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IMPORTANCE OF INFLAMMATORY MARKERS IN THE EVOLUTION OF PARKINSON DISEASE PATIENTS WITH DEVICE AIDED THERAPIES (MINI-SERIES OF CASES)

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ABSTRACT

Parkinson disease (PD) is a neurodegenerative movement disorder. Beginning with Braak's theory that hypothesized a connection between gut, inflammation, and substantia nigra degeneration, many studies were made to put a link between inflammatory bowel disease and P D. We studied several patients with advanced PD, submitted in our Neurology Center, between July and September 2022 for initiation of device aided therapy with intestinal gel that fulfilled the admission criteria. We took under consideration the demographic data, UPDRS motor part III, ADL and IADL scales at day 1, after discharge and after 3 months. We provided biological analysis for D-Dimers, Fibrinogen, C Reactive Protein, ESR, and we compared the values from the 1st day of hospitalization and after 3 months; fecal samples were collected to evaluate the presence and the levels of fecal calprotectin (FC). In more than 60% of the cases, fecal calprotectin was higher than 100 ug/g (5 times normal), 80% more than 400, 20% more than 1000 ug/g, associating with modified inflammatory marks and clinical evaluation scores with no significant improvement in motor abilities in 3 months after discharge. In only 2 cases where calprotectin was below 22, there was a positive evolution in UPDRS motor part III score from 52 to 36 and from 29 to 21(from day 1 and after 3 months), alongside with 2 points in ADL, IADL scales. Inflammation biomarkers and fecal calprotectin in high ranges seem to associate difficulties in obtaining a good therapeutical response in advanced PD stages.

Keywords: parkinson disease, inflammatory markers, fecal calprotectin

Introduction

The researchers' aim and desire for progress in medicine is based on a passion for knowledge, understanding of pathophysiological mechanisms to optimise therapeutic schemes. Dopamine (happiness hormone) is one of the main neurotransmitters in the nervous system, responsible for feelings of contentment, happiness and joy. Some patients develop neurodegenerative disorders, in particular Parkinson's disease, defined by the loss of dopaminergic neurons, with the formation of Lewy bodies and the accumulation in the substantia nigra of a protein called Alpha Syn Nuclein (1).

All the definitions cited in the literature point to a chronic, disabling, multifactorial neurodegenerative pathology (PD) with important psychosocial consequences for the patient. involves multisystemic (dopaminergic, cholinergic, noradrenergic and serotonergic) damage. has a genetic susceptibility of approximately 10%. Onset is frequently insidious, generally unilateral, with bilateral involvement as it progresses. Overriding symptoms are often motor (bradykinesia, postural tremor, extrapyramidal rigidity) but also non-motor (intestinal transit disturbance, dysphagia, nocturnal rhythm distress, depression, cognitive dysfunction) (2, 3). As known by now,

there have been a serial of interesting studies and research done in the aim of achieving the best possible knowledge for better understanding the etiology, progression, and evolution of Parkinson's (2). Beginning with Braak's theory that hypothesized a connection between gut, inflammation, and substantia nigra degeneration starting from olfactory tracts, many studies were made to put a link between inflammatory bowel disease and P D (4, 5). But what if there was a connection between the microbiota and the clinical evolution of these incurable patients that experience advanced assisted therapy? Could this be a particular finding that can provide better treatment management and outcome for Parkinson's patients? (6, 7).

Objectives

The purpose of our study is to demonstrate a possible correlation between the values of several inflammation biomarkers, faecal calprotectin, and the therapy response in a series of cases of advanced PD patients treated with Levodopa-Carbidopa vs Levodopa-Carbidopa-Entacapone intestinal gel.

Material and MEthods

In this study participate all the patients (8) with PD submitted in the Neurology Clinic of "Saint Andrew" Clinical County Emergency Hospital of Constanta, for initiating advanced assisted treatment with Levo Dopa- Carbidopa (Duo Dopa) and Levo Dopa- Carbidopa-Entacapone (Lecigon) intestinal gel, that fulfil the admission criteria. Study inclusion period July-September 2022. We performed biological analysis of the peripheral blood count of some inflammatory markers such as: D-Dimers, Fibrinogen, C Reactive Protein, ESR, and we compare the values from the 1st day of hospitalisation and after 3 months; we collected faecal samples in sterile containers to evaluate the presence and the levels of faecal calprotectin. As for the clinical evaluation of the subjects we note the following: the demographic data, UPDRS motor part III, ADL and IADL assessment tools at day 1, after discharge and after 3 months.

Study inclusion criteria: a) patients from Dobrogea belonging to the University Centre of Constanta, diagnosed with Parkinson's Disease; b) patients who do not follow chronic treatment with NSAIDs; c) patients with preserved cognitive status or mild cognitive decline (Mild Cognitive Disorder); d) patients eligible for device-assisted therapy who have tolerated the PEG-J device probe fitting.

Study exclusion criteria: a) patients with Parkinson's disease previously diagnosed with inflammatory bowel disease; b) patients who are non-collaborative or unable to travel; c) patients who we are unable to monitor during the study in terms of compliance with the treatment regimen (no relatives, no contact details); d) patients whose family has refused to include the patient's personal data in the medical study; e) patients with gastric/ intestinal neoplasm/ recent surgery/ septic condition.

Results

We evaluated 8 urban patients. A total of 6 patients received treatment with LECIGON, the remaining 2 with DUO DOPA. Over 60% had faecal calprotectin values above 100 (5 x normal reference value), 80% of them above 400.

In all cases, inflammatory markers were altered and the clinical neurologic evaluation 3 months after discharge did not reveal significant improvements in activities of daily living, reduction of 'on' periods or improvement of non-motor symptoms. Only in two cases, in which the faecal calprotectin values were below the threshold value of 22, the UPDRS- part III motor score changed significantly from 52 points to 36 points, associating 2 points increase in the ADL and IADL scales (both at discharge and 3 months after). Patients who benefited from Lecigon triple therapy had an overall better clinical and biological outcome than those who received the DUO DOPA device. Overall, these patients have a much-improved life expectancy, with a therapeutic regimen adapted to their daily needs, compared to the classical oral drug treatment.

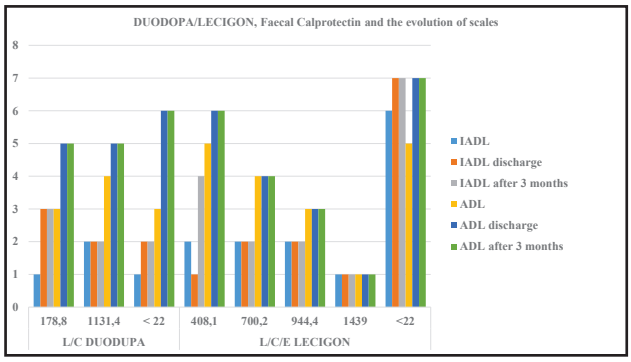

Figure 1: correlations between the types of intestinal gel, the improvement of the patient's evaluation scales and the values of faecal calprotectin determinations.

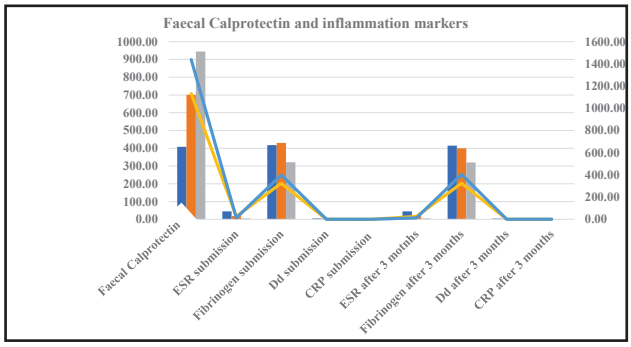

Figure 2 association between the results of the calprotectin samples and the inflammatory markers.

Discussions and Conclusions

We can support the idea that calprotectin values above 950 ug/g (3 cases) may be associated with difficulties in obtaining a rapid favorable response to state-of-the-art therapy, requiring repeated dose adjustments for optimized management. This paper is a review of clinical experience in the use of intestinal gel therapy in medical practice in patients with advanced stages of PD.

We also aimed to emphasize the efficacy of this therapy by reducing on/off periods and postural rigidity. It is important to mention that patients received prophylactic antibiotic treatment prior to PEG J device fitting.

All patients were responsive to treatment with levo-dopa, being ideal candidates for device-assisted therapy, as they had motor complications, fluctuating on-off periods on oral drug therapy (often modified during the course of the disease). Continuous infusion (morning dose, continuous dose, and extra dose) of intestinal gel with levodopa still reduced the range of rigidity, with increased quality of life, except for one case with fecal calprotectin values above 1400 ug/g.

Further studies and a larger number of patients are needed to determine a cutoff point of the fecal calprotectin value that would associate an unfavorable prognosis and a real impediment in the favorable outcome of the causes.

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