CASE REPORT

Point to ponder while prescribing phenytoin sodium infusion in septic shock patients: A case-based discussion

Habib Md Reazaul Karim1, Ghazal Ahmed2, Md Yunus1, Prithwis Bhattacharyya1

1Department of Anaesthesia & Critical Care, North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences, Shillong, Meghalaya, India, 2Department of Dermatology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India

Abstract

Extravasations of many drugs can lead to phlebitis to soft tissue necrosis. Phenytoin sodium has also been implicated for such events in a few case reports with varying success of treatments. We present a case with due consent from the patient party where a single loading dose phenytoin sodium leads to phlebitis and rapidly progressed to gangrene of the hand in a critically ill patient ultimately requiring amputation despite providing possible treatments. The intention of presenting the case is to share our bad experience along with a point to ponder which probably would give an opportunity to critical care physicians to get rid of such avoidable traumatic problem while managing such patients in future.

Keywords
Gangrene, phenytoin sodium extravasations, septic shock, vasopressor

Introduction

Despite the advent of newer antiepileptic, phenytoin sodium still remains one of the most commonly used and preferred antiepileptic both for the management of status epilepticus and long-term maintenance therapy by the physicians. This is probably because of the lower cost, wider availability, and decades of promising results. It is a very alkaline drug with a pH of 12. Extravasations of such alkaline drug can cause chemical injury and tissue necrosis. Phenytoin sodium extravasations leading to gangrene and amputation have been rarely reported in the literature. However, single dose intravenous (IV) phenytoin sodium extravasations leading to gangrene is rarely known. We present this case to emphasize on possible contributing factors for which the single dose IV phenytoin sodium extravasations rapidly progressed to gangrene despite the initiation of possible treatments.

Case Report

A middle-aged lady, a known case of epilepsy on irregular medication, presented to the emergency department of our hospital with complaints of difficulty in breathing, fever, and altered sensorium. In the emergency department, she had an episode of seizure and injection midazolam 2 mg followed by injection lorazepam 4 mg slow IV was given to control it. Injection phenytoin sodium 18 mg/kg body weight was infused after diluting with 0.9% normal saline at the rate of 50 mg/min as loading dose through a 20 G peripheral venous cannula newly placed in the dorsum of the hand. The seizure was controlled, and the patient was intubated due to disease condition and was shifted to intensive care unit (ICU) for further management. In ICU, the patient was diagnosed as community acquired pneumonia with multiorgan dysfunction syndrome (MODS), and the patient was started on a broad spectrum antibiotic and other supportive care. Triple lumen central venous catheter (CVC) was inserted for monitoring as well as medication port, and the peripheral cannula was removed. Patient’s blood pressure was not improving despite adequate fluid resuscitation and was started on injection noradrenaline infusion for management of septic shock. Injection phenytoin sodium was replaced with injection levetiracetam for seizure considering MODS. The patient was also started on low molecular weight heparin (LMWH) for deep venous thrombosis (DVT) prophylaxis. Next day, swelling and erythematous lesion was noted over the dorsum of the hand where cannula was inserted. Thrombophob (zydus) ointment was started for local
application; however, blisters were noted by the evening and blackening of the area by next day [Figure 1]. In next 3 days time, necrosis [Figure 2] of the area happened and ultimately gangrene set in by 7 days. During the initial 3 days, both ipsilateral and contralateral radial and ulnar artery pulsations were palpable which later on became very feeble, and this was explainable by shock. Culture swab taken from necrosis area showed no growth of microorganism. The regular antiseptic dressing of necrosis area was going on, and surgical colleague was following up the case and lastly opined for amputation.

**Discussion**

Over last decade, newer antiepileptic drugs have come into the role for management of convulsion.[1] Phenytoin sodium use is still recommended for emergent, urgent, and refractory treatment in the management guidelines for status epilepticus.[2] IV administration of phenytoin is common in critically ill patients.[3] Due to the high alkaline nature, it causes chemical injury and thrombophlebitis. Rare reports of even tissue necrosis and gangrene are also found in the literature with varying success with treatment.[4,5] The diluting solution compatibility, infusion rate restriction, careful and repeated evaluation of the site, and flushing the cannula with saline are recommended after use of injection phenytoin sodium.[6] The present patient received nearly 500 ml crystalloid through the same line after single dose phenytoin sodium infusion and following the placement of triple lumen CVC the peripheral cannula was removed. There was no redness and swelling of the area at that time but a feature of thrombophlebitis developed from next day and rapidly progressed. As she was non-diabetic and there was no other obvious cause like trauma, infection, peripheral vascular disease, nor she was tobacco, nicotine user, the causative factor most probably was the extravasations of phenytoin sodium. Anti-inflammatory agents and local application of heparin benzoate (thrombophob ointment from zydus) were done along with the slight elevation of affected hand for initial days. Moreover, the patient also received sc LMWH for prevention of DVT. Despite all these management and in the absence of infection, affected hand went to gangrene, and a painful decision like amputation of the hand became necessary.

While introspecting the case that why the progression was fast or why treatment provided was not effective in preventing progression to gangrene, one question raised in our mind that “was it aggravated by something else?” The present patient was in septic shock also. Although septic shock causes vasodilatation, cellular perfusion mismatch leads to mitochondrial dysfunction and cellular injury culminating to cellular death.[7,8] On the other hand, vasopressor like noradrenaline, which was used to treat shock in this patient, causes intense vasoconstriction.[9] Probably, these two factors contributed to the aggravation of the situation and fast progression to gangrene despite timely treatment was provided. Although this explanation appeared physiologically acceptable and satisfied our mind, another question raised as the incidence of phenytoin extravasations is high and fosphenytoin not reported for so, should fosphenytoin be the first choice over phenytoin in such patients?

**Conclusion**

Phenytoin sodium-induced chemical thrombophlebitis probably is aggravated by sepsis and vasopressor use. It is probably better and wise to replace it with newer antiepileptic drugs without evidence of extravasations injury in such critically ill patients as far as possible.

**References**
