

WHICH IS THE BETTER DOPAMINOMIMETIC THERAPY IN PD? TRANSDERMAL Angelo Antonini

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Rotigotine is a potent DA that differs from other marketed molecules in its pharmacological activity, and, given the transdermal route of administration, also in its pharmacokinetics. Its pharmacological activity is broader as it stimulates all the dopamine receptor subtypes: it is an agonist of D2 and D3 receptors that also acts on D1, D4 and D5 receptors, at the same time stimulating 5-HT1A receptors and blocking alpha-2B adrenergic receptors. It has no effect on 5-HT2B receptors. It is believed that rotigotine exerts its beneficial effects in PD through the activation of D3, D2 and D1 receptors in the caudate-putamen complex in the brain. Rotigotine, which is administered as an adhesive transdermal patch, results in plasma concentrations that are flat and stable over 24 hours. Analysis of blood samples drawn before and one hour after patch replacement from 142 patients with advanced PD on treatment with rotigotine (up to 16mg/24h), studied during the titration period and later during the 16-week maintenance period, showed that rotigotine levels (unconjugated rotigotine measured by validated liquid chromatography with tandem mass spectrometry) did not exhibit any major fluctuations due to patch replacement and remained stable throughout the four-month maintenance phase. In the subgroup of 27 patients in whom rotigotine was titrated up to 16 mg/24h, a dose-proportional increase in rotigotine plasma concentrations was recorded during titration. Dose proportionality was not influenced by gender or age, making plasma concentrations highly predictable. Thus, the rotigotine patch offers the advantage of stable and predictable plasma levels, reducing pulsatile stimulation of dopamine receptors. In addition, pharmacokinetic studies have shown that, unlike pramipexole, the dosage of rotigotine does not have to be adjusted in patients with impaired renal function.

It has proven to be particularly effective in controlling early morning hypo- and akinesia, possibly as a consequence of continuous and predictable transdermal drug delivery for 24 hours, which reduces the pulsatile dopamine receptor stimulation associated with intermittent oral administration. This feature of the drug makes it particularly suitable for the management of motor complications. It also raises the hope that providing stable dopaminergic stimulation from the beginning of the disease may reduce the supposed long-term effects of pulsatile stimulation.

Rotigotine has also proven to be effective in controlling non-motor symptoms, such as sleep and mood disturbances, anhedonia and pain. Its efficacy in controlling not only motor, but also non-motor symptoms results in significant improvement in health-related quality of life in PD patients.