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## [Intervention Review]

# Dopamine agonist therapy in early Parkinson's disease

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# ABSTRACT

## Background

Dopamine agonists are being used increasingly as first line treatment for Parkinson's disease, but there remains uncertainty about their clinical and cost-effectiveness relative to levodopa.

## Objectives

This meta-analysis aims to quantify more reliably the benefits and risks of dopamine agonists compared to placebo or levodopa in early Parkinson's disease.

## Search methods

We searched CENTRAL (*The Cochrane Library*), MEDLINE, EMBASE, PubMed, LILACS and Web of Science, plus major journals in the field, abstract books, conference proceedings and reference lists of retrieved publications.

#### **Selection criteria**

Randomised trials comparing an orally administered dopamine agonist (with or without levodopa) versus placebo or levodopa or both placebo and levodopa in participants with early Parkinson's disease.

## Data collection and analysis

Two authors independently extracted data on clinician-rated disability, motor complications, other side-effects, treatment concordance, levodopa dose and mortality.

## **Main results**

Twenty-nine eligible trials, involving 5247 participants, were identified. Participants randomised to a dopamine agonist were less likely to develop dyskinesia (odds ratio (OR) 0.51, 95% confidence interval (CI) 0.43 to 0.59; P < 0.00001), dystonia (OR 0.64, 95% CI 0.51 to 0.81; P = 0.0002) and motor fluctuations (OR 0.75, 95% CI 0.63 to 0.90; P = 0.002) than levodopa-treated participants. However, various 'non-motor' side-effects, including oedema (OR 3.68, 95% CI 2.62 to 5.18; P < 0.00001), somnolence (OR 1.49, 95% CI 1.12 to 2.00; P = 0.007), constipation (OR 1.59, 95% CI 1.11 to 2.28; P = 0.01), dizziness (OR 1.45, 95% CI 1.09 to 1.92; P = 0.01), hallucinations (OR 1.69, 95% CI 1.13 to 2.52; P = 0.01) and nausea (OR 1.32, 95% CI 1.05 to 1.66; P = 0.02) were all increased in agonist-treated participants (compared with levodopa-



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treated participants). Agonist-treated participants were also significantly more likely to discontinue treatment due to adverse events (OR 2.49, 95% CI 2.08 to 2.98; P < 0.00001). Finally symptomatic control of Parkinson's disease was better with levodopa than with agonists, but data were reported too inconsistently and incompletely to meta-analyse.

#### Authors' conclusions

This meta-analysis confirms that motor complications are reduced with dopamine agonists compared to levodopa, but also establishes that other important side-effects are increased and symptom control is poorer with agonists. Larger, long-term comparative trials assessing patient-rated quality of life are needed to assess more reliably the balance of benefits and risks of dopamine agonists compared to levodopa.

## PLAIN LANGUAGE SUMMARY

### Dopamine agonist therapy in early Parkinson's disease

This 'umbrella' meta-analysis assesses dopamine agonists as a drug class in early Parkinson's disease. Twenty-nine eligible trials, involving 5247 participants, were identified. It confirms reports from individual trials that motor complications are reduced with dopamine agonists compared to levodopa, but also demonstrates that other important side-effects are increased and symptom control is poorer with agonists. Unfortunately, the balance of risks and benefits remains unclear highlighting the need for further studies assessing patient-rated overall quality of life and economic measures as their primary outcomes.