

Prevalence of *Helicobacter pylori* infection in patients with Dementia who underwent Percutaneous Endoscopic Gastrostomy (PEG) and the effect of preventive single dose ceftriaxone plus pantoprazole therapy on *Helicobacter pylori* infection

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ABSTRACT

Objective: This was a retrospective study of the hospital database from April 2020 to January 2021 to reveal the rate of *Helicobacter pylori* infection among Dementia patients who underwent percutaneous endoscopic gastrostomy (PEG) procedure. Other aim of this study is examine the effect of a single dose (two grams) intravenous ceftriaxone plus pantoprazole (40 mg) before PEG procedure on *H.pylori* infection in Dementia patients.

Material and Methods: This is a retrospective observational study of hospital database from April 2020 to January 2021 examining the effect of using a single dose (two grams) of intravenous ceftriaxone plus pantoprazole (40 mg) on *H.pylori* infection in Dementia patients. A total of 77 patients, (43 (64%) of them were female) with Dementia were included whose 67 had previously been diagnosed as Dementia and underwent PEG procedure. The control group (67 subjects; 40 of them were female and the mean age was 75.8±11 years) was selected from age and gender-matched dyspeptic subjects who underwent endoscopy

Results: While the mean age in the Dementia group was 75.8±12 years, the mean age of the control group was 77.8 ±11 years (p=0.054). There were also no gender differences between groups (p=0.594).

While the mean levels of serum albumin, urea, creatinine, hemoglobin were significantly lower than control subjects (All p values were below 0.001), the mean of serum ferritin level was higher than control subjects (p<0.01). The presence of *H.pylori* on gastric biopsy specimens was significantly lower in the Dementia group compared to control subjects (19.4% versus 55.2%).

Conclusion: Our study indicated that the rate of *H.pylori* infection was lower than estimated and using single-dose intravenous ceftriaxone at a dose of 2 grams could be beneficial for treating *H.pylori* infection in patients with Dementia who faced difficulties related to lack of swallowing many drugs against *H.pylori* infection.

Keywords: *Helicobacter pylori*, Dementia, Percutaneous Endoscopic Gastrostomy, ceftriaxone, pantoprazole

INTRODUCTION

When the pathogenesis of Dementia is examined according to epidemiological data, it has been proven that *H. pylori* play an important role in the pathogenesis. *H. pylori* is a gram-negative bacterium that causes disorders associated with the upper gastrointestinal tract (chronic gastritis, peptic ulcer, and gastric cancer).

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H. pylori may initiate neurodegeneration by damaging the blood-brain barrier, cause the release of systemic proinflammatory cytokines and allowing these cytokines to easily cross the barrier. It has also been revealed that the rate of H. pylori infection was higher among patients with Dementia than control subjects (1,2). Percutaneous endoscopic gastrostomy (PEG) procedure, which is a minimally invasive method that provides internal nutrition with high efficiency and safety, is the method that is frequently preferred for Dementia patients. PEG application is especially recommended when malnutrition is detected while the patient is in the middle stage. Because, PEG insertion at more advanced stages cannot contribute to the lifetime of the patients. In many studies conducted so far, it has been revealed that internal nutrition has many advantages compared to parenteral nutrition (3).

In particular, internal nutrition has important contributions to human health in the regulation of intestinal microbiota and bacterial translocation events (4). Otherhand, preventive treatment with ceftriaxone before the PEG procedure has been accepted for decades to reduce the risk of peristomal infections (5).

However, there was no study involving the effect of single-dose ceftriaxone plus pantoprazole on H. pylori infection in patients with Dementia. Based on this, in this study, it was aimed to examine and evaluate gastric mucosal biopsy samples in patients who applied PEG in order to determine the effect of single dose of ceftriaxone plus pantoprazole on H. pylori infection.

MATERIAL and METHODS

This is a retrospective observational study of hospital database from April 2020 to January 2021 examining the effect of using a single dose (two grams) of intravenous ceftriaxone plus pantoprazole (40 mg) on H.pylori infection in Dementia patients.

Table 1. Demographic and clinical characteristics of groups

	Peg		Control		p
	n	Mean (95%CI)	n	Mean (95%CI)	
Age(year)	67	77,8 (74,7-80,9)	67	75,8 (73-78,6)	0,054
Glucose(g/dL)	67	133 (118-147)	65	121 (110-131)	0,209
AST(IU/L)	66	25 (21-29)	64	27 (20-33)	0,742
ALT(IU/L)	67	21 (16-26)	67	22 (17-27)	0,104
Total protein(g/dl)	60	5,2 (8,94-6,18)			
Albumin(g/dL)	64	3,1 (2,9-3,2)	21	4,4 (4,1-4,6)	<0,001
ALP(IU/L)	60	85 (115-94)			
GGT(U/L)	56	31 (53-36)			
Urea(mg/dL)	67	65,1 (52,5-77,7)	63	35,3 (31,7-39)	<0,001
Creatinin(mg/dL)	67	0,8 (0,66-0,95)	67	0,86 (0,8-0,92)	0,004
Calcium(mmol/L)	65	8,53 (8,91-8,72)			
WBC(mcL)	62	9,37 (8,12-10,63)	67	7,94 (7,16-8,73)	0,189
Haemoglobin(g/dL)	62	10,4 (9,9-11)	67	12,6 (12-13,2)	<0,001
Haemotocrit(%)	62	31,7 (29,8-33,6)	67	39,1 (37,5-40,7)	<0,001
Platelet(x10 ⁹ /L)	62	246 (214-278)	67	290 (214-366)	0,290
Ferritin(ng/mL)	15	220,22 (81,95-358,5)	14	62,36 (36,81-87,91)	0,010
TSH(mIU/L)	43	1,846 (1,152-2,541)	45	2,28 (1,463-3,098)	0,126
sT4(mIU/L)	42	0,989 (2,051-1,271)			
PT(sec)	64	12,4 (13,3-12,7)			
HbA1c(%)	24	5,66 (6,81-6,1)			

A total of 77 patients, (43 (64%) of them were female) with Dementia were included whose 67 had previously been diagnosed as Dementia and underwent PEG procedure. The control group (67 subjects; 40 of them were female and the mean age was 75.8±11 years) was selected from age and gender-matched dyspeptic subjects who underwent endoscopy. Patients with gastric and esophageal cancer and those who have taken proton pump inhibitors plus antibiotics before six weeks of PEG procedure were excluded. At least two gastric biopsy samples were taken from antral gastric mucosa during PEG procedure and were evaluated by pathologists in terms of the presence of H. pylori infection.

Statistical analyses: All statistical analyses were performed with Statistical Product and Service Solutions (SPSS) 23.0 software (SPSS, Chicago, IL, USA). Normality analysis of quantitative data was done with Kolmogorov-Smirnov test. If comparison of data that did not fit normal distribution was made with Mann Whitney U test. The comparison of qualitative data was made with Pearson Chi-square. Data were presented as mean (95% confidence interval) and n (%). Statistical significance value was accepted as p<0.05.

RESULTS

While the mean age (±SD) in the Dementia group was 75.8±12 years, the mean age of the control group was 77.8 ±11 years (p=0.054). There were also no gender differences between groups (p=0.594) (**Table-1**). While the mean levels of serum albumin, urea, creatinine, hemoglobin were significantly lower than those control subjects (All p values were below than 0.001), the mean of serum ferritin level was higher than control subjects (p<0.01). Finally, the presence of H.pylori on gastric biopsy specimens by histopathologic examination was significantly lower in the Dementia group compared to control subjects (19.4% versus 55.2%) (**Table-2**).

Table 2. Presence of H.pylori on gastric biopsy specimens by histopathologic examination

		Peg	Control	p
Gender	Male	24 (35,8)	27 (40,3)	0,594
	Female	43 (64,2)	40 (59,7)	
HBS	Negative	40 (97,6)		
	Positive	1 (2,4)		
antiHBS	Negative	29 (76,3)		
	Positive	9 (23,7)		
NASH	No	41 (93,2)		
	Yes	3 (6,8)		
H. pylori	No	54 (80,6)	30 (44,8)	<0,001
	Yes	13 (19,4)	37 (55,2)	
Atrophy	No	62 (92,5)	48 (71,6)	0,002
	Yes	5 (7,5)	19 (28,4)	
Metaplasia	No	58 (86,6)	65 (97)	0,028
	Yes	9 (13,4)	2 (3)	

DISCUSSION

Until the date of work, there was no report involving using single-dose intravenous ceftriaxone plus pantoprazole on H.pylori infection among patients with Dementia in the literature. We found an extremely low rate of H. pylori infection among the studied population. Current study was also revealed that using ceftriaxone plus pantoprazole before the PEG procedure could also be beneficial to treat H.pylori infection in addition to prevention of PEG-related peristomal infections in patients with Dementia.

The prevalence of Dementia increases markedly after the age of 65, and is thought to be approximately 50% at the age of 85 years. It is known that the expected human lifespan is getting longer due to advances in medicine over the years. Nevertheless, a significant increase in the prevalence of Dementia is expected in the future(6).

Dementia is generally a chronic and progressive neurodegenerative disease that causes impairment in multiple cognitive functions (with memory decline and at least one of the territory such as executive functions, language or visuospatial abilities). Apparently, an intellectual destruction, with clouding of consciousness, causing activity inabilities of daily living may occur. The patient has developed a decline in previous cognitive functions, and behavioral disorders are often added to the clinic. Depending on the nature of the disease causing Dementia. Motor, autonomic system and sleep disorders may also occur. Alzheimer's disease most commonly causes dementia syndrome when the pathophysiological changes in the central nervous system(7).

Nutritional problems often occur in patients with Dementia, especially as the disease progresses, and these patients are at risk of malnutrition. Nutritional problems that cause malnutrition are either due to trying to eat substances that are not food as a result of the loss of the ability to recognize food.

Additionally behavioral problems as agitation and disturbed eating behavior, attention deficit, impaired decision-making ability, executive dysfunction as shopping or preparing food, loss of eating skills, as well as anosmia and taste dysfunction, impaired sense of hunger and thirst, as well as refusal to eat, dysphagia, or from disruption of the entire eating process may be observed (8).

The prevalence of dysphagia in patients with Dementia ranges from 13 to 57%. Dysphagia, malnutrition, increased weight loss, aspiration pneumonia may develop, and even death may result (9).

In the middle and late stages of Dementia, dependency to caregivers develops gradually, as in the act of preparing and eating. In advanced Dementia dysphagia and indifference to eating may develop. When caregivers think that the nutritional status or fluid intake of these elderly people is inadequate, they should search for an alternative way of feeding. At this stage, unless there is a contraindicated situation, it should be recommended to continue feeding by enteral means. First of all, it should be a continuation of the recommended oral assisted feeding. However, enteral nutrition with a PEG tube is considered for adequate nutrition and hydration in individuals with advanced Dementia whose oral feeding is irreversibly declining (10).

However, according to these reports, the frequency of H. pylori in mucosal biopsies applied to these patients was found to be significantly higher than the control group. In addition to all these, there is a direct correlation between cognitive impairment and the presence of anti-H. pylori immunoglobulin G antibodies in Alzheimer's patients. In other words, between anti-H. pylori and IgG levels in cerebrospinal fluid and cognitive impairment in Alzheimer's patients are directly proportional (11).

Otherhand, treatment of *H.pylori* in patients with Dementia could be problematic due to lack of ability to take of many drugs which are given by oral route against *H pylori* infection. Thus, we conducted the presented study in this unique patient population with using single-dose ceftriaxone plus pantoprazole by intravenous route.

A recent study to explore antibiotic resistance in patients with *H.pylori* infection which was detected by a C-labeled urea breath test revealed that ceftriaxone resistance was 49.6%, and cefuroxime resistance was 25% (12).

Another invitro study in USA also revealed that minimally inhibitory concentration (MIC) of ceftriaxone against *H.pylori* infection was determined after 24 to 48 hours of incubation at 37°C by a micro broth dilution method and calculated as 0.125–0.25 µg/ml at stock cultures (13).

Interestingly, as discussed above, patients with Dementia had higher rates of *H.pylori* infection compared to age-matched counterparts. We found significantly lower *H.pylori* infection among patients with Dementia. It could be related to preventive ceftriaxone and pantoprazole treatment by intravenous route.

The limitation of the study is that the type of Dementia could not be determined because our patients were admitted to the hospital, especially at the advanced stage of Dementia, and the clinical data at the onset of their symptoms could not be accessed in their medical records retrospectively.

CONCLUSION

As expected and as we revealed; *Helicobacter pylori* is a curved, microaerophilic, gram-negative bacterium, thus ceftriaxone plus pantoprazole could be used in the treatment of *H.pylori* infection. Further large scale prospective studies are needed to confirm those findings.

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Ethical approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by Local Ethical Committee. All procedures performed in studies with human participants met the ethical standards of the Institutional Research Commission and the 1964 Declaration of Helsinki and its subsequent amendments or comparable ethical standards. Ethical approval was taken from Samsun Coastal Blacksea University Hospital (GOKA/2020/4/4).

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