Adverse Events Related to Anti-D Immunoglobulin (Ig): Prescription, Administration and Sensitisation n=409

14

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Definition:

An adverse event related to anti-D immunoglobulin (Ig) is defined as related to the prescription, requesting, administration or omission of anti-D Ig which has the potential to cause harm to the mother or fetus immediately or in the future.

Key SHOT messages

- A total of 409 reports related to errors involving anti-D Ig were reviewed by SHOT in 2016, of which 81.4% related to the omission or late administration of anti-D Ig. This is a continuing and worrying trend that is resulting in a large number of women being put at risk of sensitisation to the D antigen
- There continues to be a lack of knowledge by both clinical and laboratory staff regarding the theory underpinning the clinical need for both routine antenatal anti-D Ig prophylaxis (RAADP) and also anti-D Ig prophylaxis in response to a potentially sensitising event (PSE), including labour. This has again resulted in both inappropriate administration of anti-D Ig and incorrect, most importantly insufficient doses of anti-D Ig being administered
- While 75.8% of the errors reported this year occurred in the hospital environment, there are numerous examples of errors that have occurred as a result of poor communication between hospital and community teams
- The term 'early pregnancy' is defined by The National Institute for Health and Care Excellence (NICE) as up to 13 completed weeks of pregnancy (NICE 2012), whereas the British Society for Haematology (BSH) guideline defines this as up to 12 weeks (BSH Qureshi et al. 2014). It is therefore important, as previously recommended by SHOT in 2014, that there is consistency of practice within hospitals, regardless of which professional guideline may influence the detail of local policy

Recommendations

- Hospital Transfusion Committees should ensure regular and active participation from obstetric and midwifery teams including those based both within the hospital and the community, in order to develop and oversee local policies for the requesting, issue and administration of anti-D Ig and the investigation of adverse incidents associated with anti-D Ig

Action: Hospital Transfusion Committees, Obstetric Departments, Midwifery Teams

- All staff involved in the requesting, issuing or administration of anti-D Ig should have appropriate training and education in relation to anti-D, such as completion of the anti-D module within the Learn Blood Transfusion (LBT) e-learning package (www.learnbloodtransfusion.org.uk)

Action: Hospital Transfusion Laboratories, Hospital Transfusion Committees, Trust/Health Board Chief Executive Officers (CEO), Obstetric Departments, Community Midwifery Teams

- All clinical facilities, both NHS and private clinics, that provide care to women and are involved in the administration of anti-D Ig should report errors associated with anti-D Ig to SHOT

Action: Trust/Health Board/Private clinic Chief Executives

Good practice points:

- Hospitals should consider implementing, via a Blood Service reference laboratory, high throughput non-invasive prenatal testing for fetal D genotype, as recommended by NICE (NICE 2016). The testing will identify D-negative women carrying a D-positive fetus with the aim being to streamline the RAADP programme and prevent the administration of an unnecessary medicinal blood product when the fetus is D-negative and is therefore not at risk of haemolytic disease of the fetus and newborn (HDFN)

  There should also be a robust system for making sure that fetal blood group results are acted upon appropriately and an awareness that fetal blood group results may be different in subsequent pregnancies so that any results linked to a maternal record should be accurately recorded and indexed to a specific pregnancy

- Hospitals should have a team consisting of consultant obstetricians, hospital and community-based midwives and laboratory staff to help develop a clear policy regarding the use of anti-D Ig. The introduction of midwifery champions as a point of reference in hospital and community teams will ensure education is continuous and lead to a better understanding of the policy. A named contact(s) in the laboratory should be available to ask for advice in understanding Blood Service reference laboratory reports, including antibody levels and additional sampling requirements

- Hospital blood transfusion laboratories should have systems in place to identify any anti-D Ig that has been issued for a woman but not collected from the laboratory. The system should include a mechanism to escalate the urgency of the anti-D Ig administration to ensure that it is administered before the 72-hour time limit has elapsed

- Hospitals should have clear pathways of communication between the hospital and community teams. Regular meetings between the teams to discuss communication failures are essential in improving the service for the users

Learning points

- Hospitals should ensure a robust system is in place for the regular education of emergency department (ED) staff and midwives regarding the clinical indications for anti-D Ig. Rapid early pregnancy pathways should be available for the administration of anti-D Ig following a potential sensitising event in D-negative women

- Hospitals should develop clear processes for checking historical blood group records prior to the requesting of anti-D Ig by clinical staff or issue of anti-D Ig by laboratory staff in order to prevent inappropriate requests and administration

- Where mother and cord samples are received in the laboratory, a system should be in place to ensure that the results of the cord sample are linked to the maternal record. This will guarantee that any required postnatal anti-D Ig is appropriate (i.e. infant blood group has been confirmed as D-positive) and that the correct dose has been issued (i.e. based on the fetomaternal haemorrhage (FMH) testing result). There must be a robust system in place for entering results into the laboratory information management system (LIMS), including any received from the Blood Service reference laboratory. This will ensure that all information, including the infant blood group, is easily retrievable in the event of a query from clinical staff

- Positive patient identification means asking a woman 'What is your name?' not asking 'Is this your name?'

Commentary

This year's report again highlights recurring key issues in the provision of anti-D Ig. These include poor knowledge and understanding by both clinical and laboratory staff about appropriate use of anti-D Ig, failure to follow standard operating procedures and failure to refer to the blood grouping results of both women and infants before both requesting and issuing anti-D Ig.

These errors all emphasise the need for clear and unambiguous local protocols in both the clinical area, most importantly in clinical areas outside the maternity departments e.g. the ED and in the blood transfusion laboratory.

These protocols should be complemented by robust training programmes for clinical and laboratory staff that ensure all staff are able to correctly request and issue anti-D Ig for a woman that may present with a need for anti-D Ig regardless of the department she presents in.

The use of a checklist in the laboratory in order to escalate the requirement for anti-D Ig issued but not collected should ensure that it is administered before the 72-hour deadline. A key contact (champion) in the clinical area should be identified to act on these cases.

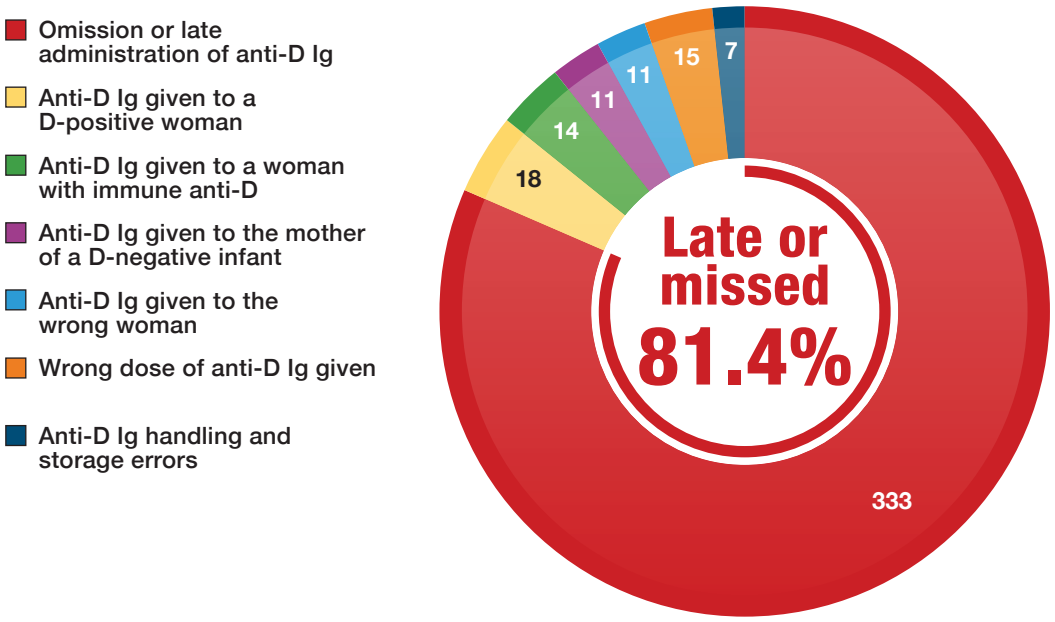


Figure 14.1: Distribution of anti-D Ig-related reports

Most errors occurred in hospital, 310, 75.8%, and 99, 24.2% in the community.

Deaths n=0

There were no deaths reported related to errors associated with anti-D Ig in 2016.

Major morbidity n=2

Two women developed immune anti-D following errors in clinical management. One was failure to administer anti-D Ig following a PSE, and the other was failure to administer anti-D Ig appropriately during a first pregnancy in 2012 which resulted in sensitisation and detection of immune anti-D in a subsequent pregnancy in 2015.

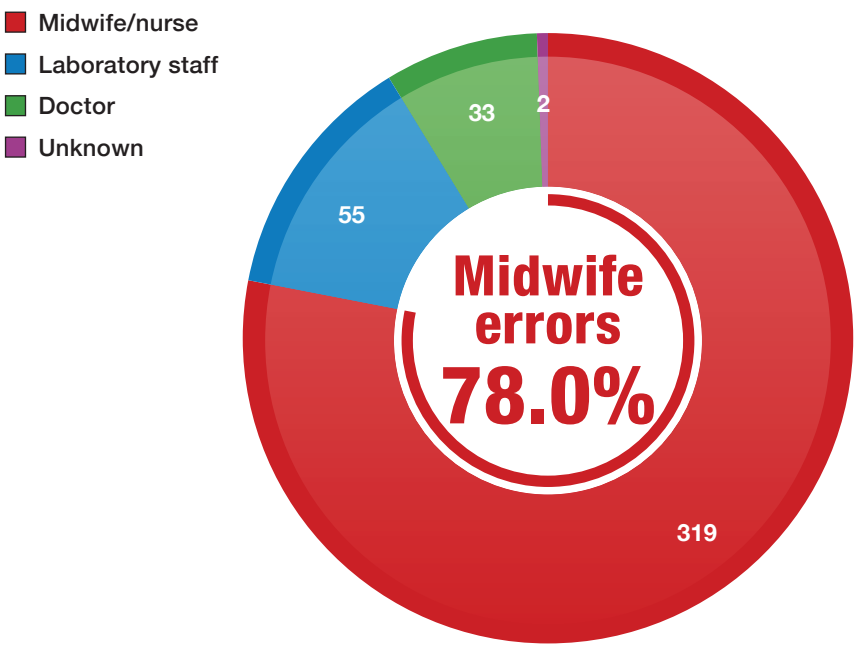
Potential for major morbidity n=331

In addition to the 2 sensitisations above, 331/409 (80.9%) case reports related to the omission or late administration of anti-D Ig. This is a worrying situation, putting many women at risk of potential sensitisation to the D antigen.

Overview of cases

Most errors (377/409, 92.2%) occurred during normal working hours.

Figure 14.2: Staff group responsible for primary error associated with anti-D Ig



Clinical staff were responsible for 352/409, 86.1%, of the errors reported with 33/409, 8.1%, involving doctors, including consultant obstetricians.

The majority of errors by laboratory staff were made by biomedical scientists (BMS); however there were also errors involving unregistered staff e.g. associate practitioners (AP), including errors in the selection and issue of anti-D Ig from the blood transfusion laboratory.

Omission or late administration of anti-D Ig n=333 (81.4%)

A total of 333/409 (81.4%) case reports related to the omission or late administration of anti-D Ig. The majority, 305/333 (91.6%) were caused by clinical staff, and 28/333 (8.4%) by laboratory staff. Most errors occurred in hospital (244/333, 73.3%) and 89 (26.7%) in the community.

Common themes identified in this category include:

- Failure to administer anti-D Ig within 72 hours when a woman attended the ED for a PSE
- General lack of understanding of national guidance on administration of anti-D Ig following a PSE
- Failure of timely collection of anti-D Ig from the laboratory
- Late administration of postnatal anti-D Ig following early discharge of the woman from hospital
- Communication failures when women have shared care between hospital and community midwifery teams

Case 14.1: Failure to administer postnatal anti-D Ig results in the formation of immune anti-D

A D-negative woman developed an immune anti-D in her second pregnancy. It is possible she did not receive all appropriate anti-D Ig during her first pregnancy. The woman was informed that her first baby was D-negative and anti-D Ig was not required. As no cord blood sample was ever received for this pregnancy, it is unclear where this information came from. It does appear as if the woman had been sensitised to the D antigen prior to her second pregnancy. It has been highlighted that the same woman probably did not receive the postnatal standard dose of anti-D Ig at the time of her first pregnancy, as clinicians believed it was only given if the Kleihauer test indicated so.

Case 14.2: Lack of knowledge by clinical staff in the ED about the need for administration of anti-D Ig for a PSE resulting in sensitisation to the D antigen

At approximately 18 weeks gestation a D-negative woman attended the ED following a road traffic accident (RTA). No anti-D Ig was administered, as a result it appears that this woman has been sensitised to the D antigen. The routine 28-week blood sample showed the presence of low level immune anti-D. The woman previously had a negative antibody screen at booking.

Handling and storage errors related to anti-D Ig n=7 (1.7%)

These 7 incidents originated in the clinical area in 6 and one in the laboratory; 4 incidents occurred in the community and 3 in hospital.

Case 14.3: Failure to return product ordered in error to the laboratory

RAADP was requested for a woman by a community midwife. This was not administered on the date originally required because the midwife who had completed the request form wrote an incorrect date. The anti-D Ig that was issued was not returned to the laboratory and was kept in a drawer in the community midwives' office. The woman was given the anti-D Ig 3 weeks later but required a further dose of RAADP as the one given may not have been sufficient to protect her against D-sensitisation. This is because it is unclear if the product would still remain effective as the storage conditions specified by the manufacturer were not followed. The product manufacturer states that it is stable at 4-8°C but can be kept at room temperature for a maximum of 4 days.

Case 14.4: RAADP issued during previous pregnancy administered after expiry

1500IU anti-D Ig was administered to a woman for whom it had been prescribed and issued during her previous pregnancy 15 months earlier. The dose had expired.

Anti-D Ig given to D-positive women n=18 (4.4%)

Staff groups and locations involved: 9 clinical staff and 9 laboratory staff errors; 17 in hospital and 1 in the community.

Four errors that occurred in the laboratory related to women typed as 'weak D-positive' and therefore should be regarded as D-positive. Two occurred as a result of failure to investigate equivocal D-typing results.

These errors also highlighted a lack of knowledge by laboratory staff regarding the classification of women typed as 'weak-D' as D-positive who therefore do not require anti-D Ig prophylaxis at any stage of pregnancy or at delivery (BSH Qureshi et al. 2016).

It is important to note however that where clear cut results cannot be obtained in D-typing, women should be classified as D-negative until the D status is confirmed and anti-D Ig prophylaxis administered accordingly. This is particularly important in cases where samples are referred to a Blood Service reference laboratory for confirmation of D-typing where the result is not available within 72 hours of a PSE.

The main theme identified in this category was failure to check the woman's blood group on historical records prior to ordering/issuing anti-D Ig.

Case 14.5: Historical blood group record not checked prior to issuing anti-D Ig

Cord and maternal blood samples were received in the laboratory for a postnatal woman despite her being grouped as D-positive. The cord sample was typed unnecessarily and anti-D Ig issued inappropriately by a BMS before checking the maternal blood group.

Anti-D Ig given to women with known immune anti-D n=14 (3.4%)

Staff group and locations involved: 7 clinical staff, 3 laboratory staff and 4 involved both groups; 13 were in hospital and 1 in the community.

The themes identified within this category include:

- Failure to check historical records
- Laboratory staff ignoring flags on the LIMS
- Lack of understanding by clinical, particularly midwifery staff, and also a consultant obstetrician

Case 14.6: Lack of knowledge by clinical staff about immune anti-D

It was standard practice for midwives to administer anti-D Ig to all women that deliver a D-positive baby. A postnatal dose of anti-D Ig was issued and administered to a D-negative woman who was under a fetal medicine unit for the management of HDFN due to high levels of immune anti-D. She had undergone previous intrauterine transfusions (IUT) (described in Case 10.1).

Case 14.7: Lack of knowledge by consultant obstetrician

Postnatal anti-D Ig was requested for a woman known to have immune anti-D (>15IU/mL), but although the BMS informed the consultant who made the request that anti-D Ig was not indicated, the consultant insisted that it was administered regardless.

Anti-D Ig given to the mother of a D-negative infant n=11 (2.7%)

The staff involved in the primary error associated with the administration of anti-D Ig to the mother of a D-negative infant were laboratory staff in 8/11 cases (often where postnatal anti-D Ig was issued before the infant blood group had been confirmed as D-positive), and clinical staff in 1/11. In one it was unclear and in the other case, both were implicated. All errors reported in this category occurred in hospital.

Anti-D Ig given to the wrong woman n=11 (2.7%)

Nine errors were made by a midwife or nurse, 2 by doctors. Nine occurred in hospital and 2 in the community.

The themes identified in this category of reports were:

- Insufficient identification checks of the woman prior to administration of anti-D Ig
- Anti-D Ig administered was labelled with details of a different woman

Case 14.8: Patient misidentification followed by a deliberate deviation

Both Woman A and Woman B attended the antenatal clinic for administration of RAADP. The midwife called out the name of Woman B but Woman A followed her into the clinic room. The midwife mentioned the name of Woman B again and Woman A acknowledged this was her name. RAADP was administered, but then following discussion Woman A stated that this was not her name. When questioned Woman A thought that it was her name being called. Woman B was then called into a separate clinic room and administered a dose of RAADP despite it being labelled for Woman A.

Wrong dose of anti-D Ig given n=15 (3.7%)

Eight were caused by clinical staff, 6 by laboratory staff and 1 was unclear.

In 12/15 cases in this category the dose of anti-D Ig administered exceeded the recommended minimum dose. This was either in breach of local policy or occurred as a result of a clinical or laboratory error that resulted in the incorrect dose being administered, for example the patient was dosed twice, or where the local policy was to give 500IU but 1500IU was given, or the dose was based on an erroneous Kleihauer result. In 3/15 cases insufficient anti-D Ig was administered.

The theme identified in this category was errors in selection of the appropriate dose required for a PSE, particularly when women had repeated bleeding during pregnancy.

Case 14.9: Insufficient postnatal anti-D Ig administered following confirmation of a large fetomaternal haemorrhage

A Kleihauer test confirmed a fetomaternal bleed following delivery which would require additional anti-D Ig prophylaxis. The sample was sent to the reference laboratory who confirmed a bleed of 21mL. The BMS in the laboratory miscalculated the dose of anti-D Ig required and only issued 2000IU. This was administered. Laboratory checks identified that 3000IU anti-D Ig was required and a further 1500IU anti-D Ig was issued and administered however this was administered more than 72 hours following delivery.

Near miss anti-D Ig cases n=29

Point in the process	Type of error made	Number of cases	%
Request	Requested for a D-positive woman	2	13.8
	Requested for a woman with immune anti-D	1	
	Requested for the incorrect patient	1	
Sample receipt	Entered into the incorrect record	1	3.5
Testing	Incomplete testing prior to issue	4	24.1
	Transcription error	2	
	Misinterpretation	1	
Component selection	Issued to a woman with immune anti-D	5	17.2
Component labelling	Anti-D Ig mislabelled	5	17.2
Collection	Collection of incorrect anti-D Ig	1	3.5
Administration	Anti-D Ig not given in timely manner	4	20.7
	Attempted administration to the wrong patient	1	
	Inappropriate storage in the clinical area	1	
Total		**29**	**100**

Table 14.1: Near misses that could have led to errors related to anti-D Ig n=29

Midwives are one of the largest staff groups who make sampling errors leading to wrong blood in tube (WBIT) incidents, 197/776 (25.4%) (Figure 12.5). This appears to be an over-representation when compared to data supplied by the Oxford University Hospitals NHS Foundation Trust, which indicates midwives take 10.2% of all samples.

Information technology (IT)-related anti-D Ig cases n=21

Error	Reports	Unnecessary anti-D Ig administered	Failure to administer anti-D Ig or excessive delay	Wrong dose anti-D Ig
Error when manually transcribing data	**2**	1	1	
LIMS not updated with reference laboratory result	**3**	2	1	
Failure to consult historical record	**5**	3	1	1
Failure to use flags, logic rules	**6**	4		2
Electronic device not working	**1**			1
Computer downtime	**4**		4	
Total	**21**	**10**	**7**	**4**

Table 14.2: IT-related anti-D Ig cases n=21

In Table 14.2 above and cases below there are a number of examples where the use of IT systems flags, logic rules or algorithms would have prevented women getting anti-D Ig unnecessarily (10 cases), ensured that the correct dose of anti-D Ig was given (4 cases) and perhaps prevented omissions or delays in anti-D Ig prophylaxis (7 cases).

Case 14.10: LIMS can prompt correct anti-D Ig administration, but only if you put the right information in

A woman with a D-negative baby was given postnatal anti-D Ig unnecessarily. The LIMS was configured to guide whether anti-D Ig was needed postnatally if the cord blood group was recorded against the maternal FMH test request. On this occasion a locum BMS recorded the cord blood group somewhere else on the LIMS so it did not prevent issue of anti-D Ig.

Case 14.11: Highlighting changes in advice on electronic records

A woman was typed as O D-positive at booking and did not receive any RAADP or postnatal anti-D Ig. However, repeat samples requested to investigate a D-grouping anomaly and sent to a reference laboratory for testing, showed a D variant that does require anti-D Ig. However despite this report being uploaded onto the LIMS and a paper copy sent to the maternity unit the clinical team continued to act on the original (incorrect) result.

Case 14.12: RAADP worklist failed after computer downtime

After a laboratory computer failure was fixed the RAADP list was printed but four patients were missed and did not get timely RAADP although all had appropriate postnatal anti-D Ig prophylaxis.

Case 14.13: Manual transcription of the wrong result onto maternity records

A D-negative woman had a D-positive baby and was given anti-D Ig. Unfortunately the RAADP had been missed because the wrong blood group had been transcribed onto the maternity system manually.

Commentary

It is possible to use the LIMS or other IT systems to support anti-D Ig prophylaxis to make the process more robust and to ensure the right women receive anti-D Ig.

Ideally the LIMS is used to record and then use the **results of testing** to support laboratory and clinical policies for **anti-D Ig prophylaxis**. This includes:

During pregnancy

- The maternal blood group and the outcome of any anomalous D-typing investigations
- The maternal antibody screen and results of any associated reference tests used to distinguish passive from immune anti-D

At delivery

- The fetal blood group
- The maternal Kleihauer test and results of any additional confirmatory FMH tests

Flags or logic rules can be used to guide when anti-D Ig prophylaxis is needed and when contraindicated based on these testing results. For example to identify:

- D-negative women with no immune anti-D who need RAADP
- D-positive women or D-negative women with immune anti-D who do not need RAADP

The risk for error is greater when manual transcription is required. Entering the results of reference tests into the LIMS, along with the interpretation and associated clinical advice has resulted in errors in anti-D Ig administration. Similarly, mistakes can occur when copying the blood grouping results into the maternity record. Electronic transmission of data is preferred because it reduces the risk of transcription error and provides the ability to see real-time and updated results which supports effective decision-making and correct anti-D Ig prophylaxis.

Finally the benefits of having anti-D Ig assigned to a named patient in the LIMS enables audit of the completeness of the process. Another development is that some electronic blood management systems are now able to control the issue of anti-D Ig as well as other blood components and this is a useful and positive step.

Learning points

In the future high-throughput non-invasive prenatal testing (NIPT) using cell-free-fetal deoxyribonucleic acid (DNA) will be available for D-typing the fetuses of D-negative women to see if anti-D Ig prophylaxis is required in pregnancy (NICE 2016). It is of some concern that similar patterns of errors could arise as have been seen in this anti-D Ig prophylaxis pathway already. For example, care should be taken to avoid:

- Transcription errors when putting paper-based reference laboratory results into the LIMS
  - Think! Right patient – Right result – Right pregnancy
- Transcribing both the correct fetal genotyping result and the correct maternal D-typing result into the maternity record

There have been no errors reported to SHOT that fall into this category but laboratories and antenatal clinics should be vigilant to prevent such errors when implementing this new technology

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