

## CASE REPORTS

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# Successful Perioperative Management of a Patient with Parkinson's Disease by Enteral Levodopa Administration under Propofol Anesthesia

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PARKINSON'S disease (PD) is a relatively common neurologic disorder. Many drugs currently used for the treatment of PD may have significant interactions with anesthetic and cardiovascular drugs.<sup>1</sup> Even brief interruption of anti-PD drugs during surgery may result in exacerbation of Parkinson's symptoms.<sup>2</sup> However, safe and effective ways to administer anti-PD drugs during surgery are not widely known.<sup>3</sup>

We used the enteral administration of levodopa (LD) in a patient with PD who had experienced exacerbation of PD during emergence from general anesthesia in two previous operations. This method of LD administration successfully prevented the exacerbation of the symptoms in this patient.

## Case Report

A 70-yr-old man with PD was scheduled for right hepatic lobectomy for metastatic disease from colon cancer. He had been suffering from PD for 10 yr and had been treated with oral administration of carbidopa/levodopa (10/100), a LD preparation in tablet form, five times daily. He manifested fluctuations of motor nerve disturbance, which progressed to severe immobility whenever the effects of LD disappeared. He had undergone two operations in the past 7 months during general anesthesia with nitrous oxide and isoflurane in combi-

nation with epidural anesthesia. During emergence from anesthesia, he had exhibited pill-rolling tremor of the hands. As prompt resumption of spontaneous ventilation and response to direct commands had been confirmed, the trachea had been extubated. He then exhibited sustained rigid extension of his extremities, which progressed to total body rigidity. He also experienced progressive difficulty in swallowing until he was unable to manage his secretions. Oxygen saturation was 100%, and there were no visible fasciculations or other evidence of seizure activity or shivering. These symptoms were improved by intravenous administration of LD. However, after LD administration, severe hypertension and premature atrial and ventricular contractions were recognized, probably resulting from adverse effects of LD.

In the current case, the patient had taken his usual medications 1.5 h before the operation. On arrival to the operation room, he showed neither muscle rigidity nor resting tremor. Anesthesia was induced with 100 mg propofol and 8 mg vecuronium to facilitate tracheal intubation. Anesthesia was maintained with continuous intravenous infusion of propofol at  $5 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$  and epidural infusion of 4–5 ml/h of bupivacaine, 0.25%, and 5  $\mu\text{g}/\text{ml}$  fentanyl. Proper position of a nasogastric tube was confirmed radiographically. One tablet of carbidopa/levodopa (10/100) was dissolved with 10 ml of saline, and the solution was given into the stomach through the nasogastric tube every 2 h during the operation. Perioperative plasma concentrations of LD in arterial blood were measured by high performance liquid chromatography (HPLC).<sup>4</sup> All plasma LD concentrations in the operative day were above minimum therapeutic concentration of 0.3  $\mu\text{g}/\text{ml}$ <sup>5</sup> and could be kept stable, but they were lower than those measured 2 days before with his regular medications.

After the hepatic lobectomy, we proposed the surgeon place a duodenostomy tube in the mid-duodenum for intermittent administration of LD and enteral feeding in the early postoperative period. Despite a 2,000-ml blood loss, which was replaced with whole blood, flesh frozen plasma, and crystalloid solution, he was hemodynamically stable during the operation. Immediately after surgery, he emerged from anesthesia smoothly and exhibited no dystonic muscle rigidity. Total epidural dose of fentanyl was 185  $\mu\text{g}$ , and he showed no adverse reactions such as muscle rigidity. Plasma LD concentrations measured in the intensive care unit (ICU) were slightly higher than those during the intraoperative period. For the first 3 postoperative days, he was given his usual medications *via* the duodenostomy tube. His postoperative course was uneventful, and he was discharged 1 month after the operation.

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## Discussion

Because brief interruption of medications often results in severe skeletal muscle rigidity, it is the prevalent opinion that a therapeutic concentration of LD in plasma should be maintained in the perioperative period in patients with PD.<sup>1</sup> However, LD's half-life is short (1–3 h), and further, LD's equilibration half-life between plasma and effect-site concentration was fivefold shorter on average in fluctuating patients than in stable patients.<sup>6</sup> Therefore, in lengthy surgeries, the effect-site concentration of LD was below the therapeutic threshold if LD was not given during surgery, even if given immediately before induction. Specifically, in clinically fluctuating patients, plasma LD instability easily produced the Parkinsonian symptoms.<sup>7</sup>

The feasibility and efficacy of enteral LD infusions in nonsurgical patients with advanced PD was first demonstrated by Kurlan *et al.* in 1986.<sup>8</sup> LD is absorbed mainly in the proximal small intestine.<sup>9</sup> Gastric emptying plays an important role in its absorption.<sup>10</sup> Delivery of LD distal to the pylorus makes its absorption rapid and may keep plasma LD concentration stable.<sup>11,12</sup> However in fasting patients, the anti-Parkinsonian effect of LD paralleled plasma drug concentration,<sup>13</sup> and there were few differences in mobility score and in plasma LD concentration between gastric and duodenal infusion.<sup>11</sup> Accordingly, intraoperative enteral LD administration should be considered for patients with PD, and further, enteral administration of LD should provide greater comfort and safety by avoiding dysphagia and aspiration in the early postoperative period. However, we have noted no reports in which LD was given through the enteral route perioperatively, and the efficacy of enteral LD infusion has not been studied for patients during general anesthesia. One previous report describes intraoperative administration of oral LD during spinal anesthesia ameliorating intraoperative exacerbation of PD,<sup>2</sup> suggesting usefulness in surgical patients.

In this case, intermittent gastric LD infusion during surgery kept plasma LD concentrations above the minimum therapeutic threshold but lower than those measured 2 days before surgery. The reasons for this phenomenon are thought to be dilution caused by replacement of blood loss and inadequate intestinal absorption of LD during surgery. During laparotomy, transport from the stomach to the small intestine

might be impaired, and absorption also could be reduced. Because the plasma LD concentration measured in the ICU, where LD was administered through the duodenostomy tube, was higher than those measured intraoperatively, delivery of the LD distal to the pylorus *via* a nasoduodenal tube may be more reliable than gastric administration *via* the nasogastric tube.

We did not use intravenous administration of LD in this case for two reasons: (1) the intravenous formulation of LD available in Japan does not contain carbidopa (dopa decarboxylase inhibitor); and (2) treatment with and drug titration of LD for intravenous administration alone may be dangerous during general anesthesia because of interactions with anesthetic agents. It may increase the risk of a variety of arrhythmias or hypertension as reported previously. These side effects of LD are mediated through its metabolite, dopamine. Previous inhibition of peripheral dopa decarboxylase prevents the conversion of LD to dopamine and abolishes the immediate hypertensive and tachycardia responses to intravenously administered LD.<sup>14</sup> Thus LD is normally given in combination with a peripheral dopa decarboxylase inhibitor such as carbidopa, which reduces the LD requirement and dose-related side effects.

In conclusion, we report the perioperative treatment of a patient with PD by using intraoperative administration of LD through a nasogastric tube during propofol anesthesia and through a duodenostomy tube in the early postoperative period. The perioperative management described in this report is practical and prevented the exacerbation of Parkinsonian symptoms during the postoperative period.

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## Post-transplant Lymphoproliferative Disease May Present with Severe Airway Obstruction

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POST-TRANSPLANT lymphoproliferative disease (PTLD) occurs in patients treated with cyclosporine or tacrolimus after organ transplantation. Associated with Epstein-Barr virus (EBV) infection, PTLD may be insidious, resembling infectious mononucleosis, or may present as an aggressive form of lymphoma. Its prevalence has been reported to be 4% among children and 0.8% among adults.<sup>1,2</sup> Lesions occur in the head and neck, gastrointestinal tract, and the transplanted allograft. Although PTLD commonly causes

upper airway narrowing in children, previously reported cases have primarily involved Waldeyer's ring.<sup>3</sup> We describe a case of PTLD with severe enlargement of the epiglottis and aryepiglottic folds causing life-threatening airway obstruction after the induction of anesthesia.

### Case Report

A 14-month-old boy who had a liver transplant for biliary atresia at the age of 6 months presented with progressive stridor. The stridor was mild at rest, with minimal subcostal retractions, but worsened with crying. Despite normal liver function, weight gain was poor (weight, 8.4 kg). Fiberoptic examination of the airway at an outside hospital revealed laryngomalacia and possible tracheomalacia. Viral serology revealed past infection with EBV. Further evaluation at our hospital included normal fluoroscopy of the trachea and a sleep study that noted three 6- to 7-s episodes of obstructive apnea over 8 h, associated with a decrease in SpO<sub>2</sub> from 97-99% to 89-90%. Fiberoptic examination of the airway revealed an enlarged epiglottis and aryepiglottic folds with minimal enlargement of the tonsils. The patient was scheduled for tonsillectomy and supraglottoplasty.

Medications included tacrolimus, prednisone, acyclovir, and trimethoprim-sulfamethoxazole.

Laboratory values included a hematocrit of 32% and a normal serum HCO<sub>3</sub><sup>-</sup> of 23.

The pediatric otolaryngologist performing the procedures requested that the patient breathe spontaneously during direct laryngoscopy to allow assessment of vocal cord function. Anesthesia was

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