

Thiopentone Induced Paralytic Ileus in Super Refractory Status Epilepticus: Erythromycin to the Rescue

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ABSTRACT

Neurocritical care, a unique specialty requiring skill and adeptness presents us with many challenging situations. Management of super refractory status epilepticus warrants the use of intravenous anaesthetic agents and along with it comes its various complications such as paralytic ileus which need to be diagnosed accurately and managed appropriately. We report a case of a patient diagnosed with super refractory status epilepticus who developed paralytic ileus because of thiopentone infusion which was refractory to the conventional prokinetic therapy resulting in the decision to initiate Total Parenteral Nutrition (TPN) but responded dramatically to intravenous erythromycin. Hence, we would like to highlight this as an important tool in the armamentarium in paralytic ileus management.

CASE REPORT

A 21-year-old male presented with continuous high grade fever of one-week duration followed by complex partial seizures characterized by facial twitching and jerky movements of both upper and lower limbs lasting for two to three minutes. Despite administering intravenous lorazepam and fosphenytoin this progressed to repeated episodes of generalized tonic clonic seizures, necessitating the institution of intravenous anaesthetics for the control of seizures. Without further ado, he was admitted to the neuro-medical intensive care unit with the diagnosis of refractory status epilepticus, where his trachea was intubated and he was mechanically ventilated while the midazolam infusion was titrated with the aim to achieve seizure control. Despite reaching the maximum infusion dose of midazolam, persistent epileptic activity was observed on follow up EEGs, Hence, he was initiated on intravenous thiopentone. A bolus dose of 3mg/Kg was given followed by an infusion of 3mg/Kg/hr. The infusion dose was gradually increased till seizure control was achieved at 5mg/kg/hr. The cardiac depression caused was countered by a continuous infusion of Inj.Noradrenaline at 0.02mcg/kg/min. Continuous electrographic monitoring proved the seizures to be controlled. Within three hours of commencing the thiopentone infusion, the patient developed a mild abdominal distension associated with high Nasogastric aspirates. Auscultation of the abdomen revealed sluggish bowel sounds. Six hours into the thiopentone infusion, there was further worsening of the abdominal distension and a silent abdomen. This predicament compelled us to stop the enteral feeding.

In this patient, abdominal distension with absence of bowel sounds, high nasogastric aspirates and X-ray of the abdomen showed multiple dilated bowel loops which lead to the diagnosis of paralytic ileus. The varied reasons for this were appraised during the resident rounds. Electrolyte abnormalities of hypokalemia and hypomagnesemia were ruled out. There was no focus of sepsis to indicate the cause of paralytic ileus. The inotropic support provided by nor adrenaline was only a small dose of 0.02mcg/kg/min which was unlikely to result in hypoperfusion of the bowel to cause the clinical manifestations as seen in our patient. Furthermore, patient was not on any other drugs known to be culprits of paralytic ileus such as morphine or anticholinergics. Hence the diagnosis was zeroed on as thiopentone infusion induced paralytic ileus. It was decided to initiate Inj.Metoclopramide 10mg twice a day as was the routine practice. This prokinetic failed to have any clinical effect on the patient's

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abdominal problems. Thus, we were further obliged to consider the option of parenteral nutrition to maintain caloric requirement; as the decision to initiate TPN was being contemplated we decided to give a trial of intravenous Inj.Erythromycin 250mg as suggested during the ICU rounds. Ninety minutes after the erythromycin was administered there were sluggish bowel sounds heard. Eight hours later there was a dramatic decrease in the nasogastric aspirates, hence, nasogastric test feeds were reinstated and well tolerated. After three doses of IV erythromycin, full caloric requirement was met through the Nasogastric feeds thereby obviating the need for parenteral nutrition and adverse effects associated with it.

DISCUSSION

In neurological intensive care units, we commonly encounter paralytic ileus in patients with neurological conditions affecting autonomic function e.g., high cervical lesions, Guillain-Barre syndrome, medication (anticholinergics, opioids), meningitis, and spinal cord infarction. It is also a well-known complication of barbiturates occurring in about 10% of patients with high dose thiopentone infusion [1]. There have been many instances where TPN had to be initiated for a few days to tide over the crisis and there are case reports of emergency colostomies done to relieve the intestinal obstructive symptoms caused by thiopentone infusions [2,3].

As neuro-intensivists we acknowledge that enteral feeding should be commenced as soon as possible due to its varied advantages such as protection against peptic ulceration, decreasing catabolism, retaining intestinal integrity and thus decreasing the occurrence of bacterial translocation and the incidence of nosocomial infections. When enteral feeding fails, immediate search for means to resolve the ileus is required as this would alter the prognosis. The management of ileus may vary greatly depending on the nature of etiology, in our institution we begin with correction of electrolyte and acid base abnormalities, discontinuation of medications that produce ileus and initiation of prokinetic therapy with metoclopramide. In our patient, though we knew that thiopentone was the culprit for the paralytic ileus, it was crucial to continue the same for the control of the super-refractory status epilepticus. Premature stopping of the anaesthetic would have a negative impact and poor outcome.

After repeated dosing of metoclopramide and facing a refractory ileus, we were forced to consider TPN as an alternative to maintain the caloric requirement as any hypoglycemic episode would lower the

seizure threshold resulting in a catastrophic outcome. The adverse events associated with TPN such as sepsis, hypercholesterolemia, refeeding syndrome, deranged liver function, hyperchloremic metabolic acidosis, immunosuppression; to mention a few, would add to the already chaotic metabolic and clinical milieu of patients with refractory seizures.

Erythromycin is now being considered for its prokinetic properties but its use has not been mentioned for the treatment of thiopentone induced ileus. Though it has no proven advantage over metoclopramide as a prokinetic, we on a premonition that this may be the answer to our predicament gave a trial of erythromycin which proved to be successful. Erythromycin is a motilin receptor agonist with cholinergic stimulatory properties [4,5]. It increases the lower esophageal sphincter pressure, improves antroduodenal coordination, and causes gastric emptying of solids and liquids [6,7]. Erythromycin has been proved to be useful in diabetic gastroparesis since it allows expulsion of large food particles from the stomach without retarding liquid emptying [8]. Studies in premature infants, the critically ill and postesophagectomy patients also confirms erythromycin's prokinetic effects [9-11]. The most commonly used dose range in adults is 200-250mg or 2.0-3.0mg/Kg. Although its use is not without risk, erythromycin is readily available, inexpensive, has a low dose-dependent side effect profile and is compatible with most drugs [12]. It has a different mechanism of action and does not possess the wide spectrum of side effects of metoclopramide.

CONCLUSION

Erythromycin, a motilin receptor agonist with cholinergic stimulatory properties is effective in case of drug induced paralytic ileus. Erythromycin is easily available, with few drug interactions and cost-effective must be in the armamentarium of drugs while treating patients with impaired gastric emptying.

Consent: Prior to submission of this case report a written informed consent was obtained from the parent.

REFERENCES

- [1] Cereda C, Berger MM, Rossetti AO. Bowel ischemia a rare complication of thiopental treatment for status epilepticus. *Neurocrit Care*. 2009;10:355-58.
- [2] Parviainen I, Uusaro A, Kalviainen R, Kaukanen E, Mervaala E, Ruokonen E. High-dose thiopental in the treatment of refractory status epilepticus in intensive care unit. *Neurology*. 2002;59(8):1249-51.
- [3] Claassen J, Hirsch LJ, Emerson RG, Mayer SA. Treatment of refractory status epilepticus with pentobarbital, propofol, or midazolam: a systematic review. *Epilepsia*. 2002;43(2):146-53.
- [4] Delooste E, Vos R, Janssen P, Van den Bergh O, Van Oudenhove L, Depoortere I, et al. The motilin receptor agonist erythromycin stimulates hunger and food intake through a cholinergic pathway. *American Journal of Clinical Nutrition*. 2016;103(3):730-37.
- [5] Czarnetzki C, Elia N, Frossard JL, Giostra E, Spahr L, Waeber JL, et al. Erythromycin for gastric emptying in patients undergoing general anaesthesia for emergency surgery: a randomized clinical trial. *JAMA Surgery*. 2015;150(8):730-37.
- [6] Boivin MA, Carey MC, Levy H. Erythromycin accelerates gastric emptying in a dose-response manner in healthy subjects. *Pharmacotherapy*. 2003;23(1):5-8.
- [7] Chaussade S, Michopoulos S, Sogni P, Guerre J, Couturier D. Motilin agonist erythromycin increases human lower esophageal sphincter pressure by stimulation of cholinergic nerves. *Dig Dis Sci*. 1994;39:381-84.
- [8] Janssens J, Peeters TL, Vantrappen G, Tack J, Urbain JL, De Roo M, et al. Improvement of gastric emptying in diabetic gastroparesis by erythromycin: Preliminary studies. *N Engl J Med*. 1990;322:1028-31.
- [9] Tomomasa T, Miyazaki M, Koizumi T, Kuroume T. Erythromycin increases gastric antral motility in human premature infants. *Biol Neonate*. 1993;63:349-52.
- [10] Deane AM, Wong GL, Horowitz M, Zaknic AV, Summers MJ, Di Bartolomeo AE, et al. Randomized double-blind crossover study to determine the effects of erythromycin on small intestinal nutrient absorption and transit in the critically ill. *American Journal of Clinical Nutrition*. 2012;95(6):1396-402.
- [11] Walsh TN, Caldwell MTP, Fallon C, McGeown G, Kidney D, Freyne P, et al. Gastric motility following oesophagectomy. *Br J Surg*. 1995;82:91-94.
- [12] Dive A, Miesse C, Galanti L, Jamart J, Evrard P, Gonzalez M, et al. Effect of erythromycin on gastric motility in mechanically ventilated critically ill patients: a double blind, randomized, placebo-controlled study. *Crit Care Med*. 1995;23(8):1356-62.

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