

Rhesus Disease information for clinicians

Atypical antibodies causing fetal disease

- Common
 - D incidence high may be severe
 - c (cE) incidence high disease common, may be severe
 - Kell: incidence high disease uncommon, but maybe severe
 - E: incidence high, disease common, usually mild, rarely may be severe
 - C: incidence moderate, disease common, usually mild rarely may be severe
- Uncommon
 - k: rarely present but when present may be very severe
 - Kp^a: rare, very rarely may be severe
 - Jk^a: uncommon, may require treatment, rarely may be severe.
 - Fy^a uncommon, usually mild, rarely severe
- Rarely, if ever cause Haemolytic disease
 - S, U, M, Fy^b, N, Do^a, Di^a, Di^b, Yt^a, Jk^b
- Never cause haemolytic disease
 - Le^a, le^b, P

Management of Rhesus D antibodies.

Rhesus D antibodies are the commonest we encounter and therefore the discussion below will centre on this condition. The management principle is the same for all the antibodies causing haemolytic disease.

As a general rule low levels of antibodies, less than 4 international units, will rarely cause a problem. Although the principle the higher the level of antibody the more likely it is to cause problem holds true in the majority of cases, severe haemolytic disease can be seen with low levels in one women and mild disease with high antibody levels in another. Therefore once above 4 IU the management will be the same.

Assessment of the paternal genotype.

It is worth testing the father to identify whether he is homozygous or heterozygous for the D antigen. If homozygous then all of his offspring will be Rh Positive however if heterozygous then only 50% will be.

Prediction of fetal rhesus genotype.

It is now possible to obtain an accurate, but not absolute, prediction of the fetal genotype from a maternal blood sample using free fetal DNA. For more information re this procedure click on the following link

http://www.blood.co.uk/IBGRL/Reference%20Services/RefSer_genotyping.htm (for a request form click on

http://www.blood.co.uk/hospitals/library/pdf/fetal_DNA_typing.pdf The sample needs to be sent to Bristol. All the information is found on the website. Note the amount and the fact that the sample needs to arrive early in the

week and not be sat in the post office over a weekend. If this reports the fetus is Rh negative then surveillance will be minimal but we would still recommend growth and MCA Doppler at 28 , 32 and 35 weeks.

Surveillance in pregnancy

Surveillance in pregnancy is now based on the middle cerebral artery Doppler (MCA). There is very good evidence to support the value of MCA Doppler in the detection of fetal anaemia from any cause. To obtain a measurement the fetal head should be magnified as large as possible. Using colour flow the MCA is identified and the Doppler gate placed over the vessel with the aim of having a zero angle between the beam and the vessel. Multiple measurements are obtained and assuming the measurements are all similar the highest value is recorded. This figure is compared with the normal range for that gestation (see below). A value above 1.55MoM indicates a significant risk of fetal anaemia and would be an indication for a fetal blood sample.

The value can be artifactually increased by excess pressure from the transducer on the fetal head and poor angle correction.

The trend of values is often a good indication of when intervention is likely to be required.

Measurements should be performed on a weekly basis and any values reaching 1.5 MoM warrants urgent referral back to fetal medicine.

Other signs of fetal anaemia include ascities or hydrops. If either of these were seen even with a normal MCA Doppler it would suggest significant fetal anaemia and would require same day referral to fetal medicine as at this point the fetal Hb is likely to be at least 7g below that expected for the gestation and an urgent transfusion is required.

The MCA Doppler becomes of less value after 35 weeks so we will usually review at that time and use the trend, the maternal antibody level, past history and value at 35 weeks to plan the mode and time of delivery.

When should surveillance begin?

The usual rule of thumb is to start monitoring 10 weeks before the first transfusion occurred or delivery whichever is the earlier.

How often should we check the maternal antibodies?

These will usually be checked on a monthly basis; however, once weekly scanning of the MCA is instigated management will be based on that result rather than the maternal antibody level.

Transfusion

Transfusions occur with the mother awake under local anaesthetic. The site of transfusion depends on ease of access but is usually into the cord insertion, umbilical vein or very rarely intracardiac. All of these occur under direct ultrasound visualisation. A fetal blood sample is sent for analysis of fetal blood group and haemoglobin. The amount of blood transfused will depend on the

gestation, the fetal Hb the Hb of the donated blood. Most transfusion will be between 50 and 150 mls and will take about an hour. Where possible we obtain a post transfusion Hb. After the procedure we perform a CTG and assuming this is reasonable then allow the mother to go home.

We would expect to repeat the transfusion every 1-3 weeks for the remainder of the pregnancy. The exact timing is dependant on the MCA Doppler at subsequent visits, however there have been some concerns raised about the value of MCA Doppler in this situation.

Risks of transfusion

1% risk of fetal death. This could be due to preterm labour, PPROM or cord occlusion. As transfusions need to be repeated more than once the absolute risk will be higher. Obviously other factors are important such as ease of procedure size of mother, and gestation.

Delivery.

For a fetus under 34 weeks showing signs of anaemia we would consider transfusion as the best option. Once beyond 34 weeks it is probably safer to deliver and treat the baby post delivery. If a mother is known to have antibodies and delivery is planned it is essential that the local blood bank is aware and that blood is available for either a top up transfusion or an exchange transfusion.

Mode of delivery

This obviously depends on many factors such as previous obstetric history and perceived severity of the fetal condition. It would be inappropriate to induce a severely anaemic fetus, however that may well be acceptable with a fetus who was thought to be only mildly affected.

Fetal medicine involvement.

We would like to see all women with significant antibodies (above 4IU) reasonably early in the pregnancy (20 weeks) so that we can plan the management for the remainder of that pregnancy. However, assuming you are happy there is no reason why the weekly MCA Doppler should not be carried out locally and the women only referred back to fetal medicine once the 1.5MoM threshold has been crossed or hydrops has developed. We would obviously be happy to see at any other time and would be happy to review at 35 weeks to help make plans for timing and mode of delivery if required.

Further reading

Mari G. Middle cerebral artery peak systolic velocity for the diagnosis of fetal anemia: the untold story. [Review] [61 refs] *Ultrasound in Obstetrics & Gynecology*. 25(4):323-30, 2005 Apr

Reference range of fetal middle cerebral artery peak systolic velocity (MCA-PSV) median and 1.5 multiples of the median (MoM) values during pregnancy

| GA (weeks) | MCA-PSV (cm/s) | |
|------------|----------------|---------|
| | Median | 1.5 MoM |
| 14 | 19.3 | 28.9 |
| 15 | 20.2 | 30.3 |
| 16 | 21.1 | 31.7 |
| 17 | 22.1 | 33.2 |
| 18 | 23.2 | 34.8 |
| 19 | 24.3 | 36.5 |
| 20 | 25.5 | 38.2 |
| 21 | 26.7 | 40.0 |
| 22 | 27.9 | 41.9 |
| 23 | 29.3 | 43.9 |
| 24 | 30.7 | 46.0 |
| 25 | 32.1 | 48.2 |
| 26 | 33.6 | 50.4 |
| 27 | 35.2 | 52.8 |
| 28 | 36.9 | 55.4 |
| 29 | 38.7 | 58.0 |
| 30 | 40.5 | 60.7 |
| 31 | 42.4 | 63.6 |
| 32 | 44.4 | 66.6 |
| 33 | 46.5 | 69.8 |
| 34 | 48.7 | 73.1 |
| 35 | 51.1 | 76.6 |
| 36 | 53.5 | 80.2 |
| 37 | 56.0 | 84.0 |
| 38 | 58.7 | 88.0 |
| 39 | 61.5 | 92.2 |
| 40 | 64.4 | 96.6 |

GA, gestational age. (Modified from G Mari *et al.* *N Engl J Med* 2000; **342**: 9-14[1].)