COCHRANE PRIMARY HEALTH CARE FIELD

PEARLS Practical Evidence About Real Life Situations

Balance of risks and benefits unclear for dopamine agonist therapy in early Parkinson's disease

Clinical question	Compared to placebo or levodopa, how effective and safe are dopamine agonists (DAs) in early Parkinson's disease (PD)?
Bottom line	Compared to placebo or levodopa, DAs reduce motor complications (dystonia, dyskinesia and motor fluctuations) in patients with early PD[1]. However, symptom control is poorer with DAs, and 'non-motor' side-effects are increased (oedema, somnolence, constipation, dizziness, hallucinations, nausea and headaches). Patients on a DA were more than twice as likely to discontinue treatment prematurely due to adverse effects than control patients, suggesting that the 'non-motor' side-effects were of sufficient severity to have a meaningful impact on patient's quality of life and were perhaps at least as clinically important as the motor complications.
Caveat	Unfortunately the balance of risks and benefits remains unclear, as only one trial included overall quality of life and cost-effectiveness as outcome measures. Larger, long-term comparative trials assessing patient-rated quality of life are needed to assess more reliably the balance of benefits and risks of DAs compared to levodopa. It is also important that cost-effectiveness is assessed, as there is a need for better evidence on the cost-effectiveness of the considerably more expensive DAs.
Context	Parkinson's disease is a progressive disorder affecting over six million people worldwide, making it the most common neurodegenerative disease after Alzheimer's disease[2]. In the absence of curative therapy, treatment is directed towards alleviating the characteristic symptoms of PD such as bradykinesia, tremor, rigidity and postural instability[3]. Levodopa combined with a peripheral dopa-decarboxylase inhibitor provides effective symptomatic control. However, long-term levodopa use is associated with the development of motor complications such as involuntary movements (dyskinesia) and motor fluctuations ('wearing-off' phenomenon and unpredictable 'on-off' fluctuations). Since levodopa was introduced in the 1960s, two other drug classes have also become widely used[4]. These are dopamine agonists and monoamine oxidase type B inhibitors (MAOBIs) and are used either alone (as first-line treatment) or in

	combination with levodopa, in an attempt to control symptoms or delay the onset of motor complications or both in early PD.
Cochrane Systematic Review	1. Stowe RL et al. **Dopamine agonist therapy in early Parkinson's disease.** Cochrane Reviews 2008, Issue 2. Art. No.: CD006564. DOI: 10.1002/14651858.CD006564.pub2. This review contains 29 trials involving 5,247 participants. 2. Schapira AH. BMJ 1999 ;318 :311-314. 3. Clarke CE. Neurology, Neurosurgery and Psychiatry. 2002 ;72 :122-127. 4. Quinn NP. Baillieres Clinical Neurology 1997 ;6 :1-13.
Pearls No. 72 May 2008 (Brian R McAvoy)	