Chronic functional vomiting syndrome: Psychiatric morbidity and response to antidepressant drugs

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Abstract

The study was conducted to assess psychiatric morbidity in functional vomiting syndrome in adults and to do an open trial of tricyclic Antidepressants drugs (TCAs) Patients participating in the study were recruited from the outpatient clinics of tropical medicine department of Zagazig University hospital over two years period from January 1998 to December 1999.All patients who were proved free from medical or metabolic causes were subjected to Semi-structured psychiatric interview for data collection and diagnosis according to DSM -1V operational criteria. The patients were given one of the following drugs (imipramine 10-100 mg, Amitryptiline 10-100 mg, dothiapin 25- 100 mg or clomipramine 25- 100mg). Treatment response was graded as follow: 0 = no improvement or worse 1 = slight improvement, but requiring treatment change 2 = moderate improvement, stable regimen but not completely resolved 3 = clinical remission. The number of patients was103 (age range 18-47& mean±s.d 34±6.2 years and 61 were females and 42 males).all patients were free from any medical disorders explaining symptoms. 17%of patients had a major depressive episode either current or past. 11.7% had dysthymic disorders. 2% had panic disorder and 6.5% were substance abusers mostly codeine and bango. 21% of patients were diagnosed as having somatoform disorders.

Results of tricyclic antidepressant drugs treatment: A total of 146 trials were used in the 103 patients. Imipramine was used in 47 trials; Amitriptyline was used in 34 trials, Dothiapin in 37 trials and Clomipramine in 18 trials. Side effects necessitating discontinuation of medication or change of medication were noted in 51 trials (34%of trials).26 patients (25%) had complete remission of symptoms (had score 3), partial response was noted in 42patients(had score 2) and 25 patients were unresponsive to treatment (score 0 or 1).

Introduction:

Nausea and vomiting are common gastrointestinal complaints caused by a variety of abnormalities in the brain-gut axis. The diagnosis of functional nausea and vomiting is made when the symptoms are chronic and unexplained ***(Drossman et al 1990; and Tally and Philips, 1988.).*** However the symptoms can also occur alone or in conjunction with other functional bowel disorders ***(Agreus et al 1995).*** The mechanism of symptoms production is poorly understood. At least in the case of dyspepsia , hypersensitivity to visceral distension and abnormal motor function may be contributors-mechanisms shared by other functional disorders ***(Lehman et al 1991).*** Histopathologic abnormalities usually are not found; if they are found, they correlate poorly with the symptoms. Evidence may indicate altered physiologic activity (e.g., symptomatic diffuse esophageal spasm, delayed gastric emptying,) or psychiatric disorder (conversion disorder , somatization disorder). In many patients, more than one of these factors is involved ***(Anderson et al 1997).*** Regardless of etiology, experiencing and reporting of symptoms vary, depending on

the patient's personality, the psychological meaning of the illness, and sociocultural influences. Symptoms of nausea and vomiting may be minimized or reported indirectly or even bizarrely by a severely depressed patient but presented with dramatic urgency by a histrionic patient. Although distressing, the illness may satisfy certain psychologic needs for some patients. Secondary benefits from chronic illness help explain why many of these patients may have unexpected side effects to medication and seem resistant to improvement. Finally, cultural influences may affect the reporting of symptoms. ***(Fleisher Dr. 1995)***

No singular treatment is of proven benefit in functional vomiting, and treatment reports are largely restricted to the pediatric age group, however prophylaxis is more important as a goal and there are reports of the efficacy of propranolol, cyproheptadine and tricyclic antidepressants as prophylactic agents

(Fleisher Dr. 1995, Andersen. etal. 1997,) but little information is available about prophylaxis in adults.***(Prakash and Clouse.1999)***

Antidepressants appear to have beneficial effects in irritable bowel syndrome ***(Gorard et al 1995)*** and more recently in the treatment of functional vomiting in adults ***(Prakash et al 1998)*** and in cyclic vomiting syndrome in adults ***(Prakash 1999)***

Aim of the work:

1- To assess psychiatric morbidity in functional vomiting syndrome in adults
2- To do an open trial of tricyclic Antidepressants drugs (TCAs) in functional vomiting syndrome in adults

Subjects & methods:

Patients participating in the study were recruited from the outpatient clinics of tropical medicine department of Zagazig University hospital over two years period from January 1998 to December 1999

Medical assessment:

All patients were subjected to full medical examination, history taking, barium meal, abdominal ultrasonography& gastroscopy to exclude medical or metabolic condition in addition to routine investigations including complete blood picture, renal &liver function tests as well as hormonal essay when endocrinal causes were suspected. Abdominal CT scans were done to most patients.

Psychiatric assessment:

All patients who were proved free from medical or metabolic causes were subjected to Semi-structured psychiatric interview for data collection and diagnosis according to DSM -1V operational criteria.

Antidepressant trial:

Identified subjects were considered if the following criteria were satisfied: (1) the symptoms were present for a minimum of three months. (2) There was no diagnosis of psychosis or an eating disorder (3) the subject returned for at least one follow-up visit (4) there was no structural or metabolic explanation for the symptoms.

The patients were given one of the following drugs (imipramine 10-100 mg, Amitryptiline 10-100 mg, dothiapin 25- 100 mg or clomipramine 25- 100mg)

Treatment response was graded as follow: 0 = no improvement or worse 1 = slight improvement, but requiring treatment change 2 = moderate improvement, stable

regimen but not completely resolved 3 = clinical remission

Adverse effects were categorized into the following types: Anticholinergic effects, sedation, cardiovascular effects and other side effects. This process was continued through the duration of follow-up.

Statistical methods: Data are reported as Mean±S.D. Grouped data were compared using Fischer exact test or two-tailed Student t test.

Results:

General characteristics of patients:

The total number of patients attending the outpatient clinics of general medicine and tropical medicine departments presenting with functional nausea and vomiting during the years 1998 & 1999 was 103, with an age range " 18-47 "years. With a mean of 34 ± 6.2 years, of these 103 patients 61 were females and 42 were males, duration of nausea and vomiting ranged from 3 months to 11 months with a mean of 6.2 ± 3.4.Chronic persistent symptoms were present in 57 subjects whereas the remainder had an intermittent relapsing pattern. Most patients (96 patients) were seen by more than 3 physicians of various specialties including: general practitioner, gastroentrologists and internists ranging from 3 to 7 physicians before our assessment (23 patients had visited 3 physicians ; 61 patients had visited 4or5 physicians ; and 12 patients were assessed by 6 or 7 physicians) . Patients had received many types of various drugs with no benefit moreover 4patients were operated for exploration.

Results of medical assessment:

All patients were medically free apart from 30 patients who showed hyperemia of the lower esophagus and upper stomach considered to be secondary to the repeated vomiting.

Results of psychiatric assessment: 17% of our sample had a major depressive episode either current or past. 11.7% had dysthymic disorders. 2% had panic disorder and 6.5% were substance abusers mostly codeine and bango. 21% of patients were diagnosed as having somatoform disorders including somatization disorder; hypochondriasis and somatoform disorder NOS

Results of tricyclic antidepressant drugs treatment: A total of 146 trials were used in the 103 patients. Imipramine was used in 47 trials, Amitriptyline was used in 34 trials, Dothiapin in 37 trials and Clomipramine in 18 trials. Side effects necessitating discontinuation of medication or change of medication were noted in 51 trials (34%of trials).

26 patients (25%) had complete remission of symptoms (had score 3), partial response was noted in 42patients(had score 2) and 25 patients were unresponsive to treatment (score 0 or 1).

Table (1): Socio-demographic comparison between functional vomiting patients with psychiatric disorders and patients without psychiatric disorders

Items	f.v. patients with psychiatric disorders no.(62)	f. v. patients without psychiatric disorders no. (41)	t (x2)	P
Age (mean± s.d)	37±1.5	26± 3.3	22.599	<. 0001
Sex - Male - Female	22 40	20 21	1.298	(NS)
Education 0-7 years > 7 years	16 46	23 18	8.381	0.0038
Marital status Married Unmarried	51(11	15 26	20.43	<0.0001
Occupation Housewife Students Manual workers Professionals	33 4 22 3	20 5 16 0	3.094	0.3773 (NS)
Residence Urban Rural	32 30	18 23	0.32	(NS)

The patients with associated psychiatric disorder were older in age, more educated and most of them were married.

Table (2) Comparison between functional vomiting patients with psychiatric disorders and patients without psychiatric disorders

Item	Patients with psychiatric disorders no. (62)	Patients without psychiatric disorders no. (41)	t(x2)	P
No. of stressors before onset	2± 0.8	0.7± 0.3	9.94	<. 0001
Duration of symptoms (months)	8 ± 2.2	3 ± 2.2	11.29	<. 0001
No. of previous visits to physicians	6 ± 1.8	3 ± 0.7	10.16	<. 0001
No. of visits to traditional healers	2 ±1.1	1 ± 0.6	4.05.3 2	<. 0001

The patients with associated psychiatric disorders had more stresses before the onset, and had visited more physicians and traditional healers.

Table (3): Results of psychiatric assessment of 103 functional vomiting patients

Diagnosis DSM IV	NO.	%
Somatoform disorders	22	21.4%
Dysthymic Disorder	12	11.7%
Panic disorder	2	1.9%
Substance abuse	7	6.8%
Major depression	18	17%

Table (4): Results of tricyclic antidepressants treatment

TCA	No. of trials	Partial response Or remission	Median (dose range)	No response
Imipramine	47	37	50 mg (10-100)	8
Dothiepin	37	33	50 mg (25-100)	4
Clomipramine	18	11	50 mg (25-100)	7
Amitryptline	34	28	50 mg (10-100)	6

Discussion:

Functional upper GI complaints are common in the primary care setting accounting for 30 to 50 % of referrals to gastroenterologists. Referring physicians and GI specialists find functional upper GI complaints difficult to understand and treat ,and uncertainty may lead to frustration ,judgmental attitudes and the ordering of inappropriate tests in a futile attempt to find a biologic cause (Vanderhoof, etal. 1993).

The Results of Psychiatric Assessment: The most common psychiatric disorders were somatoform disorders 21,4% (hypochondriasis, somatization disorder, and somatoform disorders NOS) followed by major depression 17% (current or past

episode) and dysthymic disorder 11,7% next was substance abuse 6,8%

And the least frequent was panic disorder1.9%

The patients with associated psychiatric disorders were older in age, more educated, mostly married, had more stresses before the onset and had visited more physicians and traditional healers.

To our knowledge we are not aware of published studies in Medline assessing the psychiatric morbidity of functional vomiting patients.

Antidepressant trial:

The results of treatment by tricyclic antidepressant drugs suggest that functional nausea and vomiting responds favorably to TCAs in low daily dosages (68 out of 103 patients had either full remission or partial response). This outcome is less than the reported response in the study of Prakash etal (1998) where they found that more than 50% of trials resulted in full remission and partial remission was reported in more than 80% of the trials. This difference could be due to the small number of cases in study of **Prakash** (37 patients) and also the only psychiatric disorders reported were anxiety and depression who had better response to antidepressant drugs than somatoform disorders and associated substance abuse in addition to mood and panic disorders in our study.

Our results are similar to the open-label response to antidepressants in irritable bowel syndrome. When measured in a similar fashion symptom remission occurred in 61%of 138 irritable bowel syndrome patients treated with a variety of antidepressant agents (mostly TCAs) ***(Clouse et al 1994).***

The reported success may indeed represent important benefits of TCA treatment for these unexplained symptoms.

Whether equal success would be seen with placebo is not known. functional bowel disorders have a recognized placebo response and a modest spontaneous remission rate over short periods of observation (Klein,1988 and Tally etal,1992). However all subjects had been treated unsuccessfully with other medications before the TCA trials and the response to TCAs was evident and sustained in all who initially responded. This combination of findings would be unexpected from placebo ***(Rothschild and Quitkin, 1992).***

Antidepressants may be effective for functional nausea and vomiting through several mechanisms ***(Clouse, 1994).***

First the agents may interfere with exaggerated afferent input from the gut to the central nervous system. Such visceral hypersensitivity is now recognized as an important mechanism participating in symptom production from irritable bowel syndrome and functional dyspepsia as well as unexplained chest pain ***(Mayer and Gebhart, 1994)***.The ability of TCAs to affect visceral hypersensitivity remains somewhat conjectural ***(Prakash et al 1998)***

A second potential mechanism of benefit is the effect of TCAs on the central pathways involved in the vomiting process . Acetylcholine, serotonine, dopamine, and histamine all participate as relevant transmitters in the afferent pathways projecting to the vomiting canter and medications blocking receptors for these neurotransmitters can be effective anti-emetic agents ***(Mitchelson, 1992)***

So a central benefit of TCAs through interference with input to the vomiting center should remain in consideration as a potential mechanism of action of these drugs.

Third potential mechanism of benefit of TCAs is through their antidepressant effect, however the dosage used to reach symptomatic response is lower than that usually required for management of clinical depression ***(Cole 1988)***. Reduction in symptoms in other functional GIT disorders also occurs at a similar low dose range ***(Magni 1991).***

Advantages of our study

1- Relatively large number of patients (103 patients)

2- Experienced psychiatrists did psychiatric assessment for several times and consensus was achieved.

3- Our work was a prospective follow-up study to assess response to tricyclic antidepressants

The Only Limitation was that our work was an open trial non-placebo controlled

Conclusion:

1- Functional vomiting patients have a high percentage of psychiatric disorders and thus are in need for conjoint management by both gastro-enterologists and psychiatrists.

2- These patients responded to low doses of tricyclic antidepressants and thus we suggest the addition of these agents to the regimen of treatment of functional vomiting patients.

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الاضطرابات النفسية في مرضى متلازمة القيء الوظيفي في الكبار

كان الهدف من البحث هو تقييم الاضطرابات النفسية في مرضى متلازمة القيء الوظيفي في الكبار وكذلك تقييم استجابة عينة منهم لمضادات الاكتئاب ثلاثية الحلقات و أخذت العينة من المترددين على عيادة الأمراض المتوطنة الخارجية بمستشفيات جامعة الزقازيق على مدار عامين من يناير ١٩٩٨ حتى ديسمبر ١٩٩٩ ، أجريت مقابلة إكلينيكية للمرضى الذين ثبت خلوهم من أي أسباب طبية

عضوية للقيء و جمعت خلال المقابلة كل المعلومات الخاصة بتاريخ الحالة كما تم التشخيص الطب-نفسي حسب التقسيم الأمريكي الرابع ،وكان مجموع الحالات ١٠٣ تتراوح أعمارهم بين ١٨و٧٤ عاما و كان عدد الإناث ٦١ و عدد الرجال ٤٢ ' و استعمل كل من العقاقير التالية : إميبرامين (١٠-١٠٠ مجم) ، أميتربتللين (١٠-١٠٠مجم) دوثيبين (١٠-١٠٠مجم) وكلوميبرامين (١٠-١٠٠ مجم)

و صنفت استجابات المرضى للعلاج كما يلي :

٠ = عدم تحسن أو تدهور للأعراض ، ١ = تحسن طفيف و يحتاج لتغيير الدواء

٢ = تحسن متوسط في الأعراض و ٣ = تحسن تام أو شفاء ٠

و وجد أن الاضطرابات النفسية شبيهة العضوية هي أكثر الاضطرابات النفسية شيوعا في هؤلاء المرضى ٢١% و يتلوها اضطراب الاكتئاب الجسيم حيث كانت هناك نوبة اكتئاب حادة واحدة على الأقل وحالية أو سابقة في ١٧ % من الحالات و يتلوه اضطراب عسر المزاج في ١١.٧% منهم ثم اضطراب نوبات الهلع في ٢% و كان نسبة المتعاطين للأدوية المخدرة ٦.٥ % ٠ و أما عن نتيجة العلاج بمضادات الاكتئاب ثلاثية الحلقات : فقد تحسن ٢٥% من العينة تحسنا تاما = ٣ و حصل حوالي ٤١% من الحالات على تحسن متوسط = ٢ بينما لم يستجب ٢٤ % من الحالات لهذه الأدوية

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