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Alimentary Tract

Comparison of paroxetine and amitriptyline in the treatment of refractory globus pharyngeus

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ABSTRACT

Background: Clinical trials of antidepressants for treatment of globus are generally rare, let alone for refractory globus pharyngeus.
Aims: To illustrate the efficacy and side-effects of antidepressants between paroxetine and amitriptyline for refractory globus patients.
Methods: Refractory globus patients were randomized into paroxetine group; amitriptyline group and lansoprazole group for 6-week treatment. All the subjects were asked to complete the following questionnaires pre- and post-therapy: Glasgow Edinburgh Throat Scale (GETS), Pittsburgh Sleep Quality Index, Hamilton Rating Scale Anxiety/Depression and Medical outcome short-form 36. Treatment response was defined as a >50% reduction in the GETS score.
Results: One hundred and forty-eight patients completed the study. After 6 week treatment, 71.7% of paroxetine group (33/46) were calculated as treatment response, significantly higher than that in amitriptyline group (46.2%, 24/52) and lansoprazole group (14.0%, 7/50). Compared with lansoprazole group or amitriptyline group, a more distinct improvement of emotional well-being, quality of life and quality of sleep were observed in paroxetine group after 6-week treatment.
Conclusion: Paroxetine therapy is more efficacious than empirical high-dose antisecretory treatment, or even the low-dose amitriptyline therapy in alleviating globus symptoms, and producing global improvements for refractory globus patients.

1. Introduction

Globus pharyngeus, demonstrating as a sensation of a lump or something stuck in the throat, is a well-defined clinical condition that is usually long-lasting, difficult to treat, and has a tendency to recur [1]. Our recent investigation [2] had found that up to 24% of general globus pharyngeus should be recognized as refractory globus pharyngeus (RG) which was characterized by a more severe, intrusive symptoms and are refractory tocurrent conventional treatment options, leading to substantial reduction in quality of life and psychological distress. It is also noteworthy that simple reassurance or routine therapy may not be adequate for them [3,4].

Antidepressant agents are frequently used in patients with functional gastrointestinal disorders (FGIDs) and showed a promising efficacy, even though for refractory FGIDs [5,6]. Our previous study [7] manifested that low-dose amitriptyline is well tolerated and effective for general globus pharyngeus patients with a 75% treatment response rate, which was significantly greater than that of pantoprazole group. However, there are still few trials involving antidepressant therapies for globus pharyngeus, let alone in treating RG. Furthermore, it is well recognized that different antidepressant agents have different pharmacodynamic effects on gastrointestinal functions for treating various FGIDs.

Therefore, we would like to further explore the efficacy as well as side-effect difference between paroxetine (PAR) and amitriptyline (AMT) in treating RG.

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2. Materials and methods

2.1. Patient selection

The study subjects were recruited by referrals from either the department of gastroenterology or Ear, Nose and Throat (ENT) Clinics at Guangzhou Nansha Central Hospital. All of them were then further screened by gastroenterologists in the research team and were considered eligible to join the study, if they satisfied the inclusion criteria: they had to be older than 18 years of age and had to fulfill the Rome III consensus criteria [8] for the diagnosis of globus pharyngeus. All patients underwent otolaryngological assessment, neck/thyroid palpation and upper gastrointestinal endoscopy or laryngoscopy, to exclude the presence of any organic disease. In addition, patients had to show a lack of response to a minimum of 3-month therapy with routine treatments, including education, explanation, reassurance, and at least two medical treatments (e.g., proton pump inhibitors (PPIs), prokinetics, or pharyngitis medicines). These patients should be recognized as RG patients [2] and were recruited into the study. Exclusion criteria were as follows: (1) age below 18 or over 80; (2) known allergy to lansoprazole, AMT or PAR; (3) severe hepatic or renal dysfunction; (4) prostatic disease; (5) known glaucoma; (6) serious heart disease; (7) history of seizures; (8) pregnancy or breast feeding; (9) recent use of monoamine oxidase inhibitors; and (10) absence of informed consent or refusal to join the study.

2.2. Ethics statement

This study was a prospective, randomized controlled trial for RG and was approved by the hospital ethics committee, while registered in the Chinese Clinical Trial Registry center (Registration number: Chi-CTR-TRC-14005097). Written informed consent was obtained from all the subjects.

2.3. Sample size

Previously [7], we reported that the treatment response of low-dose AMT for globus patients was 75%, significantly higher than that of 35.7% in RT groups. Moreover, we performed a preliminary trial before conducted the present study to evaluate the efficacy of PAR for globus patients, found that 80% (16/20) of globus patients could be classified as treatment response. For estimate the sample size of the study, a significance level of the test was set at 0.05 (equate to $\alpha = 0.05$), while power of the test was 0.9 (equate to $1 - \beta = 0.9$). Twenty-eight patients per group (total $n = 84$) would be required. Additionally, drop-out rates in our previous study was less than 10%. Therefore, recruiting up to 32 patients for each of these three groups in this study should be sufficient to enable us to recruit and randomize sufficiently.

2.4. Study design and procedures

After a thorough initial evaluation and assessment, the study was described to eligible patients. And then they were randomly assigned by an independent investigator using a computer-generated random numbers table into one of three treatment groups, including routine treatment group (RT group), receiving lansoprazole (Takepron; 30 mg/tablet; Takeda Pharmaceutical Company, Osaka, Japan) 30 mg twice daily, one tablet in the morning and another tablet in the afternoon; AMT group, receiving 25 mg AMT (AMT; 25 mg/tablet; HuNan DongTing Pharmaceutical Co., Ltd. HuNan, China) once daily before bedtime; and PAR group, receiving PAR (Seroxat; 20 mg/tablet; Glaxo SmithKline Pharmaceutical Co., Ltd.) 20 mg once daily before bedtime. The treating period was 6 weeks.

2.5. Assessments

Patients were assessed by the following scales pre-treatment (regarded as baseline) and at the end of the 6-week trial:

(1) The Glasgow Edinburgh Throat Scale (GETS) [9] questionnaire which was composed by globus symptom scores and scores that evaluating the psychological impact of patient's symptoms was used to assess the severity of globus symptom. In this study, we only used the globus symptom score section, for which higher scores represent more severe symptoms.
(2) The Pittsburgh Sleep Quality Index (PSQI) [10] was used to assess the quality and patterns of sleep over the previous month. A higher total score represents worse sleep quality, with scores >7 indicating the presence of a sleep disorder.
(3) The 17-item Hamilton Depression Rating Scale (HAMD) [11] was used for evaluating the severity of depression, and higher scores indicate more severe depression, with scores >7 indicating the presence of depression.
(4) The 14-item Hamilton Anxiety Rating Scale (HAMA) [12] was applied for measuring the severity of anxiety, for which higher scores indicating more severe anxiety, with scores >7 indicating the presence of anxiety.
(5) The Medical outcomes study 36-item short form health survey (SF-36) [13] was used for assessing patients' quality of life, for which higher scores represented better quality of life. It covers 8 domains of physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). Each domain scored from 0 to 100.

The main efficacy endpoint was the subjective feeling of globus symptom relief assessing by the GETS. The secondary efficacy endpoints included patients' quality of life measuring by SF-36, quality of sleep as assessed by PSQI as well as psychological state as valuating by HAMD and HAMA. All patients entering this study were contacted over the phone and were required to make a return visit to the treating clinician every two weeks, reporting the treatment efficacy and the occurrence of any adverse events.

The following examinations were completed at baseline, at the end of the 6-week treatment, and, additionally, at any time during the trial the treating clinician considered such tests necessary: routine blood tests; blood biochemistry to determine liver function, kidney function, and fasting blood glucose; inflammatory markers; a urine pregnancy test (women only); and a 12-lead electrocardiographic examination.

2.5.1. Treatment response

Treatment response [7] was defined as a >50% reduction in the GETS score. The response was calculated as: [(score at treatment − score at baseline)/score at baseline] × 100%. The treatment responses of these three groups were calculated separately.

2.6. Statistical methods

Data analysis was performed using SPSS 13.0 software (SPSS Inc., Chicago IL, United States). Paired *t*-test or Mann–Whitney *U*-test was used to compare measurement data before and after treatment. Continuous variables were compared across groups using one-way ANOVA or Kruskal–Wallis method, as appropriate. Categorical variables were compared across groups using the χ^2 test or Fisher's exact test, as appropriate. Bonferroni test was used for multiple comparisons. Significance tests were 2-tailed and managed at the 0.05 significance level.