A PROSPECTIVE STUDY: DOES CITALOPRAM INCREASE THE REFLUX SYMPTOMS?

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[Uno studio prospettico: Citalopram aumentare i sintomi di reflusso?]

ABSTRACT

Objective: Selective serotonin reuptake inhibitors (SSRIs) induce some adverse effects on gastrointestinal system. We aimed to investigate the role of citalopram, a well-known SSRI, on the reflux symptoms.

Methods: Seventy patients with gastro-oesophageal reflux disease (GERD) were included to the study. Anxiety and depressive symptoms were measured with the Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI), version II, respectively. Participants were divided into two groups: Group 1 (n=35) treated with only esomeprazole + sodium alginate and Group 2 (n=35) who were classified as moderate-severe depression and/or anxiety treated with esomeprazole + sodium alginate + citalopram.

Results: At the beginning, BDS and BAS were significantly higher in Group 2 than in Group 1 (both p<0.001) and BAS and BDS were significantly decreased with the treatments in both groups (both p<0.001). Moreover, the numbers of the patient who said the reflux symptoms improved were significantly higher in Group 1 than in Group 2 (p=0.001).

Conclusions: The administration of citalopram to patients with GERD caused the distribution of recovery of the reflux symptoms. This relation should be taken into account when managing depression in the patients with severe reflux symptoms.

Key words: Gastro-oesophageal reflux disease, citalopram, anxiety, depression

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Introduction

Gastro-oesophageal reflux disease (GERD) is a chronic and a common health problem; it affects approximately 10–20% of adults. Depression is also a most common health problem. At the same time, an association between GERD and depression has been shown in several studies. Selective serotonin reuptake inhibitors (SSRIs) induce some gastrointestinal adverse effects such as anorexia, nausea, dyspepsia, diarrhea and upper gastrointestinal bleeding. Otherwise, SSRIs may be a beneficial option for treatment of hypersensitive esophagus. However, the effects of SSRIs on the reflux symptoms remain controversial.

Although based upon the side effects of SSRIs on gastrointestinal system mentioned above, no research study has been performed yet to show the effect of SSRIs on reflux symptoms. By this way, we aimed to investigate the role of citalopram, a well-known antidepressant drug and a SSRI, whether the treatment increases or not the reflux symptoms.

Material and method

Study population

The study was conducted in a prospective way in our gastroenterology outpatient unit and 70 patients diagnosed GERD were included. At the beginning, the study protocol was reviewed and approved by the local ethics committee, in accordance with the ethical principles for human investi-
gations, as outlined by the Second Declaration of Helsinki, and written informed consent was obtained from all the patients.

Exclusion criteria included a past history of gastrointestinal surgery, gastric and duodenal ulcer, the concurrent presence of organic diseases including cancer and unwillingness of questionnaire.

GERD diagnosis was made by occurring of typical symptoms (heartburn and/or regurgitation) at a frequency higher than twice a week and for a period longer than 4 weeks\(^8,9\). All participants in the current study were administered esomeprazole 40 milligram twice a day and sodium alginate 4 x 500 milligram for three months. Anxiety symptoms were measured using the Beck Anxiety Inventory (BAI) and depressive symptoms were measured with the Beck Depression Inventory (BDI), version II (10-12). Patients who had BAI score (BAS) > 15 and/or BDI score (BDS) > 16 were treated additionally with citalopram 10 milligram/day for three months, which were classified as moderate-severe depression and/or anxiety. Participants were divided into two groups: Group 1 (n=35) treated with only esomeprazole + sodium alginate and Group 2 (n=35) treated with esomeprazole + sodium alginate + citalopram. At the end of the study patients were asked for the recovery of present reflux symptoms and categorized as i) Completely resolved, ii) Significantly reduced, iii) Slightly reduced and iv) Unchanged.

**Statistical analysis**

All statistical analyses were performed using SPSS 15.0 for Windows (SPSS, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were expressed as percentages. Either \(\chi^2\) test or Student’s unpaired t-test were used to compare the categorical or continuous variables, respectively. Paired t-test was used to analyze changes within the groups. A two-sided \(p\) value < 0.05 was considered to be statistically significant.

**Results**

There were no significant differences in baseline demographic features and clinical findings other than BDS and BAS between two groups (Table 2). BDS and BAS were significantly higher in Group 2 than in Group 1 at the beginning (both \(p<0.001\)). BAS and BDS were significantly decreased with the treatments in both groups (both \(p<0.001\)). Moreover, the numbers of the patient who said the reflux symptoms improved were significantly higher in Group 1 than in Group 2 especially in the terms of patients who said “Completely resolved” (\(p=0.001\)).

**Discussion**

The data of this study reveal that i) depression and anxiety scores were decreased in both treatment group suggest us that the association between anxiety, depression and reflux; ii) reflux symptoms were not resolved in the citalopram group suggest us that citalopram has worsening effect on reflux.

The previous study by Jansson et al. demonstrated the correlation between the anxiety, depression and reflux symptoms and they found that 2.8 times increased reflux symptoms in present of anxiety and depression\(^9\). Marti’N-Merino et al. found an increased incidence of GERD among patients with depression\(^13\). At the same time anxiety, but not depression, has found to be independent factor for the determining of health care utilization in dyspeptic patients\(^46\). Patients with GERD have impaired quality of life compared with general populations and psychological factors could affect the clinical manifestations of reflux disease\(^14,15\). We showed that treatment of reflux disease provided improvement in depression and anxiety scores independent from anti-depressant treatment.

SSRIs had a direct damaging effect on the gastrointestinal mucosa and related with the increased prevalence of gastric mucosal damage\(^16,17\). However, it has been showed that citalopram can mitigate inflammation-induced exacerbation of gastric ulcers and augment the gastric mucus barrier\(^18\). SSRIs augment the availability of physiologically released 5-hydroxytryptamine (5-HT) which is a neurotransmitter in the enteric nervous system and play a key role in the control of gastrointestinal motility\(^19,20\). Acute effects of citalopram as a selective 5-HT reuptake inhibitor include decreasing of basal gastric tone, impairing gastric accommodation to a meal, enhancing gastric emptying of solids and increasing the volume of nutrient drink ingested before maximal satiation\(^20\). Citalopram significantly decreases the of mechanical and chemical sensitivity the esophagus and SSRIs treatment may be a reasonable and beneficial option for the hypersensitive esophagus\(^7,21\).

Besides all of this knowledge, the effect of
citalopram on the symptoms of GERD is not known. We found that reflux symptoms were not resolved in citalopram treated group as well as other treatment group that not include citalopram. The side effects of citalopram related with gastrointestinal system especially on reflux disease seem to occur over the inhibition of 5-HT reuptake. As discussed above, citalopram may be a treatment option for hypersensitive esophagus. However, present study unable to exclude patient with hypersensitive esophagus because of lack of upper gastrointestinal system endoscopy and 24 hour pHmeter. It is the most important limitation of our study.

Conclusion

In the present study, the administration of citalopram to patients with GERD caused the distribution of recovery of the reflux symptoms. This study provides further evidence for the relationship between citalopram and GERD. This relation should be taken into account when managing depression in the patients with severe reflux symptoms.

References