LETTER TO THE EDITOR

To the Editor

Levodopa-Carbidopa-Related Rash in Parkinson's Disease: A Case Series

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Rash on levodopa is usually related to compounding dye. It does not require stopping levodopa, but can resolve if the formulation is switched.

Although there are various formulations of levodopa-carbidopa used for the symptomatic treatment of Parkinson's disease (PD), levodopa-carbidopa 100/25 mg remains the main formulation used in North America. Skin rash related to levodopa-carbidopa 100/25 was first reported by Goetz in 1983.[1] However, awareness of the occurrence of this skin reaction is low even among movement disorder neurologists,[2] and the inappropriate classification of this rash as a levodopa allergy can result in significant limitations in the symptomatic management of patients with PD. We describe a case series of three patients who developed a diffuse maculopapular rash a few months after the initiation of levodopa-carbidopa 100/25 mg and discuss an approach to managing this skin reaction.

A 26-year-old woman diagnosed with early-onset PD at the age of 19 years developed a diffuse rash upon resumption of levodopa-carbidopa 100/25 mg after brief interruption of therapy for perceived cognitive side effects. She had previously been on levodopa-carbidopa for 6 months. A possible link to levodopa-carbidopa was considered, as there were no known obvious precipitating factors or other concomitant medications. She was switched from levodopa-carbidopa 100/25 mg to the 100/10-mg formulation. A complete resolution of the rash was observed after 8 weeks.

A 54-year-old woman who had recently been diagnosed with PD and started on levodopa-carbidopa 100/25 mg developed a diffuse pruritic rash involving the neck and face about 4 months into treatment. Alternative causes or triggers for the rash could not be identified, and a link to levodopa-carbidopa 100/25 was most likely. The rash gradually resolved over a period of 3 months after a switch to levodopa-benserazide 100/25 mg.

An 82-year-old woman with recent diagnosis of PD developed a diffuse pruritic rash after 6 months of therapy with levodopa-carbidopa 100/25 mg. Alternative causes including a possible drug allergy to an anti-depressant were ruled out as she had been on the anti-depressant for several years without any dose changes. This rash resolved within 6 months after the substitution with levodopa-benserazide 100/25 mg.

Skin rash as a reaction to levocarb-carbidopa 100/25 mg is considered uncommon, but its incidence is probably underestimated. A review of our patients and data from previous case reports suggest a common presentation with a maculopapular rash that is often disseminated or diffuse but can have predilection for limbs, upper trunk or face. The patients are more likely to complain of associated pruritus.

On the basis of available case reports and the fact that the rash resolved in all cases after substituting levodopa-carbidopa 100/25 mg with an alternative formulation, the skin rash represents a manifestation that is related to neither levodopa nor carbidopa[1,2] but rather to the compounding components that are exclusive to this formulation of levodopa-carbidopa. The compounding ingredients in these drugs are D&C Yellow No. 10 Aluminum Lake and E104 that give the pill its yellow appearance.[3,4] Given that these two dyes are contained in other drugs other than levodopa-carbidopa 100/25 mg, the use of any such drugs is best avoided in patients demonstrating such a skin rash. Skin rash has been reported with certain doses of warfarin containing one of the above compounding agents.[5]

The development of rash in all three cases was not immediate, and resolution was gradual over a period of 2-6 months. This is in keeping with a delayed reaction and would suggest a cumulative effect of the dye in question specific to this formulation of levodopa-carbidopa (100/25 mg). However, it is also possible that this could represent an immune-mediated drug reaction, which in a mild presentation is limited to a skin rash without systemic involvement. A more systemic and fulminant reaction is possible as has been reported by Niedermaier and Briner[6] in a single case report of Henoch-Schoenlein syndrome induced by levodopa-carbidopa 100/25 mg.

We recommend that neurologists strongly consider the possibility of a dye-related skin rash or allergic reaction in the differential diagnoses of a rash in any PD patient treated with levodopa-carbidopa 100/25 mg formulation and attempt switching to a formulation that is devoid of the implicated dye as a pure allergy to levodopa is rare. Various levodopa formulations that do not contain the yellow dyes and would be safe alternatives include levodopa-carbidopa 100/10 and 200/25 mg, levodopa-benserazide and levodopa-carbidopa-entacapone.[1,2,6] Furthermore, the extended-release (CR) formulation of levodopa-carbidopa could also be considered.

We also recommend that any reported levodopa-related allergy be investigated or reviewed where appropriate, as such a determination in patients with PD if inaccurate can result in wrongful withdrawal or avoidance of levodopa therapy, which remains the most effective symptomatic therapy in PD.[2] Such avoidance would result in undertreatment and functional impairment.

Disclosures

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References

1. Goetz CG. Skin rash associated with Sinemet 25/100. N Engl J Med. 1983;309:1387-8.

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2. Chou KL, Stacey MA. Skin rash associated with Sinemet does not equal levodopa allergy. Neurology. 2007;68(13):1078-9.
3. SINEMET (carbidopa and levodopa) tablets. Product monograph, Merck Sharp & Dohme Corp 1996-2018, White Station, USA, revised 4/2018. Downloaded May 25, 2018 from https://www.merck.com/product/usa/pi_circulars/s/sinemet/sinemet_pi.pdf.
4. Sarfaraz KN. Handbook of pharmaceutical manufacturing formulations: compressed solid products, Vol. 1, 2nd ed. New York: Informa Healthcare USA; 2009, p. 238.
5. Bogart MA, Cheema A, Wooten JM, Bogart DB. Warfarin allergy: an easy solution. Clin Cardiol. 2010;33:E31-2.
6. Niedermaier G, Briner V. Henoch-Schönlein syndrome induced by carbidopa/levodopa. Lancet. 1997;349:1071.

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