The quality use of rasburicase in tumour lysis syndrome
A retrospective review

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**Background**

- Tumour lysis syndrome (TLS) is a life-threatening metabolic complication of malignancies that may occur in response to cytotoxic therapy.1
- In TLS, tumour cells release large amounts of intracellular components, resulting in hyperuricemia, hyperkalaemia, hyperphosphatemia, hypocalcaemia and acute kidney injury.2 Currently there are three treatment options available for patients with TLS: hydration, allopurinol and rasburicase.3
- Rasburicase is a recombinant urate oxidase. It functions to convert uric acid to allantoin, a substance five to ten times more soluble than uric acid and readily excreted in the urine.2
- The Children’s Hospital at Westmead protocol follows the Fasturtec® Product Information recommendation of 0.2 mg/kg/dose given once daily for 5–7 days. This recommendation applies to both paediatric and adult patients and no information is presented about dose capping. Rasburicase is a high cost medication ($A 124 per milligram) and evaluation of usage is important to promote safe and quality therapy.

**Aim**

To evaluate the efficacy of a single dose of rasburicase for prophylaxis or treatment of TLS in a tertiary paediatric hospital and to review the potential for dose capping.

**Method**

Approval to conduct the study was obtained from The Children’s Hospital at Westmead Clinical Governance Unit.

- A systematic review on the use of rasburicase in TLS was conducted on Embase and Medline.
- Nine Australian paediatric hospitals were contacted regarding the use and availability of a protocol for rasburicase in paediatric patients.
- A retrospective review of medical and laboratory records from July 2010–June 2015 was conducted. The indication, dose, duration of treatment and uric acid levels were documented. Calcium, phosphate and potassium were also noted.
- A cost analysis for the use of rasburicase during the period of July 2010–June 2015 was completed.

**Results**

Systematic literature review

- The systematic review yielded 143 articles from Medline and 484 articles from Embase.
- Evidence showed that 0.2 mg/kg/dose as a daily dose was effective in reducing uric acid levels to the normal range (0.14 to 0.42 mmol/L) and a capped dose of 7.5 mg was used in many studies.

Survey of hospitals

- None of the hospitals contacted had a policy or guideline in place for the use of rasburicase.
- Three hospitals had capped doses of 3 mg per dose.
- One hospital had capped doses of 7.5 mg per dose.

Medical record review

- Between July 2010 and June 2015, 44 patients (30 male) at The Children’s Hospital at Westmead received rasburicase for prophylaxis or treatment of TLS (Table 1).
- A total of 48 episodes of treatment were administered, where 22 (46%) of the cases were prophylaxis and 26 (54%) were treatment of TLS.
- The median dose was 0.2 mg/kg/dose given once daily (Table 1).
- The median number of doses administered per episode was 2.8. Additional doses were administered in 6 patients, with one patient receiving a total of 12 doses.
- One patient, weighing 99.9 kg received three capped doses of 7.5 mg (0.08 mg/kg/dose) and a normal uric acid level was achieved after one dose of rasburicase.
- Prior to the first dose of rasburicase, the median uric acid level was 0.44 mmol/L which decreased to 0.16 mmol/L within 24 hours (Figure 1).
- After the first dose of rasburicase, 92% of uric acid levels were within the normal range.

**Summary of findings**

- A single dose of rasburicase appears to be effective in reducing uric acid levels to the normal range in most patients.
- A treatment duration of 5–7 days may not be necessary, offering potential cost-savings without compromising patient care.
- There is potential for dose capping in obese patients.

**Conclusion**

These findings were used to inform the clinical practice guidelines of rasburicase for the prevention and treatment of TLS at the Children’s Hospital at Westmead. The dosing guidelines were amended to include a dose cap of 7.5 mg for each dose; duration of treatment of 24 or 48 hours and monitoring of uric acid and other parameters at 48 hours following a single dose and before subsequent administrations.

References


Cost analysis

- The cost for 48 episodes of treatment with rasburicase was $A115,071.
- If patients had received a single dose of rasburicase, the estimated cost would have been $A 40,816 representing a 64% decrease in cost.

**Table 1: Characteristics of 44 patients treated with rasburicase**

<table>
<thead>
<tr>
<th>Male: $30/44 (68%)</th>
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<tbody>
<tr>
<td>Median age: 7.9 years (Range: 0.1–16.8)</td>
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<tr>
<td>Diagnosis: T-cell lymphoid leukemia (15/44 (34%)), Burkitt’s lymphoma (8/44 (18%)), Other (21/44 (48%))</td>
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<td>Episodes of treatment: 48</td>
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<tr>
<td>Median dose of rasburicase administered: 0.2 mg/kg/dose (Range: 0.1–0.5 mg)</td>
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<tr>
<td>Median number of rasburicase doses administered: 2.8 (Range: 1–12)</td>
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**Figure 1: Monitoring parameters pre- and post-rasburicase single dose (n=48 episodes of treatment)**

- Pre-rasburicase: Uric acid, Potassium, Phosphorus, Calcium.
- Post-rasburicase: Uric acid, Potassium, Phosphorus, Calcium.

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