Feto-maternal/neonatal alloimmune thrombocytopenia (FMAIT/NAIT)

Version: 2.1
Published: 05 July 2016

Condition for which IVIg has an emerging therapeutic role.

Specific Conditions	• Feto-maternal/neonatal alloimmune thrombocytopenia (Antenatal) • Feto-maternal/neonatal alloimmune thrombocytopenia (Neonatal)
Indication for IVIg Use	• Prevention or treatment of fetal thrombocytopenia or haemorrhage. • Prevention or treatment of neonatal thrombocytopenia or haemorrhage.
Level of Evidence	Insufficient data (Category 4a)
Description and Diagnostic Criteria	FMAIT/NAIT develops because of maternal sensitisation to fetal platelets that possess a paternally inherited antigen. In Caucasians, the antigen is human platelet antigen (HPA) 1a in 80% of cases and HPA-5b in 15%, but other antigens are also implicated. The mother's antibodies cross the placenta and coat the baby's platelets, with accelerated platelet clearance leading to thrombocytopenia. This may result in serious and potentially life-threatening bleeding in the fetus or neonate. Pathogenesis is analogous to that of haemolytic disease of the newborn due to red cell antigen–antibody incompatibility. The aim of management of the thrombocytopenic fetus or neonate is to increase the platelet count. If fetal blood sampling reveals thrombocytopenia, intravenous immunoglobulin (IVIg) may be administered weekly to the mother, with or without steroids, until delivery. Recent studies using IVIg weekly from around 20 weeks' gestation, without fetal blood sampling, have shown reduced fetal and neonatal morbidity. This approach may be used for current pregnancies where the condition in a previous pregnancy was not associated with a fetal death or severe haemorrhage. Where a previous pregnancy was affected in the context of demonstrated maternal antibodies, the subsequent pregnancy is likely to be more severely affected where the fetus is positive to the relevant paternal antigen. Testing on maternal blood for fetal DNA or early genetic testing of the fetus (for platelet genotype) by aminocentesis may predict the need to use IVIg. Management of this condition is a specialised area and may include administration of HPA-compatible intrauterine and/or neonatal platelet transfusions. Further information regarding specialised platelet support is available from the Blood Service. Random (non-HPA-matched) platelets may be of benefit in the neonatal setting when matched platelets are not available (Kiefel et al 2006).
Justification for Evidence Category	Evidence from randomised trials (Berkowitz et al 2006, Bussel et al 1996), case series (Kiefel et al 2006, Yinon et al 2006) and a review (Spencer and Burrows 2001) shows that IVIg modulates the course of this condition. A 2004 Cochrane review (Rayment et al 2005) reported on one randomised controlled trial (RCT) comparing IVIg plus dexamethasone with IVIg alone. This RCT was methodologically sound, but too small to detect differences among comparison groups.

Qualifying Criteria for IVIg Therapy	Prevention or treatment of fetal thrombocytopenia or haemorrhage. Clinical suspicion of FMAIT in the antenatal setting based on clinical and laboratory features. • Evidence of fetal thrombocytopenia. OR • Evidence of spontaneous fetal haemorrhage. OR • Unexplained previous fetal death or previously affected sibling and maternal platelet-specific alloantibodies known or suspected to cause this condition and directed against current paternal antigens (most commonly HPA-1a or HPA-5b). Where fetal blood sampling demonstrates there has been a a failure to improve the platelet count, national guidelines recommend the consideration of intrauterine platelet transfusion rather than further Ig therapy. (Ref: *Patient Blood Management Guidelines — Module 6 —Neonatal and paediatric, Section 4.2*) Prevention or treatment of neonatal thrombocytopenia or haemorrhage. Clinical suspicion of NAIT in the neonatal setting based on clinical and laboratory features. • Evidence of thrombocytopaenia in neonate OR • Increased risk of bleeding

Review Criteria for Assessing the Effectiveness of IVIg Use	Prevention or treatment of fetal thrombocytopenia or haemorrhage. Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy. Cease treatment after the date of confinement/delivery of the baby. Clinical effectiveness may be demonstrated by: • Reduced fetal or neonatal morbidity or mortality. OR • Reduced occurrence and severity of thrombocytopenia in the neonate. Neonates with NAIT are eligible under the indication for prevention or treatment of neonatal thrombocytopenia or haemorrhage. Prevention or treatment of neonatal thrombocytopenia or haemorrhage. Review is not mandated for this indication however the following criteria may be useful in assessing the effectiveness of therapy. Clinical effectiveness of Ig therapy may be demonstrated by: • Reduced occurence and severity of thrombocytopenia in the neonate.
Dose	Prevention or treatment of fetal thrombocytopenia or haemorrhage. • **Dose during pregnancy** - Maternal dose: 1 g/kg (up to a maximum weight of 100 kg) weekly throughout pregnancy, with starting time tailored to individual risk profile and history, if relevant. Other doses and schedules have been used and some studies have used IVIg in conjunction with steroids. **The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.** **Refer to the current product information sheet for further information.** Prevention or treatment of neonatal thrombocytopenia or haemorrhage. • **Dose** - 1 g/kg. Occasionally more than one dose is required if thrombocytopenia persists. A second dose may be required. **The aim should be to use the lowest dose possible that achieves the appropriate clinical outcome for each patient.** **Refer to the current product information sheet for further information.**

Bibliography

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Generated on: 1 April 2019