Review: Several drugs are efficacious for symptomatic treatment of Parkinson disease


**Question**
In patients with Parkinson disease (PD), what are the optimal treatments for preventing disease progression, controlling motor symptoms, managing and preventing motor complications, and treating nonmotor symptoms?

**Data Sources**
Studies were identified by searching electronic databases and by checking the references of review articles and relevant studies.

**Study Selection**
English-language studies were selected if they were published full reports of randomized controlled trials (RCTs) that enrolled ≥ 20 patients with PD, used objective scales for outcome measurement, and had ≥ 4-week follow-up.

**Data Extraction**
Data were extracted on study quality, and studies were assessed for efficacy, clinical usefulness, and safety. To be considered efficacious, the intervention had to show a positive effect on outcomes based on data from ≥ 1 high-quality RCT and have no conflicting data from other RCTs.

**Main Results**
The therapeutic interventions evaluated were drugs, surgery, and rehabilitation procedures. Interventions were evaluated with respect to prevention of disease progression, treatments of signs and symptoms, symptomatic treatment and prevention of motor complications, and symptomatic treatment of nonmotor features. The Table shows efficacious interventions. No interventions were shown to be efficacious for neuroprotection in PD. In patients with nonmotor features of PD, 1 drug was shown to be efficacious for drug-induced psychosis; no drugs were efficacious for such other nonmotor features as dementia, depression, or orthostatic hypotension. No strong RCT evidence supports the efficacy of surgery or rehabilitation.

**Conclusions**
In patients with Parkinson disease, several drugs are efficacious for controlling motor symptoms and motor complications and preventing motor complications. Recent surgical interventions have not been adequately assessed in RCTs. Insufficient evidence exists for prevention of disease progression and control of most nonmotor features and to support rehabilitation.

**Sources of funding:** 8 funding agencies.
For correspondence: Profesor O. Rascol, Toulouse University Hospital, Toulouse, Cedex, France. E-mail rascol@ccica.fr.

**Interventions for Parkinson disease (PD) shown to be efficacious in randomized controlled trials (RCTs)**

<table>
<thead>
<tr>
<th>PD indicators</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs and symptoms in patients with early PD not receiving levodopa</td>
<td>Standard levodopa, controlled-release levodopa, dihydroergocryptine, pergolide, pramipexole, ropinirole, selegiline</td>
</tr>
<tr>
<td>Signs and symptoms in patients with advanced PD already receiving levodopa</td>
<td>Controlled-release levodopa, bromocriptine, cabergoline, pergolide, pramipexole, entacapone, tolcapone</td>
</tr>
<tr>
<td>Motor fluctuations and dyskinesias</td>
<td>Pergolide, pramipexole, ropinirole, entacapone, tolcapone, amantadine</td>
</tr>
<tr>
<td>Psychosis</td>
<td>Clozapine</td>
</tr>
<tr>
<td>Prevention of motor complications in levodopa-naive patients</td>
<td>Cabergoline, pramipexole, ropinirole</td>
</tr>
</tbody>
</table>

Efficacious interventions showed a positive effect on studied outcomes based on data from ≥ 1 high-quality RCT and had no conflicting data from other RCTs.

The most solid evidence in this review is the labeling of interventions as non efficacious. Controlled-release levodopa does not prevent motor complications, which further supports the complementary observation that dopamine agonists delay the onset of such complications.

The analysis does not deal with dopamine agonists as a group but evaluates individual studies of each drug. The clinical use of dopamine agonists spans more than 30 years, but most of the older studies were not RCTs. Thus, insufficient evidence exists for the use of apomorphine (the only dopamine agonist with a potency similar to that of levodopa) as monotherapy, although the same drug is considered a likely efficacious adjunct to levodopa.

Finally, off-period motor fluctuations and on-period dyskinesias were considered together as “motor complications,” although they have different pathophysiology (3) and require different clinical interventions.

Alberto Albanese, MD
Istituto Nazionale Neurologico Carlo Besta
Milano, Italy

**References**