Clinical Guideline

Guidelines for the management of hyperhaemolysis in patients with Sickle Cell Disease, including the use of intravenous immunoglobulins (IVIg)

Summary
Hyperhaemolysis is a well-recognized but rare complication of blood transfusion in patients with sickle cell disease (SCD).
It is characterised by rapid haemolysis following a blood transfusion, and the post-transfusion haemoglobin (Hb) will often be lower than the pre-transfusion Hb, implying the destruction of recipient as well as donor red cells.
This Guideline describes the management of this complication, including the use of immunoglobulin, which is a 'blue' indication according to the Department of Health Immunoglobulin Demand Management Programme.

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30/10/2014	Use of Immunoglobulin has changed from a grey to a blue indication	

Background

Hyperhaemolysis is a well-recognized but rare complication of blood transfusion in patients with sickle cell disease (SCD).
It is characterised by rapid haemolysis following a blood transfusion, and the post-transfusion haemoglobin(Hb) will often be lower than the pre-transfusion Hb, implying the destruction of recipient as well as donor red cells. It may be associated with a fever and with pain typical of sickle cell disease. It may be associated with a delayed haemolytic transfusion reaction and the development of a new red cell allo-antibody but may occur with no evidence of new red cell allo-antibody formation. In this situation the direct antiglobulin test (DAT) is usually negative and there may be a reticulocytopenia.
Additional transfusion has been associated with increasing haemolysis and worsening anaemia, and should be avoided if possible. The haemolysis can be treated with intravenous immunoglobulins (IVIg) and IV Methylprednisolone.
In cases where there is very rapid haemolysis and critical anaemia, additional transfusion will be required and this should be preceded by IVIg and IV Methylprednisolone.
Erythropoetin, iron replacement, B_{12} and folate replacement should also be considered.
Hyperhaemolysis can recur following blood transfusions several months or years after the initial episode, and patients should be retreated with IVIg and Methylprednisolone prior to future transfusion.

The Department of Health immunoglobulin guidelines have changed this indication from grey to blue..IVIG use for this indication has been approved by the Immunoglobulin assessment panel 30th November 2010.

Patient Groups

1) IVIg and IV Methylprednisolone should be considered in patients with SCD who present with evidence of severe haemolysis following a blood transfusion.

2) Patients with SCD and hyperhaemolysis who continue to haemolyse despite initial treatment and have worsening anaemia who need a further transfusion. This should be preceded by IVIg and IV Methylprednisolone.

3) Patients with SCD and a history of hyperhaemolysis are at risk of recurrence and if transfusion is necessary should be pre-treated with IVIg and IV Methylprednisolone.

Diagnosis

Hyperhaemolysis should be considered in any patient with SCD who presents with increasing haemolysis after a blood transfusion. Patients typically present at 7-14 days post transfusion, but may develop symptoms sooner if they are re-challenged with transfusion.

Clinical features: Increasing jaundice, dark urine ('coca-cola' coloured), anaemia. They may also have a fever, back leg or abdominal pain, hepatomegaly or hepatic discomfort. It is often associated with severe bone pain, typical of sickle crisis.

Investigations:

FBC: increasing anaemia – Hb may often fall to below the pre-transfusion level

Haemolysis: raised bilirubin, raised LDH

Reticulocytes: may be raised (in keeping with haemolysis) or decreased, due to suppression of red cell production

Direct Antiglobulin Test (DAT): may be positive if hyperhaemolysis is associated with a new allo-antibody, but may be negative.

Group and Antibody Screen: Hyperhaemolysis often occurs without evidence of new red cell allo-antibody formation but regular group and screens should be performed as red cell allo-antibodies may become apparent up to 3-4 months after the haemolytic episode.

Haemoglobin electrophoresis: A rapid increase in HbS% indicates haemolysis of the transfused blood

Ferritin, folate and B12 levels: This may aid in decisions about replacement.

Differential diagnosis is a delayed haemolytic transfusion reaction due to new allo-antibodies and blood must be sent to the transfusion laboratory for the investigation of new allo-antibodies.

Treatment

Discuss with Haematology Consultant (Contact the on-call Consultant if out-of-hours)
Prescribe Folic acid 5mg.
Primary treatment is with immunosuppression: IV Methylprednisolone and IVIg
Consider treatment with erythropoietin and IV iron replacement
Consider B_{12} replacement.

When a case of hyperhaemolysis is suspected and having discussed with the haematology consulant it is important to communicate the suspected diagnosis to the transfusion biomedical scientist who will add a comment to the patient record.

Blood transfusion should only be given after discussion with the Haematology Consultant.
Blood transfusion may be necessary if clinically indicated (profound symptomatic anaemia)
Phenotyped blood should be given (CDE and Kell matched).

Dosage

Intravenous immunoglobulin (IVIg)
Discuss dose with haematology consultant. Use 1g/kg for brisk haemolysis but consider lower doses (0.5g/kg) for pre-treatment

Adult and paediatric dose (unlicensed indication)
Up to 1g/kg once daily for 2 days (total dose = 2g/kg)
Administration and choice of preparation as per Trust guidance
Round dose to nearest vial size (2g, 5g, 10g and 20g vials available)

The prescribing doctor (Specialist Registrar or Consultant) MUST complete an IVIg form on EPR. This must be printed out and given to pharmacy at the same time as prescription. **Pharmacy can not supply IVIg without this form.**

Methylprednisolone
Adults: 500mg IV for 2 days
Paediatrics 10mg/kg IV for 2 days (maximum dose 500mg)

Review dose after 2 days.

Erythropoietin
NeoRecormon® 300units/kg subcutaneously once daily for 5 days, followed by 300units/kg once daily on alternate days (i.e. 3 times per week)

Ferritin, B12 and Folate
Erythropoietin needs adequate haematinics to work properly.

If ferritin <100ng/ml – prescribe IV Ferinject® (ferric carboxymaltose)
Dose is based on the patient weight and Hb; refer to full Summary of Product Characteristics for dosing information
If ferritin >100ng/ml – prescribe oral iron (ferrous sulphate)

If serum B_{12} <200 pg/ml or active B12 <70 pmol/L
Prescribe B12 i.e. Hydroxocobalamin 1mg IM 3 times a week for 2 weeks

Folate: prescribe Folic acid 5mg once daily

Monitoring of treatment:

Haemoglobin:
Target is return of haemoglobin to baseline
Stop erythropoietin if haemoglobin returns to baseline or if lack of response after full treatment dose.

Monitoring of this Guideline

Use of IVIg for this indication will be monitored via the DH Immunoglobulin Demand Management Programme Database.

References

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