Seizures in Renal and Hepatic Failure and Endocrine Disease

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SUMMARY

Hepatorenal failure and endocrine disease are associated with seizures. Seizures arise either as a direct result of the organ failure or as a result of a secondary metabolic disturbance, including toxins arising from the disease process or changes in serum electrolytes. Correction of electrolyte abnormalities or medical management of the underlying disease process will often prevent further seizures. Organ failure and endocrine abnormalities are commonly seen in the critically ill population, and these patients are more prone to seizures. Organ failure can influence the treatment of both new-onset and pre-existing seizure disorders by altering the pharmacokinetics of major anticonvulsants. Alternatively, anticonvulsants can precipitate organ failure. Therefore pharmacotherapy of seizures in these settings should be undertaken cautiously.

Key Words: Hepatic failure; renal failure; endocrinopathy; diabetes; dialysis; encephalopathy.

INTRODUCTION

Seizures are a common complication of organ failure and endocrine disease, either as a result of general biochemical and metabolic abnormalities or as a specific syndrome related to the primary disease process. Critically ill patients may be hospitalized as a result of the organ failure or endocrine disease, or these conditions may arise as complications of another disease process. The acuity of onset of these problems may determine the overall response of the organism to the factors that alter seizure threshold. Even acute organ failure typically occurs in progressive stages, each of which may be associated with differing susceptibility to seizures. Endocrine disease is typically more indolent in onset, but the effects are dependent
on the hormone cascade involved and the organism’s natural storage of the relevant hormone: hypothyroidism is rarely acute unless there is sudden loss of large amounts of thyroid tissue, whereas Addisonian crisis may develop quickly because of daily requirements for steroid hormone production.

The principles of seizure management in this group of patients follow an algorithm common to seizures complicating other medical conditions. Acute seizures should be controlled, seizure prophylaxis with antiepileptic agents should be instituted, and any causative factors should be corrected, including acute control of biochemical/metabolic abnormalities and treatment of the primary disease process.

This chapter reviews the features of seizures in hepatorenal failure and endocrine disease including their incidence, treatment, and clinical implications for critical care. Seizure medications are metabolized and excreted by the hepatorenal system and, therefore, management of seizures in the setting of renal or hepatic failure must be undertaken cautiously.

ORGAN FAILURE

Hepatic Failure

Hepatic failure is a common indication for admission to an intensive care unit (ICU), and in addition hepatic failure frequently complicates other serious illnesses. More than 2000 cases of acute hepatic failure occur in the United States every year, with an estimated mortality of 80% (1). Acute hepatic failure is most commonly caused by infection, inflammation, acute hypotension, toxin exposure, or fulminant primary liver disease. The biochemical effects of hepatic failure include significant alterations in glucose metabolism, buildup of tissue and serum ammonia, failure to remove metabolites and toxins from the circulation, and changes in the bioavailability of drugs normally cleared by the liver. This combination of events can cause progressive encephalopathy, a spectrum of neurological dysfunction classically divided into four stages. Stage I is euphoria or depression, with mild confusion, slurred speech, and disordered sleep; stage II is lethargy and moderate confusion; stage III is marked confusion, incoherent speech, and somnolence; stage IV is coma with cerebral edema formation and elevated intracranial pressure (ICP).

Seizures can arise in any of the stages of hepatic failure either as a result of the encephalopathic process or secondary to other changes in serum levels of electrolytes, glucose, or other metabolites. The incidence of seizures in hepatic encephalopathy has been reported as varying from 2 to 33% (2). Ellis et al. enrolled 42 patients with stage III and IV hepatic encephalopathy in a controlled trial to evaluate the benefit of prophylactic phenytoin administration (3). Subclinical seizure activity as documented by continuous electroencephalography (EEG) was seen in 3 of 20 patients in the treated group, compared with 10 of 22 in the untreated group. One study has reported the incidence in hepatic encephalopathy of status epilepticus (SE) that was refractory to anticonvulsants but responded to lactulose therapy with a reduction in the serum ammonia levels (4). The pathophysiology of hepatic encephalopathy is unclear, but it has been postulated to arise from a combination of