

**The aim of our study was to identify all previously reported cases of phenytoin- or fosphenytoin-associated purple glove syndrome (PGS) and summarize the most current understanding of the pathophysiology, clinical presentation, diagnosis, and treatment of the disease” Garbovsky et al (2015).**

Abstract:

The aim of our study was to identify all previously reported cases of phenytoin- or fosphenytoin-associated purple glove syndrome (PGS) and summarize the most current understanding of the pathophysiology, clinical presentation, diagnosis, and treatment of the disease. We searched the English language references from MEDLINE, EMBASE, CINAHL, TOXNET, and gray literature that featured one or more case descriptions of phenytoin- or fosphenytoin-associated PGS after administration and provided information on the clinical setting of the event and associated outcome(s). Descriptive statistics were employed to summarize relevant facts about the cases. We identified 82 unique cases of parenteral phenytoin-associated PGS and 5 cases of fosphenytoin-associated PGS that were published from 1984 to 2015. Additionally, we found two cases of PGS associated with oral formulation of phenytoin published from 1999 to 2015. The spectrum of tissue injury ranged from mild local cutaneous reactions around the infusion site to frank limb ischemia. Just over a half of cases reported symptoms after one dose of IV phenytoin. Pathologic findings included evidence for microvascular thrombosis and possible microvascular or subclinical extravasation as a contributing mechanism. Doppler ultrasound and conventional angiography were used in some patients to identify arterial or venous thrombosis. Various treatments were documented including the use of supportive care such as limb elevation and heat or cold application, utilization of systemic antibiotics, anticoagulants, or vasodilators, and local infiltration of hyaluronidase, heparin, or other compounds. In a small number of patients, invasive interventions such as regional anesthesia, thrombectomy, fasciotomy, and debridement were described. Time to resolution varied from days to weeks. Resolution of PGS without deficits was documented in the majority of cases. Skin changes followed by sensory and motor deficits were described in 16, 6, and 5 cases, respectively. Four patients underwent skin grafting and eight patients required limb amputation. Death as a result of PGS was documented in two patients. PGS associated with oral and injectable phenytoin or parenteral fosphenytoin has been documented in the literature and sometimes

includes significant vascular thrombosis and potentially limb-threatening ischemia. Avoidance of small hand veins, adherence to recommended IV administration guidelines and monitoring of the infusion site for reactions should be considered to decrease the morbidity of IV phenytoin or fosphenytoin use. Patients with PGS and evidence of decreased distal perfusion should undergo prompt vascular imaging and potential intervention to avoid ischemic sequelae. Alternative anticonvulsant drugs should be considered in patients at risk for PGS when possible.

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Garbovsky, L.A., Drumheller, B.C. and Perrone, J. (2015) Purple Glove Syndrome after Phenytoin or Fosphenytoin Administration: Review of Reported Cases and Recommendations for Prevention. *Journal of Medical Toxicology*. 11(4), p.445-59. doi: 10.1007/s13181-015-0490-z.