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Vascular Parkinsonism: Motor and Non-Motor Response on Treatment with Rotigotine

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Abstract

To date dopaminergic therapy has shown unsatisfactory effect on vascular Parkinsonism symptoms and related disturbances. In this case series we describe the effect of rotigotine treatment in patients with subacute onset of Parkinson's like movement (3-6 months) after ischemic stroke of thalamus or internal capsule areas with concomitant leukoencephalopathy. Rotigotine treatment seems to improve both motor and cognitive symptoms of our sample; further studies are needed to clarify the effect of continuous dopaminergic stimulation on nigro-striatal functions in vascular patients with Parkinsonism like disturbances.

Keywords: Vascular Parkinsonism; Rotigotine; Dopaminergic therapy

Introduction

Vascular Parkinsonism (VP) is currently defined as a parkinsonian syndrome associated with vascular encephalopathy. It is very important to differentiate VP from Parkinson's disease because of prognostic and therapeutic options [1,2]. VP is characterized by postural instability and falls rather than bradykinesia and upper limb rest tremor these latter present in PD [3]. Furthermore, VP shows the absence of a clear correlation between clinical presentation, radiological features, degree of preservation of presynaptic dopaminergic function assessed by [^{123}I] FP-CIT SPECT and a good response to dopaminergic therapy [4,5]. Rotigotine is a non-ergoline dopamine agonist formulated in a silicone-based transdermal patch. The transdermal delivery system maintains a stable drug release profile allowing for a steady-state plasma concentration of rotigotine [6]. For this reason, given the capacity for continuous drug delivery it has been evaluated for management of motor complications in patients with VP. In this study we describe the clinical response to treatment with rotigotine on non-motor and motor symptoms in patients with VP.

Materials and Methods

In this cross-sectional study, we selected 13 patients (mean age 73.45 ± 6,05 years), who had a diagnosis of VP applying the criteria of Zijlmans et al. [2] and followed-up in the Movement Disorders Clinical Trials Center (San Raffaele Cassino, Italy). The patients showed subacute onset of Parkinson's-like movement (3-6 months) after ischemic stroke (thalamus or internal capsule areas) with concomitant finding of leukoencephalopathy detected by brain imaging Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). All patients also had neuropsychological alterations such as depression, apathy, impaired memory or attention. Exclusion criteria included orthopedic, rheumatologic or spinal cord disease responsible for impaired score during motor scales, past medical history of brain trauma or tumor, well documented visual abnormalities. At T0, considered as clinical onset of VP, it was carried out the NIH scale with scores between 2 and 8. They were then subjected to the following scales: Unified Parkinson's disease rating Scale (UPDRS sections I-III) [7], Beck Depression Inventory II (BDI-II) [8], the Neuropsychiatric Inventory (NPI) [9], Mini Mental State Examination (MMSE) [10], and Montreal Cognitive Assessment (MOCA) [11]. After clinical evaluation, all patients were treated with transdermal rotigotine (at baseline, 2 mg/24 h increased after 30 days to 4 mg/24 h), for a total of 12 months of treatment. Two patients were excluded to the study because reported skin reactions during the first month of treatment. The remaining 11 patients underwent the same evaluations as mentioned above, after 6 (T1) and 12 months (T2).

Statistics

Descriptive results for all continuous variables were reported as mean ± standard deviation (DS) (for normally distributed data) or median with range (for data not normally distributed). For comparisons between data a non-parametric Friedman's two-way analysis of variance by ranks for repeated measures test was performed. A p value <0.05 was considered significant. SPSS 21.0 statistical package was used for the analysis.

Results

We evaluated 13 patients (46.15% were male), who had a diagnosis of stroke in previous 6 months. The patients showed subacute onset of Parkinson's-like movement (3-6 months) after ischemic stroke (thalamus or internal capsule areas) with concomitant finding of leukoencephalopathy detected by brain imaging Computed Tomography (CT) or Magnetic Resonance Imaging (MRI). All patients also had neuropsychological alterations such as depression, apathy, impaired memory or attention.

At baseline, the MDS-UPDRS Part III score was 18 points (as median; min 8, max 25), MoCA score was 28 points (as median; min 25, max 30), MMSE score was 26.8 points (as median; min 25 max 29.1), NPI score was 3 points (as median; min 1 max 7) and BDI II score was 13 points (as median; min 8 max 20). All patients experienced an overall

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reduction in scores of sections I-III UPDRS at T1 and T2 respect to T0 scores ($p<0.005$). Regard to the cognitive response, the MMSE and MoCA not showed a significant improvement of the scores at both T1 and T2 respect to T0. In NPI we observed a scores reduction at time T1 and T2 ($p<0.05$). Furthermore, a significant change in the BDI-II was observed in T1 and T2 respect to T0 scores ($p<0.005$).

Discussion

In our study, the clinical response to dopaminergic treatment with transdermal rotigotine showed a significant improvement in symptoms of motor and non-motor sphere in patients with VP. Previous studies reported poorly response to L-dopa in only one-fifth of the patients with VP or a transient response to treatment in only 38 % of the patients [12,13]. On the other hand, Zijlmans et al. had shown a good response to L-dopa in VP principally in patients with macroscopic infarcts or lacunae caused by enlarged perivascular species in the basal ganglia or lesions close to nigrostriatal pathway [14]. Rotigotine is a potent agonist at dopamine D1 receptors as well as at dopamine D2 and D3 receptors but shows a lower potency at D4 and D5 receptors [15]. Rotigotine represents a new drug with a good efficacy and tolerability used as transdermal patch in patients with early (in monotherapy) or advanced (in combination with levodopa) PD and also in restless legs syndrome [16-18]. The transdermal delivery of rotigotine allows obtaining continuous dopaminergic stimulation during 24 h which in turn leads to continuous receptor stimulation thus miming physiological nigrostriatal function.

Conclusion

Even though it is an open label, non-randomized and consists of a small sample not controlled, it is interesting to note that the dopaminergic treatment with transdermal dopamino-agonist rotigotine seems to possess extreme rational, despite the pharmacological management of these patients remain in part conditioned by personal experience.

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