

FROM THE FAMILY PRACTICE INQUIRIES NETWORK

What is the best initial treatment of Parkinson's disease?

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■ EVIDENCE-BASED ANSWER

No studies clearly demonstrate the best initial treatment for Parkinson's disease. Levodopa improves motor function in Parkinson's disease; however, long-term use is associated with irreversible dyskinesias and motor fluctuations. Compared with placebo, selegiline improves the motor symptoms of Parkinson's disease and allows a physician to delay the introduction of levodopa by 9 to 12 months (strength of recommendation [SOR]: **A**, based on randomized controlled trials).

Dopamine agonists—alone or combined with levodopa—have fewer associated dyskinesias and other motor complications but produce lower scores on activities of daily living and Unified Parkinson's Disease Rating Scale (UPDRS) when compared with levodopa alone (SOR: **A**, based on systematic reviews of randomized controlled trials). Drug choices should be based on each patient's individual symptoms and response to medication (**Table**).

Medications for Parkinson's disease

Medication	Starting dose	Usual daily dose	Approx cost/mo
Selegiline	5 mg every morning	5 mg every morning and at noon	\$29 for 10 mg/d

Carbidopa/levodopa	25/100 mg tab 3 times daily	25/100 mg 3 times daily	\$76 for 75/300 mg/d
Pergolide	0.05 mg/d	2–3 mg/d divided 3 times daily	\$223 for 2 mg/d
Pramipexole	0.375 mg/d divided 3 times daily	1.5–4.5 mg/d divided 3 times daily	\$177 for 3 mg/d
Ropinirole	0.25 mg 3 times daily	3 mg divided 3 times daily	\$185 for 3 mg/d

■ EVIDENCE SUMMARY

Five randomized controlled trials¹⁵ have shown improved motor function and activities of daily living with selegiline vs placebo in early Parkinson's disease. Two of these trials^{1,2} found that selegiline delayed the need for levodopa for 9 to 12 months.

One large randomized controlled trial showed no difference in disability scores and an increase in mortality at 5.6 years when comparing selegiline combined with levodopa to levodopa alone.⁶ A re-analysis of this study, as well as subsequent studies, have not supported this conclusion and found no increase in mortality in patients with a history of selegiline use.⁷⁻¹⁰

Two Cochrane reviews found that patients who tolerated the dopamine agonist bromocriptine—when administered alone or with levodopa—had delayed dyskinesias and motor complications compared with levodopa alone.^{11,12} There was no change in off-time with the combination.¹² A large randomized controlled trial comparing bromocriptine with levodopa demonstrated that at 3 years, disability scores were lower in the patients initially assigned to bromocriptine, but the difference was no longer significant at 9 years.¹³

The bromocriptine group in this trial showed a lower incidence of dyskinesias when data from all patient groups were combined. However, when moderate to severe cases were analyzed separately, there was no significant difference.¹³ There was no difference in mortality between patients initially treated with bromocriptine vs levodopa.^{13,14}

Studies of other dopamine agonists show results comparable with bromocriptine. Lisuride (not available in the US) with rescue levodopa vs levodopa alone had fewer motor complications at 4 years but lower UPDRS and activities of daily living scores.¹⁵ Another study comparing lisuride (with or without levodopa) vs levodopa alone found no difference in motor complications at 5 years.¹⁶ Studies with cabergoline, pramipexole, and pergolide—alone or combined with levodopa—vs levodopa alone showed a decrease in motor complications with the dopamine agonist but lower activities of daily living and UPDRS scores.¹⁷⁻¹⁹

■ RECOMMENDATIONS FROM OTHERS

In 2002, the American Academy of Neurology published practice parameters for the initiation of treatment for Parkinson's disease based on literature from 1966 to 1999. The authors concluded:

- selegiline has mild symptomatic benefit and may be tried as initial therapy, but confers no neuroprotective effect
- either levodopa or a dopamine agonist can be used for the initial treatment of symptomatic Parkinson's disease
- levodopa has a higher risk of dyskinesias than a dopamine agonist but superior motor benefits,²⁰ and is less likely to have other side effects (nausea, hallucinations, somnolence, and edema).

CLINICAL COMMENTARY

Family physicians play a key role in monitoring Parkinson's

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Parkinson's disease has a profound impact on a patient's physical and psychological wellbeing. Difficulties with movement, autonomic nervous system abnormalities, neuropsychiatric symptoms, and problems with medication effectiveness and side effects all occur throughout its course. Consultation with a neurologist skilled in this disorder can be quite helpful, particularly in younger patients or when the diagnosis is unclear. The family physician plays a key role in monitoring of the patient's condition. Active management of symptoms (and comorbidities as they arise) is crucial in helping patients maintain their functional status and quality of life.

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