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TOXIC ENCEPHALOPATHY – BACLOFEN INDUCED

Internal Medicine

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ABSTRACT

Baclofen is an antispasmodic drug, which reduces the frequency and intensity of muscular spasms by acting on spinal cord nerves in patients with specific spinal cord diseases. It is commonly used in patients above 12 years to treat spasticity. It is excreted via the kidney, unchanged in the urine. Therefore, in patients with renal dysfunction, there are chances of accumulation of baclofen and leading to toxic effects like encephalopathy. One such condition in which a patient with end-stage renal disease had just taken baclofen is described here. The patient had toxic encephalopathy, which was treated.

KEYWORDS

Encephalopathy, Baclofen, GABA

INTRODUCTION

Baclofen is an analogue of the inhibitory transmitter GABA acts as a selective GABA-B receptor agonist. Its primary action is to decrease the release of excitatory transmitters and depress both polysynaptic and monosynaptic reflexes. It is an effective therapy for spasticity, chronic hiccups and in many neurological disorders like multiple sclerosis, amyotrophic lateral sclerosis, spinal injuries, etc(1). It is well absorbed orally and is excreted unchanged in urine. It reduces muscular tone at the spinal level when administered in therapeutic quantities. However, with increasing doses of the drug, other involvement of the central nervous system has been noted, especially with toxic doses. Caution should be considered in administering baclofen to patients with decreased renal function. Patients with impaired renal function have a longer half-life and increased blood-brain barrier bridging. From the previous literatures, it is evident that baclofen even at a low dose induced encephalopathy(2). Generalized CNS effects like fatigue, syncope, hypotension, ataxia, psychological disturbances, and cardiovascular and respiratory depression are seen in such cases(2). The toxicities are generally ruled out from encephalopathic symptoms, EEG reports and medical history. The patients developed encephalopathy which was treated with haemodialysis and immediate stoppage of the drug

Case

A 74-year-old male patient with a past medical history of renal disease, diabetes mellitus type 2, hypertension, dyslipidemia, and old cerebrovascular disease presented for altered mental status, vertigo, slurring of speech and decreased urine output. He also had right upper and lower limb weakness and increased sleep habits for 1 day. The patient had a recent local clinic visit with concern for pain due to muscle spasms a week ago, from where he was started on a baclofen tablet 10 mg b.i.d. On the day of admission, the patient had 1 episode of vomiting after coming to the ER and was admitted to the intensive care unit as he was drowsy and GCS was 9/15.

The vital signs were the following: temperature 100.1°F, respiratory rate 18 breaths/minute, pulse 76 beats/minute, blood pressure 180/90 mmHg, and pulse oxygenation 96% on room air. On initial presentation, the patient was febrile and drowsy with a GCS score of E2V3M4 and bilateral plantar mute. Laboratory tests showed the following: sodium 138 mEq/L, potassium 5.86 mEq/L, chloride 106 mEq/L, calcium 7.87 mg/dl, phosphorus 4.94 mg/dl, bicarbonate 19.8 mEq/L, blood urea nitrogen 54.2 mg/dL, creatinine 4.86 mg/dL. A white blood cell count was 9300 cells/, haemoglobin 10.9g/dL, lymphocyte 17%, platelet counts 2.90 lakh cells/ µl and ESR 88 mm/hr. A venous blood gas included a pH of 7.28, oxygen of 34.6 mmHg and carbon dioxide of 45.9 mmHg. A hepatic function panel had a total bilirubin of 0.34 mg/dL, AST 14u/L, ALT 13 u/L, alkaline phosphatase 92u/L and ammonia 52u/L. A thyroid panel was sent and it was within normal limits.

Chest X-ray showed aspiration pneumonia. ECG - T inversion in L1, aVL, V6, LV strain pattern. MRI brain was performed with bilateral periventricular ischaemic changes and pontine right thalamic and left external capsule micro haemorrhages. An abdominal ultrasound found the liver grossly normal, both kidneys showed increased renal cortical echotexture, the pancreas obscured by bowel gas and no significant free fluid. 2D ECHO showed poor echo window bradycardia, adequate lv systolic function with LVEF = 50%, concentric LVH, no definite RWMA, normal valves and no vegetation. The EEG report showed a mild degree of generalised non-specific disturbance of electrical function and the presence of triphasic waves. Blood and urine culture was negative. Viral markers were sent and were non-reactive. The patient's bystander confirmed consumption of the baclofen 5 days before admission.

The neurology consultant advised giving Inj. Levipil 500mg BD. Ophthalmic consultation was sought and they found no signs of papilledema. Nephrology consultation was sought because of raised creatinine and they advised on conservative management.

His final diagnosis was Aspiration pneumonia, Toxic encephalopathy - baclofen induced, Hypertensive urgency, Type II Diabetic mellitus- HbA1c- 8.1, Old cerebrovascular disease- left side 2 years back, Systemic hypertension- 6 years, DLP- 3yrs and Acute on chronic kidney disease

The patient was treated with Inj. Meropenem 0.5g for 5 days because of aspiration pneumonia and other supportive medications, including Levipil. He regained consciousness in a few days without any RRT. He had significant improvement in mental status without any residual symptoms. Upon discharge, the patient was stable with GCS 15/15. Hence this can be reported as a complaint of BACLOFEN INDUCED TOXIC ENCEPHALOPATHY

DISCUSSION

The patient was a 70-year-old male patient who is a known case of CKD, who recently commenced low-dose baclofen for muscle spasms. Baclofen is mainly excreted by the kidneys unchanged, with only about 15% of absorbed baclofen metabolized in the liver through deamination. Our patient had a normal liver function but an impaired renal function. So half-life of baclofen is increased resulting in its accumulation and drug intoxication with neurological side effects. The side effects include transient drowsiness, sedation, dizziness, fatigue, coma, and respiratory depression. The onset of symptoms was typically 2-3 days after taking baclofen, while end-stage renal disease

patients have also reported experiencing them as soon as 24 hours after taking the drug. However, our case presented with altered mental status, vertigo, slurring of speech and decreased urine output after taking 20 mg/day for a few days. The impaired excretion is responsible for the toxic effects of baclofen even with normal therapeutic doses as it accumulates and induces neurotoxicity. The mainstay of treatment is supportive and close monitoring for possible respiratory compromise. Haemodialysis is also a very reliable method of treatment as it decreases baclofen half-life in ESRD patients. In our case, the patient was symptomatically treated and all monitoring was done. It is important to decide when to start, decrease or discontinue the dose of baclofen to be used in patients with impaired kidney function

CONCLUSION

Baclofen toxicity is a serious, life-threatening condition, mainly for those with altered renal function. The diagnosis of baclofen poisoning should be made in patients with impaired renal function who report altered mental status and a history of ingesting the drug. Clinicians who prescribe baclofen or oversee patients who need it long-term need to be aware of several potential toxicity-increasing variables. Patients must be counselled of the potential adverse effects of baclofen and encouraged to stop taking medicines at the first sign of any symptom. The clinical case demonstrates that severe baclofen toxicity can occur even at low dosages, especially in CKD patients. Therefore, it is better to avoid baclofen in such patients because the accumulation in the CNS is cumulative and dependent on the renal excretion ability

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Conflicts Of Interest

There are no conflicts of interest.

Abbreviations

GABA- Gamma-Aminobutyric acid
EEG- Electroencephalogram
CNS- Central Nervous System
ER- Emergency Room
GCS- Glascow Coma Scale
ECG- Electro Cardiogram
LV- Left Ventricular
DLP- Dyslipidaemia
CKD- chronic kidney disease
ESRD- End Stage Renal Disease

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