as systemic inflammatory response syndrome.[3,4] However, we disagree that it is a single-insult model of organ injury. The hemorrhage and resuscitation method is actually a "two-insult model" of multiorgan injury, as this model requires a period of controlled hemorrhage followed by resuscitation with shed blood. Resuscitation with shed blood exacerbates as well as causes multiorgan injury by promoting systemic inflammatory response, platelet activation, increased neutrophil recruitment and microthrombi formation.[4]

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Physostigmine and Restless Legs Syndrome

To the Editor:

Restless legs syndrome (RLS) is a common neurologic disorder that uncommonly manifests in the perioperative period. Its anesthetic implications were recently discussed,[1,2] but the reviewers did not reference a 2005 case report that described rapid relief of symptoms with physostigmine.[3] Their perioperative recommendations for prevention and treatment were based on the current theory of causation involving dysfunctional central iron and dopamine metabolism and six case reports in which no patient experienced prompt resolution of symptoms. Oral administration of the dopamine D2/D3 receptor agonist, 0.125 mg pramipexole, produced relief after 30 min.[4] We report the second case of prompt relief of RLS symptoms with intravenous physostigmine.

A 65-yr-old man presented for endoscopic ultrasound and fine needle aspiration of a submucosal gastric lesion. The patient met the international standard essential criteria for RLS: irresistible urge to move his legs, accompanied by unpleasant sensory complaints in his legs; increased agitation when the nursing staff insisted that he remain still; symptoms at home relieved by walking; and symptoms that are worse in the evening but reasonably controlled with dopamine D2/D3 receptor agonist therapy.[1,5] His daily dose of pramipexole, extended-release 1.5 mg after dinner, was twice the maximum daily dose usually recommended for RLS[6] and may reflect the severity of the syndrome. However, it is less than the average dose used to treat early Parkinson disease.[7] His other comorbidities (medications) included obesity, obstructive sleep apnea, diabetes mellitus type 2 (insulin, metformin, glipizide), hypertension (lisinopril), coronary artery disease (aspirin, lovastatin), gastroesophageal reflux (omeprazole), and osteoarthritis (oxaprozin).

Anesthesia was provided with 2 mg midazolam, 440 mg propofol, and 10 mg ketamine intravenously (IV). He also received 4 mg ondansetron, 0.2 mg glycopyrrolate, and 20 mg IV esmolol and oxymetazoline intranasally before insertion of a nasopharyngeal airway. He was conversant on arrival in the recovery room. Within minutes he became agitated and tried to get off his stretcher to walk. He exhibited severe restlessness in both legs and complained of lower extremity tingling and tugging. The differential diagnoses in this setting included hypoxia (Spo_2 98%), hypoglycemia (blood glucose 168 mg/dL), emergence delirium (conversant, oriented), neuroleptic-induced akathisia (no droperidol given), peripheral neuropathy, and a RLS flare (patient stated, "It's my restless legs"). Administration of 1 mg IV physostigmine attenuated these symptoms within 3 min. Symptoms completely resolved with a second dose of 1 mg physostigmine. Five hours later, he was free of symptoms, despite not yet taking his usual evening dose of pramipexole.

It is difficult to reconcile this apparent effectiveness of physostigmine with the current view of the pathophysiology of RLS – central iron insufficiency altering the dopaminergic system with a decrease in the number of D2 receptors in the putamen, increased activity of tyrosine hydroxylase, and increased dopamine transporter density in the caudate, putamen, and striatum.[1,8,9] But the cholinergic and dopaminergic systems do interact in certain brain regions, *e.g.*, striatal cholinergic output is dopamine D2 receptor-mediated.[10]

In summary, two patients with acute manifestations of RLS syndrome obtained prompt sustained relief after administration of physostigmine. A clinical trial in the nonperioperative setting is needed to confirm this beneficial effect. A positive outcome could spur a different line of research into the mechanisms involved.

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