

# Duodopa Infusion Treatment: a Point of View from the Gastroenterologist

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## Abstract

In patients with advanced Parkinson's disease, the continuous delivery to the small intestine via a jejunal tube of levodopa/carbidopa, formulated as a gel suspension (Duodopa) represents a new treatment method. The continuous release results in less variability in levodopa concentrations and fewer motor fluctuations and dyskinesias than with oral administration. The method which requires a very good collaboration between the neurologist and the gastroenterologist is used with increasing frequency in selected centres especially in severe patients. First, a classic PEG gastrostomy kit is placed under propofol sedation. This allows the passage of a pig tail catheter which is deployed in the jejunum and it is attached to a portable pump via a special tubing system. We present our experience of seven cases (5 males, mean age 60 years) with a follow up of one year. One patient died due to respiratory failure and aspiration pneumonia probably related to the endoscopic procedure. At one year, all patients agreed that the neurological benefit offsets the procedure related problems and the technical issues related to the enteral infusion system.

## Keywords

Duodopa – PEG gastrostomy – complications.

## Introduction

Although the traditional orally administered medication represents the mainstay of therapy in Parkinson's disease (PD), some innovative drug delivery methods have the potential to reduce or avoid many side effects of current treatment, such as dyskinesia, wearing-off type fluctuations,

on-off phenomena or bouts of motor freezing [1]. Several methods are used, such as delivery via rectal, intranasal, sublingual, subcutaneous or percutaneous ways [1].

In some patients with advanced PD, a treatment by continuous delivery to the small intestine via a jejunal tube of levodopa/carbidopa, formulated as a gel suspension (Duodopa®, Solvay Pharma) has been proposed [2]. The continuous delivery via an electronic portable pump attached to a special tubing system results in less variability in levodopa concentrations and fewer motor fluctuations and dyskinesias than with oral administration [2].

The selection of patients implies a good cooperation between a neurologist and a gastroenterologist. First, a 24-48 hours trial of Duodopa® is done with delivery via a nasojejunal tube. If there is a good clinical response, a classic PEG gastrostomy is placed allowing the passage of a pigtail catheter that is deployed in the jejunum.

A study regarding the challenges and complications of this technique from the point of view of the gastroenterologist has never been published. We present our experience of seven cases with a follow up of one year and we discuss the main complications and the evolution of the patients after the procedure.

## Case series

The Duodopa infusion programme started in our hospital in June 2009. The Ethics' Committee of the hospital approved the study. All patients signed a special informed consent regarding the procedure. An international protocol regarding Duodopa® (Solvay Pharma) treatment was adopted and applied.

Seven patients were included into the study (five males) with a mean age of 60.2 years (ranges 22 and 79) (Table I).

The neurology team decided on the inclusion to the programme. The patients had a gastroenterological consultation one or two days before the procedure.

## Technique

A test of effectiveness was realized in all patients in order to avoid futile gastrostomy. This test consisted of naso-

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**Table I.** Characteristics of Duodopa-treated patients

Number	Gender	Age	Mean duration of endoscopic procedure (minutes)	Hospitalisation duration (days)	Current Levodopa mg/ 24 h
1	M	73	32	17	1.150
2	M	22	30	17	980
3	M	63	40	5	1.560
4	M	60	29	14	2.050
5	M	69	23	14	3.150
6	F	67	17	13	deceased
7	F	68	22	8	1.980

duodenal / jejunal administration of the Duodopa gel and the registration of on and off periods for at least 24 hours. The nasojejunal tube was inserted in the endoscopy unit under propofol sedation and with endoscopic guidance. We performed an abdominal X-ray to verify the tube positioning but only in the first three patients. Two patients were less compliant and necessitated repositioning or reinsertion of the nasojejunal tube due to unintentional removal in the first 24 hours after procedure.

The percutaneous endoscopic gastrostomy was realised using a standard gastrostomy PEG kit (Freka gastric kit FR/CH15 from Fresenius®). Antibiotic prophylaxis was realized with amoxicillin clavulanate 1g i.v. one hour before the procedure. The procedure was performed by two experienced endoscopists under general sedation with propofol.

After placing the PEG tube, an inner pigtail catheter (Freka intestinal tube FR/CH 9, Fresenius®) was positioned using the endoscope and a rat tooth forceps to the duodenal-jejunal transition. The procedure took on average 20 minutes. We did not have any complications during the PEG tube placement procedure. The main technical challenge was related to the difficulties of positioning the PEG in a patient with partial gastric resection and gastroduodenal anastomosis. The procedure took 10 minutes longer. All patients had mild pain to the puncture site, which was treated with analgesics.

## Evolution

We observed one death in a patient with a lot of comorbidities (parkinsonian dementia, obesity, chronic obstructive pulmonary disease and respiratory failure). Six days after the PEG placement she died due to severe respiratory failure secondary to aspiration pneumonia. Although initially she seemed to have a good evolution, she developed respiratory failure necessitating admission to ICU. The CT scan revealed aspiration pneumonia, probably related to the endoscopic procedure, although no complications were seen during anaesthesia and the procedure time was the shortest of all.

After the procedure all the other patients had spectacular improvement in their neurological status, most of them regaining an acceptable quality of life. They were seen

regularly by their neurologists every three months and whenever necessary. The doses were continuously adjusted in order to maximise the efficacy of the treatment.

QUALY questionnaires and neurological examinations were done during the visits. The questionnaires included questions regarding the PEG tube and electronic pump management. All our patients agreed that the technical challenges posed by the enteral infusion system were offset by the improvement in motor fluctuations and dyskinesias offered by this technique.

During the follow up, three patients presented complications related to the delivery system requiring a gastroenterological consultation.

### Case 1

Approximately four months after the system placement, the 22-year-old patient who regained a very active lifestyle, dislodged his jejunal tube. It was repositioned with the help of its guide wire without endoscopic control. Two months after, he consulted his neurologist for apparently a pump malfunction (high pressure alarm; blockage) and an aggravation of his symptoms. After a check up of the infusion system, which worked fine, we verified the patency of its tubing system. Tube clogging is a frequent complication after PEG placement [3] and this was our initial suspicion. An attempt to pass a guide wire over the jejunal tube showed in fact a blockage after 40 cm. The decision of tube removal was made and the patient had an upper endoscopy. The PEG gastric tube was in place, but the jejunal tube was knotted in the stomach around a bezoar. We decided to extract it with a polypectomy snare after cutting its abdominal side. The extraction was made easily and without complications.

A new tube was placed and the patient restarted the therapy with rapid improvement of his neurological symptoms. Five months later we encountered the same problem in this patient and a new tube was placed after the knotted old tube removal by polypectomy snare.

This is to our knowledge the first incident of this type occurring with the Duodopa® delivery system; blockages due to a knot of the jejunal tube have not been reported yet. The first time we thought that the knot was formed due to the presence of the gastric bezoar. After the second incident of this type (and also after the change of three pumps due to accidental damage) we believed that the patient's lack of care manipulating its pump and the delivery system were playing a role. The second time the knotted tube was removed, we started to believe that the way he was manipulating the tubing system was responsible.

### Case 2

Another patient, a veterinary doctor, called emergency for aggravation of his symptoms and pump blockage (high pressure alarm, probably due to the clogging of the jejunal tube). He never came to the hospital, because he saw the cause of the malfunction: the tube was trapped in one of his waistcoat buttons. The system regained perfect functioning after the removal of the exterior compression. This complication has never been reported before.

### Case 3

The third patient dislodged the jejunal tube 5 months after the placement. She was admitted due to an aggravation of her neurological status requiring escalation of the Duodopa® doses. She had an endoscopy which revealed that the jejunal tube was in the stomach forming a large loop; a new tube was placed with spectacular improvement. We concluded that this dislodgement was probably related to the motility disorders associated with Parkinson's disease (she was diagnosed with gastroparesis and vomiting related to its neurological condition).

In all six patients, a significant clinical improvement was seen and permanent administration was decided.

### Discussion

The experience of European centres with this technique is increasing slowly mainly due to cost related issues. Only some studies and case reports are published to date.

One of the largest series recently published included 65 patients followed for a medium period of 10.7 years [4]. Fifty-two patients were treated for more than one year. The adverse effect profile of levodopa/carbidopa infusion was comparable to that noticed after oral administration. Seven patients died, but all deaths were secondary to other causes and not to the procedure or the treatment. The most frequent problems were related to the intestinal tube placement, including dislocation to the stomach and occurred in 69% of the patients during the first year [4].

In a French study of seven patients adverse events were due to PEG positioning for four patients, the equipment (pump, connection, inner tube) for all patients and levodopa for four patients [5]. In our study we did not encounter problems with the PEG placement and we had (repeating) problems regarding the jejunal tube placement in only one patient—the 22-year-old man. Remarkably, in this comparable French study no improvement in the quality of life was observed [5]. However, in a larger study that included all patients treated by Duodopa infusion system in France [6], more than 90 percent of the patients reported improvement in their quality of life, autonomy and neurological condition.

Several issues related to our experience must be discussed.

Before the start of the study a specialised training was assured for the neurologists. The training for the gastroenterologists was programmed but it never took place

due to lack of funding. Only a training video was presented before the first procedure, and we started the programme hoping that our previous experience with gastrostomies would be sufficient.

Now, after a one-year experience, we believe that training is required before the start of such a programme. The procedure itself is not complicated but it must be carefully explained and the selection of patients must be done in a multidisciplinary approach.

Our experience showed spectacular neurological improvements in all patients with no major drawbacks related to the delivery system montage or functioning. Placing a PEG gastrostomy has a number of well-known complications, but it is a common endoscopic procedure and in expert hands these are rarely seen, as in our series [4].

Careful enrolment of patients should be done to avoid the kind of issues we encountered with our youngest patient. For this patient a closer follow up was established to avoid future complications.

Although seen by some experts as a salvage method offered as compassionate treatment in desperate cases, in our series the patients returned to a normal life with major neurological improvement and without complications.

### Conflicts of interest

None to declare.

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