EFFECTIVENESS OF DULOXETINE IN TREATING EARLY STAGE OF SOMATOFORM DISORDER AT KOSHI ZONAL HOSPITAL

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ABSTRACT

Introduction

Somatoform disorder (SD)is group of psychiatric disorders that disrupt multiple physical symptoms, accompanied by disturbance in thoughts, impairing activities of daily living due to muscle and joint pain, low back pain, headache, chronic tiredness, palpitation, stomach upset, dizziness and sleeplessness which may cause occupational and social dysfunction.

Objective

Evaluation of patients by Numeric Pain Rating Scale (NPRS), Pain Disability Scale (PDS) and complications duloxetine medication during treating of patients with somatoform disorder at Koshi Zonal Hospital.

Methodology

50 patients with first time diagnosis of SD were selected by in this cross sectional study on the basis of diagnostic and statistical manual (DSM-5), pain and other symptoms, were treated with Duloxetine medication in early stage of Somatoform Disorder and results were evaluated at 2ndweek, 6thweek and 12th week. The study was conducted from March 2016 to July 2017 at Koshi Zonal Hospital.

Results

Out of 50 early SD patients, total mean age was 41.38 years (range 20-60), 21 patients recovered at 6th week and 22 patients recovered at 12th week but 7 patients needed other medications after 12 weeks. Duloxetine was well tolerated with nausea and headache being the most common compliant following use of duloxeting.

Conclusion

Duloxetine can be both effective and well tolerated in the treatment of early stage of somatoform disorder.

KEYWORDS

Duloxetine, pain, somatoform disorder,

INTRODUCTION

Somatoform Disorders (SD) are a group of problems in which sufferings are a spectrum of multi system symptoms; such as generalized symptoms (arthralgia, backache, non-specific chest pain, chronic tiredness, headache), gastrointestinal symptoms (constipation, nausea, chronic bloating), genitourinary symptoms (erectile dysfunction, ejaculatory disturbance, impotence, dyspareunia, dysuria) and pseudone urologicsymptoms (amnesia, loss of consciousness, paresthesias, impaired coordination). Somatoform disorder is more common in women than in men, with life time prevalence of 0.2-2 percent in women while less than 0.2 percent in men.[1,2]

Vague symptoms of SD overlap with fibromyalgia, chronic fatigue, irritable bowel disease, anxiety, mood disorder, hypochondriasis, malingering and factitious disorder which may occur together or separately and poses a challenge in diagnosis. There is no single cause for SD so the diagnosis becomes difficult due to huge spectrum of symptoms. The etiology of SD is unclear. Studies suggest that multi-drug approach may be better whereas some suggest cognitive behavior therapy is most efficacious, others having a supportive role.[3] Duloxetine is a serotonin-norepinephrine reuptake inhibitor; it inhibits serotonin more than it does norepinephrine. The management requires a multifaceted approach fitted and tailored to the individual patient such as educating patient, cognitive behavior therapy and pharmacotherapy. Among pharmacotherapy, Duloxentine has been suggested for management of early stage of somatoform disorder.[4,5,6,7] Duloxetine is a serotonin-norepinephrine reuptake inhibitor; it inhibits serotonin more than it does norepinephrine. Duloxetine is approved by the FDA USA for use in fibromyalgia, diabetic neuropathic pain, major depressive disorder and generalised anxiety disorder.[3] In a study double-blind placebo controlled trail, it was found that Duloxetine 60mg was superior to placebo from week three to week eleven, and showed significant improvements in scales used for assessment of disability and pain, Roland-Morris Disability Questionnaire-24 and Brief Pain Inventory.[4] We were unable to find any studies of use of duloxetine in SD patients in Nepal, hence to find the effectiveness in our population we conducted this study.

METHODOLOGY

This cross sectional descriptive study was conducted on 50 patients in psychiatry outpatient department (OPD) who were diagnosed with somatoform disorder for first time and were naïve to treatment with duloxetine. The study was conducted from March 2016 to July 2017. Using Epi Info 7 statcalc we calculated sample size of 52 using 2% prevalence for somatoform disorder.[2] Of the 52 patients 2 were excluded following initial enrolment because they did not

A. One or more somatic symptoms that are distressing or result in significant disruption of daily life.
B. Excessive thoughts, feelings, or behaviors related to the somatic symptoms or associated health concerns as manifested by at least one of the following:
   - ❖ Disproportionate and persistent thoughts about the seriousness of one's symptoms.
   - ❖ Persistently high level of anxiety about health or symptoms.
   - ❖ Excessive time and energy devoted to these symptoms or health concerns.
C. Although any one somatic symptom may not be continuously present, the state of being symptomatic is persistent (typically more than 6 months).

We used duloxetinein a range of 20-60 mg doses. Higher range of the given dosage were used in unresponsive patients, according to severity of pain and other symptoms. We used Numeric Pain Rating Scale (NPRS) which is 11-point scale used to assess the pain intensity, which is scored 0 (no pain) through 10 (worst possible pain) to assess the severity of the pain.[8,9] We also used Pain Disability Index (PDI) with functioning from 0 (no disability) to 10 (total disability) to assess disability in seven broad areas: family/home, responsibilities, recreation, social activity, occupation, sexual behaviour, self-care, and life-support activity.[8,9] The PDI is an instrument that has been used to assess the degree to which chronic pain interferes with various daily activities. The NPRS requires minimal reading skills and hence can be used across all cultures. The PDI was translated to Nepali for this study. The results were analysed by using SPSS 22.

RESULTS

In our study all, except 7 patients showed good response. Thirty-five female patients mean age 40.28 (range 20-40) years, 15 male patients mean age 44.13 (range 30-60) years were included in our study.

Table 1: Distribution of age, male, female and duration of illness

	6th week improved	12th week improved	Not responded
Mean Age (year)	41.38	40.14	50.14
Mean Age Female	36.61	40.176	50.2
Number of Female	13	17	05
Mean Age Male	45.25	40	50
Number of Male	08	5	02
Duration of Illness	8.9 month	10.95 month	13.57 month

Among 35 female patients, 13 improved at 6th week, 17 patient improved at 12th week and 5 patients not satisfied with good responses. Among 15 male patients, 8 patient improved at 6th week, 5 patient improved at 12th week and 2 patients had not good responses.

NPRS (Numerical Pain Rating Scale) show significantly good responses as per follow up in table 2

Table 2: Average scores according to NPRS before and after use of Duloxetine

Before medication	2nd week	6th week	12th week
4.52	3.18	1.88	1.06

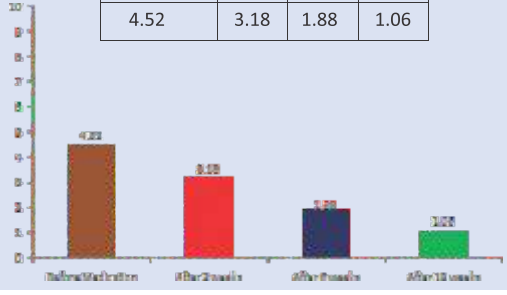
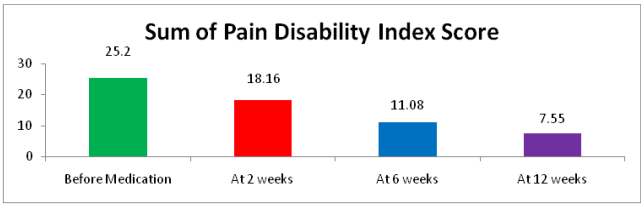


Table 3: Pain Disability Index before medication and at 2nd week, 6th week and 12th week.

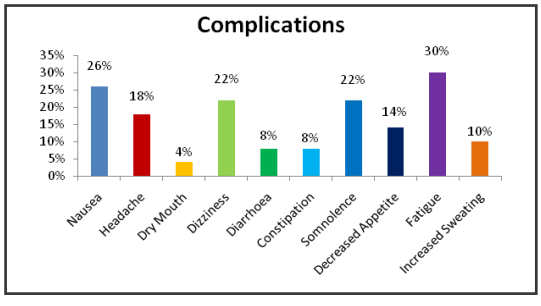
	Before Medication	2nd week	6th week	12th week
1.Family/Home Responsibilities	4.5	3.18	1.84	1.06
2.Recreation	4.38	3.04	1.74	1.06
3.Social Activity	4.38	3.04	1.64	0.96
4.Occupation	3.98	2.58	1.38	0.89
5.Sexual Behavior	2.68	2.26	1.8	1.93
6.Self Care	1.98	1.68	1.28	1.03
7.Life-Support Activities	3.4	2.38	1.4	0.58
Sum	25.2	18.16	11.08	7.55



According to patients' compliance dose was adjusted for good responses of patients.

Table 4: Complications during medication

Adverse event	Number (%)
Nausea	26
Headache	18
Dry mouth	4
Dizziness	22
Diarrhea	8
Constipation	8
Somnolence	22
Decrease appetite	14
Fatigue	30
Increased sweating	10



According to adverse event we changed in duloxetine doses.

DISCUSSION

Somatoform disorders are frequently encountered in all branches of medicine. There are difficulties to effectively treat somatoform disorders because it is related to medically unexplained symptoms, time consuming, requires patience and understanding, lack of definitive laboratory evidence and lack of compliance to treatment. Organic causes must be ruled out and sometimes it becomes a diagnosis of exclusion. Awareness and identification of risk factors helps limiting the expenses and harm of unnecessary investigations.[11,12] Clinical characteristics on the literature on SD indicate a common condition that can be severe and disabling. It is a psychiatric condition which is being treated by non-psychiatricphysician with patient unwilling to consult psychiatrists due to taboo, especially in scenarios like ours where lack of education/awareness prevails and psychiatric evaluation in early stage is difficult.[13] In our study most of patients referred in psychiatric Out Patient Department from medicine OPD, Oncology OPD, Orthopedic OPD, Gynaecology OPD and other hospitals. Pharmacological treatments commonly implemented are Duloxetine, Dothiepin and others. In this study we focused on Duloxetine effectiveness in SD.

Duloxetine is safe and well tolerated at the dosage of 60 mg once daily; dose can be adjusted to maximum of 120mg daily in divided doses. Duloxentine can be used in Gateway to Fibromyalgia, Premenstrual Dysphoric Disorder, Chronic Pain Conditions, Chronic Musculoskeletal Pain. Clinical trials reported that the patients tolerated the drug well and were safer in the treatment of SD. Adverse events can be seen during medication such as nausea, headache, dry mouth, dizziness, diarrhoea, constipation, somnolence, decrease appetite, sweating as well as Hyponatremia. Clinically appreciable and with the help of laboratory analysis hyponatremia can be diagnosed easily, and is manageable side effect in patient undergoing treatment with duloxetine.[7,14,15] Close monitoring, both clinically and laboratory based for hyponatremia is essential in patients with depression and somatic disorders being treated with duloxetine. Lack in clinician knowledge of SD may delay the diagnosis due to delay in referral for consultation. Medically unexplained symptoms may make difficulty in diagnosis and management. Early SD are active as depression and anxiety in primary care, early treatment decrease costs and disability and improves outcome.[16,17]In our study early stage SD was treated with duloxetine (low dose 20 mg to higher dose 60mg). There is very little work done regarding the pharmacological treatment of SD in Nepal, paroxetine was found to be effective in somatization disorder.[18] Antidepressants has shown to improve symptoms in patients with medically unexplained symptoms, but we could not find any studies where duloxetine was used in patients with SD.[19] However a report of two cases of SD in adolescents showed marked improvement in symptoms after 3weeks of treatment with good drug tolerability.[7] In a placebo-controlled double blind study for management of chronic low back pain without any radiculopathy, done to assess the effectiveness of duloxetine, these also authors used scales to assess impressions of improvement and decrease of pain. They found improvements were greater for 60mg and 120 mg of duloxetine starting from week 3 but significance was lost after week 12.[4]In a single-blind placebo run-in trail of 60-90mg duloxetine for patients with osteoarthritis Sullivan et al. gave the subjects 2 weeks of placebo followed by 10 weeks of duloxetine. They found that duloxetine improved pain intensity and self-reported function as report on Western Ontario and McMaster University OA Index (WOMAC).[20]Though the condition assessed in our study is different to this study, our results on the effectiveness of duloxetine is similar with progressive improvement found on the disability and pain perception scales. For tolerability, a previous review that explored

effectiveness and tolerability of duloxetine in chronic musculoskeletal pain stated nausea as the most common adverse event. Other adverse events that were noted were dry mouth, insomnia, somnolence, constipation, dizziness, and fatigue.[3] In our study fatigue was the most common complaint followed by nausea, though the frequency was different the adverse events were similar. SD is considered a chronic condition and many physicians have negative views regarding its treatment. Ignorance of the condition, vehement attempts to rule organic disease, or a fear of missing an organic condition and the uneasiness felt by physicians to explore psychological issues are the four main reasons for the difficulty that doctors face during management of somatoform disorders.[21]SD is a has a great economic burden on patients, and they have an inconsistent pattern of care by their physicians; are often not satisfied with their treatment and referred inappropriately; which can lead to unnecessary iatrogenic damage.[22,23] Simth et al., randomised somatising patients into treatment and non-treatment groups and found that cost of health-care decreased by 53% when SD patients were appropriately treated.[24] Duloxetine has been found be effective and well tolerated in many conditions of chronic pain like osteoarthritis and fibromyalgia.[3] Most patients with SD also complain of pain and duloxetine could be a good option in the early stages. This could be especially beneficial in resource poor countries like ours where there is a lack of mental health professionals and the government spending on mental health is close to negligible.[25]

CONCLUSION

In patients with somatoform disorder in our population where there is lack of professionals who can impart psychological therapies such as cognitive behavioural therapies, Duloxetine is a good treatment option that can be considered in the early stages. Duloxetine shows to have good efficacy in SD in the initial period, with improvements in pain intensity and overall interference to daily activity due to SD. It is also well tolerated by most of the patients.

RECOMMENDATION

In developing countries where the is gross lack of infrastructure and travel to a hospital may be very cumbersome, non-pharmacological treatments may not be suitable. Non-pharmacological treatments require frequent visit to the hospital the access to which may be difficult. Hence our study result recommends that duloxetine is one of the medication for treating somatoform disorder, it can be used in the treatment of early stage of somatoform disorder.

LIMITATION OF THE STUDY

This is an open label study, done in a single centre. During the course of study, we used flexible dosing as opposed to a fixed dose regimen, hence dosage was adjusted if the subjects had an adverse effect. This study was limited in time whereas somatoform disorder is a chronic illness with many complexities hence the long-term outcome of the illness could not be assessed within such a short time frame of our study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

FINANCIAL DISCLOSURE

None

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