Sickle Cell Disease and Thalassaemia:
Acute Complications of Thalassaemia

Profile	
Version:	*V3.0*
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Executive/Divisional sponsor:	*Dr Lisa Pickering, Divisional Chair*
Applies to:	*All staff involved in the care of patients with Thalassaemia*
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Approval	
Approval person/Committee:	*MedCard Divisional Governance*
Date:	*14th February 2019*

Contents

Policy Gateway

Please complete the checklist and tables below to provide assurance around the policy review process.

☒ I have involved everyone who should be consulted about this policy/guidance

☒ I have identified the target audience for this policy/guidance

☒ I have completed the correct template fully and properly

☒ I have identified the correct approval route for this policy/guidance

☒ I have saved a word version of this policy/guidance for future reviews and reference

Please set out what makes you an appropriate person to conduct this review:
Lead consultant for adult haemoglobinopathy service

Please set out the legislation, guidance and best practice you consulted for this review:

- West Midlands Review Service – Quality Standards: Health Services for People with Haemoglobin Disorders (2018/19)
- Guidelines for the Management of Transfusion Dependent Thalassaemia, 3rd Edition (2014) TIF. Cappellini MD et al., https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-3rd-edition-2014/
- American Heart Association (AHA) Consensus Statement. Cardiovascular Function and Treatment in B-thalassaemia Major. Pennel D, et al. July 2016 Circulation. 2013;128:00-00

Please identify the key people you involved in reviewing this policy why, and when:
Dr Lisa Anderson (2015, 2019) – Consultant cardiologist Dr Mark Haden (February 2019) – link consultant for Emergency Department

Summarise the key changes you have made and why:
Updated contact details Specified details for management of acute heart failure to make easier to manage and be aware of concerns

Executive Summary

Patients with thalassaemia (both transfusion dependent and non-dependent) are at risk of emergency presentations and admissions with an unpredictable nature. This is rare and may not be encountered by many medical staff.

This guideline contains up to date advice based on both evidence and expert opinion to support the management of these patients.

1. Introduction

In the local population, that St Georges Healthcare NHS Trust serves, β-Thalassaemia Major (Transfusion Dependent Thalassaemia (TDT) is not as prevalent as sickle cell disease. It is also uncommon for patients with thalassaemia to present acutely unwell and require inpatient or emergency admission. However it is important to be aware of conditions that these patients are particularly at risk of and for them to be managed appropriately and speedily.

Patients with TDT have most of their clinical management as outpatients and are red cell transfusion dependent from early childhood. Most clinical emergencies are actually due to the complications of the transfusion (significant iron overload effecting heart, pituitary gland and liver) or the side effects of medication treating this siderosis (chelation agents such as desferrioxamine, deferasirox and deferiprone.)

2. Status and Purpose

This document is part of the Haematology Department's guidelines on the management of patients with SCD and is applicable to all staff involved in the care of these patients.

3. Definitions

Transfusion dependent thalassaemia (TDT) – Beta thalassaemia major - inherited life long condition due to abnormal haemoglobin varient

4. Scope

This guideline is relevant to the care of patients with thalassaemia presenting acutely to the Emergency Department at St George's site and being admitted to a ward at St George's

5. Roles and Responsibilities

5.1 Haemoglobinopathy team (Consultant haematologists, Clinical Nurse Specialist and Clinical Health Psychologist) – Responsible for the care of these patients, developing and updating guidelines to be reflective of good practice and to deliver the training to ensure good safe care

5.2 Medical staff involved in the care of patients with thalassaemia. Responsible with the oversight of the haemoglobinopathy team to deliver the care of these patients in line with guidelines where possible.

5.3 Nursing staff and allied health professionals involved in the care of patients with thalassaemia on wards, day unit and other areas of St George's Responsible with the oversight of the haemoglobinopathy team to deliver the care of these patients in line with guidelines where possible.

6. Content

6.1 Infection and Fever

Patients may present with overwhelming sepsis due to a range of bacteria and are susceptible to such infections due to many factors. Hyperferritinaemia is a risk in itself for infection, some patients will also have been splenectomised and others are at risk of myelosuppression due to medications such as deferiprone.

Presentation of sepsis is as in patients without thalassaemia and prompt treatment is essential.

- Follow hospital guidelines for antibiotic choice
- Consider source of infection – pneumonia, billiary tract and urinary tract are all particularly common

Infection is now one of the leading causes of death in patients with thalassaemia

Special consideration should be given to

- **Neutropenia** due to deferiprone: Stop the medication and treat as per the St Georges Healthcare NHS Trust Febrile Neutropenia Policy.

- **Central venous catheters:** if these are present consider broad-spectrum gram-positive cover such as vancomycin or teicoplanin (in discussion with microbiology) and discuss whether the line needs to be removed.

- ***Yersinia enterocolitica* infection:** This is more common in patients with high iron levels and those who are chelated. They present with fever, abdominal pain, diarrhoea and vomiting. The chelation should be stopped, microbiological samples sent and discussion with the on call microbiologist about starting ciprofloxacin.

- **Transfusion transmitted infections:** these are rare in the UK now but the possibility of HIV, Hepatitis B and Hepatitis C should be considered.

Whilst patients are septic, their transfusion requirements may increase, as they are less able to tolerate their anaemia.

6.2 Biliary Obstruction and Hepatic Emergencies

Biliary Obstruction

Patients with Thalassaemia are more susceptible to biliary obstruction and stones than their non-thalassaemia peers. Patients presenting with abdominal pain, jaundice with or without fever should be investigated for such conditions.

HepaticFailure

Decompensated liver failure may rarely be a cause of presentation to the emergency department. In these case hepatic siderosis is usually the underlying cause with or without the presence of viral hepatitis (B or C).
Management is that of other causes of acute hepatic failure and its elements (ascites, encephalopathy and coagulopathy) requiring early involvement of the hepatology team and consideration of intensive chelation.

6.3 Cardiac Emergencies

Patients with iron overload should be monitored in the outpatient setting and this should include annual cardiac MR for cardiac T2* and cardiology review so patients with cardiac involvement should be known.

Despite close monitoring, some thalassaemic patients find compliance difficult and are known to be at risk with moderate or high levels of cardiac iron. Cardiac T2* time of <10ms represents significantly severe iron overload and these patients are at highest risk of arrhythmyias or decompensated heart failure (HF).

In these individuals, any reports of increasing fatigue, palpitations or worsening breathlessness should be investigated with echo and 24 hour tape and any patient for whom you have any immediate concerns should be discussed with Dr Lisa Anderson (secretary extension 1220 or mobile via hospital switchboard).

All other transfusion dependent patients presenting with cardiac failure or atrial or ventricular arrhythmias should be referred to the Heart Failure team (via Dr Anderson or via Heart Failure Nurses Specialists on bleep 7376 or extension 4404). These patients need assessment at the earliest opportunity with cardiac MR for possible cardiac iron overload.

Patients may still present with **sudden arrhythmias or acute heart failure**. These are significant, sometimes fatal, events that need urgent treatment and involvement of a cardiologist from the earliest point. These patients should be managed on the cardiothoracic intensive care unit.

Key points

- The first line of treatment is to control the cardiac toxicity related to free iron by urgent commencement of a continuous, uninterrupted infusion of high-dose intravenous deferoxamine, augmented by oral deferiprone.
- As the cause of the heart failure is iron toxicity this is potentially reversible.
- Care is required to not exacerbate cardiovascular problems from overuse of diuretics or inotropes because of the unusual loading conditions in TDT.
- TDT patients with cardiac iron overload may also have iron overload in many endocrine and primary myocardial dysfunction can be caused by hypoparathyroidism and hypothyroidism and these conditions may exacerbate iron cardiomyopathy.
- Decreased adrenal reserve is also common in TDT and patients in HF should be treated as though they have adrenal insufficiency until proven otherwise.
- The chronic anemia and ineffective erythropoiesis of thalassemia are associated with a hypermetabolic state that leads to deficiencies in many vitamins such as thiamine, B6, and folate so consideration should be given to replacement of thiamine, carnitine, or vitamin D.

Treatment of Acute Decompensated HF With Reduced Ejection Fraction

Acute decompensated HF is recognized as a clinical syndrome that includes progressive shortness of breath and significant fluid retention.
A significant presenting feature in TDT can be abdominal (or other location) pain from distended organs such as the liver. This is usually associated with reduced ventricular function and raised BNP.

Acute HF in TDT is associated with a significant mortality rate that improves with the use of continuous intravenous desferrioxamine.

The aim of treatment in acute HF is to keep the patient alive so that iron chelator treatment can detoxify the cardiac iron.

1. Immediate commencement of 24-hour-per-day continuous (uninterrupted) intravenous iron chelation treatment with deferoxamine 50 mg/kg/day

2. The patient should have continuous electrocardiographic and hemodynamic monitoring.
3. As soon as is practical, perform bedside echocardiography to confirm the diagnosis of HF and exclude other cardiovascular conditions, including pulmonary embolism.
4. Introduce deferiprone as soon as possible at a dose 75mg/kg/day - the total dose given in 3 divided doses)
5. Supportive hemodynamic therapy should be geared to maintain cerebral and renal perfusion, avoiding aggressive inotropic therapy, which can be detrimental. Blood pressure is typically low in TDT patients and should not attract specific therapy if renal and cerebral perfusion is maintained.
6. Only minimum diuretic treatment should be used because of the importance of maintaining preload. Consideration should be given to the alternative of venous ultrafiltration to remove excess fluid as a means to prevent reduction in preload, but there is not conclusive evidence to support this.
7. Cardiac arrhythmias are common and often respond to continuous iron chelation treatment.
8. Normalisation of electrolyte abnormalities, and consideration should be given to the use of magnesium infusion to stabilize ventricular arrhythmia. Nevertheless, amiodarone is the drug of choice to treat hemodynamically significant arrhythmias.
9. β-Blockers can be used if the hemodynamic status allows. There is no published evidence for the use of these interventions.
10. Maintain meticulous glucose control with insulin/potassium infusion. This may also help with cardiac inotropic status.
11. Give hydrocortisone on the presumption of inadequate adrenal response to stress.
12. Check thyroid, liver, and renal function and calcium, magnesium, vitamin D, carnitine, and other metabolic parameters and correct these when necessary.
13. Maintain hemoglobin between 100 and 120 g/dL. This may require frequent small-volume transfusions.
14. Search for precipitating conditions such as infections.
15. There is no evidence to support the initiation of angiotensin-converting enzyme inhibitors or angiotensin 2 receptor blockers to manage acute decompensation, and the successful introduction of these drugs is often compromised by poor tolerance caused by low blood pressure. The introduction of β-blockers as an antifailure treatment has the merit of reducing the propensity to arrhythmia and may take priority over angiotensin-converting enzyme inhibitors/ angiotensin 2 receptor blockers. The introduction of these drugs can be considered for management of chronic HF, after the patient is stabilized and is past the acute decompensation period.
16. Cardiac T2* should be performed as soon as is practical: If cardiac T2* is >20 ms, then myocarditis should be considered as a cause of HF, using a standard CMR myocarditis protocol

- Clinical stabilization can occur within 14 days after commencement of continuous iron chelation treatment but can also take months.
- Patients with renal failure may need dialysis or renal replacement
- Consideration towards mechanical support devices to support both ventricles should be considered.

6.4 Endocrine Emergencies

These are rare but can occur due to iron overload in the pituitary gland

Marked hypothyroidism and acute hypoparathyroidism can cause patients to present via the emergency department.

Diabetic emergencies can also present in the acute setting.

Adrenal insufficiency should also be considered in all patients

These should be treated and investigated urgently and involve the care of the endocrinology team

6.5 Admissions and Discharge

Patients are admitted directly under the haematology team and a bed on Ruth Myles Ward (St James' Wing) or Gordon-Smith Ward (Lanesborough Wing) should be requested.

The haemoglobinopathy team consists of a Consultant Haematologist, Haematology Registrar, a Clinical Health Psychologist and a Clinical Nurse Specialist.

During admission patients will be seen regularly by different members of the teams. There are multidisciplinary (Consultant, CNS and Psychologist) ward rounds twice a week.

Specific things to consider

- Observations should be done 4 hourly
- Constipation, mobility, VTE prophylaxis, antibiotic rationalisation and mood should all be considered daily
- Is fluid intake sufficient? Is Hb baseline sufficient?
- Do work or college need to be informed of admission?
- Are there child care issues that need to be addressed?
- Are there any safeguarding or capacity issues?
- Would referral to Full Circle Therapy Team be appropriate to offer?
- Would individual nursing or psychology input be useful?
- Are there discharge plans in place including an estimated discharge date?

Our **Clinical Nurse Specialist** will see patients on regular ward rounds but can also see patients at separate times and support nursing staff on the ward if needed. She can be contacted by telephone (see contacts later)

Our **Clinical Health Psychologist** will see patients twice a week on the multidisciplinary ward round too and patients can ask to see her at other times and nursing staff or medical staff can also discuss issues with her. She can be contacted by telephone or email (see contacts later)

Discharge planning

This should include a planned date of discharge, consideration of whether further time will be needed off work or college, who will help look after or support the patient if further recuperation is required at home and what pain relief will be needed post discharge.

There should also be follow up plans discussed. Many patients may not need increased follow up other than their routine clinic appointment but other options include a day unit review, earlier clinic appointment with either the doctor or the CNS, clinic appointment with the Clinical Psychologist and or review by a community sickle cell nurse specialists.

Other points

Patients should not be moved between wards without discussion with the clinical team looking after them. In particular patients should not have multiple ward moves and if moves are essential this should be explained to the patient and not happen overnight if possible. Moves can worsen pain and delay discharges.

Behavioural Challenges

The St George's Healthcare NHS Trust Zero Tolerance (Violence an Aggression) Policy should be adhered to at all times. Although pain, fear of illness and hospitals can be challenging for patients intimidating, violent or aggressive behaviour will be acted upon and not tolerated. If nursing staff become concerned about behaviour this should be discussed with a senior nursing member of staff – including the site managers out of hours and a member of the haemoglobinopathy team in hours.

Some patients who do find admission to hospital very difficult may have individual care plans that cover all aspects of care and admission (medication, other treatment options as well as discussions about behaviour) and these can be found uploaded on EPR. They are also available from members of the haemoglobinopathy team.

Concerns related to safeguarding, unacceptable or unusual behaviour should be raised with the Consultant Haematologist for Haemoglobinopathies or the Clinical Psychologist. Acute psychiatric concerns out of hours should be discussed with the Liaison Psychiatrist on call (bleep 6501)

All concerns regarding safeguarding or unacceptable behaviour should be recorded in the medical notes, and nursing staff should be encouraged to do the same.

Hospital Contact Details

Dr Elizabeth Rhodes	Haematology Consultant	ext 0885
Dr Julia Sikorska	Haematology Consultant Haematology Registrar	ext 0885 bleep: 7080
Carol Rose	Sickle Cell CNS	mobile: 07500835735
Full Circle	See referral form on haematology intranet or fullcircle intranet page	

Out of hours

Haematology Registrar	via switchboard
Haematology Consultant	via switchboard

Useful Numbers

Safeguarding Adults	David Flood	Bleep 8031
Liaison Psychiatry	On Call	Bleep 6501
Chaplain Contacts		ext 3285

7. Dissemination and implementation

7.1 Dissemination:

Guidelines will be available on the departmental intranet page and available in paper form in the junior doctor office in haematology.

7.2. Implementation

Guidelines will be promoted by the haemoglobinopathy team

8. Consequences of Breaching the Policy

Failing to follow this policy could lead to action under the Trust's disciplinary policy.

9. Monitoring compliance

The table below outlines the process for monitoring compliance with this document.

Monitoring compliance and effectiveness table					
Element/ Activity being monitored	**Lead/role**	**Methodology to be used for monitoring**	**Frequency of monitoring and Reporting arrangements**	**Acting on recommendations and Leads**	**Change in practice and lessons to be shared**
WMQRS peer review quality standards	*Consultant haematologist*	*As required (every 2-3 year)*	*The lead or committee is expected to read and interrogate the report to identify deficiencies in the system and act upon them. Consider stating this responsibility in committee terms of reference.*	*Required actions will be identified and completed in a specified timeframe. Consider stating this responsibility in committee terms of reference.* *These will be discussed at Divisional governance board*	*Required changes to practice will be identified and actioned within a specific timeframe. A lead member of the team will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders.*

10. Associated documentation

List related Trust documents
List other associated and supporting documentation

11. References

- West Midlands Review Service – Quality Standards: Health Services for People with Haemoglobin Disorders (2018/19)
- Guidelines for the Management of Transfusion Dependent Thalassaemia, 3rd Edition (2014) TIF. Cappellini MD et al., https://thalassaemia.org.cy/publications/tif-publications/guidelines-for-the-management-of-transfusion-dependent-thalassaemia-3rd-edition-2014/
- American Heart Association (AHA) Consensus Statement. Cardiovascular Function and Treatment in B-thalassaemia Major. Pennel D, et al. July 2016 Circulation. 2013;128:00-00