

Perioperative sublingual levodopa in Parkinson's Disease: A useful alternative!

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ABSTRACT

Timely administration of dopamine agonists is of the essence in Parkinson's disease. The perioperative period especially for abdominal surgeries under general anaesthesia poses a challenge to oral drug administration. Alternatives such as rotigotine patches and subcutaneous apomorphine administration have been described but unavailability restricts their use. Sublingual administration of tablet levodopamine as an alternative worked well in our patients and we would like to describe the same.

Key words: Anaesthesia, Parkinson's disease, perioperative levodopa, sublingual drugs

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INTRODUCTION

Parkinson's disease was formally described by James Parkinson, which he termed as "the shaking palsy." It comprises of hypokinesia, rigidity and rest tremor.^[1] The characteristic pathological feature is the destruction of dopamine-containing nerve cells in substantia nigra of basal ganglia.^[2] Crude prevalence rates of Parkinson's disease in India ranges from 7 to 328 per 100,000 above the age of 50 years.^[3] With advances in surgical and anaesthesia techniques and increasing geriatric population, more such patients will require medical attention during the perioperative period. The regular administration of anti-Parkinson medication is of utmost importance to prevent aggravation of symptoms. However, the administration of levodopa can be challenging in certain situations such as gastrointestinal surgery or in cases where Ryles Tube (RT) is not *in situ*. We discuss two case scenarios where sublingual levodopa administration worked successfully as an alternative to oral administration of levodopa.

CASE REPORTS

Case report 1

A 73-year-old male diabetic patient with Parkinson's disease since 12 years presented with subacute

intestinal obstruction and was scheduled to undergo an emergency colostomy. The patient was on a combination of oral levodopa 100 mg and carbidopa 25 mg (Syndopa Plus™, Sun Pharmaceuticals), 2 tablets thrice a day and one controlled release preparation of oral levodopa and carbidopa (Syndopa CR™ 125 mg, Sun Pharmaceuticals) tablet thrice a day. He was also taking tablet ropinirole 0.5 mg twice a day and tablet metformin 500 mg thrice a day. The procedure was completed uneventfully under subarachnoid block.

A month later, he was scheduled for repair of prolapsed bowel through colostomy which was performed under combined spinal epidural anaesthesia technique. The patient maintained stable haemodynamics throughout the procedures. Since both the surgeries were performed under regional anaesthesia, perioperative levodopa was administered orally.

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An exploratory laparotomy with total colectomy with ileorectal anastomosis was planned later for repeated bowel prolapse through the colostomy. A low thoracic epidural with balanced general anaesthesia was instituted. Intraoperatively, the patient had hypotension nonresponsive to fluid boluses and 30 mg of ephedrine. It responded to intravenous infusion of noradrenaline at 0.1 $\mu\text{g}/\text{kg}/\text{h}$ which was tapered off postoperatively over 2 h in the surgical intensive care unit. It was difficult to administer anti-Parkinson medication orally since the patient had a bowel surgery, continuous RT aspirate and was ventilated postoperatively. Hence, Syndopa Plus and Syndopa CR tablets were administered at the scheduled time in the crushed form sublingually for the first 12 h till the extubation. The patient remained stable and did not manifest exacerbation of Parkinson symptoms. In view of Parkinson's disease, prolonged major surgery, fluid shifts and the need for blood transfusion the patient was electively ventilated postoperatively and successfully extubated after 12 h. Oral levodopa was commenced after extubation.

Case report 2

An 83-year-old male patient with hypertension, diabetes and Parkinson's disease was posted for the right shoulder hemiarthroplasty. Hypertension was controlled with a combination of tablet benzthiazide 25 mg and triamterene 50 mg once a day and tablet telmisartan 40 mg once a day. He was on insulin therapy for diabetes. He was diagnosed with Parkinson's disease 3 years back and was on a combination of tablet Syndopa Plus™ (levodopa 100 mg and carbidopa 25 mg) four times a day, and tablet amantadine 100 mg twice a day. His cardiovascular status was evaluated preoperatively and was found to be stable. The surgery was planned in beach chair position, and a general anaesthetic combined with interscalene block was planned. After induction of anaesthesia, the patient had severe hypotension unresponsive to fluid boluses and bolus doses of ephedrine (42 mg). The patient responded to an intravenous infusion of noradrenaline 0.1 $\mu\text{g}/\text{kg}/\text{h}$ which was tapered off in post-operative period. The duration of surgery was expected to last before the next scheduled dose of Syndopa. However, surgery was unexpectedly prolonged. The patient being in beach chair position, the insertion of an RT tube was difficult. Hence, the scheduled dose of Syndopa Plus was administered during surgery, sublingually in crushed form as per schedule. Extubation and post-operative course were uneventful without exacerbation of Parkinson symptoms. His anti-Parkinson medication was resumed orally in the postoperative period. He had an uneventful recovery.

DISCUSSION

Prime anaesthetic challenges faced in both our cases were the perioperative administration of anti-Parkinson medications and profound hypotension.

Patients with Parkinson's disease are dependent on timely administration of dopaminergic agonists to avoid worsening of symptoms. This contributes to the challenge during the perioperative period especially with general anaesthesia and abdominal surgeries.^[4-6] Levodopa can be administered via the RT, but its effect can be suboptimal due to delayed gastric emptying.^[7,8] A duodenal tube is advocated when normal feeding is interrupted for a prolonged duration.^[9] Rotigotine transdermal patch or subcutaneous (sc) apomorphine is an alternative in these patients, however nonavailability limits their use in our setup.

Sublingual drug administration has advantages like relatively rapid onset of action due to high vascularity of oral mucosa, avoidance of hepatic first pass metabolism and ease of administration in unconscious or incapacitated patients.^[10] Levodopa absorption is affected by delayed gastric emptying time, gastric pH, liver metabolism and a simultaneous high protein diet.^[11] These factors seem to be successfully averted by the sublingual route of administration of levodopa.

Levodopa methyl ester (LDME), a prodrug of Levodopa has been studied through sublingual and subcutaneous (SC) routes in humans and the intranasal route in animals.^[12,13] In humans, it was found to be ineffective by the SC and sublingual use whereas in animals it is in experimental stages. Furthermore, the sublingual dose we administered was tablet levodopa whereas the drug studied by Kleedorfer *et al.* was the liquid formulation of LDME.

There have been no published studies of oral levodopa being administered by the sublingual route except for a small trial comparing sublingual versus SC liquid LDME in 10 patients.^[12] Hence, there is no data available for the therapeutic serum concentration of dopamine by the sublingual route.

Our first patient underwent total colectomy with continuous RT aspirate, followed by elective ventilation whereas our second patient underwent unexpectedly prolonged shoulder surgery in beach chair position under general anaesthesia making RT insertion and drug administration difficult. Hence

in both the patients crushed form of tablet Syndopa Plus was administered sublingually at the scheduled time. Neither of them manifested exacerbation of Parkinson symptoms. Our observation of the efficacy of sublingual crushed tablet levodopa being in only two patients, it would be worth investigating this route further in a larger group of patients.

We observed profound hypotension under general anaesthesia in both the patients. Advanced age, effect of levodopa and dopaminergic agonists, autonomic disturbances due to Parkinson's disease may have contributed to it.^[14] Autonomic dysfunction due to Parkinson's disease or diabetes mellitus, dehydration due to intestinal obstruction, sitting position under anaesthesia could be additional causative factors for hypotension. Intravenous infusion of noradrenaline, normalised haemodynamics. Noradrenaline mainly acts on peripheral alpha receptors causing vasoconstriction and cardiac beta 1 receptors contributing to its inotropic action, hence is preferred as an inotrope in Parkinson's patients.^[15] Ephedrine having a direct and indirect stimulant effect on alpha and beta adrenergic receptors competes with noradrenaline for uptake at the synaptic vesicles and hence increases noradrenaline levels. Hence, its use is justified in the management of hypotension due to subarachnoid block in Parkinson's disease.

Regional anaesthesia has its own advantages in these patients, where deemed applicable. First, it avoids delay in oral intake associated with the use of general anaesthetics and muscle relaxants. Second, the chances of post-operative nausea vomiting are reduced which in turn ensures minimal interruption of oral anti-Parkinson medication. The patient can be given oral levodopa as per schedule throughout the perioperative period under regional anaesthesia. However, the presence of rigidity can pose a problem with positioning for the administration of regional anaesthesia.^[5] Intraoperative frequent adjustments in upper limb positioning may be needed to ensure patient comfort. In view of all these advantages, regional anaesthesia was successfully administered in our first case for his initial two surgeries.

CONCLUSION

We would like to suggest the possible use of sublingual administration of levodopa when recommended

methods such as through Ryle's tube, oral or patches cannot be used. A balanced anaesthesia technique in addition to timely administration of perioperative Parkinson medication, low threshold for treating hypotension form the cornerstones for perioperative management of patients with Parkinson's disease.

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Conflicts of interest

There are no conflicts of interest.

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