

■ Clozapine and dyskinesia in Parkinson disease

Durif et al. studied the effect of clozapine on levodopa-induced dyskinesias (LID) in 50 parkinsonian patients in a 10-week randomized placebo-controlled study. The duration of LID was reduced by 2 hours and their intensities by 50%. The mean clozapine dose was 40 mg. Three patients in the clozapine group developed hyper eosinophilia, which resolved rapidly after stopping the drug.

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■ Progress in combating levodopa-induced dyskinesia

Commentary by Robert L. Rodnitzky, MD

Levodopa-induced dyskinesia (LID) is a source of motoric or social disability in a significant percentage of patients undergoing treatment for Parkinson disease (PD). This complication appears in approximately 40% of patients who have received levodopa therapy for 4 to 6 years.¹ In their mildest form LID may be apparent to family members, but not the patient. When more severe, these abnormal involuntary movements can impair gait and balance, interfere with ordinary activities of daily living such as feeding, or result in social withdrawal due to embarrassment. Patients with moderate or severely advanced PD are most commonly affected by this adverse effect, but patients with young onset PD of any severity are prone to develop early and severe LID.

There has been some progress in treating this complication. Medical therapy with amantadine, an NMDA antagonist, and surgical therapies such as pallidotomy, pallidal stimulation, or subtha-

lamic nucleus stimulation may help.² Still, many patients cannot tolerate or are not improved by the former treatment, and are not suitable candidates for the latter.

There is clearly a need for additional effective therapies of this condition, and a host of potential approaches have been suggested ranging from blockade of the adenosine A_{2A} or alpha 2 adrenergic receptors, to treatment with 5HT_{1A} serotonin agonists, to mention only a few. Durif et al. provide evidence, based on a double-blind placebo-controlled study, that the atypical antipsychotic agent clozapine effectively reduces the severity and duration of LID in PD patients. Whereas this result has been suggested in previous open-label studies, the more rigorous demonstration of clozapine's antidyskinetic properties in this study is a welcome development. The exact mechanism by which clozapine improves LID is still unclear, mirroring our incomplete understanding of the physiochemical basis of this complication.

Whereas these data may appropriately lower the clinician's threshold to prescribe clozapine for the treatment of LID, the use of this agent must still be balanced by awareness of its relatively high side effect profile, including the rare, but potentially fatal, complication of agranulocytosis.³ However, as LID are potentially disabling for so many PD patients, this caveat should be considered a precaution, not a prohibition for the use of this otherwise useful medication.

References

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