Rasburicase for Acute Kidney Injury

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Background: Acute kidney injury (AKI) continues to have significant mortality and morbidity and the search is on for any novel therapeutic intervention. **Case characteristics**: Two cases of AKI with elevated SUA (serum uric acid). **Intervention**: Rasburicase. **Outcome:** In Case 1 (late preterm male with AKI) rasburicase resulted in a significant reduction of SUA along with improvement in renal parameters. In Case 2 (6 yrs old boy with multi organ failure), rasburicase failed to provide any significant benefit despite fall in SUA.Message: The effect of rasburicase in AKI needs to be studied.

Keywords: *Acute kidney injury, Child, Rasburicase.*

Incidence of acute kidney injury (AKI) remains high and the search is still on for a specific therapy which will avoid dialysis and decrease the associated morbidity and mortality [1]. Recently few case reports have shown rasburicase (recombinant urate oxidase) to be effective in various forms of AKI [2-7] with raised serum uric acid. We herein report our experience of using rasburicase in 2 children with AKI (non-tumour lysis syndrome related).

CASE REPORT

Case 1: A late preterm male baby was admitted on day 4 (D4) with anuria and progressive body swelling from D2. The baby was born by normal delivery with an APGAR of 6 at 10 min. On admission his mean arterial pressure (MAP) was 35 mmHg, creatinine 5.8 mg/dL, potassium 6.5 mmol/L and sodium 121 mmol/L. He stayed anuric despite fluid boluses and ionotropes. Usual AKI measures were initiated along with urgent medical steps for reducing serum potassium. Anuria persisted even after 24 hours, with worsening renal parameters (creatinine peaked at 6.3) and hence peritoneal dialysis was considered. The parents did not consent to an invasive procedure. As his serum uric acid was elevated at 14 mg/dL, after parental consent and ruling out glucose 6 phosphate dehydrogenase (G6PD) deficiency, rasburicase was given on late D5 at 0.2 mg/kg and within 12 hours he started to produce urine. Subsequently there was a steady improvement in his urine output with a concomitant fall in creatinine which became normal by D30 (***Fig.* 1**). Post-rasburicase, serum uric acid was 0.5 mg/dL on D7 and 2.8 mg/dL on D10.

Case 2: A 6-years-old boy with multiple special needs was transferred from another hospital intubated and severe respiratory distress. He had been anuric for 48 hrs with rising urea and creatinine. He had quadriplegic cerebral palsy and epilepsy. On admission to our institute, his transaminase was >7000, creatinine phosphokinase 45000, INR was un-recordable, creatinine 3.01 mg/dL and serum uric acid 8.9 mg/dL. A provisional diagnosis of rhabdomyolysis was made but due to anuria, myoglobinuria could not be confirmed. His ventilation was stabilized and because of impaired perfusion and low arterial pressure he received normal saline boluses as well as inotropes. Despite this he remained hemodynamically unstable and anuric with worsening renal parameters along with significant coagulopathy. Dialysis was contemplated but in presence of severe coagulopathy both hemodialysis (as we do not have facilities of hemofiltration in our unit) and peritoneal dialysis were considered risky. His uric acid on the next day had risen to 9.7 mg/dL and after parental consent rasburicase was administered at 0.2 mg / kg (G6PD level

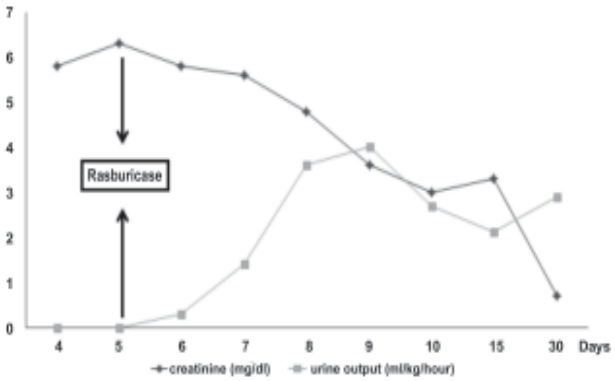

FIG. 1 *Urine output and creatinine post-rasburicase in Case 1.*

was normal) around 24 hrs after admission. Despite a dramatic fall in uric acid (0.3 mg/dL by 24 hours) he passed 4 mL of urine within four hours with no further improvement in urine output and renal parameters continued to worsen. Sustained low efficiency dialysis (SLED) had to be ultimately initiated by D3 of admission but he suffered from a massive pulmonary bleed and died on D4 of admission.

DISCUSSION

Rasburicase is a recombinant urate oxidase, an enzyme which breaks down uric acid to 5-10 times more soluble allantoin. Although it has become a standard intervention for prevention / treatment of AKI secondary to tumor lyses syndrome [8] it has only recently been proposed as a novel treatment modality for other causes of AKI [2-7].

Over the last decade there has been increasing experimental evidence suggesting alternative pathways for uric acid induced AKI apart from the well-known intra tubular crystal deposition. The proposed mechanism includes uric acid induced renal vasoconstriction secondary to inhibition of neuronal nitric oxide synthase, and thickening of pre-glomerular arterioles secondary to endothelial damage, all of which results in impaired renal blood flow auto-regulation. Elevated uric acid has also been shown to have pro-inflammatory property including stimulating release of monocyte chemo-attractant protein-1 (MCP-1) [9]. Epidemiologically also it has been seen that elevated preoperative uric acid (≥7 mg/dL) is associated with a 35-fold increased risk for AKI in adults undergoing cardiovascular surgery [9]. Further confirming the role of uric acid in AKI, a recent randomized control trial among adults undergoing cardiac surgery showed lower urinary AKI biomarker (NGAL) in cases of pre-emptive reduction of uric acid particularly in patient with impaired baseline glomerular filtration rate (<45mL/min/1.73m^2) [10].

A logical corollary from the above mentioned evidence would be to explore whether treating hyperuricemia benefits established AKI. This was first explored by Hobbs, *et al.* [2] and subsequently there have been few more positive case reports [2-7]. However, as shown by the negative response in our Case 2, much more needs to be learned before we adopt it routinely. Although we did not experience any related side effects one should watch for anaphylaxis as well as always document a normal G6PD levels before administrating rasburicase [8].

In conclusion, evidence is mounting in favour of uric acid as a novel clinical biomarker and its estimation should be included in any AKI work up. Despite the high cost (Rs 15,000 for 1.5 mg ampoule) of rasburicase, if it can be demonstrated that it is effective in AKI and can reduce need for dialysis, it is likely to prove to be cost effective. *Acknowledgements*: Dr Amit Ray, Consultant Neonatologist; Dr Bichitrovanu Sarkar, Consultant Pediatric Intensivist, Vision Care Hospital, Kolkata; and Dr L Pandey for patient management.

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REFERENCES

1. Hsu CW, Symons JM. Acute kidney injury: can we improve prognosis? Pediatr Nephrol. 2010;25:2401-12.
2. Hobbs DJ, Steinke JM, Chung JY, Barletta GM, Bunchman TE. Rasburicase improves hyperuricemia in infants with acute kidney injury. Pediatr Nephrol. 2010;25:305-9.
3. Hooman N, Otukesh H. Single dose of rasburicase for treatment of hyperuricemia in acute kidney injury: a report of 3 cases. Iran J Kidney Dis. 2011;5:130-2.
4. Lin PY, Lin CC, Liu HC, Lee MD, Lee HC, Ho CS, *et al*. Rasburicase improves hyperuricemia in patients with acute kidney injury secondary to rhabdomyolysis caused by ecstasy intoxication and exertional heat stroke. Pediatr Crit Care Med. 2011;12:e424-7.
5. Canpolat FE, Cekmez F. Rasburicase for hyperuricemia in an extremely low birth weight infant. Indian Pediatr. 2011;48:573-4.
6. Acosta AA, Hogg RJ. Rasburicase for hyperuricemia in hemolytic uremic syndrome. Pediatr Nephrol. 2012;27:325-9.
7. Jarmoliñski T, Zaniew M, Tousty J, Runowski D. Is it the right time to subject children with acute kidney injury to rasburicase trials? Pediatr Nephrol. 2012;27:1201-2.
8. Wilson FP, Berns JS. Onco-Nephrology: Tumor lysis syndrome. Clin J Am Soc Nephrol. 2012;7:1730-9.
9. Ejaz AA, Dass B, Kambhampati G, Ejaz NI, Maroz N, Dhatt GS, *et al*. Lowering serum uric acid to prevent acute kidney injury. Med Hypotheses. 2012;78:796-9.
10. Ejaz AA, Dass B, Lingegowda V, Shimada M, Beaver TM, Ejaz NI. Effect of uric acid lowering therapy on the prevention of acute kidney injury in cardiovascular surgery. Int Urol Nephrol. 2013;45:449-58.