Rhabdomyolysis-Induced Acute Kidney Injury Treated with Medium Cut-Off Membrane: A Case Report

Abstract

Acute kidney injury can complicate rhabdomyolysis in 10-40% patients. Myoglobinuria and elevated creatine kinase (CK) form the basis of diagnosis. When associated with azotemia and/or oliguria, intermittent hemodialysis is a treatment option. 31-year-old young man came with lower limb pain after doing 800 sit ups. At the presentation, blood pressure was high, serum creatinine was 15.7mg/dl and creatine kinase(CK)>20000 IU/L. Intermittent dialysis was initiated. He developed posterior reversible encephalopathy syndrome, generalized tonic clonic convulsions and a further rise in CK. He underwent extracorporeal removal of myoglobin with medium cut-off (MCO) membrane. After 3 sessions with MCO membrane, myoglobin and CK levels reduced. He was transitioned to conventional dialysis and discharged in a stable condition with complete renal recovery. Medium cut-off membrane effectively removes circulating myoglobin without significant albumin loss and is cost effective.

Keywords: *Acute kidney injury, dialysis, medium cut off membrane, rhabdomyolysis*

Girish V. Kumthekar, Urvi Shukla[1], Veena Purandare[2]

Departments of Nephrology, [1]Critical Care Medicine and [2]Internal Medicine, Symbiosis University Hospital and Research Center (SUHRC), Symbiosis Medical College for Women (SMCW), Symbiosis International University (SIU), Lavale, Pune, Maharashtra, India

Introduction

Acute kidney injury (AKI) is a life-threatening complication of rhabdomyolysis. AKI develops in 10%–40% of patients with severe rhabdomyolysis.[1]

The released myoglobin is rapidly cleared by hepatic metabolism. Therefore, tests for myoglobin in plasma or urine (normal range: 0–100 mg/L with chemiluminescence-based immunoassay CLIA) are not a sensitive diagnostic procedure. It is also readily filtered by glomeruli. Water is progressively reabsorbed, and the concentration of myoglobin rises proportionately until it precipitates and causes obstructive cast formation and thus AKI.[2] Management of rhabdomyolysis intends to increase the clearance of myoglobin, to treat hypovolemia, and to balance electrolyte and pH changes.[3]

Mortality due to AKI secondary to rhabdomyolysis is 59% versus 22% in the case of patients with normal renal function.[4,5] This makes it imperative to treat rhabdomyolysis-induced AKI with precision aimed at clearing circulating myoglobin to prevent systemic complications. We present a case of young male patient who presented for exercise-induced rhabdomyolysis with severe AKI and getting complicated with tonic-clonic seizures further accentuating muscle injury.

Case details

A 31-year-old man presented with 8-day history of lower extremity pain, reduced urine output, and abdominal pain. He developed pain immediately after prolonged lower extremity exercise (800 sit-ups). The patient had gross hematuria, back pain, and fever afterward. He had no history of any previous medical conditions or medications except for taking anabolic steroids for muscle building for more than 2 years. He was taken to a nearby hospital and was found to have very high blood pressure and creatinine of 15.7 mg/dL. He was initiated on intermittent hemodialysis and was found to have CK of more than 20,000 IU/L. He underwent seven sessions of intermittent hemodialysis (IHD) before shifting to Symbiosis University Hospital and Research Centre, Lavale (SUHRC) for further management.

The patient was found to have proteinuria (3+) with urine occult blood positive. His blood pressure was 150/100 mm Hg, and body weight was

How to cite this article: Kumthekar GV, Shukla U, Purandare V. Rhabdomyolysis-induced acute kidney injury treated with medium cut-off membrane: A case report. Indian J Nephrol 2023;33:468-71.

Received: 01-05-2022
Revised: 13-07-2022
Accepted: 30-07-2022
Published: 21-02-2023

Address for correspondence:
Dr. Girish V. Kumthekar, Symbiosis Medical College for Women and Symbiosis University Hospital and Research Centre, Lavale, Pune – 412 115, Maharashtra, India.
E-mail: drgirishkumthekar@gmail.com

Access this article online

Website: https://journals.lww.com/ijon/

DOI: 10.4103/ijn.ijn_151_22

Quick Response Code:

97 kg. Laboratory work-up showed a CK of 20,000 IU/L, alanine aminotransferase (ALT) of 106 IU/L, aspartate aminotransferase (AST) of 375 IU/L, and urine myoglobin (Mb) of 1003 µg/L. His blood urea and serum creatinine (S.cr) were 168 mg/dL and 9.30 mg/dL, respectively. Based on his markedly elevated CK, myalgia, and myoglobinuria, he was diagnosed and hospitalized as a case of exercise-induced rhabdomyolysis with AKI KDIGO stage 3.[6] Other laboratory parameters were as follows: calcium 7.8 mg/dL, phosphorus 6.9 mg/dL, uric acid 5.6 mg/dL, serum albumin 2.5 g/dL, hemoglobin 13.3 g%, WBC 17200/mm^3, and platelets 186/mm^3. His auto-immune workup (ANA, ANCA, C3, C4) was inconclusive. He was treated with salt and water restriction, alternate-day hemodialysis with ultrafiltration, and supportive care. He was requiring three tablets (prazosin, clonidine, and nifedipine) to keep his blood pressure under control. He was improving gradually, with urine output increasing to 700 mL/24 h.

He developed accelerated hypertension (BP: 221/140 mm Hg) with hypertensive encephalopathy and had three episodes of tonic-clonic seizures and was shifted to ICU (31/1/2022). On imaging, he was found to have PRES and started on parenteral labetalol and nitroglycerine. Seizure control was achieved with levetiracetam. His creatinine increased to 11.2 mg/dL, and urine output dropped to 40 mL/24 h. This was the second hit of rhabdomyolysis and AKI [Table 1].

As urine output dropped significantly after seizures, the decision was taken to offer extracorporeal removal of myoglobin. We had options of using a plasma filter (therapeutic plasma exchange), medium cut-off (MCO) membrane (Theranova, BAXTER), or high cut-off membrane HCO (Theralite, BAXTER). After comparing the three filters, it was decided to use MCO Theranova, BAXTER. After three consecutive sessions, myoglobin level decreased to 537 mcg/L and CK decreased to 3517 IU/L. Urine output increased 1100 mL/24 h (February 5, 2022). After three sessions with the MCO membrane, the patient was started with a conventional dialyzer (FX8). His urine output increased to 1300 mL/24 h, and intermittent dialysis was stopped (February 8, 2022). The dialysis access catheter was removed (February 9, 2022), and the patient was discharged in stable condition.

Presently, the patient remains stable with serum creatinine at 1.6 mg/dL and urine output of more than 1.5 L without diuretics.

Discussion

The predominant cause of kidney damage in patients with rhabdomyolysis is the massive release of myoglobin into the circulation, with myoglobinuria. Myoglobinuria, which becomes visible when urine myoglobin excretion exceeds 100–300 mg/dL, causes cast formation and accumulation of iron in proximal tubules, with intratubular obstruction and proximal tubular cell injury.[1]

Treatment consists of volume resuscitation, urine alkalization, diuresis, and hemodialysis when necessary for rhabdomyolysis-induced AKI. Various forms of dialytic therapy have been used if AKI develops, but there is no evidence supporting the use of a specific dialysis modality. The techniques and devices used for classic dialytic techniques have displayed a limited capacity for the removal of circulating myoglobin. The use of hyper-permeable membranes might represent a novel approach for the treatment of acute rhabdomyolysis not only because efficient renal replacement is provided but also because of a potential protective effect in the rapid and efficient removal of circulating myoglobin.[7] There are multiple

Table 1: Biochemical and clinical parameters

Date	Creatinine	Urea	CK NAC	Myoglobinuria	Urine output	Dialysis filter type
24/01/22	9.3	168	20,000		200	FX8
26/01/22	11.6	215	3517		250	FX8
27/01/22	10.0	161			320	FX8
28/01/22	-				600	FX8
30/01/22	-			1003	700	FX8
31/01/22	11.2	140			40	FX8
01/02/22	9.9	114			50	THERANOVA
02/02/22	8.4	91			NIL	THERANOVA
03/02/22	7.4	82	857		50	THERANOVA
04/02/22	6.21	69			720	NIL
05/02/22					1100	FX8
07/02/22				506	1300	NIL
08/02/22					500	FX8
Outpatient follow-up						
21/02/22	2.1	36	-	-	2100	-
03/03/22	1.6	26	-	-	1850	-

Table 2: Membranes available for extracorporeal myoglobin clearance

Membrane Type	Mode of Clearance	Advantage	Disadvantage	Cost involved per Filter/Membrane
Plasma filter	Therapeutic plasma exchange	It gives removal of myoglobin with other mediators of inflammation.	Plasmapheresis resulted in higher sieving coefficients, but the final clearance is minimal because of the limitations imposed by low volume exchanges.	18,000 INR
Theralite	High cut-off membrane	The Theralite dialyzer, featuring the proprietary High cut-off (HCO) membrane.	Albumin replacement is needed. Average albumin loss per hour of treatment (g/h) ≤7.0	1,25,000 INR
CytoSorb	Adsorption	Myoglobin has a mass of 17 kD [12-14] and is effectively adsorbed by CytoSorb®, which resulted in the approval of the device for conditions with increased myoglobin levels such as rhabdomyolysis.	The device may adsorb other known and unknown molecules, which may potentially be useful. Dialysis is not possible with CytoSorb as it an adsorbent column with no dialysate compartment.	93,260 INR
Theranova	Medium cut-off membrane	It effectively targets the removal of large middle molecules. There is no need for albumin replacement (Sieving coefficient for albumin is 0.008). It can perform dialysis as well.	Multiple sessions may be needed.	3990 INR
Conventional hemodialysis does not eliminate myoglobin				
CRRT improves myoglobin clearance but does not change mortality				

options for extracorporeal removal of myoglobin, including CytoSorb®, high cut-off membrane, therapeutic plasma exchange, and high-volume CRRT/CVVHF.[3,8,9] Attempts to use plasmapheresis have resulted in higher sieving coefficients, but the final clearance is minimal because of the limitations imposed by low volume exchanges.[6] The limitation imposed by high-flux membranes in convective therapies such as hemofiltration is that in the presence of a low sieving coefficient for myoglobin, even high-volume hemofiltration or pulse high-volume hemofiltration may be inefficient for removing the desired amount of circulating myoglobin.[8] Potential drawbacks due to unwanted loss of beneficial molecules such as albumin are inherent to both of the above mentioned modalities. In this regard, an MCO membrane (Theranova BAXTER) has sieving coefficient for myoglobin at 0.9 and for albumin at 0.008. This membrane appears to be tailor-made for middle molecule without any need for albumin replacements.

In a small retrospective observational study, reduction in myoglobin during dialytic procedure was significant for both HCO and MCO membranes. This preliminary study showed comparable effectiveness of a novel MCO (Theranova BAXTER) and "standard" HCO dialysis membrane (Theralite BAXTER) for serum myoglobin removal in patients with severe AKI.[10]

There are multiple options for extracorporeal removal of myoglobin [Table 2]. The process of selection of an appropriate filter for a patient with rhabdomyolysis involves sieving coefficients for myoglobin and albumin, cost per filter, loss of useful substances such as immunoglobulins in the process, and ease of doing the therapy as per unit protocols. We chose the MCO membrane as it is relatively cost-effective, gives good dialysis, and friendly with operating technicians and nurses.

A novel class of membranes, MCO membranes, are designed to remove middle and large middle molecules in hemodialysis (HD) treatments. These membranes were compared with online hemodiafiltration (OL-HDF) and were found to be equally effective. The MCO filter could remove molecules such as β_2-microglobulin, myoglobin, prolactin, α_1-microglobulin, and α_1-acid glycoprotein while retaining albumin.[11,12]

Conclusion

The patient recovered well with an MCO membrane and was not required to supplement albumin. The cost of three dialysis sessions was much lower compared to other membranes. The timing for initiation of extracorporeal blood purification in rhabdomyolysis-induced AKI needs

to be determined in larger randomized and controlled trials aimed at preventing the need for dialysis in these subsets of patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Pasquale E, Luca E, Nicoletta S, Lorenzo P, Stefania B, Teresa R. Rhabdomyolysis-associated acute kidney injury. Am J Kidney Dis 2018;71:A12-4.
2. Vanholder R, Sever MS, Erek E, Lameire N. Rhabdomyolysis. J Am Soc Nephrol 2000;11:1553-61.
3. Hannah C, Bernhard MW, Schmidt LC. Effects of hemoadsorption with CytoSorb during severe rhabdomyolysis. Blood Purif 2021;50:268-9.
4. De Meiejer AR, Fikkers BG, de Keijzer MH, van Engelen BGM, Drenth JPH. Serum creatine kinase as predictor of clinical course in rhabdomyolysis: A 5-year intensive care survey. Intensive Care Med 2003;29:1121-5;
5. Woodrow G, Brownjohn AM, Turney JH. The clinical and biochemical features of acute renal failure due to rhabdomyolysis. Ren Fail 1995;17:467-74.
6. Summary of Recommendation Statements. Kidney Int Suppl 2012;2:8-12.
7. Ronco C. Extracorporeal therapies in acute rhabdomyolysis and myoglobin clearance. Critical Care 2005;9:141-2.
8. Brendolan A, D'Intini V, Ricci Z, Bonello M, Ratanarat R, Salvatori G, Bordoni V, *et al*. Pulse high volume hemofiltration. Int J Artif Organs 2004;27:398-403.
9. Olcay D, Can I, Ben van der Hoven, Sjoerd T, Patricia O, Hilde RH. Successful reduction of creatine kinase and myoglobin levels in severe rhabdomyolysis using extracorporeal blood purification (CytoSorb®). Blood Purif 2020;49:743-7.
10. Jerman A, Andonova M, Persic V, Gubensek J. Extracorporeal Removal of Myoglobin in Patients with Rhabdomyolysis and Acute Kidney Injury: Comparison of High and Medium Cut-Off Membrane and an Adsorber Cartridge. Blood Purif. 2022 Mar 25:1-5. doi: 10.1159/000521923. Epub ahead of print. PMID: 35340002.
11. Maduell F, Rodas L, Broseta JJ, Gomez M, Xipell M, Guillen E, *et al*. Medium cut-off dialyzer versus eight hemodiafiltration dialyzers: Comparison using a global removal score. Blood Purif 2019;48:167-74.
12. RONCO, C. (2017). *Expanded hemodialysis: innovative clinical approach in dialysis*. https://search.ebscohost.com/login.aspx?direct=true&scope=site&db=nlebk&db=nlabk&AN=1604256.