

WORSENING OF PARKINSONISM AFTER THE USE OF VERALIPRIDE FOR TREATMENT OF MENOPAUSE

Case report

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ABSTRACT - We describe a female patient with stable Parkinson's disease who has shown a marked worsening of her motor functions following therapy of menopause related symptoms with veralipride, as well as the improvement of her symptoms back to baseline after discontinuation of the drug. We emphasize the anti-dopaminergic effect of veralipride.

KEY WORDS: Parkinson's disease, menopause, veralipride.

Piora de parkinsonismo após uso de veraliprida para tratamento da menopausa: relato de caso

RESUMO - Relatamos o caso de uma paciente com doença de Parkinson idiopática em tratamento com levodopa, com boa evolução clínica, sem flutuações e discinesias, que apresentou piora acentuada do quadro clínico após utilização de veraliprida para tratamento de sintomas psicofuncionais da menopausa. Com a retirada da veraliprida ocorreu melhora do quadro clínico aos níveis prévios à introdução do fármaco. A ação antidopaminérgica da veraliprida é enfatizada.

PALAVRAS-CHAVE: doença de Parkinson, menopausa, veraliprida.

Secondary parkinsonism has been presenting a marked increase in its incidence, mainly as a consequence of increasing development and use of drugs with dopaminergic-blocking properties. In some countries, like Brazil, this group now represents the second leading cause of parkinsonian syndromes (PS)¹.

The antidopaminergic drugs most often related to PS are the calcium channel blockers, the neuroleptics and the anti-emetic drugs¹⁻⁴. These drugs are also reported to worsen motor symptoms when used in persons with stable idiopathic Parkinson's disease (IPD)¹⁻⁴.

We report a patient with stable IPD who developed a marked worsening of her motor function shortly after initiation of therapy with veralipride, as well as the improvement of her motor symptoms back to baseline after discontinuation of the aforementioned therapy.

CASE

A 59-year old female patient had a slowly progressive levodopa responsive PS that had initiated three years

earlier. Her right side was predominantly affected with rigidity, bradykinesia and rest tremor, in keeping with the diagnosis of IPD. Due to worsening climateric symptoms, she was started by her gynecologist on veralipride. She noticed a marked increase of her motor symptoms, and was examined by her neurologist. There was an obvious deterioration of her motor function, and her "on" period rating in the motor scale of the Unified Parkinson's Disease Rating Scale increased from 13 to 23.

Veralipride was then withdrawn, and after 30 days her motor function returned back to baseline without any other concomitant increase in her levodopa dosage.

DISCUSSION

The PS is characterized by the combination of at least two of the following signs: tremor, rigidity, bradykinesia and postural instability. Its most common cause is IPD¹⁻⁵.

In a large number of series, secondary parkinsonism represents the second most common cause¹⁻⁴. In Brazil, the studies of Cardoso et al.¹ and Herdoiza (personal communication) have found that the second leading cause of the syndrome was drug-

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induced parkinsonism (predominantly due to calcium-channel blockers). Similar results were reported by Errea-Abad et al and Kuzuhara^{2,3}. Commonly recognized drugs are the neuroleptics, the dopamine depletors and the anti-emetics¹⁻⁵. These drugs should generally be avoided in parkinsonian patients due to their anti-dopaminergic effects.

Other small series or case reports have suggested an increasing number of drugs as responsible for the development of PS or a worsening of the motor function in an already parkinsonian patient. Included in this category are frequently used drugs such as methyl dopa, verapamil, captopril, lithium, amiodarone, cimetidine, valproic acid, phenytoin and meperidine, among others¹⁻⁵.

Veralipride (N-[(1-allyl-2-pyrroli dinil)metil]-5-sulfamoyl-o-veratramida) is a substituted benzamide with an antidopaminergic action similar to neuroleptics, with a consequent elevation of prolactin levels⁶⁻⁸. The luteinizing and follicle-stimulating hormones have their serum levels reduced by veralipride, as a consequence of hyperprolactinaemia⁶. The central nervous system effects of veralipride, specially on the hypothalamus, are described as secondary to hyperprolactinaemia, either as a feedback in tubero-infundibular dopamine neurons or secondary to an opioid agonistic effect^{6,9}.

The recent increase in the use of veralipride is due to its generally well tolerated effect on menopause-related symptoms, as an alternative to hormonal therapy⁷⁻¹¹.

There is a small number of reports of a variety of veralipride-induced movement disorders in the medical literature, such as respiratory dyskinesias, tardive dystonia, parkinsonism and acute dyskinesias¹²⁻¹⁷.

The parkinsonian syndrome was described as a case report by Milandre et al. in 1991 and Franchignoni and Tesio in 1995^{15,16}. Masmoudi et al, in 1995, also reported on a parkinsonian syndrome, adding four other veralipride-induced dyskinesias¹⁷. Surprisingly, despite the paucity of reports, Llau et al. found in a pharmaco-vigilance center that among the drug-induced parkinsonian syndromes, 6% were related to veralipride⁴. Symptoms are reported to start either

early or late after initiation of therapy, and the discontinuation of therapy usually resolves the syndrome^{4,12-17}.

In the present report, we briefly describe a patient with an established diagnosis of IPD that had a marked worsening of her motor function induced by therapy with veralipride, as well as the improvement back to baseline after discontinuation.

We emphasize in this report the possibility of not only the development of a *de novo* parkinsonian syndrome, but the worsening of a previously stable IPD upon initiation of this commonly used drug.

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