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Charcoal Hemoperfusion –An Effective Tool in Phenytoin Intoxication

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Abstract

Phenytoin is a commonly prescribes antiepileptic drug having a narrow therapeutic range and a total serum level >20mcg/ml is associated with clinically relevant toxicity(1). It is responsible for a number of intentional and unintentional overdoses. Besides supportive care and management of dysarryhtmias in phenytoin intoxication, specific treatment recommendations to enhance the elimination of the parent compound have been discussed controversially and it is still under debate.MARS (Molecular Adsorbent Recirculating System), Albumin haemodialysis,charcoal hemoperfusion, tandem plasmapheresis in phenytoin intoxication is still not well established(2).we present a case of intentional overdosage of phenytoin that was successfully treated with two sessions of charcoal hemoperfusion,resulting in both clinical improvement and normalisation of serum phenytoin concentration**.**

Keywords : Phenytoin intoxication ,Charcoal Hemoperfusion , extracorporeal therapy, Dialysis

Case History

A 30 year old previously healthy male diagnosed one week back as a case of seizure disorder and started on Tablet Eptoin (phenytoin) 100mg p.o BID, was admitted in our hospital emergency department with intentional overdosage of 100 tablets of 100mg phenytoin around 10:00pm i.e 12 hours approximately before hospitalization . patient gave history of giddiness, headache, depressed mood, numbness over his both upper limb and lower limbs. On clinical examination, he had bilateral horizontal nystagmus,conscious oriented , GCS15/15 (e4m6v5). Cognitive functions were normal, tones and reflexes l were normal. A diagnosis of phenytoin intoxication was made. Laboratory investigations including serum phenytoin levels were ordered and he was started in initial supportive management. Gastric lavage was done and he was kept nil per oral. Serum phenytoin levels were elevated and above therapeutic range(37.9 mcg/ml). cross consultation with neurologist and nephrologist was done . patients relatives were counseled for charcoal hemoperfusion and hemodialysis in view of continual neurological symptoms despite care. They consented for charcoal Hemoperfusion and hemodialysis. A right femoral vein access for dialysis catheter was obtained under standard aseptic precautions . Charcoal hemoperfusion was done with a cellulose coated activated charcoal

hemoperfusion column, charcoal hemoperfusion catridge(GAMBRO ADSORBA 300C, GERMANY) adult size with membrane thickness 3-5micrometer, pore size 450micrometer was done with regular heparin using hemodialysis machine for 8 hours.Day 2 serum phenytoin levels were 23.91mcg/ml. patient continued to have nystagmus.other neurological symptoms started to disappear. He was again subjected to second session of charcoal hemoperfusion and hemodialysis for 8 hours. Serum phenytoin levels were repeated on day 4, it had reduced to 13.21mcg/ml(within therapeutic range).He was clinically normal with no neuro deficts. The only complication noted in the above treatment was mild thrombocytopenia(1.30-1.40 lakh cells/cu.mm). patient was haemodynamicaly stable and was discharged subsequently.

Discussion

The narrow therapeutic index, and its wide inter individual variability in the rate of phenytoin metabolism is responsible for wide clinical spectrum of adverse effects(3).The mechanism behind phenytoin intoxication is that when large doses of the drug are ingested , the cytochromep450 system becomes saturated leading to zero order kinetics in which only a fixed amount of phenytoin is eliminated over a period of time. This results in too prolonged half life (24 to 230 hours) in overdose and rapid rise in serum concentration of the drug. Only free unbound phenytoin is biologically active. Blood vessels reflect the total serum concentration of the drug(4). In charcoal hemoperfusion , the charcoal in the catridge will compete with the plasma proteins for phenytoin molecules and the molecules will adsorb on the charcoal surface(5), subsequently the free phenytoin is eliminated by dialysis. In our case the prolonged half life(t1/2) of the drug was reduced from 230 hours to 48 hours. There have been very little reports previously based on this modality of therapy(6). The role of charcoal can be explained by the fact that bound phenytoin has been found to dissociate from albumin in the presence of activated charcoal and subsequently becomes adsorbed to the activated charcoal.

Conclusion

There have been no reports of usage of any of these modalities in treatment of phenytoin overdose in adults . charcoal hemoperfusion was planned in view of evidence indicating neurological symptoms with phenytoin overdose(6). The absolute indications for a hemoperfusion in phenytoin toxicity are not described as reports of this conditions are very few. Through this report we suggest an effective and cost friendlier modality of treatment in phenytoin intoxication.

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