UK NATIONAL SCREENING COMMITTEE

Review of antenatal screening for fetomaternal alloimmune thrombocytopenia

13 November 2012

Aim of the paper

This note provides background to the agenda item addressing the review of antenatal screening for fetomaternal alloimmune thrombocytopenia.

Current policy

The current policy is that screening should not be offered.

The policy was developed on the basis of a review against the criteria which was published in *Vox Sanguinis* 2002.

Screening would aim to prevent severely affected cases (eg intracranial haemorrhage and intrauterine fetal death) in first affected pregnancies. The paper found that the incidence of the FMAIT, as a whole, was unclear and in addition the incidence of severely affected cases was unclear. There was also uncertainty about the long term clinical effects of FMAIT as a whole. A suitable predictor of severely affected cases had not been identified and, consequently, a test which could identify pregnancies which would benefit from intervention was lacking. Finally the lack of a clear management strategy for anti-HPA-1a women was identified as an obstacle to the introduction of a screening programme.

SPH were asked to review the literature and the resulting document is attached.

Review process

The review addresses literature produced between 2002 and January 2011.

The document was considered by the FMCH in March 2012. A three month consultation was hosted on the UK NSC website and this closed in August 2012. The following stakeholders were contacted directly: British Committee for Standards in Haematology, NHS Blood and Transfusion Service, RCM, RCOG, RCPH, FortuNAIT, NAIT Babies

A positive endorsement of the review and its conclusions was received from the BCSH. Detailed comments on the text were received from the NHS Blood and Transfusion Service and the National Perinatal Epidemiology Unit. These raised no significant concerns with the document's conclusions and have been used to develop the document where possible. The three sets of comments are attached.

Consultation

A public consultation on the screening review took place for three months ending 22nd August 2012. Three responses were received to the consultation which are available at Annex A.

Proposed policy position statement

It is proposed that the current policy position should be retained.

Action

The UK NSC is asked to consider the above.

Annex A

Consultation Responses

Feedback from the British Committee for Standards in Haematology (BCSH) Transfusion Task Force (TTF)

Four members of the BCSH TTF replied that they agree with the findings / policy.

One member provided a more in-depth reply:
"It is clear that more evidence is required.
There seems to be no standard anti-HPA-1a antibody test, and only a small proportion with positive tests will go on to have an intracranial haemorrhage. Using the maternal antibody level to predict FMAIT will depend on where the cut off is set, but the specificity of 63% (Killie et al 2008) is really not good enough.
What one does with the test result is also uncertain. Practice seems to have changed after Arnold et al (2008) published their study. In the four years since then I am sure there will still be no consensus on initial clinical management/ investigation of severity. Even in confirmed FMAIT choosing the right treatment is a problem."

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FMAIT - an evidence review

Feedback from NHS Blood & Transplant

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
Page 13, section 39	Neonatal transfusion with platelets	We published a response to an article in 'Blood' in which we showed that the response to HPA-1a/-5b negative platelet transfusion to neonates affected by anti-HPA-1a or HPA-5b mediated NAIT was better than the response to random donor platelet transfusion. We observed both a higher increment and a longer survival with the 'matched' platelets. (Platelet transfusion in neonatal alloimmune thrombocytopenia. [2007]. Blood; 109: 388-389).
Page 6, section 11	The Condition	Reference is made to the paper by Knight et al but the reference does not appear in the list of references.
Page 8, section 20	The Test	Radioimmunoprecipitation is not routinely used as a diagnostic assay and is primarily a research tool. Other than the MAIPA assay, the Platelet Immunofluorescence Test (Europe), solid-phase adherence assays (Japan) and various forms of Antigen Capture ELISA (USA) are the main diagnostic assays (Allen 2007) (Porcelijn et al, Transfusion, 2008, 48, 1699-1706)

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Feedback from National Perinatal Epidemiology Unit

Section and / or page number	Text or issue to which comments relate	Comment *Please use a new row for each comment and add extra rows as required.*
Page 6, paragraph 12	If the paediatrician does not initially consider FMAIT-related ICH as a possible cause of the newborn's neurological deficits, the platelet count may not be determined for several days after delivery, by which time it may have returned to normal so that the diagnosis of FMAIT will be missed (personal communication from Professor Kjeldsen-Kragh).	We believe that it is unlikely that in the context of an unexplained ICH the platelet count would not be measured and thus that FMAIT would be considered as part of the differential diagnosis. Thus it is unlikely that a significant number of severe cases are not clinically detected. As no evidence is provided to support this comment, we suggest that it should be removed.
Page 13, paragraphs 37 and 38	a non-randomised controlled trial is planned, following these different national guidelines.	Can the authors confirm that this study will go ahead and/or is in progress? It would be helpful to have clear dates by which results are expected.
Page 18, footnote 4	A population of approximately 800,000 women (i.e. approximately the entire number of births each year in the UK) would be needed for a study that has 90 per cent power to detect a fifty per cent difference in the risk of ICH and IUFD at a significance level of five per cent.	The suggested study is clearly unlikely to be feasible. However, a study with an alternative endpoint would be, and it may be helpful to comment on this.
Page 18, footnote 5	It is difficult to say how long it will take to complete these trials, but if the results of the phase III trial are as expected, a drug for prevention of HPA 1a-immunization may be on the market within a period of around 5 years	This is very speculative, and we would suggest better removed.