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## Acute Carbamazepine Poisoning

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Carbamazepine is an anticonvulsant useful in the treatment of tonic clonic sei-

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*Received for publication February 12, 1991;  
 Accepted August 28, 1991*

zures and partial seizures with complex symptoms. Patients on long term therapy show mainly hematologic, dermatologic and hepatic derangements. There are very few cases reported, of acute toxicity mainly in adults, showing chiefly cardiovascular and neurologic dysfunctions(1-4). Here, we report our observations on a child with carbamazepine poisoning with a brief review of literature in relation to clinical spectrum and management of acute carbamazepine intoxication.

### Case Report

A 3-year-old female child weighing 11 kg was admitted with a history of ingestion of eight tablets (200 mg each) of carbamazepine prescribed for her mother. During transportation child started having tonic clonic seizures. On examination she was mainly responsive to deep painful stimuli and was having intermittent decerebrate posturing. Vital signs were maintained. Pupils were semidilated and sluggishly reacting. Meningeal signs were absent. Doll's eye response was absent. The gag reflex was diminished and tendon reflexes were not elicitable. Plantar response was flexor bilaterally. Chest examination revealed evidence of bronchopneumonia in the right inframammary region. Other systems were essentially normal.

Laboratory investigations revealed hemoglobin of 8.3 g/dl, TLC of 7000/cu mm, DLC P<sub>60</sub> L<sub>38</sub> E<sub>1</sub> M<sub>1</sub> and platelets were reduced to 60,000/cu mm. Lumbar tap was normal. Blood culture was sterile. X-ray chest revealed right lower zone pneumonia probably secondary to aspiration of vomits enroute to hospital.

Stomach wash was done. Patient was treated with antibiotics, and intravenous fluids. Vitals were monitored. Convulsions

were controlled with intravenous diazepam. Mannitol was given to reduce intracranial pressure. Metabolic acidosis was corrected. On day four, the patient developed hepatomegaly, icterus, oliguria and generalized bleeding in the form of purpuric rashes and echymotic patches all over body.

Further investigations revealed rise in blood urea while serum creatinine was normal, serum bilirubin was 1.6 mg/dl with elevation of liver enzymes (ALT/AST-216/118). Platelet count was 60,000/cu mm, while coagulation profile was essentially normal. Blood gas analysis revealed severe metabolic acidosis with pH 7.076 and base excess 22.5 mEq/ml. Patient was given platelet transfusion. In spite of all measures, the child continued to be in deep coma and finally expired.

Post mortem liver biopsy showed evidence of toxic hepatitis in the form of periportal mononuclear and polymorphonuclear infiltration with increased vacuolation of hepatocytes. However, there was no liver cell necrosis or biliary stasis.

## Discussion

Carbamazepine is a carbamylated iminostilbene chemically related to imipramine(5). Side effects from long term administration include hepatic, hematologic and dermatologic dysfunctions(1,5), while acute toxicity reported mainly in adults showed cardiovascular and neurologic impairment(2-4). Our patient interestingly, presented with hepatic, hematologic, renal and neurologic dysfunctions. Consistent with earlier reports, our patient had prolonged deep coma with raised intracranial pressure. She did not develop any cardiovascular toxicity. Isolated thrombocytopenia as found in our patient without any

other coagulation abnormality has been reported(6). Hepatic involvement is documented in patients on chronic treatment with carbamazepine but is not reported in acute poisoning(7,8). Toxic hepatic damage confirmed by histopathologic finding in one case has also been reported earlier(9). Oliguria with rising BUN found in our case suggested renal impairment hitherto unreported.

Treatment of carbamazepine poisoning is mainly supportive. The extent of protein binding (75-85%) and large volume of distribution (1-1.2 mg/kg) of carbamazepine are kinetically unfavorable for rapid clearance(10). Peritoneal dialysis and hemodialysis have been reported to be ineffective in enhancing the plasma clearance of carbamazepine(10). Recently, oral activated charcoal and charcoal hemoperfusion have been shown to be of some benefit, but further trials are warranted to determine the efficacy of such a therapy(11,12). More recently, a specific drug Flumazenil (Anexate) has been tried in an adult female with severe intoxication with transient recovery of sensorium(13). Though well known as a specific antidote of benzodiazepines, the role of flumazenil is yet to be ascertained in carbamazepine toxicity.

## Acknowledgement

The authors are thankful to Dr. B.L. Jaikhani, Department of Neurochemistry, All India Institute of Medical Sciences for the help rendered by him.

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## Vincristine Neurotoxicity

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The prognosis for children with malignancies has improved significantly in the past two decades as a result of comprehensive care of these children and increasingly vigorous chemotherapy. Vincristine sulfate (Oncovin [R], Eli Lilly and Company, Indianapolis), a VINCA alkaloid, has been one of the most widely used chemotherapeutic agents in the past decade. Arnold *et al.*(1) noted significant increase in neurotoxicity of vincristine (VCR) since a ready-to-use form of the drug became available. Warriar and Ducos(2) reported a 10-year-old child with severe abdominal pain, syndrome of inappropriate antidiuretic hormone secretion (SIADH), and generalized seizures following the first dose of VCR. We have retrospectively reviewed the charts of all children who received VCR before and after the introduction of the ready-to-use VCR preparation to look for any significant change in the degree of toxicity.

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*Received for publication May 26, 1990;  
Accepted December 4, 1991*