ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 04 | April - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A PROSPECTIVE STUDY FOR USE OF FIXED, LOW DOSE 1.5 MG RASBURICASE FOR THE TREATMENT OF HYPERURICEMIA IN ADULT ONCOLOGY PATIENTS

Oncology

Dr Rudresha AH	Associate Professor, Kidwai Memorial Institute of Oncology, Bengaluru
Dr Indani Madhavi*	Senior Resident, Kidwai Memorial Institute of Oncology, Bengaluru *Corresponding Author
Dr Suresh Babu MC	Professor, Kidwai Memorial Institute of Oncology, Bengaluru
Dr Lokesh KN	Associate Professor, Kidwai Memorial Institute of Oncology, Bengaluru
Dr Rajeev LK	Associate Professor, Kidwai Memorial Institute of Oncology, Bengaluru
Dr Smitha CS	Associate Professor, Kidwai Memorial Institute of Oncology, Bengaluru
Dr Kasturi Baruah	Senior Resident, Kidwai Memorial Institute of Oncology, Bengaluru

ABSTRACT

Tumor lysis syndrome (TLS) is a serious condition with high morbidity and mortality, primarily due to hyperuricemia. This prospective study assessed the efficacy of a single 1.5 mg dose of rasburicase in 60 oncology patients with hyperuricemia (uric acid >8 mg/dL). At 24 hours, 75% achieved uric acid normalization, increasing to 81.66% by day five. The overall response rate, including those requiring an additional dose, was 95%. Patients with uric acid <12 mg/dL had better responses, with weak correlations to weight, BSA, and total leukocyte count. A single low dose of rasburicase is effective and cost-efficient, though further research is needed to optimize dosing strategies.

KEYWORDS

low dose rasburicase, oncology, tumor lysis

INTRODUCTION:

Tumor lysis syndrome (TLS) is a medical emergency and can lead to significant morbidity and mortality. Hyperuricemia, is an important manifestation of TLS and can lead to renal insufficiency[1]. Rasburicase, a recombinant urate oxidase, rapidly lowers uric acid levels.While the approved dose is 0.2 mg/kg/day for 5 days, cost constraints often limit its use.[2] We evaluated the efficacy of a single fixed dose of 1.5 mg rasburicase in patients with established TLS.

METHODS: We conducted a single-center prospective study and enrolled oncology patients (>15 years) with hyperuricemia (uric acid >8 mg/dl) and ECOG PS ≤ 3. Patients received a single 1.5 mg dose of rasburicase and inpatient monitoring was done. Blood samples were collected at 12 hrs, 24hrs, Day 3 and Day 5 of rasburicase administration. Additional doses were given at clinician discretion. All patients received allopurinol or febuxostat. Primary objective was to estimate plasma uric acid response rate (defined as percentage fall in the uric acid levels from the normal value of less than 8mg/dl recorded at 24hrs and at 5day). Secondary objectives were to assess need for additional doses of rasburicase needed, response rates based on baseline uric acid levels, Tumor lysis-related mortality, safety, and co-relation to weight, Body Surface area (BSA), Body Mass Index (BMI), Baseline Uric acid level and Baseline Total Leucocyte Count (TLC).

RESULTS:

1. Patient Characteristics:

A total of 60 patients were enrolled in the study. The baseline features and malignancy distributions are summarized in table 1 and 2 below.

Table 1: Baseline patient characteristics

Characteristic	Number of Patients (%)
Total patients	60 (100%)
Male	42 (70%)
Female	18 (30%)
Age (mean in years)	42 years
Weight (mean)	53.84 kg
Height (mean)	156.84 cm
BMI (mean)	22.3 kg/m2
ECOG PS 1	26 (43.33%)
ECOG PS 2	29 (48.33%)
ECOG PS 3	5 (8.3%)
Average TLC	1.4 lakh/mm3
Average Baseline UA	12.1 mg/dl
Average Baseline Creatinine	1.58 mg/dl
Average Baseline Urea	26.8 mg/dl

Table 2: Distribution of malignancies in the population

Diagnosis	Number of patients	(%)
ALL	17	28.33
CML	15	25
NHL	13	21.66
AML	6	10
CLL	5	8.33
MM	4	6.66
Total	60	100

2. Plasma Uric Acid Response:

Plasma uric acid normalized at 24 hours in 45 out of 60 patients (75%) and at day 5 in 49 out of 60 patients (81.66%) with a single dose of rasburicase. 10 patients received 1 additional dose of rasburicase with an overall response rate of 57 out of 60 patients (95%).

Table 3: Response in overall population

	Number of pt (of 60)	Percentage (%)
Response at 24 hrs with single dose	45	75
Response at 5 days with single dose	49	81.66
Response rate with single or two dose	57	95

3. Subgroup Analysis:

In the cohort with uric acid levels less than 12 mg/dl at baseline (n=31), 29 patients (93.54%) had normalization at 24 hrs. and remained normal at day 5. Only 1 patient (3%) required an additional dose of rasburicase, and at 5 days overall, 30 patients (96.77%) had a sustained response.

Table 4: Response rate in population with Uric acid <12mg/dl

	Number of pt (of 31)	Percentage
Response at 24 hrs	29	93.54
Response rate at 5 days with single dose	29	93.54
Response at 5 days with one or two dose	30	96.77

In the cohort with baseline uric acid levels more than 12 mg/dl (n=29), 16 patients (55.17%) had a response at 24 hrs., and 20 patients (68.96%) had sustained normal uric acid levels at 5 days. 9 patients (31%) received an additional one dose of rasburicase, and at 5 days overall, 27 patients (93.10%) had a sustained response.

Table 5: Response rate in population with Uric acid >12mg/dl

	Number of pt (of 29)	Percentage
Response at 24 hrs.	16	55.17
Response rate at 5 days with single dose	20	68.96
Response at 5 days with one or two dose	27	93.10

4. Correlation Analysis:

Pearson correlation analysis showed weak correlations between certain patient characteristics (such as weight, BSA, TLC, baseline uric acid, creatinine, and BMI) and the doses of rasburicase needed. Though the P value was <0.05 the associations were weak. A modest negative corelation was found for the dose of rasburicase and weight of the pt (corelation coefficient -0.11, p value <0.05)

Table 6: Pearson Correlation Coefficients

Variable	Pearson Correlation coefficient	P-Value
Weight vs Rasburicase Doses	-0.11	<0.05
BSA vs Rasburicase Doses	0.0073	<0.05
TLC vs Rasburicase Doses	0.0245	<0.05
Baseline Uric Acid vs Rasburicase Doses	0.4410	<0.05
Creatinine vs Rasburicase Doses	0.4240	0.00424599
BMI vs Rasburicase Doses	0.0275	<0.05

No patients developed hypersensitivity reaction, cardiac dysfunction, hemolysis or methemoglobinemia. No death occurred due to TLS / Hyperuricemia

DISCUSSION:

This study explored the efficacy and safety of a single fixed dose of 1.5 mg rasburicase in adult oncology patients with hyperuricemia associated with tumor lysis syndrome (TLS). Findings demonstrate that this lower dose effectively reduced plasma uric acid levels, with normalization in 75% of patients at 24 hours and 81.66% by day five. These results align with prior research indicating that low-dose rasburicase can be sufficient for hyperuricemia management in oncology settings, providing a potential alternative to the standard weight-based regimen of 0.2 mg/kg. [1-3]

Notably, our subgroup analysis revealed that patients with baseline uric acid levels below 12 mg/dL had a higher response rate with a single fixed dose compared to those with initial uric acid levels above 12 mg/dL. This suggests that lower baseline levels may predict a more favorable response to fixed-dose rasburicase. Identifying such baseline characteristics could support individualized treatment strategies, allowing clinicians to tailor rasburicase dosing more effectively according to patient needs.[4]

The safety profile observed in our study further supports the use of this fixed dose. No severe adverse effects, such as hypersensitivity, hemolysis, or methemoglobinemia, were reported, which underscores the practicality and safety of low-dose regimens. This is consistent with previous studies suggesting that low-dose rasburicase is well-tolerated in adult cancer patients, making it a safe choice.[5,6]

A major benefit of the fixed-dose approach is its cost-effectiveness. Rasburicase is expensive, and its high price often limits its application, particularly those in low- and middle-income regions. Demonstrating that a single fixed dose of 1.5 mg rasburicase can yield results comparable to higher, weight-based doses provides an economically viable solution. Several studies have similarly highlighted the economic and therapeutic advantages of low-dose rasburicase, reinforcing the relevance of our findings.[7-9]

Limitations:

This study has limitations, including its single-center design and relatively small cohort size, which may affect the generalizability of the findings. Future studies might explore more refined dosing approaches based on factors such as tumor burden, renal function, and baseline uric acid levels, which could further optimize the use of rasburicase in TLS treatment.

CONCLUSION:

Our study supports the use of a single fixed dose of 1.5 mg rasburicase as a cost-effective, safe, and efficient option for managing hyperuricemia in adult oncology patients with TLS, especially in those with baseline uric acid levels below 12 mg/dL. Given the potential to reduce costs and expand access, this approach may have significant implications in resource-limited settings. Future research will be instrumental in establishing this regimen as a viable standard in oncology practice.

REFERENCES:

1. Cairo MS, Coiffier B, Reiter A, et al. Recommendations for the evaluation of risk and prophylaxis of tumor lysis syndrome (TLS) in adults and children with malignant diseases: an expert TLS panel consensus. Br J Haematol. 2010;149(4):578-586.
2. Herrington JD, Dinh BC. Fixed, low-dose rasburicase for the treatment or prevention of hyperuricemia in adult oncology patients. J Oncol Pharm Pract. 2015;21(2):111-117.
3. Thorat J, Bhattacharya S, Nair R, et al. Fixed Dose Rasburicase is Effective in the Management of Hyperuricemia in Adult Cancer Patients. J Evid Based Med Healthc. 2016;3(85):4643-4647.
4. Coiffier B, Altman A, Pui CH, et al. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. J Clin Oncol. 2008;26(16):2767-2778.
5. Pui CH, Mahmoud HH, Wiley JM, et al. Recombinant urate oxidase for the prophylaxis or treatment of hyperuricemia in patients with leukemia or lymphoma. J Clin Oncol. 2001;19(3):697-704.
6. Becker MA, et al. Safety and Efficacy of Rasburicase in the Treatment of Tumor Lysis Syndrome in Different Age Groups. Clin Oncol. 2018;30(3):189-195.
7. Lima J, et al. Low-Dose Rasburicase for the Management of Tumor Lysis Syndrome: A Cost-Effective Approach. J Pharm Pract. 2020;33(5):657-663.
8. X. Feng, et al., Efficacy and cost of single-dose rasburicase in prevention and treatment of adult tumour lysis syndrome: a meta-analysis, J. Clin. Pharm. Ther. 38 (4) (2013) 301–308.
9. X. Yu, et al., The optimal single-dose regimen of rasburicase for management of tumour lysis syndrome in children and adults: a systematic review and meta-analysis, J. Clin. Pharm. Ther. 42 (1) (2017) 18–26.