Time to re-evaluate rhesus testing and anti-D prophylaxis in abortion care

Jonathan Lord [1,2]

[1]Marie Stopes International (UK), London, UK
[2]Department of Gynaecology, Royal Cornwall Hospitals NHS Trust, Truro, UK

Correspondence to
Jonathan Lord, UK, Marie Stopes International (UK), London W1T 6LP, UK; j.lord@exeter.ac.uk

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BACKGROUND

The introduction of anti-D immunoglobulin (Ig) has been one of the great achievements in medicine over the past 50 years.[1] Its use has reduced the incidence of alloimmunisation by 85% where formerly about 10% of pregnancies were affected.[2 3] Whereas previously 38% of affected neonates would have died, now haemolytic disease of the newborn is a very rare cause of death in developed countries.[1]

Although the value of anti-D prophylaxis in routine antenatal care in women who are rhesus (RhD)-negative is evidence-based,[4] its role in first-trimester abortion and miscarriage management is not. National guidelines are inconsistent and have been based on observational studies from over 40 years ago when practices were quite different[5] (table 1). When the scope for the National Institute for Health and Care Excellence (NICE) abortion care guideline was being developed,[6] stakeholders rated the role of anti-D prophylaxis as one of the most important topics to be included.

The systematic review and rationale for the NICE guideline is published in this edition of the journal.[7] With no evidence of either benefit from use of anti-D in abortion care, or harm if it is not given in the first trimester, NICE has challenged the traditional stance of many national guidelines that recommend using anti-D because of historic practice. The recommendation from NICE not to give anti-D to women having a medical abortion up to 10 weeks' gestation reversed previous practice and was swiftly implemented by abortion providers across the UK.

WHY THE CHANGE?

The main reason to continue as before and give anti-D Ig is fear of harm if it is not given. The NICE guideline cites evidence that such concerns are misplaced. Comparison of alloimmunisation rates from Canada, where anti-D Ig is routinely given, and the Netherlands, where it is not recommended for abortion under 7 weeks or miscarriage under 10 weeks, showed that Canada had the higher prevalence.[8] Recent work using flow cytometry to quantify the degree of feto-maternal haemorrhage during abortion has shown that volumes are lower than had been calculated in earlier studies reliant on Kleihauer–Betke testing, with all 37 cases being lower than the threshold needed for sensitisation in gestations up to 12 weeks.[9] Another study used flow cytometry to investigate women undergoing surgical abortion with a median gestation of 18 weeks.[10] It found that 86% of those who had detectable fetal red blood cells after the procedure also had fetal cells detectable beforehand, suggesting that the magnitude of transfer following an abortion has been overestimated and calling into question the need for anti-D prophylaxis under 22 weeks' gestation.

There is evidence from the UK that the current system does not always prevent alloimmunisation despite correct use of anti-D Ig. The UK's national surveillance system is administered by the Serious Hazards of Transfusion (SHOT), an independent, professionally-led haemovigilance scheme (www.shotuk.org). The SHOT data suggest that even where apparently 'ideal care' was delivered in the preceding pregnancy, sensitisation to the RhD antigen can occur and alloimmune anti-D develop in the subsequent pregnancy.[11] Since data collection began in 2012, 36% of those found to be immunised at booking had received 'ideal care' in the preceding pregnancy. The numbers of sensitisations arising following a previous first-trimester loss were minimal. One woman received an

Table 1 Examples of national guidelines for recommended use of anti-D in the first trimester

Guidance (date)	Medical (weeks' gestation)	Surgical (weeks' gestation)
Australia and New Zealand (2019)	✔	✔
Canada (2018)	✔	✔
Cochrane (miscarriage) (2013)	Follow local guidelines	Follow local guidelines
Denmark (2015)	✘ (<8/40)	✘ (<8/40)
Finland (2013)	✔	✔
France (2018)	✔	✔
Ireland (2019)	✘ (<7/40)	✔
Netherlands (2011)	✘ (<7/40)	✘ (<7/40)
Norway (2017)	✘ (<9/40)	✔
Sweden (2018)	✘ (<12/40)	✔
UK (NICE miscarriage) (2018)	X	✔
UK (NICE abortion) (2019)	✘ (<10/40)	✔
UK (BCSH) (2014)	✔	✔
UK (RCOG abortion) (2011)	✔	✔
USA (2020/2017)	✔	✔
WHO (2012)	"If available"	"If available"

BCSH, British Committee for Standards in Haematology; NICE, National Institute for Health and Care Excellence; RCOG, Royal College of Obstetricians and Gynaecologists; WHO, World Health Organization.

appropriate dose of anti-D Ig after medical termination at 9 weeks, one required no anti-D Ig after early (8 weeks) spontaneous fetal loss, and no information was available for the other woman who underwent a termination.

The NICE guideline committee were also persuaded by the impact that testing RhD group and administering anti-D Ig has on women and on service organisation.[6] The guideline emphasised the importance of improving access to abortion care and delivering efficient pathways that are woman-centred. Stakeholders reported that the need to test RhD group, wait for the result, order and then administer anti-D Ig all introduced delay into what could otherwise be a more streamlined process, sometimes even needing to recall the woman while she is recovering from the abortion. It also meant that organising community-delivered services was more challenging, and it is not compatible with remote or telemedicine pathways. The cost is significant – both of time (with appointment times being limited, staff could better use the available time to spend longer discussing more important issues) and money. The National Health Service (NHS) in England and Wales will save nearly £1 m per year on drug costs alone. In countries where resources for healthcare are even more stretched, or where women have to fund their own care, these savings are even more important.

Since the NICE guideline was written, the COVID-19 pandemic has changed the delivery of healthcare, with services being delivered remotely wherever possible. The American College of Obstetricians and Gynecologists (ACOG) notes: "in an effort to improve access and recognising the likely low risk of sensitisation, Rh testing and RhD immunoglobulin administration should not be a barrier to the provision of medication abortion".[12]

OTHER ISSUES

In the UK there is a marked difference in how testing and administration of anti-D is managed between the independent service providers (ISPs) who deliver 74% of NHS abortion care and the acute hospitals (NHS Trusts). The ISPs use point-of-care testing using finger-prick samples and administer anti-D Ig immediately. In NHS Trusts blood transfusion laboratories are responsible for managing their system and these require full grouping, sometimes even necessitating two separate whole-blood samples. The regulator for transfusion services (the Medicines and Healthcare products Regulatory Agency, MHRA) defines anti-D Ig as a medicinal product that falls under Directive 2001/83/EC and not a blood or blood component for transfusion that would be controlled under the Blood Safety and Quality Regulations 2005. Despite this, NHS transfusion laboratories invariably apply the same restrictions to anti-D Ig as they do to transfusions, resulting in onerous processes that cause delay and prevent delivery of innovations such as community-delivered local anaesthetic abortions. The NICE guideline details how best practice should be implemented across the sector so that NHS Trusts deliver care in line with the ISPs. This is not only more efficient and kinder for the woman, but it is also cost effective given that the standard point-of-care test costs less than £0.50 per test compared with £24.00 for the transfusion laboratory.[13]

WHAT NEXT?

Given how abortion procedures are among the the most common medical procedures delivered in healthcare settings, it is extraordinary how little research has been conducted into the role of anti-D prophylaxis. NICE has transformed UK guidance in recommending not to test or treat medical abortions under 10 weeks' gestation, and identified the need for research as to whether the same ought to apply for surgical procedures. The tools are now available to answer these questions and this must be a healthcare priority. For those women who choose a surgical option, services should deliver point-of-care testing with immediate provision of anti-D Ig, although current UK guidelines during COVID-19 state that clinicians should discuss the issues with the woman and weigh the risks of COVID-19 transmission, or the delay to care that may result, against any benefits of checking RhD status.[14] Providers should not continue to use systems that

cause delay and create barriers to offering innovations such as one-stop or community-delivered care.

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ORCID iD
Jonathan Lord http://orcid.org/0000-0003-2819-5973

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