to an RhD negative infant. In another incident, the staff member misinterpreted the negative antibody screen to mean the woman was RhD negative. In addition, three incidents involved RhD Ig being ordered for a named patient but then given to another patient (near miss). In all these cases, the woman

who received the product did require RhD Ig, but correct patient identification processes were not followed.

Thirty per cent (7/22) of reports were related to omission of RhD Ig doses, putting these women at risk of RhD alloimmunisation in future pregnancies. In five of the reports the antenatal dose was omitted, usually both the 28 and 34 week doses. The remaining errors related to problems with the ordering or storage of the product without any adverse clinical outcomes.

RhD Ig incident reporting to STIR is in its infancy. The equivalent UK haemovigilance program Serious Hazards of Transfusion (SHOT), a mandatory reporting system, has been receiving reports relating to RhD Ig for since 1996 and now explores the causes of RhD alloimmunisation in these reports. In the 2016 SHOT report, 409 cases due to RhD Ig administration were reported, 81.4% related to omission or late administration of RhD Ig.[4] A case of unrecognised immune anti-D resulting in severe HDFN and neonatal death was also reported. There is an increase in the number of cases reported each year, which may be due to more awareness of the need to report, but also indicates ongoing issues with RhD Ig administration.

An example of a recent case reported to STIR highlights poor communication and misinterpretation of pathology results leading to morbidity from HDFN. At the core of this incident is the failure to distinguish between an allo-antibody to RhD and passively acquired anti-D due to RhD Ig administration.

An RhD negative woman in her third pregnancy, reported to have received RhD Ig appropriately in previous pregnancies, was being cared for in a shared care arrangement. At 26 weeks gestation, a blood group and antibody screen was performed at a laboratory separate to the health service where she was booked. Anti-D was detected and no antibody titre was performed. The health service did not receive a report for this result as it was faxed to an incorrect number. A hard copy of the results was sent, addressed to the chief medical officer at the health service. At the 28 week visit to the health service, the midwife requested a copy of the results from the laboratory, but it is unclear whether the report was received. At this time, the woman was administered a routine antenatal prophylaxis dose of RhD Ig. At the 34 week visit, the original 26 week result was viewed by a midwife and medical officer; however they misinterpreted the result to be due to passive anti-D. A second dose of RhD Ig

was given. Routine blood grouping performed prior to elective caesarean section identified a strong anti D with a titre of 1:2048. The woman was contacted and asked to return urgently to the health service. Cardiotocography (CTG) was performed and found a sinusoidal fetal heart trace. An emergency caesarean section was performed and the infant was transferred to NICU on 60% oxygen and CPAP. Subsequently, the infant was intubated and ventilated. The baby's initial haemoglobin was 70g/L with a bilirubin of 161 micromol/litre, requiring a double volume red cell exchange. Despite the setting of the birth and the elevated RhD titre, the woman was administered a postnatal dose of RhD Ig.

This case highlights the problems that can occur in the care of obstetric patients with regard to red cell alloimmunisation and the use of RhD Ig. Communication between the laboratory and the health service failed, and it is unclear what communication occurred in the shared care arrangement and who was taking responsibility for reviewing results.

In the health service the staff either did not review results or did not understand the significance of the results. Opportunities to monitor the woman and her baby during the pregnancy for complications of HDFN were missed as staff were unaware of the risk. Although staff seem to have been aware of the need for an RhD negative woman to receive RhD Ig prophylaxis, they did not seem to understand the importance of the antibody testing and interpretation of the results. Titres higher than 1:4 are generally considered to demonstrate RhD alloimmunisation , but interpretation of anti-D levels requires knowledge of the clinical as well as antibody results. Alloimmunised women do not need further RhD Ig and should undergo serial antibody monitoring. Where there is uncertainty RhD Ig should be given and serial monitoring may be used to distinguish between passively acquired anti-D and alloimmunisation. A titre of 1:32 or higher, or a significantly rising titre (or preferably quantification) should indicate monitoring for fetal anaemia is required.[5,6]

Recommendations

Table 2 summarises strategies and recommendations to minimise RhD administration related errors that can be incorporated into current antenatal care systems.

All staff involved in RhD Ig administration should receive education on the use of RhD Ig. Staff require competency in interpretation of the blood bank results and should know to contact their local pathology provider or appropriately experienced clinician for expert assistance with result interpretation if there is any uncertainty. Confirmation of the maternal

RhD status is essential to ensure appropriate prescription or administration of RhD Ig. In a number of the incidents reported, the laboratory either did not routinely check the patient blood group prior to dispensing the product, or did not have the RhD status available to check. Finally, all staff should be educated about the importance of correct patient identification with regard to prescription, product request and administration. In order to introduce and maintain these recommendations each health service should have robust haemovigilance systems in place which require support of hospital executive and depending on the hospital size may include hospital transfusion committees with input from obstetric, haematology and pathology departments. Potential errors highlighted by RhD use often have overlap with other areas of transfusion practice and the broader principles of haemovigilance should be applied in this setting.[8]

Table 2. Recommendations for health services

Conclusion

The introduction of RhD Ig in Australia has been successful in substantially reducing the incidence of severe HDFN. The addition of RhD Ig incidents to STIR allows the systematic collection of data related to the use of this product and identifies potential opportunities for practice improvement and staff knowledge. However, in order to accurately identify the incidence of RhD Ig errors and assess response to recommendations made by STIR, mandatory reporting to STIR would be required. Promoting awareness of the issues around RhD Ig administration will hopefully reduce incidents. STIR will continue to monitor and report on these incidents to help health services improve patient care.

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Table 1. RhD reporting to STIR (Jan 2015-Dec 2016)

	Inappropriate administration	Omitted dose	Near Miss	Error in ordering/ request	Storage/ handling	Wrong dose	Total
Routine prophylaxis	1	5	1		1	1	9
Post sensitising event	3		1		1		5
Post-natal	4*	2	1	1			8
Total (%)	8	7	3	1	2	1	22

*one report corresponds to anti-D administered inappropriately for both prophylaxis and post-natal

Table 2. Recommendations for health services

Staff education	• Prior to registration as an antenatal care provider, all staff should receive education on the prescribing and administration of RhD Ig in accordance with national guidelines[7], for example the RhD Ig e-learning module on the Australian Red Cross Blood Service website. https://learn.transfusion.com.au/course/index.php?categoryid=85
Guidelines for dosage and prescribing RhD Ig	• Health service policies should reflect current recommendations for timing and dose of RhD Ig. • Confirmation of the maternal RhD status is essential prior to prescription or administration of RhD Ig. This must be an electronic or hardcopy result, not a result transcribed into the medical record or referral letter and should be shared with the laboratory prior to dispensing RhD Ig. • If this is not available, arrangements should be made to determine the woman's RhD status prior to RhD Ig administration.
Administration	• Positive patient identification must be used, wherever possible, to confirm the woman's identity prior to administration of RhD Ig. • All staff must be educated about what this process involves.
Governance	• Health services providing maternity care should include input from obstetrics into their Transfusion committee or equivalent. • Consideration to regular auditing processes to review systems relating to RhD Ig prescription and administration should occur. • Consider the use of checklists, with sign off that include when

	RhD Ig should be used. These may be paper or electronic records. • Health services should report incidents of administration errors, delays and missed administration to STIR.