Carbamazepine is used in the treatment of simple partial, complex partial and generalized tonic clonic seizures. It is also used in the treatment of trigeminal neuralgia and in manic depressive illness. Erythromycin is a macrolide antibiotic often used in infections like mycoplasma, legionella infections and other infections caused by aerobic gram positive cocci and bacilli. It is also used in diabetic gastroparesis and in those with an allergy to penicillin. Pharmacokinetic studies have established that erythromycin causes carbamazepine toxicity when these two drugs are given concurrently. One needs to be aware that this drug combination predictably causes adverse side effects hence, alternative antibiotic therapy should be considered for patients receiving long-term carbamazepine therapy who need antibiotic coverage. We report a case of carbamazepine toxicity induced by the concurrent administration of erythromycin.

Keywords: Carbamazepine, erythromycin, ataxia
inherited causes are stroke, trauma, tumors, infections, demyelination, nutritional, anticonvulsants, salisylates, sedatives overdosage and alcohol intoxication. Carbamazepine intoxication is common both in pediatric and adult population. Its concentration in the cerebrospinal fluid increases correspondently to the concentration of free drug in the plasma. It is metabolized primarily in the liver by oxidative enzymes, then is conjugated with glucuronic acid and is excreted in the urine. Its metabolite, carbamazepine-10,11-epoxide, is active and may achieve up to 50% concentration of the parent compound and may increase duration of the symptoms of toxicity. Children eliminate the drug more rapidly than adults. Carbamazepine toxicity should be considered in differential diagnosis of patients presenting with ataxia. Some comatose patients demonstrate complete recovery, whereas 5-38% of patients die. Central nervous system side effects are frequent at concentrations above 9 microgram/ml. Patients with serum carbamazepine levels 40 µg/ml is significantly associated with an increased risk of serious complications such as coma, seizures, respiratory failure and cardiac conduction defects. Erythromycin has been reported to interact with carbamazepine in both children and adults. Erythromycin has protein binding capacity of 70-80% and even higher for the erythromycin estolate esters. Erythromycin potentiates the effects of carbamazepine, corticosteroids, cyclosporine, digoxin, ergot alkaloids, theophylline, triazolam, valproate, warfarin by interfering with the metabolism of these drugs. The toxicity increases as plasma carbamazepine concentration increases above the therapeutic range not only by liver metabolism, but also due to plasma protein displacement by drug interactions which made the availability of carbamazepine more in cerebrospinal fluid. It inhibits the metabolism of carbamazepine by competitive binding to cytochrome P-450, blocking the metabolism to carbamazepine-epoxide. Symptoms of intoxication usually appear within 24 hours of starting therapy with erythromycin and resolve 48 to 72 hours after discontinuation of either drug. Carbamazepine is highly protein-bound and with large volume of distribution and hence hemodialysis or peritoneal dialysis have limited efficacy in acute carbamazepine toxicity. A few reports in the 1980s showed efficacy of haemoperfusion in reducing the plasma levels of carbamazepine by 25–50% in intoxicated patients. Since then, haemoperfusion has been considered to be the treatment of choice in severe carbamazepine overdosage. There is no antidote for carbamazepine overdosage. In this patient, the carbamazepine toxicity occurred due to the inhibition of its metabolism by erythromycin and it was reversed completely once the offending drug was stopped. All well-documented drug interactions are essentially avoidable. It is of utmost importance that we enquire about concurrent medications at all times and consider their potential interactions. It may be preferable that epilepsy patients keep a diary stating their drug details and the list of drugs that should be avoided in them. If it is absolutely necessary to prescribe erythromycin to patients already on carbamazepine, the carbamazepine dose should be reduced and serum levels should be closely monitored.

CONCLUSION

In this case, stopping of erythromycin resulted in dramatic reversal of carbamazepine toxicity, highlighting the importance of meticulous history elicitation, so as to avoid drug interactions. High index of suspicion is required for antiepileptic drug toxicities when an otherwise well controlled epileptic patient develops seizures or any other symptoms especially when they are started on new drugs which can modify antiepileptic drug metabolism.

REFERENCES