British Journal of Medicine & Medical Research
3(1): 75-79, 2013

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Two Cases of Baclofen-Induced Encephalopathy in Hemodialysis and Peritoneal Dialysis Patients

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Authors' contributions

This work was carried out in collaboration between all authors. Authors JL and HSS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors YSJ and HR managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

Case Study

Received 17th August 2012
Accepted 2nd November 2012
Published 8th December 2012

ABSTRACT

Hiccups are a spasmodic contraction of the diaphragm and usually transient phenomenon that affects nearly everyone. When hiccups develop, the patients are administrated antispastic agent, such as balcofen. Baclofen is widely used for the treatment of this spastic movement disorders. Also, baclofen is a gamma-aminobutyric acid (GABA) derivative that induces presynaptic motor neuron inhibition and produces a central antispastic response. Baclofen toxicity is rare and has been reported with intrathecal pump and orally administered baclofen, particularly in patients with poor renal function. Herein, we report two cases of encephalopathy in hemodialysis and peritoneal dialysis patients who received low doses of baclofen for persistent hiccups. We suggest that, in patients with chronic kidney disease (CKD), baclofen should be avoided or started at a low dose. If the renal insufficiency patient develops toxic baclofen-induced encephalopathy, hemodialysis may be the proper treatment to improve clinical symptoms.

Keywords: Baclofen; encephalopathy; hemodialysis; peritoneal dialysis; hiccups.

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1. INTRODUCTION

Baclofen is a gamma-aminobutyric acid (GABA) derivative that induces presynaptic motor neuron inhibition and produces a central antispastic response [1]. Baclofen is eliminated mostly by the kidney. The elimination half-life of baclofen is 2 to 6 hours for therapeutic oral doses in healthy volunteers and elderly patients [2] but half-life increases with renal insufficiency [3] Baclofen is widely used for the treatment of spastic movement disorders. Baclofen toxicity is rare and has been reported with intrathecal pump and orally administered baclofen, particularly in patients with poor renal function. Few cases of baclofen-induced neurotoxicity have been reported in patients with renal insufficiency treated for hiccups. These patients received high doses of baclofen [4]. Herein, we report two cases of encephalopathy in dialysis patients who received low doses of baclofen for persistent hiccups. And the patients were recovered mentality after treatment of hemodialysis.

2. CASE REPORT

2.1 Case 1

A 71-year-old man was admitted to our hospital for arteriovenous fistula (AVF) formation surgery. His past medical history included 30 years of diabetes and hypertension. One month before admission, he was diagnosed with stage 5 chronic kidney disease (CKD). He had been started on baclofen 10 mg 3 times for one day. The patient presented 3 days after baclofen treatment with mental deterioration. Neurological examination did not reveal signs of localization. Vital signs were 130/80 mmHg blood pressure, 78 times per minute heart rate, 18 times per minute respiration rate and 36.2ºC body temperature. His blood sugar was within normal limits. Laboratory tests showed 9.8 g/dL hemoglobin, 23600/uL leukocytes, 188000 uL platelets, 53 mg/dl blood urea nitrogen, 7.6 mg/dL creatinine, 139 meq/L sodium, 3.3 meq/L potassium, 95 meq/L chloride, 6.9 mg/dL calcium, 5.1 mg/dL phosphorus, 1.9 mg/dL magnesium, 11 IU/L AST, 15 IU/L ALT and 1.3 mg/dL total bilirubin. Blood gas analysis revealed 7.421 pH, 75.7 mmHg PaO, 35.4 mg PaCO, 22.5 mmol/L HCO_3 and 95.5% oxygen saturation. The finding of electroencephalography (EEG) was normal. Brain computed tomography (CT) without radio-contrast did not show acute findings (Fig. 1). Baclofen was stopped and hemodialysis was started via permanent catheter through the right subclavian vein approach. Hemodialysis was performed immediately to eliminate baclofen and the patient received 2 times (total 8 hours) hemodialysis. The consciousness of the patient returned completely after 2 times (total 8 hours) hemodialysis were completed. Serum baclofen concentration was not estimated because serum baclofen analysis was not possible. Finally, the patient received arteriovenous fistula formation and has been treated with hemodialysis.

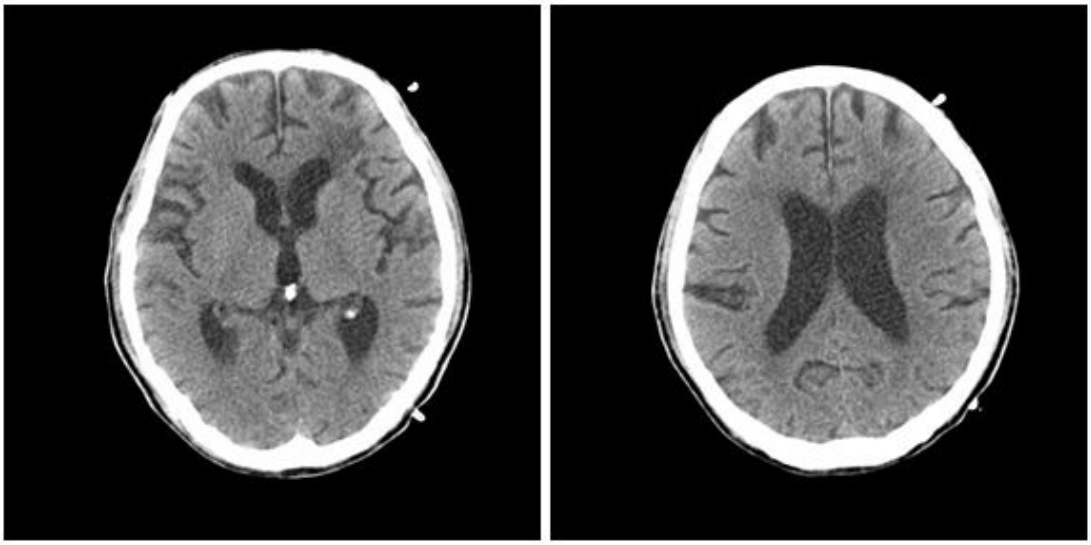

Fig. 1. Non-enhanced computed tomography (CT) of the brain in hemodialysis patient showed no recent hemorrhagic evidence was seen

2.2 Case 2

A 35-year-old woman was transferred to our unit presenting with mental deterioration. She was diagnosed with stage 5 chronic kidney disease (CKD) and had been treated with peritoneal dialysis for 3 years. Three days before admission, she was started on baclofen 10 mg twice a day for a right rib fracture. On admission, she was sent to a local hospital with symptoms with mental deterioration. There were no focal neurologic signs. The patient was transferred to our emergency department. Her vital signs were unremarkable (blood pressure 130/80 mm Hg, pulse 80/min, temperature 36.4ºC and pulse oxygenation 98%). Laboratory data were WBC count 10700 /uL, Hemoglobin 12.0 g/dL, platelet count 476000 /uL, BUN (Blood Urea Nitrogen) 26 mg/dL, creatinine 13.6 mg/dL, sodium 137 meq/L, potassium 2.2 meq/L, chloride 82 meq/L, calcium 8.7 mg/dL, phosphorus 6.8 mg/dL, magnesium 6.1 mg/dL, bilirubin total 0.4 mg/dL, AST 19 IU/L, and ALT 16 IU/L. The finding of electroencephalography (EEG) was normal. Non-enhanced computed tomography (CT) of the brain and T2-weighted imaging (T2WI) of magnetic resonance imaging (MRI) of the brain in peritoneal dialysis patient showed no gross abnormality was found (Fig. 2). Baclofen was discontinued and 3 times (total 10 hours) hemodialysis treatment via dual lumen catheter were performed to eliminate the baclofen. The patient's returned to be alert mentality during the second hemodialysis session. She changed hemodialysis to peritoneal dialysis and was discharged without any change of mentality or neurological deficits.

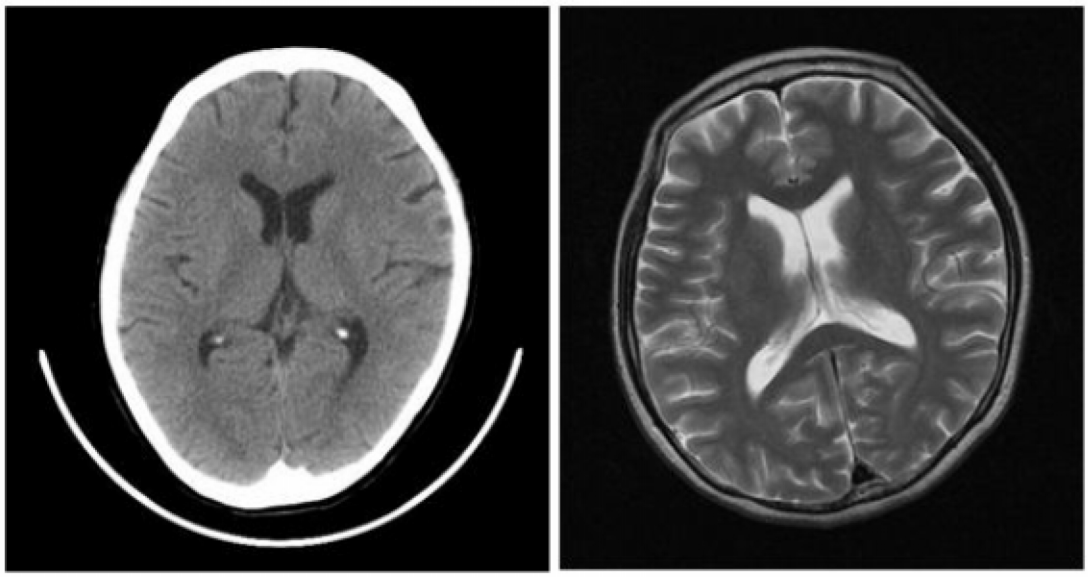

Fig. 2. Non-enhanced computed tomography (CT) of the brain (Left) and T2-weighted imaging (T2WI) of magnetic resonance imaging (MRI) of the brain (Right) in peritoneal dialysis patient showed no gross abnormality was found

3. DISCUSSION

Baclofen is primarily excreted by glomerular filtration, with a clearance proportional to creatinine clearance [5]. Thus, baclofen accumulation and encephalopathy may occur when normal doses are administered to patients with impaired renal function. Baclofen induced encephalopathy has been reported in patients with varying degrees of renal insufficiency. We report two cases of baclofen-induced encephalopathy in chronic kidney disease (CKD) patients. One patient had been treated with hemodialysis, the other patient had been treated with peritoneal dialysis. There have been case reports of baclofen-induced encephalopathy in patients with renal insufficiency showing that consciousness recovered after hemodialysis treatment [6-7] Therefore, our patients received hemodialysis treatment and mentality was restored. There are guidelines for administrating baclofen. Using baclofen is not recommended in patients with an estimated glomerular filtration rate (eGFR) of < 30 ml/min/1.73 m^2. Patients with eGFR between 30 and 60 ml/min/1.73 m^2 (stage 3 CKD) are recommended to start with low doses at long intervals. Patients taking baclofen must be monitored closely for toxicity when declining renal function is present [8]. If patients with renal impairment present with mental deterioration, physicians must consider any drugs being taken. If organic causes are ruled out and baclofen is a suggested cause of illness, it is necessary to begin hemodialysis.

4. CONCLUSION

We suggest that, in patients with chronic kidney disease (CKD), baclofen should be avoided or started at a low dose. If the renal insufficiency patient develops toxic baclofen-induced encephalopathy, hemodialysis may be the proper treatment to improve clinical symptoms.

CONSENT

In this paper, only published data from the literature were used for description. Thus, a statement of patient consent is not applicable for this paper.

ETHICAL APPROVAL

Since data from the literature, only, were used for description, ethical approval is not applicable to this paper. This study is not against the public interest. All authors hereby declare that all description have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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The peer review history for this paper can be accessed here:
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