Is the improvement of MAO-B-I clinically relevant?

László Vécsei

Special Issue on Controversies in Neurology: From the 10th World Congress on Controversies in Neurology (CONy), Lisbon, Portugal. 17–20 March 2016.

Abstract

Point of view: Yes

Selegiline is a selective, irreversible MAO-B inhibitor at therapeutic dose of 10 mg/day, but loses its selectivity at greatered dosage. The potential of selegiline to modify disease progression in PD was proposed when it was shown to prevent MPTP-induced parkinsonism in monkeys. There is no conclusive evidence from clinical trials to prove that selegiline has „disease-modification” effects. Long term clinical trials of selegiline have shown improved motor outcome and reduced levodopa requirement. Whether these findings were attributed to the symptomatic benefits of the disease-modification property of selegiline remain debate. Unlike rasagiline in which delayed-start design trials were carried out in an attempt to separate confounding symptomatic effects from disease-modifying effects, there are none for selegiline. Rasagiline is a second generation propargylamine-based selective, irreversible MAO-B inhibitors. It was reported to have potent anti-apoptotic effects independent of MAO inhibition in in vitro and in vivo experimental parkinsonian models. Unlike selegiline, rasagiline is not metabolized to L-amphetamine-like metabolites which may cause appetite supression and insomnia. In the PRESTO study the Clinical Global Impression (CGI) and the UPDRS ADL scores during „off” time showed improvement as secondary end points, with both doses of rasagiline, but not with PD Quality of Life summary score. In the LARGO study, patients who had received rasagiline had statistically significant reduction of mean daily „off” time. Recent study supports the efficacy and safety of safinamide (oral aminoamide derivative with broad mechanism of action such as reversible MAO-B inhibition, blockage of voltage-dependent sodium channels, modulation of calcium channels and of glutamate release) as an adjunct to levodopa in PD patients with motor fluctuations. In earlier clinical studies, it was shown to improve motor control in patients with PD who received it as an add-on to dopamine agonist or as an adjunct to levodopa. The dual mechanism (reversible MAO-B inhibition and glutamate release inhibition) is belived responsible for the alleviation of motor symptoms of PD.

1University of Szeged, Department of Neurology and MTA-SZTE Neuroscience Research Group, Semmelweis str. 6, Szeged, 6725-Hungary
Correspondence: vecsei.laszlo@med.u-szeged.hu

Citation: Vécsei, L. Is the improvement of MAO-B-I clinically relevant?. International Journal of Clinical Neurosciences and Mental Health 2016; 3(Suppl 1):D65
Published: 16 March 2016