Iatrogenic Baclofen Neurotoxicity in End Stage Renal Disease: A Case Report and Review of Literature

Navaneedha Lingam Mahalingam and Rizna Abdul Cader*

1Department of Internal Medicine, Faculty of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Malaysia.

Authors’ contributions

This work was carried out by both authors. Author NLM wrote the case report and the first draft of the manuscript. Author RAC did the literature search and modified the manuscript. Both authors have read and approved the final manuscript.

ABSTRACT

Baclofen is a centrally acting antispasmodic agent that is commonly prescribed to patients suffering from spinal cord problems. Nearly 85% of baclofen is excreted by the kidneys whereas the remaining 15% is metabolized by the liver. In patients with renal insufficiency, baclofen accumulates and causes central nervous system toxicity. Herein we report a case of baclofen induced neurotoxicity in a patient with end stage renal disease on maintenance haemodialysis. The patient had cervical spondylomyopathy and was started on baclofen 10 mg once daily which was subsequently increased to three times a day. Within 48 hours of the increased dose of baclofen, he developed drowsiness, confusion and became aggressive. Other causes of encephalopathy were excluded and baclofen was stopped. His confusion improved completely after three consecutive sessions of haemodialysis. Physicians should be aware of baclofen induced neurotoxicity in patients with renal insufficiency.
Keywords: Baclofen; end stage renal disease; haemodialysis; neurotoxicity.

1. INTRODUCTION

Baclofen is a synthetic derivative of neurotransmitter gamma-aminobutyric acid [1]. Although its precise mechanism of action is not fully understood, it has an inhibitory effect on the central nervous system via the gamma-aminobutyric acid B receptors at the spinal level. It is commonly prescribed to patients suffering from spinal cord problems to control spasticity. Baclofen is predominantly (nearly 85%) excreted by the kidneys whereas the remaining 15% is metabolized by the liver [2]. Due to its lipophilic properties, it crosses the blood brain barrier exerting effects on the central nervous system [3]. There have been several case reports of baclofen induced neurotoxicity in patients with renal insufficiency [4-6]. Neurotoxicity includes somnolence, respiratory depression and central nervous system depression, and delirium [7-8].

2. CASE REPORT

A 51 year old male with end stage renal disease (ESRD) secondary to hypertension on maintenance haemodialysis and cervical spondylomyopathy (wheel chair bound) was electively admitted for pre-operative assessment prior to posterior instrumentation and fusion. He was started on oral baclofen 10 mg at night due to clonus of his left lower limb. Baclofen dose was increased to 10 mg three times a day two days later due to increased spasticity. Two days later patient became delirious, drowsy and restless. His GCS was 11/15 (E3 V3 M5), he was not in respiratory distress, his vital signs were normal with a BP of 120/90 mm Hg, heart rate of 58 beats/min and afebrile. Physical examination was unremarkable, with no neurological deficit compared to his baseline and normal and reactive pupils bilaterally. There was no evidence of infection and no other new medications were prescribed. His blood investigations revealed: - white cell count 4.5 ×10⁹/L (4.0–10.0), haemoglobin 12.3 /dl (14.0– 17.0) and platelet count of 207 ×10⁹/L (150–400). Renal profile: - sodium 132 mmol/L (135–150), potassium 5.5 mmol/L (3.5–5.0), urea 18.5 mmol/L (2.5 -6.4), creatinine 1035 umol/L (62–106). Liver Function Test: albumin 38 g/L (35–50), alkaline phosphatase 186 U/L (32–104), alanine transaminase 20 U/L (< 44), Bilirubin 12.2 umol/L. Calcium 2.47 mmol/L and phosphate 2.28 mmol/L. Glucose was 6.2 mmol/L and magnesium 0.82 mmol/L. A CT brain revealed no abnormalities. A diagnosis of acute delirium secondary to baclofen toxicity was made, baclofen was stopped and patient was started on urgent haemodialysis for 4 hrs. His GCS and symptoms improved gradually and normalized after 3 consecutive sessions of haemodialysis (4 hours each). He subsequently underwent cervical spinal surgery as planned and was discharged well.

3. DISCUSSION

Patients with renal insufficiency are at higher risk of adverse effects from baclofen and reports in ESRD patients have shown neurotoxicity even after taking 5 mg of baclofen [3,5]. To the best of our knowledge, there are twenty three case reports (involving 47 patients) of baclofen induced neurotoxicity in patients with renal insufficiency but thirty three of these patients had ESRD [4,6,9-11]. The majority of the ESRD patients were on haemodialysis (> 60%) and most of the patients were elderly (more than 60 years old), with neurotoxicity at presentation that usually manifested within 2-3 days of taking baclofen [4]. Our case report has a startling resemblance to these cases where our patient had ESRD and developed symptoms of neurotoxicity within 48 hours of taking baclofen 30 mg/day.

Studies have shown symptoms of baclofen toxicity develop when serum levels are > 400 ng/ml [12]. We did not check serum baclofen levels as we had no facilities do it at our institution and is in keeping with most of the case reports. However, in the few studies that did monitor serum baclofen levels, they found that patients were still symptomatic despite levels falling to therapeutic range [2,4,13]. Thus, caution is warranted when interpreting serum baclofen levels.

Treatment of baclofen induced neurotoxicity includes supportive measures and dialysis depending on the presentation and degree of renal insufficiency [3,14-16]. Baclofen has a low molecular weight, low volume of distribution and as only 35% of it is protein bound, it is dialyzable [17,18]. Prompt recovery of symptoms post haemodialysis have been reported in ESRD patients treated for baclofen toxicity [3,4,6]. Although one study reported that a
single 4 hour haemodialysis session successfully removed 79% of baclofen, the median number of haemodialysis sessions was two sessions in the studies that reported the total number of haemodialysis sessions [3,6,13]. Our patient showed improvement of symptoms after his first session of 4 hours haemodialysis and achieved complete recovery after three days of haemodialysis (4 hours/session). Although majority of the reported literature on baclofen induced neurotoxicity in ESRD is on haemodialysis patients, there are some reports on peritoneal dialysis patients that were successfully treated with peritoneal dialysis [3].

4. CONCLUSION

The half-life of baclofen in patients with renal insufficiency and ESRD is significantly increased. Baclofen induced neurotoxicity is an under-recognized iatrogenic condition that results in significant morbidity and mortality. Haemodialysis is a treatment option for baclofen induced neurotoxicity.

Based on our literature review, we do not advocate the use of baclofen in ESRD patient as the risk outweighs the benefits.

CONSENT

All authors declare that written informed consent was obtained from the patient for publication of this paper.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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