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Evaluation of a Single Center on the Efficacy of Percutaneous Endoscopic Gastro-Jejunostomy (PEG/J) in the Therapy of Parkinson's Disease with Levodopa-Carbidopa Intestinal Gel, From the Experimental Phase to Today.

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ABSTRACT

BACKGROUND**:** The aim of this study is to evaluate the results obtained in terms of efficacy, safety, and complication rates, in the treatment of patients with Parkinson's disease, after the creation of a Percutaneous Endoscopic Gastro-Jejunostomy (PEG-J), with Levodopa/Carbidopa Intestinal Gel.

METHODS**:** We report the experience of our center, from the experimental phase performed from 2009 to 2011, and until today, using the "Pull-string Ponsky-Gauderer type gastrostomy" technique.

RESULTS**:** Since the experimental phase we have observed immediate relief of symptoms in all patients. We had no intraoperative complications, while at a distance, in the experimental phase, we had a case of pressure injuries at the gastric level and a case of severe inflammation of the stoma. In the following years we detected four cases of ostomy inflammation and only one case of bumper incarceration syndrome.

CONCLUSIONS**:** Regarding the technique, PEG/J proved to be safe both in the short and long term, with a very low complication rate: the effectiveness of Levodopa Gel therapy, in our opinion, is important, both for the rapidity of the response to symptoms and on patient compliance.

Keywords: Parkinson's disease; Endoscopy; PEG/J; Levodopa gel.

Introduction

The degeneration of Central Nervous System (CNS) cells, and in particular those found in the "substantia nigra", which normally produce dopamine, is the cause of one of the most common neurological disorders, Parkinson's disease. Drug treatment at the initial stage of the disease, when the symptoms may still disappear, is carried out with the administration of Levodopa in tablets. In the advanced stage of Parkinson's, conventional therapy can become inadequate, and hardly manages to obtain sufficient results to control the symptoms, mainly due to a worsening of neuronal degeneration[1-3]; moreover, in cases where these patients have a slowed gastric emptying, the absorption of Levodopa is significantly impaired. Considering this last consideration, in 2008 an international experimental study N. S187-3-004, was launched entitled “An Open-Label, 12-Month Safety and Efficacy Study of Levodopa-Carbidopa Intestinal Gel in Levodopa-Responsive Subjects with Advanced Parkinson's Disease and Severe Motor Fluctuations Despite Optimized Treatment with Available Parkinson's Disease Medications”. The study was conducted in 83 centers, including ours, in 16 countries around the world, with a duration of 4.5 years and a deadline of June 2012. The Study was a multicenter, open-label phase 3 study, the primary objective of this study was to evaluate the safety and long-term tolerability of Levodopa-Carbidopa Intestinal Gel (LCIG) over 12 months in subjects with advanced, levodopa-responsive Parkinson's disease (PD)[4]. with severe motor fluctuations, despite optimized treatment with available PD drugs. After this experimental phase, our experience has continued over the years, both in the first PEG/J plant and in the replacements over time.

Materials and Methods

The role of our Endoscopic Surgery center has been, both in the experimental phase and in the following one, to evaluate the effectiveness and compliance of PEG/J over time, observing any immediate and late complications. Literature data show a morbidity rate after PEG which varies between 4% and 25%, while mortality is about 1%[5-9]. In the experimental phase 12 patients were enrolled in the period from November 2009 to November 2011: 11 men and 1 female, with a mean age of 69 years (range 55-80). All patients suffered from an advanced form of Parkinson's disease and were already on oral levodopa therapy. After the 28-day screening phase, enrolled patients were placed with a nasodijunal (NJ) tube, for a duration of 14 days, during which Levodopa Gel was administered via an infusion pump. In this phase, the efficacy of the therapy was determined, and a psychological evaluation was carried out aimed at identifying the psycho-physical conditions of the patients, to confirm compliance and complete conviction to participate in the experimental study, all candidates were subjected to an esophagogastroduodenoscopy to exclude any pathologies of this

tract. Only one patient was considered unfit for the PEG/J procedure, because he had hemorrhagic erosive gastritis; however, subsequently inserted into the protocol after a 4-month treatment, using a therapy with proton pump inhibitors, and after the complete healing of erosive gastritis. Before the placement of the PEG / J, an evaluation was also made of the possible ethical and medico-legal problems of the procedure, which represent an important topic in the international literature, certainly the clinical conditions of patients with advanced Parkinson's justify its use of this procedure.

All procedures for the packaging of PEG/J were performed in the operating room under general anesthesia and the surgical technique used was the "Ponsky-Gauderer type gastrostomy"[10-12]. With the "pull technique", first a gastrostomy was prepared and then the jejunal catheter was inserted into the stomach through the PEG and carried with the endoscope and a foreign body forceps, through the pylorus, up to the third duodenal portion. In all subsequent years to date we have performed the same procedure.

Results

Both in the experimental phase and subsequently, the procedure for packaging PEG/J has always been successful, without intraoperative complications. With this technique all patients had the opportunity to immediately start therapy with Levodopa Gel and showed rapid and lasting clinical improvement. The long-term complications, in the experimental phase, were a case of pressure injuries at the gastric level, which resulted in the removal of only the jejunal catheter that was made of particularly rigid material, and replacement of the same, after healing the lesions, with another softer, and a case of severe inflammation of the stoma that was treated conservatively. From the experimental phase and until today, we have performed this method both as a first implant and for the subsequent replacement, in about 54 patients, in whom we have detected four cases of stomatitis and only one case of bumper incarceration syndrome. In all cases treated to date, the average time for PEG/J replacement was 12 months.

Discussion

With this retrospective study of our center, we have tried to analyze all patients, with severe Parkinson's disease, to whom in recent years we have packaged a PEG/J for the continuous administration of Levodopa/Carbidopa Intestinal Gel[13-14]. We focused in particular on the endoscopic-surgical method and on the effectiveness of this new route of drug administration, noting all the pros and cons of an invasive technique and the success of drug administration on the symptoms of the disease. As regards the issue of ethical evaluation of the procedure, the literature data refer only to the use of PEG for nutritional purposes and take

into consideration the survival of patients who have implanted a PEG, in the event of a decrease in nutritional intake. and compare their survival with that of older hospitalized patients (controls) who did not receive a PEG[15-16]. In our case we considered the PEG / J necessary, considering the clinical picture of the patients and the advanced state of Parkinson's disease.

Percutaneous PEG/J gastrojejunostomy, for the administration of Levodopa/Carbidopa Intestinal Gel, for the treatment of advanced Parkinson's disease, is a safe procedure both in the short and long term and effective with a very low and acceptable morbidity rate. The effectiveness of Levodopa Gel therapy, in our opinion, is important, both for the rapidity of the response to the symptoms and on the compliance of the patients.

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