Case report: Successful use of rectally administered levodopa-carbidopa

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Family physicians taking care of patients with Parkinson's disease (PD) might encounter situations in which their patients cannot take oral medications. Parkinson's disease frequently causes oropharyngeal dysphagia.[1] Intercurrent illness often results because patients are unable to take oral medications, and administering oral medications is usually limited perioperatively. Abrupt withdrawal of PD medications might have significant sequelae, including worsened symptoms and even death.[2]

We describe a patient with severe PD who, secondary to acute delirium, became unable to take her medication and subsequently had severe exacerbation of her PD symptoms. A rectal formulation of levodopa-carbidopa was prepared and led to clinical improvement.

Case report

An 88-year-old woman with a 16-year history of PD lived independently and was able to move about using a walker. She took levodopa-carbidopa 250/25 mg qid. She was admitted to an acute care hospital after a fall and transferred for geriatric rehabilitation.

Initially she progressed well but developed a urinary tract infection complicated by delirium. She was unable to take oral medications due to worsening of her pre-existing dysphagia and to paranoia. Nasogastric or gastrotomy tube insertion for replacing levodopa was impossible for many reasons. After 1 week without PD medications, she was bedridden with severe bradykinesia and rigidity. She could not speak but could communicate with eye movements.

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In a 1981 study, Eisler et al[3] found that rectal preparations of levodopa were ineffective and hypothesized that the alkalinity of rectal secretions could be a factor in the lack of absorption. Using this suggestion, we prepared a strongly acidic rectal suspension of levodopa-carbidopa (**Table 1**[4]). This preparation was given to our patient at a dose of 100/25 mg tid. Within 36 hours of receiving the first rectal dose, she spoke several words. Within 48 hours, she recovered spontaneous movement of her hands. Over the next 4 days she began to move her feet and was able to move her arms independently. The dosing regimen was increased to 250/25 mg qid after 4 days. After 1 week, the patient could converse and could raise both upper limbs. The maintenance dose used was 315/32 mg (1.25 mL of 250/25 mg tablet suspension) in the morning and at noon and 250/25 mg at dinner and bedtime. On this regimen there was little "wearing off" between doses and no signs of excess levodopa.

After 4 weeks the patient was able to resume taking nutritional supplements and oral levodopa-carbidopa. She could write her name legibly, move herself independently in bed, and converse for extended periods. The patient was able to resume her geriatric rehabilitation program.

Table 1. Preparation of rectal levodopa-carbidopa suspension

• Crush and pulverize 10 tablets of either 100/25 mg or 250/25 mg of levodopa-carbidopa
• Crush to a fine powder with 10 mL of 50% water, 50% glycerol mixture[4]
• Lower pH to 2.3-2.4 using 1 g of citric acid
• Administer levodopa-carbidopa suspension (1 tablet per mL) using a 3-mL syringe attached to a 6-cm catheter
• Store between 2°C-8°C in an amber bottle for <24 hours (stability of preparation is uncertain)
• Shake well before use

Discussion

A MEDLINE search for original research articles published between 1966 and 1999 used key words "levodopa/therapeutic use," "rectum," and "suppositories." A limited number of clinical studies have examined the use of rectal levodopa.

Eisler et al found that levodopa, given rectally to patients as a tablet, suppository, or powder insufflation, caused no rise in serum levodopa levels and had no clinical benefit.[3] Parkes et al[5] used an enema of 5 g of levodopa in 100 mL of water in one patient with hepatic coma and found that the patient temporarily regained consciousness 12 hours after treatment. In another case report, Beasley et al[6] used a suppository of 750 mg of levodopa qid, which led to clinical improvement and increased blood levels. Unfortunately, the method used to prepare the suppository was not published.

Apomorphine can be administered parenterally or sublingually, but its role is generally for managing "on-off" periods rather than for replacing levodopa.[7] Perioperative management using apomorphine and rectal domperidone has been reported, however.[8] Levodopa can be given intravenously, but formulations are unavailable for clinical use and can be difficult to administer.[9]

Clinical improvement seen with this preparation could be due to its low pH, the fact that it is a suspension as opposed to a solid tablet, and the fact that rectally absorbed medications are not subject to first-pass metabolism. A larger trial would help to quantify the clinical effect of the preparation. The absence of serum levodopa levels is a major limitation of this case report. Blood samples were drawn from our patient to determine the amount of levodopa absorption but could not be analyzed. Analysis would be an important component of further study.

Conclusion

Family physicians working with PD patients, particularly in long-term care, regularly encounter difficulties with oral administration of medications for PD. Our experience with this patient suggests that physicians might consider rectal administration of levodopa-carbidopa to prevent deterioration of PD symptoms in the short term when intercurrent illness or surgery prevents using oral levodopa-carbidopa.

For patients who cannot return to oral administration, inserting a feeding tube should be considered. If this is impossible, however, rectal administration of levodopa-carbidopa might have a role in long-term management of PD.

Editor's key point

- Rectal administration of levodopa-carbidopa in an acidic suspension might be effective when oral preparations are not tolerated.

Point de repère du rédacteur

- L'administration par voie rectale de lévodopa-carbidopa dans une suspension acide pourrait se révéler efficace quand les préparations par voie orale ne sont pas tolérées.

Competing interests

None declared

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References

1. Edwards LL, Quigley EM, Pfeiffer RF. Gastrointestinal dysfunction in Parkinson's disease: frequency & pathophysiology. *Neurology* 1992;42:726-32.
2. Mayieux R, Stern U, Mulvey K, Cote L. Reappraisal of temporary levodopa withdrawal ("drug holiday") in Parkinson's disease. *N Engl J Med* 1985;313(12):724-8.
3. Eisler T, Eng N, Plotkin C, Calne D. Absorption of levodopa after rectal administration. *Neurology* 1981;31:215-7.
4. McEvoy GK. *AHFS drug information 98*. 40th revised ed. Bethesda, Md: American Society of Health-System Pharmacists Inc; 1998.
5. Parkes JD, Sharpstone P, Williams R. Levodopa in hepatic coma. *Lancet* 1970;1:1341-3.
6. Beasley BL, Hare TA, Vogel WH, Desimone S. Rectal administration of L-dopa [letter; comment]. *N Engl J Med* 1973;289(17):919.
7. Lien CTC, Mutch WJ. The treatment of Parkinson's disease in older people. *Scott Med J* 1997;42:147-50.
8. Galvez-Jimenez N, Lang AE. Perioperative problems in Parkinson's disease and their management: apomorphine with rectal domperidone. *Can J Neurol Sci* 1996;23(3):198-203.
9. Mouradian MM, Heuser IJ, Baronti F, Chase TN. Modification of central dopaminergic mechanisms by continuous levodopa therapy for advanced Parkinson's disease. *Ann Neurol* 1990;27(1):18-23.