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Short and long-term safety and durability of PEG-J tube in jejunal levodopa infusion in patients with Parkinson's disease

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ABSTRACT

Aims: To investigate PEG-J related adverse events and tube durability in patients with Parkinson's disease who underwent PEG-J procedure for jejunal drug infusion.

Methods: PEG-J implanted patients, who were planned jejunal levodopa infusion, were included in the study. The demographic characteristics of the patients, tube durability, tube replacement, reason for tube replacement, number of procedures, and adverse events related to procedures were retrospectively analyzed.

Results: Thirty-four patients with a mean age of 65.7±9.8 years included in the study. The mean total PEG-J follow-up period of the patients was 33.6±21.1 months. Functions of PEG-J tubes were preserved in 82.5% at 6 months, 78.4% at 12 months, and 65.2% at 18 months. Twenty-one (% 61,8) patients required at least one PEG-J replacement. Of the PEG-J replacements, 90.4% were due to device-related adverse events. A total of 29 procedure or stoma related adverse events occurred in 21 (61.8%) patients, and a total of 28 PEG-J tube related adverse events occurred in 19 (55.9%) patients. A total of six (17.5%) early procedure-related adverse events (acute abdomen and peritonitis, prolonged bleeding, stoma leakage, stoma infection) were observed, all occurred in first 7 days. Twenty-three (67.6%) stoma-related late adverse events (stoma leakage, stoma infection, abscess) were observed. Two patients who developed peritonitis were successfully treated with conservative treatments.

Conclusion: PEG-J used for drug application is a safe method and can be used for a long time without the need for frequent replacement. Most of adverse events can be managed with conservative treatments.

Keywords: PEG-J, adverse events, Parkinson's disease, jejunal drug infusion

INTRODUCTION

Percutaneous endoscopic transgastric jejunostomy (PEG-J) is used primarily to overcome some complications that may occur due to gastric feeding in patients requiring long-term enteral nutrition, and secondarily to administer drugs that undergo gastric initial elimination when administered orally. [1,2]

In recent years, PEG-J has been widely used for continuous infusion of levodopa-carbidopa intestinal gel (LCIG) in patients with advanced Parkinson's disease who do not respond adequately to oral therapy and are not suitable for surgery.[3-6] With this method, LCIG is given as a continuous infusion directly into the jejunum with a tube that is advanced through the percutaneous endoscopic gastrostomy and extends to the proximal jejunum. In this way, undesirable fluctuations in serum levodopa level caused by gastric first elimination and problems in gastric emptying, especially in advanced Parkinson's patients, are overcome.[7] In the literature, there are few studies and limited number of patients on the early and long-term adverse events (AE) that may develop due to the PEG-J procedure used in the treatment of LCIG. The aim of this study is to investigate PEG-J related adverse events and tube durability in patients who underwent PEG-J procedure for LCIG treatment in our clinic.

METHODS

The study was carried out with the permission of Ankara City Hospital No:1 Clinical Researches Ethics Committee (Date: 20.04.2022 Decision No: E1-22-2579). All procedures were carried out in accordance with ethical rules and principles of Declaration of Helsinki.

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All patients diagnosed with Parkinson's disease who were scheduled for LCIG treatment and PEG-J implanted by the gastroenterology department in our hospital between April 2015 and April 2023 were included in the study. The LCIG treatment decision was made by the neurologist who followed the patients.

Criteria required for being a candidate for LCIG treatment and PEG-J placement were age >30 years, failure to respond to optimal oral dopaminergic therapy, and levodopa responsiveness assessed using the Levodopa Challenge test. Exclusion criteria for LCIG treatment were severe cognitive impairment, psychosis, active psychiatric illness, unresponsive Levodopa Challenge test, gastrointestinal disease or other drug use that would affect drug metabolism and lack of patient's caregiver. Exclusion criteria for PEG-J procedure were history of total gastrectomy, coagulopathy, sepsis, abdominal wall infection, ascites, lack of informed consent, gastric outlet obstruction or absence of transillumination in upper endoscopy.

The demographic characteristics of the patients, tube durability, tube replacement, reason for tube replacement, number of procedures, and AE related to the procedure were retrospectively analyzed. AE occurring in first 7 days or less were classified as early AE, and AE developing in a longer period were classified as late AE. The endpoint was tube dysfunction, tube removal for any reason and discontinuation of treatment, or death of patients for any reason. Patients who did not have data on PEG-J procedure and follow-up or who had PEG-J implantation due to enteral nutrition were not included in the study.

All patients were hospitalized before the procedure and PEG-J procedure was performed by an experienced gastroenterologist under conscious sedation provided by an anesthesiologist. Systemic antibiotic prophylaxis was administered to all patients before the procedure. Initially, endoscopy was performed to evaluate upper gastrointestinal tract. After providing skin antisepsis, a PEG tube (AbbVie 15 French PEG Kit) was placed in the region where transillumination and indentation were detected on the anterior wall of the gastric corpus-antrum junction. The inner jejunal extension tube (AbbVie 9 French intestinal tube), which was sent through the PEG tube, was held with gripping forceps and advanced to distal duodenum/proximal jejunum. Then, the endoscope was pulled back to the stomach and the gripping forceps were opened while the endoscope was inside the stomach, and the jejunal tube tip was released so that it remained in the jejunum. After the procedure, the patients in the present study were regularly checked by a nurse who was experienced in PEG-Jcare, and the control information was recorded regularly.

Statistical Analysis

IBM SPSS Statistics Version 25.0 software for Windows (IBM Corp., Armonk, NY, USA) was used to perform the statistical analysis. Descriptive statistical methods (mean, standard deviation, frequency, percentage, minimum, maximum) were used in the evaluation of the research data. The conformity of the quantitative data to the normal distribution was analyzed by Kolmogorov-Smirnov, Shapiro-Wilk test, and graphical examinations. Spearman correlation coefficient was used to compute the correlation analysis. Statistical significance was considered $p \leq 0.05$ with a confidence interval (CI) of 95%.

RESULTS

Thirty-four patients with a mean age of 65.7±9.8 years who were treated with LCIG were included in the study. Seventeen (50%) of the patients were male. Demographic characteristics of the patients are shown in Table 1.

Table 1. Demographic characteristics of patients

Total number of patients	34	
Gender	**n**	**%**
Female	17	50
Male	17	50
Age	65.7±9.8 years (48-86 years)	
Comorbid diseases	**n**	**%**
Hypertension	12	35.3
Hyperlipidemia	5	14.7
Diabetes mellitus	5	14.7
Cardiac problems	5	14.7
Osteoporosis	4	11.8
Pulmonary problems	3	8.9
Rheumatoid arthritis	1	2.9
Pernicious anemia	1	2.9
Malignancy	1	2.9

The mean total PEG-J follow-up period of the patients was 33.6±21.1 months (0-98 months). The longest period of use of a single PEG-J catheter without replacement was 52 months, and in this patient, the tube was removed while the tube was still functioning, when the patient wanted to discontinue the treatment. During the follow-up period, only one PEG-J procedure was performed in 13 patients, while two or more PEG-J procedures were performed in 21 (61.8%) patients. A total of 65 PEG-J procedures were applied (Table 2).

After initial PEG-J insertion, a total of 31 tube replacements were required due to inner jejunal tube occlusion in seven patients (Five due to drug, two due to king formation), inner jejunal tube dislocation in 10 patients, internal jejunal tube break in four patients, PEG tube damage in seven patients (Three due to

accidental cutting by the patient), peristomal infection in 2 patients, and acute abdomen and peritonitis in 1 patient. Of the PEG-J replacements, 90.4% were due to device-related AE, and 9.6% were due to procedure- or stoma-related AE. Functions of PEG-J tubes were preserved in 82.5% at 6 months, 78.4% at 12 months, and 65.2% at 18 months (Table 2).

Table 2. Number of PEG-J tubes used by patients, reasons for replacement and tube retention rate in follow-up

Average follow-up time of patients	33.6±21.1 months (0-98 months)	
Number of PEG-J used	**n (patient)**	**%**
1	13	38.2
2	14	41.2
3	5	14.7
4	1	2.9
5	1	2.9
Total	34	100
Cause of tube replacement	**n (procedure)**	**%**
Inner jejunal tube occlusion	7	22.6
Inner jejunal tube dislocation	10	32.3
Inner jejunal tube break	4	12.9
PEG tube break	7	22.6
Stoma infection	2	6.4
Acute abdomen and peritonitis	1	3.2
Total	31	100
Functional PEG-J tube ratio	**%**	
6. months	82.5	
12. months	78.4	
18. months	65.2	

Seven (20.6%) patients had no AE. A total of 29 procedure or stoma related AE occurred in 21 (61.8%) patients, and a total of 28 PEG-J tube related AE occurred in 19 (55.9%) patients. A total of six (17.5%) early procedure-related AE (acute abdomen and peritonitis, prolonged bleeding, stoma leakage, stoma infection) were observed, all occurring in first seven days. Twenty-three (67.6%) stoma-related late AE (stoma leakage, stoma infection, abscess) were detected (Table 3). There was no relation between early or late AE and comorbid diseases in the correlation analysis ($p>0.05$).

All cases with stoma leakage improved spontaneously without any intervention.

A total of 17 stoma infections and abscesses occurred in 15 patients. There was a total of 9 colonization in the wound cultures sent from 8 patients, and there was no colonization in the wound cultures of 7 patients. While Candida species were detected in five cultures; *Corynebacterium striatum*, *Enterobacter aerogenes*, *Streptococcus intermedius* and *Staphylococcus aureus* were detected in the other four cultures, respectively. While two of the patients developed two stoma infections, one stoma infection or abscess developed in the other 13 patients. Tube exchange was performed due to infection in two patients with Candida infection. In two other patients with Candida infection, the tube was removed due to prolonged infection, new PEG-J replacement was not performed because the patients wanted to discontinue the treatment. Other patients who developed infections recovered with conservative and medical treatment.

Table 3. Adverse events during follow-up

	n	Procedure %	Patient %
Stoma and procedure related early adverse events (0-7 days)			
Prolonged bleeding	1	1.5	2.9
Stoma leakage	1	1.5	2.9
Stoma infection	1	1.5	2.9
Acute abdomen	3	4.6	8.8
Total	6	9.1	17.5
Stoma and procedure related late adverse events (>7 days)			
Stoma leakage	7	10.8	20.6
Stoma infection	13	20.0	38.2
Abscess	3	4.6	8.8
Total	23	35.4	67.6
Total adverse events	29	44.5	85.1
Patient with adverse events	21		61.8
PEG-J tube related adverse events	**n**	**Procedure %**	**Patient %**
Inner jejunal tube occlusion	7	10.8	20.6
Inner jejunal tube dislocation	10	15.4	29.4
Inner jejunal tube break	4	6.1	11.8
PEG tube break	7	10.8	20.6
Total adverse events	28	43.1	82.4
Patient with adverse events	19		55.9

Acute abdomen or perforation developed in three patients. In the first patient, the tube had penetrated the left lobe of the liver, and surgically, a small liver incision was made to free the tube and the tube continued to function without replacement. In the second patient, peritonitis symptoms developed with the findings of pneumoperitoneum and intra-abdominal infectious collection, the tube was removed, and a new PEG-J was inserted when the clinical findings improved with medical treatment. In the third patient, peritonitis findings developed with pneumoperitoneum and intra-abdominal infectious collection findings, the PEG-J tube was removed, and the patient recovered with conservative methods and medical treatment without the need for surgical procedure, then the patient did not accept new PEG-J replacement.

During follow-up, mechanical ileus due to Spiegel's hernia developed in one patient and paralytic ileus due to neurological and metabolic causes in another patient, but these problems were not related to PEG-J.

Six patients died due to comorbid diseases. Three patients discontinued treatment due to complications (one patient due to peritonitis in the first week, the other two due to prolonged candida infection at 16 and 23 months). There was no death due to PEG-J procedure or tube-related complications. One patient without complications wanted to stop the treatment and the PEG-J tube was removed. At the end of the follow-up, 24 patients were still using PEG-J (Table 4).

Tablo 4. Number of patients at the end of follow-up

Patients without PEG-J exchange (n=13)	Patients without PEG-J replacement (n=21)
9 patients are still on follow-up	15 patients are still on follow-up
2 patients quit due to PEG-J complications	1 patient quit due to PEG-J complications
1 discontinued treatment without complications.	5 patients died
1 patient died	

DISCUSSION

Our study showed that PEG-J used for drug application is a safe method and can be used for a long time. 91.2% of our patients did not develop serious early complications related to the PEG-J procedure, and there was no mortality secondary to early and late complications. Conditions such as peritonitis, perforation, intestinal fistula, which are classified as severe AE in the literature, have been reported between 0-15% in different studies.[4,7-14] Viljaharju et al.[10] reported that a single case of peritonitis died among 103 patients. Cheron et al.[14] reported that one closed duodenal perforation and one intra-abdominal infectious collection were cured with conservative treatment. Ebstein et al.[13] reported that five of eight peritonitis cases treated conservatively, three of them surgically, all patients were successfully treated. All early complications observed in the present study were procedural complications that developed within first 7 days. Peritonitis and intra-abdominal infectious collection were present in two of three cases of acute abdomen. These patients recovered with medical treatment and conservative approach. Therefore, we think that conservative approaches would be more appropriate in cases of peritonitis and infectious collections without organ penetration (such as colon, small bowel, liver) in radiological imaging, if there is no finding suggesting septic shock or organ dysfunction.

During the PEG-J procedure, gastropexy is recommended to prevent serious side effects such as peritonitis and intra-abdominal abscess. However, on the contrary, other studies have reported that gastropexy application will not eliminate this risk. While no severe AE was detected after gastropexy in the study of Ishibashi et al.,[15] Yamashita et al.[16] reported that peritonitis developed in 2.9% despite gastropexy. In the present study, we detected peritonitis in 5.9% of our patients and gastropexy was not performed in any of our patients. We think that gastropexy may reduce the development of peritonitis in early period. In cases where gastropexy cannot be performed, making an incision appropriate for the diameter of the PEG catheter, and pressing the incision site more carefully while pulling the PEG tube out of the stomach through the abdominal wall may prevent the separation of the stomach and abdominal wall and the development of peritonitis and intra-abdominal infectious collections. The use of CO_2 insufflation instead of air during the procedure may reduce the development of pnomoperitoneum and therefore the risk of peritonitis. Penetration of left lob of the liver was present in one of three cases of acute abdomen in the present study. It is also important not to perform the procedure if transillumination and indentation cannot be obtained clearly, in order to avoid problems that can lead to acute abdomen, especially organ penetration.

Tube revision is required for various reasons during the follow-up of PEG-J patients. Viljaharju et al.[10] and Simoni et al.[17] found the need for at least one tube replacement in 57% and 56.6% of patients, respectively. In this study, at least one tube replacement was required at a rate of 61.8%, slightly more than in these studies. In the study by Yamashita et al.,[16] the need for tube replacement was reported in 34.9% of the patients at 12 months. In our study, tube replacement was 21.6% at 12 months and 34.8% at 18 months. We determined the durability of PEG-J tubes to be longer. Viljaharju et al. reported that over 90 percent of tube replacements were due to tube-related AE. Simoni et al.[17] also reported that 82% of the reasons for replacement were tube-related problems and the most common reason for tube replacement was inner tube dislocation. Udd et al.,[9] on the other hand, showed that the causes of tube replacement were predominantly due to tube-related AE and reported that 38% were due to accidental removal of the inner tube and 29% to the occlusion of the inner tube. In our study, similar to these studies, the majority of the replacements were related to tube-related problems and the most common cause was inner tube dislocation. Although the number of procedure- or stoma-related AE was at least as high as the number of tube-related AE, most of them responded to conservative treatments and did not require replacement.

The average number of procedures, peristomal and device-related AE per patient has been reported between 0.7 and 6 in the literature so far in patients who have been placed PEG-J for LCIG continuous infusion.[4,8,9,17] We found an average of 1.7 AE per patient. Udd et al.[9] found

71% peristomal AE and 86% tube-related AE in their patients. After accidental dislocation of the inner tube, granulation tissue formation was found to be the most common AE. Balaise et al.[4] found stoma- or procedure-related AE in 69.8% of the patients, and device-related AE in 63.5%. As common reasons: They found PEG tube dislocation with 44.4%, granuloma with 34.9%, inner tube obstruction with 31.7%, stoma infection and abscess with 30.2%, and stoma leakage with 27%. In their study, Simoni et al.[17] reported that 63.3% of the patients had AE, and they found device-related complications in 44.3% and stoma-related complications in 45.9% of them. Again, the most common complications were wound infection with 25.9% and inner tube dislocation with 18.9%. In this study, we found AE in 79.4% of our patients. Stoma- and procedure-related AE was found in 61.8% of the patients, and PEG-J tube-related AE was found in 55.9% of the patients. In our study, the main PEG-J tube related AE were inner tube dislocation, inner tube occlusion and PEG tube breaking, similar to previous studies. Half of the total AE were stoma and procedure related ones.We did not observe granulation tissue in contrast to studies[9,13,18] that detected a high rate of excessive granulation tissue. In contrast to Cococci et al.,[8] who did not report any infectious AE in their study, half of the patients in this study developed stoma infection or abscess. This finding was in line with the existing literature, and the results we found were similar to the study by Rus et al.,[18] who previously reported a 49.5% local infection rate and a 5.8% abscess rate. In earlier studies, it was reported that local infection rates were different in different centers, and the history of malignant disease, tube diameter and endoscopist experience affected the risk of infection.[19]

In the present study, only one stoma infection developed in the early period, while all remaining stoma infections and abscesses developed in the late period. This means that infections are associated with later stoma care rather than periprocedural conditions. Along with periprocedural antibiotic prophylaxis and compliance with sterile conditions during the procedure, patients and their caregivers should be well educated about stoma care and their attention should be drawn to its importance.

In the present study, wound culture was positive in half of the patients who developed peristomal infection. Patients with culture negative or bacterial colonization were treated with appropriate antibiotic therapy and conservative approach. The patient, who had previously isolated *Enterobacter aerogenes* in culture, did not respond to treatment, and candida colonization was detected in repeated culture. Four of the five patients with Candida infection were treated by removing the tube due to prolonged infection. Previous studies have shown that Candida species can colonize PEG catheters and cause serious clinical problems, especially in immunosuppressed individuals.[20-22] However, there is no evidence in the literature regarding the culture results of stoma infections developed in Parkinson's patients with PEG-J, and especially for treatment-resistant candida infections. We think that in case of treatment-resistant peristomal infections, possible Candida infection should be considered and treated with tube replacement in those who do not respond to conservative treatments.

Another stoma- and procedure-related AE that was frequently observed in the present study was stoma leakage. This AE is often caused by a large stomatal incision relative to the tube diameter or by fluid retention in the stomach. In this study, all cases with stomal leakage resolved spontaneously. Optimal size of the stoma incision, short interval and low volume diet, optimization of Parkinson's treatment and use of prokinetic agents in patients with delayed gastric emptying may reduce the incidence of stomal leakage.

One of the limitations of the present study is that it is retrospective. However, after the procedure, the patients in our study were regularly checked by a nurse experienced in PEG-J care, and the control information was recorded regularly. Another limitation of the study is the small number of patients and the absence of a control group. This study could be more powerful if the data of the patients who were placed with PEG-J for drug administration were compared with the data of the patients who were placed with PEG-J for enteral nutrition. Randomized controlled studies with larger number of patients are needed in this regard.

CONCLUSION

PEG-J used for drug application is a safe method and can be used for a long time without the need for frequent replacement. Although a few complications may develop in the early and late period, most of them can be managed with conservative treatments.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Ankara City Hospital No:1 Clinical Researches Ethics Committee (Date: 20.04.2022 Decision No: E1-22-2579).

Informed Consent: Because the study was designed retrospectively, no written informed consent from was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

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