Review: Anticholinergic drugs improve motor function and disability in Parkinson disease

Katzenschlager R, Sampaio C, Costa J, Lees A. **Anticholinergics for symptomatic management of Parkinson's disease (Cochrane Review).** Cochrane Database Syst Rev. 2003;(2):CD003735.

QUESTION

In patients with Parkinson disease (PD), are anticholinergic (ACN) drugs more effective than placebo or no treatment for improving parkinsonian symptoms and disability?

DATA SOURCES

Studies were identified by searching the Cochrane Controlled Trials Register (up to 2001), MEDLINE (1966 to 2001), Old MEDLINE (1960 to 1965), and Index Medicus (1927 to 1959); and reviewing bibliographies of relevant articles, other reviews, and book chapters.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) that compared marketed ACN drugs with placebo or no treatment and measured relevant outcomes in patients with a clinical diagnosis of idiopathic PD (de novo or receiving other antiparkinsonian treatment).

DATA EXTRACTION

Data were independently extracted by 2 reviewers on sample size, patient characteristics, disease duration and severity, concomitant medication, details of the intervention, and outcomes. Outcomes included changes in global scores of impairment and disability; changes in scores for tremor, rigidity, and bradykinesia; withdrawals due to lack of efficacy and adverse effects; and rates of neuropsychiatric and cognitive adverse effects.

MAIN RESULTS

9 RCTs (221 patients) met the selection criteria. ACN drugs were all compared with placebo in a crossover design and included bornaprine (3 RCTs), benzhexol (2 RCTs), orphenadrine (1 RCT), benztropine (1 RCT), benapryzine (1 RCT), and methixine (1 RCT). Outcome measures varied widely across studies; some scales designed by the investigators lacked detailed definitions. In 5 RCTs eligible for formal comparison, improvement in motor function and disability was greater in the ACN group than in the placebo group, based on the following: disability score (1 RCT); tremor on a 5-item scale (1 RCT); Webster scale, handwriting, drawing, and accelerometry (1 RCT); "all-round assessment of efficacy" by investigators and patients (1 RCT); and investigators' and patients' overall impression and a number of poorly defined motor function tests, including speed, coordination, and gait (1 RCT) (all P values < 0.05). 8 of 9 RCTs also reported a statistically significant improvement from baseline in ≥ 1 motor function or activity of daily living in the ACN group (all P values < 0.05).

CONCLUSION

In patients with Parkinson disease, anticholinergic drugs are more effective than placebo for improving motor function and disability.

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COMMENTARY

The review by Katzenschlager and colleagues reminds us that most of what we do in medicine is based on nonrandomized studies and clinical experience. The included RCTs are old, heterogeneous, and of such poor quality that only limited conclusions can be drawn. What can be concluded from these studies is that ACN agents are probably better than placebo in the short-term treatment of certain motor features in PD and are associated with more side effects (primarily neuropsychiatric).

The most recent RCT included in the review was published 17 years ago, and the management options in treating PD have changed dramatically since—newer-generation dopamine agonists (pramipexole and ropinirole), catechol-0-methyl-transferase inhibitors (entacapone), and expanding brain surgery options are now available. Yet many patients continue to be treated with ACN agents, and nearly 10% of patients in early PD trials are receiving ACN agents (1). Why?

In clinical practice, patients sometimes show dramatic reduction in severity of parkinsonian tremor after receiving ACN agents. Furthermore, single-dose studies have shown a predominant effect of ACN agents on tremor (2). However, ACN agents seem to have less effect on rigidity and bradykinesia, symptoms that are often more responsive to levodopa.

A concern for ACN agents is their side effects, including dry mouth, nausea, vomiting, constipation, sedation, blurred vision, urine retention, tachycardia, visual hallucinations, and invariably mental status changes with higher dosages. These agents are contraindicated in patients with closed-angle glaucoma. In addition, long-term use of ACN medications can increase Alzheimer disease pathology in patients with PD (3).

Most patients with PD can be managed without ACN agents, but if one chooses to use them, they should be used primarily to treat troubling parkinsonian tremor, either as initial treatment or if tremor continues to be bothersome despite dopaminergic therapy. They should be used cautiously. Doses should be increased slowly, and patients should be informed of the side effects. These drugs are best reserved for relatively young patients with early disease and no significant comorbid conditions. Finally, there are no data to support 1 ACN agent over another, and therefore, the physician should become familiar with the use of 1 or 2 of the available agents.

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