Birmingham Children's Hospital NHS
NHS Foundation Trust

GUIDELINE FOR THE MANAGEMENT OF TUMOUR LYSIS SYNDROME.

Version:	1.1.0
Ratified by:	Cancer Service management group
Date ratified:	27/5/2016
Name of originator/author:	Nigel Ballantine
Name of person reviewing the guidelines:	Dr Eleni Syrimi, Dr Prashant Hiwarkar
Name of responsible committee/individual:	Chemotherapy Working Group (CWG)
Date reviewed last:	February, 2016
Review date:	Document to be reviewed not less than every two years – first review not later than February, 2018
Target audience:	Medical, nursing and pharmacy staff within the Haematology Oncology Specialty

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1 Introduction

Tumour Lysis Syndrome is an oncological emergency that can occur in haematological malignancies with high tumour burden. The laboratory changes of hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia occur when dying malignant cells release purines, potassium and phosphate into the circulation faster than they can be excreted by the kidney. Unless precautions are taken uric acid or phosphate salts will deposit in the renal tubules resulting in reduced renal function. A domino effect occurs in the remaining nephrons and patients may rapidly enter established anuric renal failure.

Tumour lysis syndrome is common in the haematological malignancies of childhood. Around one in five children with acute leukaemia or non-Hodgkin's lymphoma will develop the condition. Fortunately, most can be managed medically without the need for dialysis. The condition also rarely occurs in small children with bulky stage 4S neuroblastoma or hepatoblastoma. The risk of tumour lysis syndrome depends mainly on the extent of the tumour burden, and to a lesser extent the rapidity with which the malignant cells both divide and respond to treatment.

The main principles of tumour lysis syndrome management are (1) identification of high-risk patients with initiation of preventive therapy and (2) early recognition of metabolic and renal complications and the prompt administration of supportive care, including haemodialysis.

2 Purpose

This guideline provides an outline for the management of patients at risk of tumour lysis syndrome. As with all such guidelines the recommendations below are no substitute for appropriate assessment of the patient, and response to that assessment. In all cases, advice from senior colleagues should be sought sooner rather than later if there is any uncertainty.

3 Duties

3.1 Duties within the Organisation

The lead committee (Chemotherapy Working group) for this document is identified on the title page.

3.2 Identification of Stakeholders

The following stakeholders have been identified within BCH: The Chemotherapy Working Group (CWG); nursing and support staff within the Haematology Oncology specialty.

Outside BCH: The West Midlands Children's Cancer Network Group.

4 Method for development

4.1 Consultation and Communication with Stakeholders

The original policy was drafted by Nigel Ballantine (Chair, CWG) and reviewed by the stakeholders previously identified. Comments and suggestions were incorporated until a final version was agreed by the CWG and ratified by the Head of Chemotherapy (HoC) and Lead Cancer Clinician (LCC). The latest version has gone through the same process.

5 Content

Risk stratification as per Cairo-Bishop

Three risk groups can be identified from the following pre-treatment factors:

	Low	Intermediate	High
Renal function	Normal renal function	High 'normal' serum creatinine	Pre-existing renal impairment
WCC (X 10^9/l)	<25	25 to 100	> 100
Lymphadenopathy	Minimal lymphadenopathy	Significant lymphadenopathy	Massive lymphadenopathy or malignant effusions (Stage 3 +4 Lymphomas)
Hepatosplenomegaly	None	Mild (2-3 cm)	Major
Serum Urate	low	<450 µmol/l	> 450 µmol/l
Other			L3 ALL (Burkitt's leukaemia) Rising creatinine and or phosphate

The consultant on-call will advise on the most appropriate risk group for a particular patient

Low Risk

- Dextrose Saline (usually Sodium chloride 0.45% / Dextrose 5%) by IV infusion at not less than 2000 ml/m^2/24 hours for at least 48 hours. **No added potassium unless specifically directed by consultant.**

- Monitor fluid balance - weight patient twice daily.

- Monitor U&Es, creatinine, Ca & PO_4 12 hourly for at least the first 24 hours after treatment starts, then daily until IV hydration stops.

- Give allopurinol at 100 mg/m^2 three times per day by mouth for 7 days (maximum 400mg/24hours if below 15 years old).

Intermediate Risk

- Give Allopurinol 100 mg/m^2 three times per day by mouth (Round up to nearest 50 mg, maximum single dose 200 mg). Continue for 7 days.
(maximum 400mg/24hours if below 15 years old)

- If risk status increases (see above) then consider Rasburicase (urate oxidase) – see below for dose.

- Dextrose Saline (usually Sodium chloride 0.45% / Dextrose 5%) by IV infusion at not less than 3000 ml/m^2/24 hours for at least 48 hours. **No added potassium unless specifically directed by consultant.**

- Observe strict fluid balance. Allow insensible losses of 300 - 500 ml /m^2 /24 hours depending on presence or absence of pyrexia. If urine output falls give furosemide - inform consultant if there is no response within 1 hour. Fluid challenge and/or higher dose may be required. Weigh patient twice daily.

- Monitor U&Es, creatinine, Ca & PO_4 6 hourly for at least 48 hours. Reduce to 8 hourly, then 12 hourly and then daily in consultation with the consultant in charge.

High Risk

- Inform on-call consultant paediatric intensivist.

- Rasburicase (urate oxidase) 0.2mg/kg, IV **ONE DOSE ONLY**. Infuse in 50ml of Sodium chloride 0.9% over 30 min.

- **Caution: Risk of anaphylaxis, draw up adrenaline prior to first dose, administer with doctor present. Risk increased with history of atopy.**

- **Caution: Risk of haemolysis in G6PD deficiency. Please check G6PD status prior administrating Rasburicase. If the child is G6PD deficient then Rasburicase should NOT be given.**

- **Caution: Urate assays, taken whilst patients are receiving rasburicase, must be sent to the laboratory on ice to prevent falsely low assay results. Uric acid should be checked again on day 3 of treatment. DO NOT send uric acid routinely with all samples sent to biochemistry.**

- **If a second dose of Rasburicase is indicated based on uric acid at day 3 or worsening renal function, then this should be discussed with a consultant.**

- Dextrose Saline (usually Sodium chloride 0.45% / Dextrose 5%) by IV infusion at not less than 3,000 – 4,000ml/m^2/24 hours until directed to stop by consultant. **No added potassium unless specifically directed by consultant.**

- Observe strict fluid balance. Allow insensible losses of 300 - 500 ml /m^2 /24 hours depending on the presence or absence of pyrexia. If urine output falls then give furosemide. Fluid challenge and / or higher dose may be required. Discuss with renal consultant about using higher dose of Furosemide. The patient should be weighed twice daily.

- Monitor U&Es, creatinine, Ca & PO_4 6 hourly for at least 48 hours. Reduce to 8 hourly, then 12 hourly and then daily in consultation with the consultant in charge.

- A rising creatinine and phosphate together with a falling calcium and urine output are indications that dialysis or haemofiltration may be required. Inform consultant and intensive care team **immediately** if this occurs.

- The tables – see Appendix I – should be completed for all patients with an intermediate or high risk of tumour lysis syndrome. Once renal function has returned to normal they should be filed in chronological order in the narrative section of the case notes.

6 References:

- Guidelines for the Management of Tumour Lysis Syndrome in Adults and Children with Haematological Malignancies of the British Committee for Standards in Haematology

- Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome (TLS) in adults and children with malignant diseases: an expert TLS panel consensus.

7 Approval, Dissemination and Implementation

7.1 Approval of document

This document has been approved by the CWG and ratified by the HoC and LCC.

7.2 Dissemination

A paper copy will be placed in the policy files within the Haematology Oncology Specialty.

Electronic copies will be provided via the Trust Intranet in the Oncology department and Trust policies folders.

7.3 Implementation

The policy is currently in use within the Haematology Specialty. This document brings the policy into Trust-approved format.

8.0 Associated Documentation

See Below

Appendix I

Surname:_____ Forename:_____ D.O.B. _ _ / _ _ / _ _

Hosp No:_____ Weight: _ _ _._ Kg Surface area: _ _._ m^2

Date/ Time	Sampling frequency (hours)	Weight	Minimum hourly IV rate	Minimum hourly urine volume*	Signature

- Minimum hourly urine volume equals hourly infusion rate – (13 X S.A.)

Surname:_____ Forename:_____ D.O.B. _ _ / _ _ / _ _

Hosp No:_____ Weight: _ _ _._ Kg Surface area: _ _._ m^2

Uric acid at diagnosis: _ _ _ mmol/l

Date	Time	Hb	WCC	Plat	Na	K	Creat	Ca corrected	PO_4	Urate

Date	Time	Hb	WCC	Plat	Na	K	Creat	Ca corrected	PO_4	Urate

Note on the measurement of uric acid: Measurement may be affected by both allopurinol and rasburicase (urate oxidase). Repeat measurement is only necessary if requested by consultant other than at day 3.

Committee Approval			
If the committee is happy to approve this document, please sign and date it and forward copies to the person with responsibility for disseminating and implementing the document and the person who is responsible for maintaining the organisation's database of approved documents.			
Name	Dr D Hobin	Date	27-05-2016
Signature