Treatment of refractory seizures in eclampsia with propofol: A case report

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Abstract
We describe the management of a case of refractory status epilepticus evolving in post-partum eclampsia. The seizures were refractory to therapy with benzodiazepines, MgSO4, barbiturates and phenytoin, but responded rapidly to propofol infusion.

Key Words: Refractory, Seizures, Eclampsia, Epilepticus, Propofol.

Introduction
Convulsive status epilepticus refractory to treatment with benzodiazepines, phenytoin sodium or barbiturates presents a challenge to critical care specialists. Such cases of refractory status epilepticus (RSE) are not uncommon. Prompt seizure control is probably essential to prevent mortality and morbidity.

Propofol, which is a unique non-barbiturate anaesthetic agent, has been used in nearly 33 studies in RSE with good results. However the pro- or anticonvulsant effects of propofol remain a matter of controversy, with many reports describing abnormal movements, posturing and seizure-like activity with its use. On the other hand, systematic studies in both humans and animals strongly suggest that it has anti-epileptic properties.

However, no case report so far has described the use of propofol in eclampsia-induced RSE. We describe the management of such a case.

Case Report
A 23-year-old primigravida with twin pregnancy at 38 weeks of gestation, was admitted in the late afternoon (16:55 hrs) with complaints of “leaking” since afternoon. She was a booked case but on irregular antenatal checkup. A physical examination revealed the presence of pedal edema and a blood pressure of 160/100 mm of Hg. She was fully conscious, oriented and asymptomatic otherwise. Laboratory investigations revealed mild proteinuria. Her Hb was 10 g% with a packed cell volume of 33%. Biochemical investigations were within normal limits. She was diagnosed as a case of PE (pre-eclampsia) with twin pregnancy and given prophylactic MgSO4 I/M (5g in each buttock). Induction of labor was started at 23:30 hrs. The patient developed a generalized seizure at 04:55 hrs and her B.P. was 170/110 mm of Hg, which was managed with I/V Diazepam. She had another seizure at 05:15 hrs. She was taken up for emergency Caesarian section at 06:30 hrs for which general anaesthesia (G.A.) with twin pregnancy and given prophylactic MgSO4 I/M (5g in each buttock). Induction of labor was started at 23:30 hrs. The patient developed a generalized seizure at 04:55 hrs and her B.P. was 170/110 mm of Hg, which was managed with I/V Diazepam. She had another seizure at 05:15 hrs. She was taken up for emergency Caesarian section at 06:30 hrs for which general anaesthesia (G.A.) with rapid sequence induction was given. Intra-operative course was unremarkable and she was responding to commands following extubation. Her B.P. was 140/92 mm of Hg. She was shifted to the ward at 07:30 hrs. She developed another generalized seizure in the ward at 10:30 hrs, which was treated with Inj. Diazepam (B.P.160/110) and Inj. MgSO4 4g I/V. She went into a state of “status” from 11:30 hrs with the convulsions not responding to Diazepam with the patient remaining unconscious. She was intubated at this point of time and shifted to the CCU, put on appropriate ventilatory support and started on Thiopentone infusion (2mg/kg/hr) after a bolus of 250 mg to control the seizures. Her B.P. was persistently greater than 140/100mm of Hg and a nitroglycerine (NTG) infusion was started and gradually titrated to maintain the B.P. around 140/90. One hour after starting the infusion, she again developed seizures, which was controlled with a bolus of...
Thiopentone (100 mg) and I/V Diazepam (10 mg). She however had a repeat seizure after 15 minutes, following which, she was given a loading dose of Inj. Phenytoin (1000 mg) over a period of 30 minutes. She however continued to have focal seizures and myoclonus. Arterial blood gas analysis revealed mild respiratory alkalosis. An emergency CT scan revealed only the presence of mild cerebral edema.

2 hours after starting thiopentone infusion, she still had focal seizures with a B.P. of 140/90 mm of Hg with NTG infusion of 2ug/kg/min. Her pupils were constricted and not reacting to light, plantars were equivocal. Spontaneous respiratory efforts were present.

At this point of time, thiopentone infusion was stopped and Propofol infusion was started at a dose of 4 mg/kg/ hour after an initial bolus of 50 mg. Five minutes after starting Propofol infusion, the B.P. fell to 110/70 mm of Hg and the NTG infusion was stopped. The B.P. then gradually rose over a period of 15 minutes to settle at 130/90 mm of Hg. The patient had no recurrence of focal seizures or myoclonus after starting Propofol infusion. Tab.Amlodepin 5mg was started OD via the Ryles tube and we were able to taper the dose of Propofol over the next 24 hours to 1.5mg/kg/hour. The infusion rate of Propofol was further reduced over a period of 48 hrs. and the patient was successfully extubated on the fifth day with a Glasgow coma scale (GCS) of 15!

Discussion

In the above-mentioned case, the patient had persistent seizures in spite of receiving the full therapeutic dose of MgSO4 (blood levels were 4.7 mEq/l). She had received 10g of MgSO4 I/M and then 4g I/V. Her seizure activity was not controlled even with thiopentone, diazepam and phenytoin. This patient had received an adequate dosage of thiopentone, which was borne by the fact that she had received GA some hours back in which 250mg thiopentone was used as an induction agent. She then received a further dose of 250 mg as bolus followed by an infusion of 2 mg/kg/hr & then again a bolus of 100 mg. Some authors recommend a higher initial bolus (5-20 mg/kg) followed by an infusion of 2.5 mg/kg/hr. Also, it was necessary to start NTG infusion to have her B.P. under control. However, on starting Propofol infusion, her seizure activity was rapidly brought under control and we also achieved a good control on her blood pressure. Thus, Propofol infusion not only afforded us a control of her seizure activity but also of her blood pressure. Though hemodynamic instability is known with Propofol and is in fact a consideration before using it, it was not an issue with our patient since she had hypertension. In fact, this reduction (control of her BP) after Propofol was an indicator of the its hemodynamic effects.

Propofol is a unique, non-barbiturate anaesthetic agent with proven anticonvulsant properties, although the exact anticonvulsant mechanism is unknown. It probably acts by causing a uniform depression of the central nervous system, potentiation of GABA-mediated pre and post-synaptic inhibition and by decreasing the release of excitatory transmitters, glutamate and aspartate. Stecker et al compared propofol with high dose barbiturates in the treatment of refractory status epilepticus (RSE) and they concluded that propofol resulted in a rapid control of RSE compared to high dose barbiturates. Also, recurrent seizures were common with sudden discontinuation of propofol but not with gradual tapering. In our case, we had a gradual decrease in the dose of propofol without having any recurrent seizure activity. Classen et al, in an excellent review, systematically reviewed the literature for treatment strategies of RSE using pentobarbital, propofol and midazolam. They concluded that treatment of RSE with any continuous I/V anti-epileptic drug infusion so as to attain EEG background suppression may be more effective than other strategies for RSE treatment. Harrison et al have recommended adjusting the infusion rate of anti-epileptic drug so as to attain EEG burst-suppression. In our case, we adjusted the infusion rate so as to control further seizure activity. Our patient was on respiratory support while on propofol infusion. Propofol is a potent respiratory depressant and hence it is strongly advised to have facilities for airway control and ventilatory support during its use.

References