DOI: 10.7860/JCDR/2020/44729.13998

Case Series

Internal Medicine Section

Baclofen Induced Encephalopathy in Patients with Chronic Kidney Disease

ALOK KUMAR[1], DORCHHOM KHRIME[2], NITIN BANSAL[3], SAURABH AGARWAL[4], UTKARSH SHARMA[5]

ABSTRACT

Hiccups are manifestation of uremic syndrome. Baclofen had been used in uremic hiccups, but its usage has been described in literature with development of neurotoxicity in patients with renal failure. The case series reports three patients of Chronic Kidney Disease (CKD) that were on haemodialysis. All of them had intractable hiccups, for which Baclofen was administered. They developed encephalopathy within 24-48 hours of ingestion of Baclofen. The drug was discontinued and the patients improved within 36-48 hours. They were finally discharged with no residual neurological deficit.

Keywords: Haemodialysis, Hiccups, Renal failure

INTRODUCTION

Baclofen has been used for hiccups due to various causes [1]. There are some case reports on use of Baclofen in uremic hiccups but it has been reported to cause encephalopathy in patients with renal failure [2]. This article is about three CKD patients that were prescribed Baclofen to treat hiccups. They developed encephalopathy which subsided after discontinuation of the drug.

CASE 1

An 11-year-old male child was admitted in emergency with decreased level of consciousness and somnolence. He was on haemodialysis for CKD for one week. Patient had CKD due to membrano proliferative glomerulonephritis. He was on Amlodipine 5 mg daily with metoprolol 50 mg twice a day. Other medications were calcium carbonate, calcitriol, pantoprazole and torsemide. He was started on baclofen 2.5 mg thrice daily for hiccups one day prior to admission. He was admitted in Intensive Care Unit. His Glasgow Coma Scale (GCS) was E3V2M4. His pupils were of normal size and had normal light reaction. His plantar reflex was not elicitable and deep tendon jerks were normal. He had nystagmus also. His BP was 118/72 mm Hg and respiratory rate was 21 per minute.

His investigations revealed Blood Urea Nitrogen (BUN) of 46 mg%, S. creatinine of 4.7 mg%, Serum sodium (Na^+) 141 meq /L, Serum Potassium (k^+) was 4.3 meq/L. He had Serum Calcium (Ca^{++}) of 8.7 mg%. His Liver Function Tests (LFT) were normal. The blood glucose level was 128 mg%. His haemoglobin was 10.8 gm% and TLC was 7800/mm^3. Arterial blood gas was within normal limits. His CT scan of cranium and EEG were normal. The cummulative dose of Baclofen that he received was 7.5 mg. The next day the child showed a state of confusion. He was stared on symptomatic treatment and baclofen was discontinued. A single session of dialysis was given and the child showed improvement after 36 hours of admission. Two days later he was discharged with no residual neurological deficits.

CASE 2

A 62-year-old male was admitted in ward for accelerated hypertension. He was on irregular haemodialysis for two months. He had CKD due to diabetic nephropathy. He had intractable hiccups for three days due to uraemia. Patient received 2.5 mg baclofen twice a day for two days and developed abnormal behaviour after 48 hours. His GCS was E3V3M4. Examination of eye showed normal size pupil with normal light reaction and presence of nystagmus. Patient had flexor plantar response and normal deep tendon reflexes. His BP was 150/96 mm Hg and respiratory rate was 19 per minute. His investigations revealed BUN OF 67 mg%, S. creatinine of 6.9 mg%, Serum Na^+ 144 meq /L, Sersum K^+ 4.1 meq/L. He had Serum Ca^{++} of 8.9 mg% and Serum bilirubin of 1.1 mg%. His LFT were normal, blood glucose level was 146 mg%, haemoglobin was 10.8 gm% and TLC was 7800/mm^3. Arterial blood gas was in normal limits. CT scan of cranium was normal. Patient was on Amlodipine 10 mg daily with metoprolol 50 mg twice a day and clonidine 100 mcg thrice daily. Other medications were calcium carbonate, calcitriol, famotidine and torsemide. Baclofen was stopped and dialysis was done three times. Patient was fully alert and oriented after 48 hours and his GCS was 15. He was discharged after four days without any residual neurological deficit.

CASE 3

A 44-year-old female was admitted in emergency with decreased level of consciousness. She was on haemodialysis, for CKD, for 12 weeks. She had CKD due to amyloidosis. She was started on dialysis elsewhere.

Patient was admitted in Intensive Care Unit. Her GCS was E3V2M4. Her pupils were of normal size and had normal light reaction. Her plantar reflex was not elicitable and deep tendon jerks were normal. Her BP was 142/86 mm Hg and respiratory rate was 18 per minute. Her investigations revealed BUN of 75 mg%, Serum creatinine of 7.7 mg%, Serum Na^+ 136 meq /L, Serum K^+ 4.3 meq/L and Serum Ca^{++} of 9.2 mg%. Her LFT were normal. The blood glucose level was 142 mg%. Her haemoglobin was 11.8 gm% and TLC was 4700/mm^3. Arterial blood gas was in normal range. CT scan of cranium and EEG were normal. Patient was on amlodipine 10 mg, calcium carbonate, torsemide and pantoperazole. The medical history showed baclofen ingestion 5 mg twice a day for two days. She was in a state of confusion the next day of starting Baclofen. The drug was immediately discontinued. She was given a session of dialysis on the same day of admission. She started obeying verbal command and became fully oriented after 36 hours of admission and was discharged three days later with no residual neurological deficits.

DISCUSSION

There are reports of Baclofen induced encephalopathy among patients with kidney disease. Lee J et al., described two cases of advance renal failure that were treated with Baclofen for hiccups. The patients developed encephalopathy which was treated with haemodialysis and immediate stoppage of the drug [3]. Khazneh E et al., also described a case of single dose baclofen

induced neurotoxicity in 47-year-old male [4]. Baclofen induced encephalopathy in a child has also been reported [5]. Most of the ingested Baclofen (70-85%) is excreted by the kidneys without changes in urine and 15% is metabolised by the liver to an inactive form [5,6]. However, in patients with the renal insufficiency half-life of the drug is prolonged. It is between 4.5 and 6.8 hour in subjects with normal renal function [6-8].

Neurological side effects including transient drowsiness, sedation, dizziness, fatigue, coma and respiratory depression are known adverse effects of baclofen in patients with normal renal function [8]. Baclofen is primarily excreted by glomerular filtration. Thus, its accumulation and encephalopathy may occur in patients with impaired renal function even when normal doses are administered [9]. Half-life of baclofen is significantly increased and the recommended dose or even low doses of baclofen as little as 5 mg daily or a cumulative dose of 10 mg could result in its accumulation and severe drug intoxication with neurological side effects [10].

Baclofen-associated encephalopathy has been described in patients with varying degrees of renal dysfunction. Aisen ML et al., described a patient that developed baclofen-associated encephalopathy with an estimated Glomerular Filtration Rate (eGFR) of 55-60 mL/min and creatinine of 0.8 mg/dl [9]. There are few case reports of baclofen induced encephalopathy in adult patients with advance renal failure or on renal replacement therapy for various indications. Present case series also reported a child that showed a state of confusion and ataxia after 24 hours of taking Baclofen, though he received only 7.5 mg cumulative dose of baclofen. Sanjay S et al., described baclofen toxicity with a dose of 2.5 mg baclofen single dose in patient on maintenance haemodialysis [11]. Patients in this series received 7.5 to 20 mg cumulative dose of baclofen. Most of the patients recover after discontinuation of baclofen in 24 hours to 96 hours [12-14]. All the index patients showed improvement in 36-48 hours in the case series.

Usage of baclofen is not recommended in patients with an eGFR of ≤30 mL/min/1.73m^2. Patients with eGFR between 30 and 60 mL/min/1.73m^2 (stage 3 CKD) are recommended to start with low doses at prolonged intervals [15,16].

CONCLUSION(S)

This case series highlights that lower doses of baclofen could be hazardous in advanced renal failure. If baclofen is administered in such patients then it could lead to serious neurological adverse effects. These patients should be managed with discontinuation of baclofen and if needed, with dialysis.

REFERENCES

[1] Seker MM, Aksoy S, Ozdemir NY, Uncu D, Civelek B, Akıncı MB, et al. Successful treatment of chronic hiccup with baclofen in cancer patients. Med Oncol. 2012;29:1369-70.
[2] El-Husseini A, Sabucedo A, Lamarche J, Courville C, Peguero A. Baclofen toxicity in patients with advanced nephropathy: Proposal for new labeling. Am J Nephrol. 2011;34:491-49.
[3] Lee J, Shin HS, Jung YS, Rim H. Two cases of baclofen-induced encephalopathy in hemodialysis and peritoneal dialysis patients. Ren Fail. 2013;35(6):860-62.
[4] Khazneh E, Shamlawi A, Jebrin K, Hamdan Z, Sawalmeh O. Single-dose baclofen-induced neurotoxicity in a patient with end stage renal disease: Case report. BMC Nephrol. 2018;19:352.
[5] Malak M, Barzegar M. Baclofen induced encephalopathy in a 6-year-old boy with advanced renal failure. Iran J Child Neurol. 2015;9(2):61-63.
[6] Gerkin R, Curry SC, Vance MV. First-order elimination kinetics following baclofen overdose. Ann Emerg Med. 1986;15:843-46.
[7] Vlavonou R, Perreault MM, Barrière O, Shink E, Tremblay PO, Larouche R, et al. Pharmacokinetic characterization of baclofen in patients with chronic kidney disease: Dose adjustment recommendations. J. Clin. Pharmacol. 2014;54:584-92.
[8] Leung NY, Whyte IM, Isbister GK. Baclofen overdose: Defining the spectrum of toxicity. Emerg Med Australas. 2006;18(1):77-82.
[9] Aisen ML, Dietz M, McDowell F, Kutt H. Baclofen toxicity in a patient with subclinical renal insufficiency. Arch Phys Med Rehabil. 1994;75:109-11.
[10] Wolf E, Kothari NR, Roberts JK, Sparks MA. Baclofen toxicity in kidney disease. Am J Kidney Dis. 2018;71(2):275-80.
[11] Sanjay S, Manoharan B, Arun KN, Sundar S. Baclofen in the treatment of intractable hiccups. J Assoc Physicians India. 2003;51:324-25.
[12] Chen YC, Chang CT, Fang JT, Huang CC. Baclofen neurotoxicity in uremic patients: Is continuous ambulatory peritoneal dialysis less effective than intermittent hemodialysis? Ren Fail. 2003;25:297-305.
[13] Beladi Mousavi SS, Beladi Mousavi M, Motemednia F. Baclofen-induced encephalopathy in patient with end stage renal disease: Two case reports. Indian J Nephrol. 2012;22(3):210-12.
[14] Bassilios N, Launay-Vacher V, Mercadal L, Deray G. Baclofen neurotoxcity in a chronic hemodialysis patient. Nephrol Dial Transplant. 2000;15:715-16.
[15] Wu VC, Lin SL, Lin SM, Fang CC. Treatment of baclofen overdose by haemodialysis: A pharmacokinetic study. Nephrol Dial Transplant. 2005;20:441-43.
[16] Roberts JK, Westphal S, Sparks MA. Iatrogenic baclofen neurotoxicity in ESRD: recognition and management. Seminars in Dialysis. 2015;28(5):525-29.

PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Nephrology, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India.
2. Professor, Department of Medicine, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India.
3. Professor, Department of Medicine, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India.
4. Associate Professor, Department of Medicine, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India.
5. Professor and Head, Department of Paediatrics, Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar, Dehradun, Uttarakhand, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Alok Kumar,
Shri Guru Ram Rai Institute of Medical and Health Sciences, Patel Nagar,
Dehradun, Uttarakhand, India.
E-mail: alokkraj@rediffmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 21, 2020
- Manual Googling: Jun 09, 2020
- iThenticate Software: Aug 17, 2020 (10%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Apr 20, 2020**
Date of Peer Review: **May 26, 2020**
Date of Acceptance: **Jun 10, 2020**
Date of Publishing: **Sep 01, 2020**