

DEBATE: ALL PD PATIENTS SHOULD START WITH LEVODOPA AND GO SLOW – NO

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When used for the treatment of Parkinson's Disease (PD) levodopa is the drug associated with most favorable outcomes and often associated with better quality of life (1). Despite this superiority of levodopa, starting the treatment of PD with dopamine agonists comes with some advantages. Several randomized controlled studies showed that wearing-off phenomenon and peak-dose dyskinesia are less frequent and appears later, in patients who were given a dopamine agonist from the start, when compared with the patients who were given levodopa from the start (2, 3). This benefit of having less frequent wearing off phenomenon and peak dose dyskinesia persists even when levodopa is added to the dopamine agonist group as soon as it was symptomatically needed, and reported to last as long as six years (4). In every study which found dopamine agonists superior in terms of above-mentioned motor complications, patients in levodopa groups had better symptomatic control (mostly measured by UPDRS Part 2 and/or 3). Keeping this in mind, if you first begin with dopamine agonists (protecting the patients from motor complications), and then add levodopa as soon as it is symptomatically needed (as it was performed in some studies, protecting the patients from worse symptomatic control) one can take advantage of both drug types.

CALM PD study compares the patients groups in whom either pramipexole or levodopa were chosen as the initial treatment, and though overall dyskinesia rates were reduced in the pramipexole group, the frequency of disabling dyskinesias were similar in both groups (4). There are no other studies comparing the groups in terms of disabling dyskinesias.

Some studies report peak dose dyskinesia contributing poor quality of life, and some do not (5). It may be fair to follow a policy of not to fear from dyskinesias, unless they are troublesome, since it is well-known that many patients prefer mild to moderate dyskinesia over being off (6). But when it comes to wearing off, it is really disabling, it is proven to cause poor quality of life, and it is frequent (up to 50% after two years of levodopa treatment for some studies), so every effort to prevent the patients from wearing off phenomenon (and to postpone it) seems worthwhile (7, 8, 9). To initiate the treatment with dopamine agonists (as opposed to levodopa) decreases the frequency and postpones the emergence of wearing off phenomenon. This may surmount risks of exposing the patients to awkward neuropsychiatric side-effects of dopamin agonists, which may already be infrequent in early stages.

Another option in the treatment of PD as an initial treatment, especially in the early stages of the disease is MAO-B inhibitors. Rasagiline is effective, safe, and easy to use in the beginning of the disease (10, 11). There is also quite an evidence that rasagiline may slow down the progression of the PD (10, 11).

It is well known that patient compliance is better (which leads to better symptomatic control) with once-daily drugs, which is the case for rasagiline, and most dopamine agonists (12).

Based on the data summarized above it seems wise to begin treatment with an MAO-B inhibitor, switch to a dopamine agonist as soon as it is needed, and then switch to levodopa as soon as it is needed.

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