

Treatment of Fever and Infection in Children with Transfusion Dependent Thalassaemia

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Dr Height	2	Dec 2013	Agreed
Dr Dick	2	Dec 2013	Agreed
Dr Amanda Fife and Dr Dakshika Jeyaratnam	2	March 2014	Penicillin allergy information and new trust vancomycin prescribing guidelines

Reviews and updates (including CGG comments)

Date	New version no.	Summary of Changes	Author of change/s
June 2014	2	Penicillin Allergy information	
June 2014	2	Vancomycin information	

Dissemination schedule (after ratification)

Target audience(s)	Method	Person responsible
Paediatricians and haematologists, paediatric nurses	Cliniweb and hard copies on ward	

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Abstract Page

Acute infection remains a major cause of death in thalassaemia patients. A vigilant approach to recognizing and treating serious infection will help prevent unnecessary mortality. Patients should be educated on management of fever and acute symptoms, with advanced understanding of who to call and where to seek care. Children who are at particular increased risk of serious infection are those who are splenectomised, those who have iron overload, those being chelated with desferrioxamine, and those with central venous access devices (Portacath, Hickman line). Gram-negative organisms are the major cause of bacteraemia in thalassaemia patients. Patients on deferiprone have an increased risk of neutropenia.

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Definition/Background

Acute infection remains a major cause of death in thalassaemia patients. A vigilant approach to recognizing and treating serious infection will help prevent unnecessary mortality. Patients should be educated on management of fever and acute symptoms, with advanced understanding of who to call and where to seek care. Children who are at particular increased risk of serious infection are those who are splenectomised, those who have iron overload, those being chelated with Desferrioxamine, and those with central venous access devices (Portacath, Hickman line). Gram-negative organisms are the major cause of bacteraemia in thalassaemia patients. Patients on Deferiprone have an increased risk of neutropenia due to agranulocytosis.

This guideline is aimed at staff caring for all children in King's College Hospital with significant thalassaemia who present with possible sepsis or a temperature $>38.5^{\circ}\text{C}$. The guideline applies to patients who are currently under the care of the Paediatric Haematology team. It is mainly aimed at being a tool for the medical team managing these patients, but any member of the multidisciplinary team may find it useful.

Indications

This guideline applies to patients who have transfusion-dependent thalassaemia, who may have indwelling central venous devices, who may be iron overloaded, and/or chelated with Desferrioxamine, Deferiprone or Deferasirox.

Equipment required

N/A

Guideline steps

Children should be assessed as for any child with possible infection or fever. History and examination should be focused on identifying possible sources of infection and likely organisms. The child should be admitted to hospital if the temperature $>38.5^{\circ}\text{C}$, or if systemically unwell, and the following investigations performed. The paediatric haematology team should be informed of the patient's admission.

Initial Assessment of the Febrile Thalassaemic Patient

- History to include details of iron chelation, central lines, diarrhoea, recent foreign travel and previous splenectomy.
- Full clinical examination looking for any site of sepsis, including ears, throat and possible mucositis, and examination of any central venous access device for exit-site or tunnel infection. Abdominal examination for tenderness, PEWS score.
- FBC with differential, urea and electrolytes, liver function tests and ALT, blood glucose.
- Blood cultures from each lumen of the central venous line if present, using the initial 3-5ml discard for culture, or peripheral cultures if no central line.
- Urine microscopy and culture.
- If indicated, serum for viral serology and EDTA sample for malaria screen.
- Swabs from sites of clinical infection only – include combined respiratory virus swab if respiratory tract signs.
- Stool culture and sensitivities, specifically requesting culture for detection of *Yersinia enterocolitica* infection if diarrhoea, fever, abdominal pain and vomiting.
- Electrocardiograph if tachycardia, irregular pulse, hypotension or history of palpitations.
- CXR if symptomatic/chest signs.
- Abdominal Ultrasound if abdominal pain and/or jaundice.

Prescribing in Penicillin Allergic Patients

THE SYMPTOMS OF THE PENICILLIN ALLERGY MUST BE DEFINED AND DOCUMENTED.

Drugs in RED are contra-indicated in penicillin allergy.

Drugs in ORANGE should be prescribed with caution, and only if penicillin allergy is less severe. Administer under close supervision.

Drugs in GREEN are considered safe.

Severe penicillin allergy includes anaphylaxis, collapse, hypotension, difficulty in breathing, bronchospasm, wheeze, lip swelling, angio-oedema, tracheal or laryngeal swelling, immediate rash & urticaria. Note: these symptoms can occur up to 5 days (occasionally longer) after receiving the antibiotic. These patients must not be given any beta-lactam agents (penicillins, cephalosporins, carbapenems and aztreonam). Patients with a history of Stevens-Johnson syndrome/ TEN/AGEP/DRESS after beta lactams should not be given them.

Less severe penicillin allergy = e.g. a minor, non-confluent rash >72 hours after the antibiotic dose. These patients may be given cephalosporins or carbapenems if there is no satisfactory alternative and the benefits outweigh the risks of cross reactivity.

Penicillin-containing drugs and some cephalosporins – e.g. Amoxicillin, Benzylpenicillin (Penicillin G), Co-amoxiclav (Augmentin®), Flucloxacillin, Penicillin V (Phenoxymethylpenicillin), Piperacillin - Tazobactam (Tazocin®), Temocillin, Ticarcillin + Clavulanic acid (Timentin®), **some cephalosporins** i.e. cefaclor, cefadroxil, cephalexin, cefradine.

Some Cephalosporins, Carbapenems and other beta-lactams – e.g. Cefixime, Cefotaxime, Cefuroxime, Ceftazidime, Ceftriaxone, Ertapenem, Imipenem + Cilastatin (Primaxin®), Meropenem, Aztreonam

Antibiotic Treatment of Fever and Sepsis in Children with Thalassaemia:

Empiric Treatment:

- Treatment should start urgently and within 1 hour of the child presenting with fever:
- First line:
 - **Tazocin (Piperacillin/Tazobactam)** 90 mg/kg x 4/day IV (max dose 4.5g IV every 6 hours)
 - **Gentamicin** 7 mg/kg once daily IV (check trough level prior to third dose)
NB If weight > 50kgs cap dose at 350mg od iv
 - Use **Vancomycin** (check levels), or **Teicoplanin** as 2nd line, if the child has pain/inflammation around Port or Hickman site or tunnel infection.
- If meningitis suspected use **Meropenem**:
Child aged 1 month -12 years: <50kg 40 mg/kg every 8 hours IV
> 50kg 2g every 8 hours IV
- Second line/penicillin allergy:
 - **Ciprofloxacin & gentamicin**: if line sepsis suspected add **Vancomycin or teicoplanin** (Cipro max dose: 400mg IV every 8 hours)
- The empirical regimen is the same irrespective of previous antibiotic courses unless there are known antibiotic resistance patterns guiding recommendations for an individual patient.

Please refer to KCH Vancomycin guidelines

Treatment if there is fever and diarrhoea or vomiting

Thalassaemia patients are at increased risk of Yersinia enterocolitica if they are iron overloaded or chelated with desferrioxamine, and may present with fever, abdominal pain, and diarrhoea. Stool and blood cultures should be sent; contact the lab about specific cultures for Yersinia, since this organism requires particular lab conditions for culture. However, antibiotics should be started empirically, before results are available. In general, all chelation therapy should be stopped until the child has fully recovered. **Ciprofloxacin** is the antibiotic of choice, given intravenously until gastrointestinal symptoms have resolved.

- **Ciprofloxacin** 6 mg/kg every 8 hours, intravenously
Co-amoxiclav or **cotrimoxazole** can be used if the patient has a known allergy to **ciprofloxacin**.

Transfusion-Transmitted Infections

Patients with transfusion-dependent thalassaemia are at increased risk of transfusion-transmitted infections, including hepatitis B, C and HIV. This is particularly true if the patient has received blood transfusions abroad, in countries without established safe blood supplies. This should be considered when assessing patients with acute febrile illness.

All regularly transfused patients should have been vaccinated against hepatitis A and B

- Hepatitis serology should be requested on all patients presenting with an ALT > 100 IU/l. If hepatitis is confirmed the paediatric Hepatology team should be contacted.
- If suspected sepsis occurs following a blood transfusion, the possibility of bacterial or malarial contamination of the transfused blood should be considered; in addition to taking blood cultures and treating the patient, the relevant blood unit(s) should be returned to the Blood Transfusion Laboratory for investigation and the KCH Trust 'Investigation of Suspected Transfusion Reaction' form (see cliniweb) should be completed.

Other information

Related guidelines

Clinical Guidelines on the Use of Iron Chelation in Children Receiving regular Blood Transfusion
Investigation of Suspected Transfusion Reaction

References