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BRIEF ARTICLE

Treatment of functional dyspepsia with sertraline: A double-blind randomized placebo-controlled pilot study

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Abstract

AIM: To evaluate sertraline, a selective serotonin reuptake inhibitor in the treatment of patients with functional dyspepsia.

METHODS: Consecutive tertiary hospital patients with a clinical diagnosis of functional dyspepsia (FD) according to the Rome Ⅱ criteria with a Hong Kong dyspepsia index (HKDI) of greater than 16 were recruited. Patients commenced enrolment prior to the inception of the Rome Ⅲ criteria for functional dyspepsia. All patients were ethnic Chinese, had a normal upper endoscopy and were *Helicobacter pylori* negative prior to enrolment. Study patients were randomized to receive sertraline 50 mg or placebo daily for 8 wk. HKDI symptom scores, quality of life, hospital anxiety and depression (HAD) scale and global symptom relief were evaluated before, during and after treatment. Adverse effects were monitored during and after treatment.

RESULTS: A total of 193 patients were randomized in the intention to treat (ITT), and 150 patients were included in the per protocol (PP) analysis. In both the ITT and PP, there was no difference in the primary outcome of global dyspepsia symptoms between the sertraline and placebo groups at week 8. In the ITT analysis, 98 and 95 patients were randomized to the sertraline and placebo groups respectively. A total of 43 patients withdrew from the study (22.3%) by week 8, with 23 of the 24 drop-outs in the sertraline group occurring prior to week 4 (95.8%). In contrast, in the placebo arm, 11 of 19 patients dropped out by week 4 (57.9%). Utilizing the last response carried forward to account for the drop-outs, there were no differences between the sertraline and placebo groups at baseline in terms of the HKDI, HKDI 26.08 ± 6.19 *vs* 26.70 ± 5.89, $P = 0.433$; and at week 8, HKDI 22.41 ± 6.36 *vs* 23.25 ± 7.30, $P = 0.352$ respectively. In the PP analysis, 74 and 76 patients were randomized to the sertraline and placebo groups respectively. At baseline, there were no statistically significant differences between the sertraline and placebo groups, HKDI 25.83 ± 6.313 *vs* 27.19 ± 5.929 respectively, $P = 0.233$; however by week 8, patients in the sertraline group demonstrated a statistically significant difference in their Hong Kong Dyspepsia Index compared to placebo, HKDI 20.53 ± 6.917 *vs* 23.34 ± 7.199, $P = 0.02$, respectively). There was also no statistically significant difference in overall quality of life measures or the HAD scale related to treatment in either the ITT or PP analysis at week 8.

CONCLUSION: This pilot study, the first to examine sertraline, a selective serotonin reuptake inhibitor, for the management of FD, did not find that it was superior to placebo.

Key words: Dyspepsia; Chinese; Gastrointestinal diseases; Drug therapy; Sertraline; Selective serotonin reuptake inhibitors

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INTRODUCTION

Functional dyspepsia (FD) is defined as persistent or recurrent pain and/or discomfort centered in the upper abdomen for at least 12 wk in the preceding 12 mo according to the Rome Ⅱ criteria in the absence if structural disease[1]. The Rome Ⅲ criteria, published in 2006, further refines FD into epigastric pain syndrome and/or postprandial distress syndrome with the criteria fulfilled in the last 3 mo with symptoms onset at least 6 mo prior to diagnosis, again in the absence of structural disease[2,3]. The prevalence of dyspepsia in the Asia Pacific region varies from 10% to 20%, with a FD prevalence of 7.9%-12% which is lower than that seen in the west[4-6]. FD or non-ulcer dyspepsia is a significant cause of morbidity and work-related productivity lost[7]. The pathogenesis of FD is not known. A number of studies have shown an important role of psychological factors in the pathogenesis of this condition[8-10]. We have demonstrated previously that anxiety and depression are important co-factors in its pathogenesis[11]. There is no definitive treatment for this condition. Acid suppression therapy has been shown to be ineffective for the treatment of this condition in Chinese patients[12] despite benefit of proton pump inhibitor therapy in patients with ulcer-like and reflux like dyspepsia[13]. *Helicobacter pylori* (*H. pylori*) eradication confers only small benefit relative to placebo[14] and studies of itopride, a dopamine D2 antagonist with acetyl cholinesterase effects although initially promising, conferred no benefit in a subsequent and larger study[15,16]. Visceral hypersensitivity appears to be important in the pathogenesis of FD, as evidenced by a small study utilizing capsaicin to generate a desensitization of gastric nociceptive C fibers[17]. Similarly, antidepressants were investigated in FD for their ability to modulate visceral hypersensitivity[18]. Earlier antidepressant therapy studies demonstrated some effectiveness in the treatment of functional gastrointestinal symptoms, however a recent student utilizing venlafaxine (a selective serotonin and noradrenaline reuptake inhibitor) did not show any benefit[19-23]. In terms of antidepressants studied in FD, tricyclic compounds are the class of antidepressants best studied for this application, however selective serotonin reuptake inhibitors (SSRIs) are more commonly used in clinical practice because of their safer side-effect profile. The precise mechanism of action of SSRIs in the treatment of depression is not fully understood. However, long-term treatment with SSRIs has been reported to down regulate the serotonin transmitter responsible for serotonin reuptake as well as serotonergic receptors[24], which may down regulate visceral hypersensitivity.

An open label study found that the SSRI, fluoxetine, was superior to no treatment in depressed patients with FD, however had methodological flaws including the open label nature of the study[25]. To date, there are no published randomized controlled studies on the effect of sertraline for the treatment of FD. We performed a double-blind, randomized, placebo-controlled trial consisting of 8 wk of therapy in Chinese patients with FD. We aimed to assess the efficacy of SSRI in the treatment of FD and to identify potential responders to SSRI therapy in subgroups of patients with dyspepsia as their chief symptom.

MATERIALS AND METHODS

Patient enrollment

Consecutive patients referred to the Department of Medicine, Queen Mary Hospital, Hong Kong between June 2002 and June 2008 were screened for enrolment. FD was defined as persistent or recurrent dyspepsia (pain or discomfort centered in the upper abdomen) with no evidence of organic disease, chronic severe constipation, or irritable bowel syndrome to explain the symptoms, for at least 12 wk, which need not be consecutive, within the preceding 12 mo, in accordance with the Rome Ⅱ criteria[26]. The Rome Ⅲ criteria for FD had not yet been conceived when the study was commenced[3]. Patients aged 18-80 years with symptoms of dyspepsia within two weeks prior to the endoscopy visit were eligible for the study. Informed written consent was obtained from all patients. Patients were also required to have a dyspepsia score of greater than 16 by our validated questionnaire[27] and have had no prior investigations performed for this episode of dyspepsia within the 6 mo prior to the study. All enrolled patients were ethnic Chinese. Exclusion criteria included patients who were pregnant or breast feeding, had a history of alcohol or drug abuse; recent malignancy or significant medical illnesses or concurrent medication, which may interact with or contra-indicate the use of sertraline. Patients with a history of or current anti-depressant use were excluded. Patients with classical heartburn or acid regurgitation as their only symptom without epigastric discomfort or pain were also excluded to avoid recruitment of patients with non-erosive gastro-oesophageal reflux disease. All patients had normal upper endoscopy. The study was approved by the Institutional Review Board of the University of Hong Kong/Hospital Authority Hong Kong West Cluster (EC 1774-02).

Study protocol

Patients were randomized to receive either sertraline 50

mg or placebo once daily for eight weeks. Randomization was performed by drawing a sealed envelope that contained a pre-assigned randomized treatment generated by computer on entry to the study. Both the investigators and patients were blinded to the assigned treatment throughout the study. The sertraline and placebo capsules were identical in appearance. Patients were given a diary in which they recorded side effects and symptoms during therapy. After enrolment by gastroenterologists, patients returned for follow up at four and eight weeks where one of two gastroenterologists assessed their symptoms and quality of life.

Dyspepsia symptoms were assessed by a locally validated dyspepsia questionnaire, the Hong Kong dyspepsia index (HKDI) which consisted of 12 questions (epigastric pain, upper abdominal bloating, upper abdominal dull ache, epigastric pain before meals, epigastric pain when anxious, vomiting, nausea, belching, acid regurgitation, heartburn, feeling of acidity in the stomach, loss of appetite) graded on a five point Likert scale as follows: 1 (none), no symptoms; 2 (mild), symptoms can be easily ignored; 3 (moderate), awareness of symptoms but easily tolerated; 4 (severe), symptoms sufficient to cause interference with normal activities; and 5 (incapacitating), incapacitating symptoms with an inability to perform daily activities and/or require days off work. Test-retest reproducibility and internal consistency were good, with an intra-class correlation coefficient of 0.89 and Cronbach's alpha coefficient of 0.90. A cut off score of $\geqslant$ 16 was discriminative between controls and dyspeptic patients. Moreover, the HKDI score was significantly correlated to patients who reported a subjective improvement in symptoms and those who reported no change or worsening after therapeutic intervention (Kendall's *tau* = 0.21, P = 0.02)[27]. Patients were then sub-classified into four dyspepsia subgroups according to their predominant symptoms: (1) ulcer-like dyspepsia-predominant epigastric pain; (2) dysmotility-like dyspepsia-predominant discomfort that may be characterised by upper abdominal fullness, early satiety, bloating, or nausea; (3) reflux-like dyspepsia-predominant reflux symptoms (heartburn or acid regurgitation); and (4) unspecified-symptoms do not fulfill the criteria for ulcer-like, dysmotility-like, or reflux-like dyspepsia. Although reflux-like dyspepsia was discarded in the Rome II criteria, we felt that a certain proportion of patients with FD still belong to that particular subgroup and there is considerable overlap between FD and non-erosive or negative endoscopy reflux disease[28,29]. Furthermore, inclusion of reflux-like dyspepsia allows comparison with previous randomized controlled trials[30].

Quality of life was assessed by a locally validated questionnaire [Chinese translated form of 36-item short-form (SF-36)][31]. The SF-36 consisted of 36 items to measure eight aspects of psychological general well being (physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health). A generic quality of life instrument was utilized to assess general well being as at the commencement of this study, there were no dyspepsia specific quality of life questionnaires validated in the Chinese language. The symptoms pertaining to anxiety and depression were assessed by the hospital anxiety and depression (HAD) scale questionnaire which consists of 14 questions. Finally, subjective global symptom relief was graded by patients, from a scale of 1 to 5, representing the spectrum from complete resolution of symptoms to worsening of symptoms, respectively.

Study intervention: Sertraline

The SSRI utilized in this study was sertraline (Zoloft, Pfizer Corporation) at a dose of 50 mg orally daily. Study participants were provided with pre-sealed boxes containing either sertraline or placebo and were asked to take a capsule per day for 8 wk in total. Patients were provided with a 4 wk supply of capsules and were contacted weekly to ensure compliance with treatment. Patient compliance was checked by counting returned study medications. Subjects who took less than 75% of the study medication were excluded from the final per protocol (PP) analysis.

Statistical analysis

Mean dyspepsia score, the eight aspects of the SF-36 scores and the two HAD scores before and after treatment were collected on Excel (Microsoft) databases in the two treatment groups. The change in mean HKDI, SF-36 and HAD scores from baseline, at the four and eight week visit were calculated and compared between the sertraline and the placebo groups. Patient diaries, detailing the presence and severity of symptoms, were also compared between groups at weeks 4 and 8. The primary end point was defined as an improvement in clinical symptoms at week 8. Secondary endpoints included an improvement or resolution of the clinical symptoms, or an improvement in any of the scales including HKDI, SF-36 or HAD at week 8. Continuous variables were expressed as mean ± SD, and categorical data expressed as percentages. Continuous variables were compared using Student's t tests. Categorical variables were compared using Fisher exact or χ^2 tests as appropriate. The Mann-Whitney test was used for data with a skewed distribution. The intention to treat (ITT) analysis included all patients who had taken at least one tablet. In the PP analysis, patients with poor drug compliance (< 75% intake of any study drugs) and drop outs (due to adverse effects) were excluded. Multiple logistic regression analysis was performed to determine independent factors (age, sex, *H. pylori* status, smoking, alcohol intake, dyspepsia duration, predominant symptoms, and type of treatment given) associated with treatment response.

All calculated P values were two-sided and P values < 0.05 were considered statistically significant. Statistical analysis was performed using SPSS Ver. 16.0 for Windows (SPSS Inc., Chicago, IL, United States).

Power of the study

This was a pilot study, so assuming a placebo response

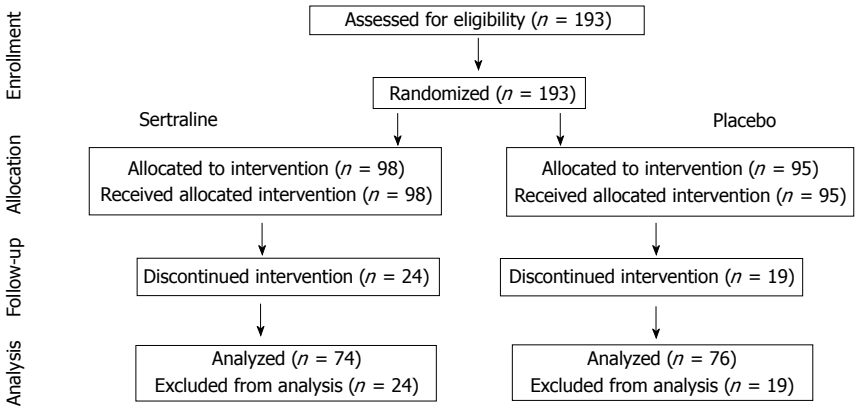

Figure 1 Study patient flow chart.

Table 1 Demographics of study patients

	Sertraline	Placebo	*P* value
Number of patients	98	95	
Age (yr)	43.0	41.6	0.515
Sex (male)	27	27	1.000
Current smokers (%)	3.2	7.3	0.122
Alcohol (%)	6.2	8.3	0.295
H. pylori positive (%)	8.4	7.3	0.843
NSAID use (%)	3.1	2.6	1.000
Predominant symptom *n* (%)			
Ulcer like	17 (44.7)	21 (55.3)	
Dysmotility like	60 (49.2)	62 (51.8)	
Reflux like	8 (57.1)	6 (42.9)	
Non-specific	13 (68.4)	6 (31.6)	

H. pylori: *Helicobacter pylori*; NSAIDs: Non-steroidal anti-inflammatory drugs.

rate of 25%-30%, a drug response rate of 30 % above placebo and a drop out rate of 20%[11], 166 patients will be needed to demonstrate 95% confidence interval with power of 0.8 and alpha of 0.05 (i.e., 166 patients with dyspepsia with 83 patients in each arm). It was aimed to recruit 190 patients.

RESULTS

Baseline demographics

We recruited 193 eligible patients (patients for the ITT analysis). A total of 98 patients were randomized to receive sertraline 50 mg and 95 patients were randomized to receive placebo (Figure 1).

All recruited patients were ethnic Chinese. Baseline characteristics of the patients in the two treatment groups are given in Table 1. 75.5% and 80% of patients took more than 75% of the medications in the sertraline and placebo groups, respectively. Poor compliance patients, those who refused follow up, and those who discontinued treatment because of adverse events were excluded from the PP analysis ($n = 150$).

Baseline characteristics of the patients and their dyspepsia subtypes are listed in Table 1. Mean age of these patients was 42.4 years (range: 18-71 years) with a median dyspepsia score of 26.5 (range: 17-46). There were 54 males (mean age 45.2 years) and 139 females (mean age 41.4 years). Mean age, sex distribution, smoking history, alcohol consumption and H pylori positivity at baseline were similar between the treatment groups (Table 1). Baseline mean HKDI score, SF-36 and HAD scales in the PP analysis (Table 2) assessments were similar between the treatment groups.

Dyspepsia scores

In the PP analysis at week 8, 28.4% *vs* 27.6%, of patients experienced complete resolution of their dyspepsia symptoms, whilst 64.9% *vs* 59.2% of patients experienced no difference in their dyspepsia symptoms in the sertraline and placebo groups ($P = 0.511$ for difference between the two cohorts) respectively. Sub group analysis for complete response at weeks 4 and 8 was also unrevealing. Complete response was similar between the treatment groups at weeks 4 and 8.

In the PP analysis the baseline mean HKDI score was 25.83 (SD = 6.313) and 27.19 (SD = 5.929) for sertraline and placebo arms respectively ($P = 0.233$). Mean HKDI score improved in all groups at week 4 compared to baseline. HKDI score in the sertraline group improved the most but was not statistically significant. By week 8, the sertraline group had a mean HKDI score of 20.53 (SD = 6.917), whilst the placebo group's mean dyspepsia score was 23.34 (SD = 7.199), ($P = 0.02$). The change in HKDI between week 0 to 8 was 5.3 and 3.85 in the treatment and placebo groups respectively ($P < 0.001$ for both sertraline and placebo groups). There were no consistent significant differences in the parameters of the quality of life assessment and the HAD scale at week 8 (Table 2).

For the ITT analysis, where the method utilized was the last response carried forward, the mean HKDI at week 0 was 26.08 and 26.70 (SD = 6.19 and 5.89, $P = 0.433$) for sertraline and placebo cohorts respectively. Although improvement of the HKDI was seen at weeks 4 and 8, the results were not statistically significant at (HKDI week 8 = 22.41 and 23.25, SD = 6.36 and 7.30 for sertraline and placebo respectively, $P = 0.352$). Again, there was no consistent significant differences in the parameters of quality of life assessment, HAD scale or complete responses at week (data not shown).

Table 2 Dyspepsia index, 36-item short-form score and hospital anxiety scale results

	Week 0	*P* value	Week 4	*P* value	Week 8	*P* value
Mean dyspepsia score						
Sertraline	25.83	0.124	22.59	0.740	20.53	0.02
Placebo	27.19		22.94		23.34	
SF36-physical functioning						
Sertraline	81.79	0.585	79.30	0.39	75.61	0.15
Placebo	83.11		81.63		80.39	
SF36-role physical						
Sertraline	57.91	0.30	52.62	0.40	52.70	0.22
Placebo	52.11		57.87		62.17	
SF36-bodily pain						
Sertraline	49.10	0.002	54.22	0.89	53.97	0.50
Placebo	41.06		53.78		51.63	
SF36-general health						
Sertraline	33.76		39.06		35.39	
Placebo	32.54	0.65	41.85	0.34	34.72	0.84
SF36-vitality						
Sertraline	47.69	0.57	47.91	0.73	49.05	0.68
Placebo	46.76		48.88		50.33	
SF36-social function						
Sertraline	67.75		72.38		68.41	
Placebo	67.68	0.98	72.19	0.96	69.74	0.73
SF36-role emotional						
Sertraline	51.82		53.49		52.70	
Placebo	50.75	0.85	54.19	0.90	51.32	0.85
SF36-mental health						
Sertraline	58.12		54.89		65.24	
Placebo	58.59	0.83	61.57	0.03	64.37	0.69
HAD scale						
Anxiety score						
Sertraline	14.27	0.52	13.58		14.29	
Placebo	13.88		13.66	0.90	13.68	0.41
HAD scale						
Depression score						
Sertraline	15.51	0.14	15.50	0.88	14.27	0.45
Placebo	14.84		15.56		13.70	

HAD: Hospital Anxiety and Depression Scale; SF36: 36-item short-form.

Adverse events

At week 8, a total of 43 patients (24 on sertraline and 19 on placebo) discontinued treatment. The main reasons for discontinuation of the study medication were drug side effect (41.2%), no reason given (41.9%) or other reason which included the development of conditions for which sertraline could interfere with prescribed treatment (7%) (Table 3). Of particular interest is the pattern of withdrawal from the study, 23 of 24 patients withdrawing from the sertraline group did so before week 4, representing 95.8% of all drop-outs from the sertraline group. By contrast, in the placebo group, approximately half of the patients withdrew prior to week 4 (57.9%), whilst the other half withdrew prior to week 8. Patients experiencing drug adverse effect were noted to have multiple symptoms including insomnia, constipation and agitation, however there was no significant difference in the rate of adverse effects experienced by the two cohorts. Nine percent of all study patients withdrew from the study without explanation (were lost to follow up).

Table 3 Default patient profile *n* (%)

	Default week 4	Default week 8	Reason for default week 8		
			No reason given[1]	Adverse effect of drug[1]	Other[1]
Sertraline	23	24	7 (16.3)	14 (32.6)	3 (7)
Placebo	11	19	11 (25.6)	8 (18.6)	0 (0)

[1]Represents percentage of all default patients; $P = 0.259$ for drug adverse effect between sertraline and placebo groups.

Factors associated with response

Age, sex, *H. pylori* status, smoking, alcohol consumption, and dyspepsia duration were not associated with response to sertraline. Multiple logistic regression analysis did not identify any independent predictors of favorable outcome.

A *post hoc* analysis comparing reflux like dyspepsia *vs* all other types of dyspepsia showed similar results to the PP analysis, in the non reflux like group the HKDI was 25.70 and 27.00 at week 0, whilst at week 8, HKDI was 20.85 and 23.42 respectively ($P = 0.004$). Similarly, the SF 36, HAD scales and complete response rates did not show any statistically significant differences (data not shown). In the reflux like group where $n = 14$, HKDI was 28.88 and 28.00 at week 0, and at week 8, HKDI was 21.00 and 23.80 ($P = 0.426$).

DISCUSSION

We have reported a double-blind, randomized, placebo-controlled pilot study of sertraline 50 mg *vs* placebo for the treatment of FD. We found that there was a statistically significant improvement in the mean HKID score at week 8 in the sertraline group compared to the placebo group in the PP but not the ITT analysis. There were also no differences in measures of quality of life, depression and anxiety and subjective global symptom resolution.

This study is a pilot study examining the effect on sertraline in patients with FD. The sertraline dose that was administered is a clinically relevant dose (the initial treatment dose for depression and obsessive-compulsive disorder and in some studies, depression)[32]. The trial duration of 8 wk seems adequate given that a steady-state plasma sertraline level is expected after 1 wk with once daily dosing and the beneficial effects of antidepressants in functional gastrointestinal disorders are often observed after shorter treatment duration than in depression[33]. However, longer term follow-up may yield more significant results given that individual responses to sertraline can vary and up to 12 wk may be required to see the full onset of action. Furthermore, although the dosage of sertraline utilized was appropriate for the reasons cited above, several studies have indicated that due to ethnic differences, Chinese patients may tolerate lower doses better[33,34].

One of the limitations of the study is the drop out rate, 17.6% at week 4 and 22.3% at week 8. Our drop

out rates are similar to those observed when antidepressants are utilized in functional gastrointestinal disorders[35]. There are many factors which could account for the drop out rate in our study. Sertraline's known side effects include sleep disturbance, headache, tremors, agitation and gastrointestinal upset[24]. In our study, adverse drug effect was the cause of study withdrawal in 41.2% of cases. Interestingly, of the patients who dropped out, 41.9% withdrew from the study without giving a reason. Multiple studies have indicated a cultural bias in the Chinese population against a diagnosis of psychiatric or functional disorders[36-38] and the authors hypothesize that the cultural stigma attached to treatment for a functional disorder with a known anti-depressant would contribute significantly to the drop out rate. Furthermore, the majority of the drop outs in the sertraline group occurred at week four, which could possibly be explained by the short term side effects of sertraline usually seen during the run in period of SSRIs[39] which could be mitigated by more intensive support and education during the first few weeks of treatment.

Another limitation of the study is the failure to discern a difference in the generic quality of life measures utilized between the sertraline and placebo cohorts. This may ostensibly be a reflection of the fact that generic quality of life instruments are not sensitive enough to detect changes in overall well being in patients with FD particularly with treatment[40]. This has been seen with other gastrointestinal disorders and has resulted in the development of disease specific quality of life instruments[41,42].

Finally, the most important limitation of the study is the failure to find a difference in global symptom scores in the ITT analysis, and only a small difference in the HKDI, but not global symptoms score in PP analysis. The authors believe this small finding suggests a possible benefit of sertraline in patients with FD, but perhaps this study was under-powered to detect this difference due to the unexpectedly high dropout rate, particularly in the first 4 wk when SSRI adverse effects are at their maximal, and for this reason warrants further larger studies utilizing sertraline to clarify the issue. We assert that our findings are important given that clinicians not uncommonly are utilizing SSRIs to treat FD despite the fact that to date, our study included, there is no strong justification for its use[43].

In conclusion, our data suggest that an SSRI, sertraline was not superior to placebo for the management of FD in Chinese patients. Further studies are warranted to confirm these results as this study was likely under powered to determine an effect in the context of a higher than expected drop out rate and there is a suggestion that with more support, a longer follow up period, and perhaps a reduction in the dose of sertraline in Chinese patients an effect may be seen.

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COMMENTS

Background

Early studies with tricyclic antidepressants demonstrated efficacy in the treatment of functional dyspepsia yet there have been no double-blind, randomized, placebo-controlled trials examining the role of selective serotonin reuptake inhibitors (SSRIs) in this condition.

Research frontiers

SSRIs, the most commonly utilized antidepressant in clinical practice, may improve the symptoms of functional dyspepsia through modulation of visceral hypersensitivity. In this study, the authors examine the effects of sertraline, a SSRI, on global symptoms, a locally validated dyspepsia index, the 36-item short-form (SF-36) and the hospital anxiety and depression scale.

Innovations and breakthroughs

Tricyclic antidepressant medication has been shown to be efficacious in functional dyspepsia, however tricyclic antidepressant medications have significant side effects, prompting the study of the utility of newer antidepressants in this condition. Venlafaxine, a selective serotonin and noradrenaline reuptake inhibitor did not show any benefit in functional dyspepsia however an open label study of fluoxetine, a SSRI, found benefit. This is the first double-blind, randomized, placebo-controlled study examining an SSRI in the treatment of functional dyspepsia.

Applications

This study found that treatment with the SSRI, sertraline, improved the Hong Kong dyspepsia index score at week 8 compared to baseline but did not find overall improvement in global dyspepsia symptoms, SF-36 or the hospital anxiety and depression scale, possibly due to the higher than expected drop out rate in the sertraline group by week 4. Larger studies are warranted to further examine the effects of sertraline in functional dyspepsia.

Peer review

This is a nicely designed study showing that SSRI sertraline is of no benefit in functional dyspepsia. The authors acknowledge the main limitation of a negative study represented by the scarce numerosity and high drop out rate, based on the optimistic calculations adopted to evaluate sample size. A more realistic hypothesis will substantially raise the number of patients needed to be included.

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