

Review: Catechol O-methyl transferase inhibitors plus L-dopa and some surgical interventions improve Parkinson disease symptoms

Levine CB, Fahrbach KR, Siderowf AD, et al. **Diagnosis and treatment of Parkinson's disease: a systematic review of the literature.** *Evid Rep Technol Assess (Summ)*. 2003 May;(57):1-4.

QUESTION

Do pharmacologic, surgical, psychiatric, or ancillary interventions improve symptoms in patients with early or advanced Parkinson disease (PD)?

DATA SOURCES

Studies were identified by searching MEDLINE (1990 to 2000), the Cochrane Library, Current Contents, the reference lists of included studies and recent review articles, and Internet web sites.

STUDY SELECTION AND ASSESSMENT

Studies were selected if they were randomized controlled trials (RCTs) of pharmacologic (dopamine agonists [DAs] plus L-dopa, selegiline plus L-dopa, or catechol O-methyl transferase [COMT] inhibitors plus L-dopa vs L-dopa alone), psychiatric (piracetam or citalopram vs placebo), surgical (pallidotomy, deep brain stimulation [DBS], and fetal cell transplantation), or ancillary (physiotherapy, speech or language therapy, and rehabilitation) interventions; were published in English; and had ≥ 10 patients.

OUTCOMES

Main pharmacologic outcomes were standardized mean change scores on the Unified Parkinson Disease Rating Scale (UPDRS).

Outcomes in surgery trials were measured for "on" time (dyskinesia present) or "off" time (dyskinesia absent) scores on the UPDRS.

MAIN RESULTS

68 RCTs met the inclusion criteria. Meta-analyses were done on 17 pharmacologic RCTs using random-effects models. 2 psychiatric trials compared citalopram (1 trial) and piracetam (1 trial) with placebo. 4 surgical trials compared the association with "on" or "off" time scores. 13 trials evaluated ancillary interventions. More patients with advanced PD had improved symptoms on L-dopa plus COMT inhibitor in the short term (≤ 7 mo) compared with L-dopa alone (Table). DA plus L-dopa or selegiline plus L-dopa groups did not differ for improvement in PD symptoms (Table). Adverse events, including dizziness, dyskinesia, and PD aggravation, were more common in advanced PD. Piracetam

did not reduce intellectual impairment or improve motor or cognitive function, and citalopram did not reduce major depression. DBS and fetal cell transplantation reduced "on" scores ($P < 0.05$) but not "off" scores ($P > 0.05$), and pallidotomy did not reduce either type of score. Evaluation of ancillary treatments was hampered by poor-quality studies.

CONCLUSIONS

In patients with advanced Parkinson disease, catechol O-methyl transferase inhibitors improve symptoms, and deep brain stimulation and fetal cell transplantation reduce "on" scores.

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Dopamine agonists (DAs), selegiline, or COMT inhibitors plus L-dopa vs L-dopa alone for improvement of Parkinson disease symptoms at 3 to 60 months†

Intervention	Number of trials	Comparisons	Standardized mean difference (95% CI)‡
Pharmacologic	17	DA + L-dopa vs L-dopa alone	0.16 (-0.016 to 0.34)
	5	Selegiline + L-dopa vs L-dopa alone	0.47 (-0.021 to 0.96)
	5	COMT inhibitor + L-dopa vs L-dopa alone	0.33 (0.22 to 0.44)

†COMT = catechol O-methyl transferase. CIs calculated from data in article using random-effects model.

‡A positive effect size indicates improvement.

COMMENTARY

The systematic review by Levine and colleagues reviewed current PD treatment, including pharmacologic, physiotherapeutic, surgical, and psychiatric interventions.

Although the authors reviewed a substantial amount of data, the literature search only included studies up to December 2000. Several studies in the use of DAs for the treatment of PD have since been published.

The review methodology is well explained, and the inclusion of studies seems reasonable. It is important to note that the studies included medications that are available in Europe and not just in North America. Pharmacologic treatment was categorized for early and advanced PD, including monotherapy and combined therapy of DAs plus L-dopa. Unfortunately, studies on DAs plus L-dopa within the past 3 years were not included in this meta-analysis. This is important because the recent studies investigating new DAs have shown the possibility of substantial reduction in motor fluctuations (1). In addition, some evidence exists that early use of DAs has neuroprotective effects, which is important for clinicians who are starting therapy in patients with PD.

High-quality studies of surgical interventions are more limited, and most of the data addressed pallidotomy and thalamotomy. Few strong studies of DBS exist, which makes it difficult for clinicians to decide which of these procedures is optimum. Information is even more limited for physical therapy interventions and speech therapy.

At present, the treatment options for PD are well established. DAs are valuable for early treatment and as adjunct treatment with COMT inhibitors and L-dopa. Surgical interventions are leaning toward DBS rather than lesioning. Allied health therapies have yet to be studied in detail to determine their efficacy.

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Reference

1. Management of Parkinson's disease: an evidence-based review. *Mov Disord*. 2002;17 Suppl 4:S1-166.