International Journal of Basic & Clinical Pharmacology
Nagabushan H et al. Int J Basic Clin Pharmacol. 2025 Jan;14(1):6-11
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20243829

Original Research Article

A prospective observational comparative study of effectiveness and adverse effects of amitriptyline versus duloxetine in the treatment of somatoform pain disorders in a tertiary care hospital

Nagabushan H. [1], P. Monika[1]*, Bhagyavathi H. D.[2]

[1]Department of Pharmacology, MIMS, Mandya, Karnataka, India
[2]Department of Psychiatry, MIMS, Mandya, Karnataka, India

Received: 04 October 2024
Accepted: 06 November 2024

***Correspondence:**
Dr. P. Monika,
Email: pmonika0905@gmail.com

ABSTRACT

Background: To compare the effectiveness and adverse effects as well as treatment compliance of amitriptyline and duloxetine in treating somatoform pain disorder.
Methods: This study was done on 100 patients, with 50 in each group, at Mandya Institute of Medical Sciences (MIMS) over 6 months. Group A was treated with amitriptyline 75 mg per day, and Group B with duloxetine 40 mg per day. Patient Health Questionnaire (PHQ-15) as well as Social and Occupational Functional Assessment Score (SOFAS) were used to compare effectiveness of treatment. For medication adherence Medication Adherence Rating Scale (MARS) was used. Adverse effects were also monitored. The baseline measurements were taken, and evaluations were conducted at 4th, 8th, and 12th weeks of follow-up.
Results: There were 31% males and 69% females. At baseline and after 12 weeks, Group A had average PHQ-15 scores of 14.72±6.13 and 3.16±0.97, respectively, while group B had scores of 17.12±5.45 and 7.22±2.46. During the same period SOFAS scores were 48.70±6.27 and 85.9±5.06 for group A, and 50.86±5.99 and 82.62±6.10 for group B. The effectiveness of Amitriptyline group showed statistically significant difference ($p<0.05$) when compared with Duloxetine. Group A experienced more adverse effects like dry mouth, drowsiness when compared to Group B.
Conclusions: Amitriptyline and duloxetine are effective in treatment of somatoform pain disorder; the effectiveness of amitriptyline was higher when compared to duloxetine in our study.

Keywords: Amitriptyline, Duloxetine, Effectiveness, Somatoform, Safety

INTRODUCTION

Chronic physical symptoms that cannot be attributed to a physical illness are a hallmark of somatoform diseases. A common feature shared by all somatoform disorder subtypes is long duration of unexplained somatic symptoms combined with significant distress and impairment.

According to international classification of diseases, 10th revision (ICD-10) "somatoform disorders"(SFD) are defined as medically unexplained symptoms accompanied by severe psychological suffering. Patients with somatoform illness frequently consult several doctors or experts.[1] Musculoskeletal pain, abdominal pain, exhaustion, fatigue, ear, nose, and throat problems, and gastrointestinal symptoms are some of the most typical somatic symptoms.

Major depressive disorder (MDD), anxiety disorders, and other psychiatric disorders are frequently accompanied by somatic symptoms, which include a variety of physical symptoms like pain (e.g., stomach ache, headache, and neuropathy), muscle tension, body shaking, difficulty

breathing, palpitations, fatigue, and gastrointestinal symptoms.[2] Antidepressants, antipsychotics, antiepileptics, and medicinal plants are some of the medications used to treat somatic symptoms. A limited number of studies have reported on the efficacy of these medications.[3-5]

To produce therapeutic effects, tricyclic antidepressants (TCA's) inhibit the reuptake of nor-epinephrine (NE) and 5-Hydroxy tryptamine (5-HT) neurotransmitters. TCA's also simultaneously block muscarinic (M1), alpha adrenergic (α1), and histamine (H1) receptors, which can result in a variety of adverse effects in clinical settings, including thirst, constipation, impaired vision, dizziness, orthostatic hypotension, drowsiness, lethargy, and weight gain.[6]

Other antidepressants include serotonin and norepinephrine reuptake inhibitors (SNRIs) like duloxetine and venlafaxine, selective serotonin reuptake inhibitors (SSRIs) like fluoxetine, sertraline, paroxetine, and citalopram, and 5-HT receptor inhibitors such as Mirtazapine are used in the treatment of somatoform disorders. Evidence suggests that 5-HT and NE neurotransmission act as analgesics through the spinal cord's inhibitory descending pain pathway to treat somatic symptoms.[7-9]

The most researched tricyclic drug, Amitriptyline, has been shown to be helpful for treating at least one of the following issues: pain, sleep, morning stiffness, general improvement, exhaustion, and discomfort. TCAs are effective in treating somatic symptoms, probably as a result of their capacity to block reuptake of NE and 5-HT.[10]

In patients suffering from depression, the SNRI, Duloxetine (60 mg/day) is effective in reducing all types of pain, including back, shoulder, and general discomfort.[11,12] There are no studies comparing amitriptyline and duloxetine for treating somatoform pain disorders.Hence in our study effectiveness and safety of amitriptyline was compared with duloxetine for treatment of somatoform pain disorder. The aim of our study is to compare the effectiveness and to determine adverse effects as well as treatment compliance of Amitriptyline versus Duloxetine in treatment of somatoform pain disorders.

METHODS

Study design

This was a prospective, observational comparative study. The approval (Ref. No. MIMS/IEC/2023/804) to conduct the study was obtained from the Institutional Ethics Committee of MIMS, Mandya before starting the study.

Study place

The study was conducted at MIMS, Mandya, a tertiary care teaching hospital in Karnataka, India.

Study duration

The study was conducted during the period from December 2023 to July 2024. The duration of the study was of 6 months.

Sample size

The study was conducted in Department of Psychiatry in 100 patients diagnosed with somatoform pain disorder according to the International Classification of Diseases (ICD-10).

Inclusion criteria

Patients of either gender, aged between 18-65 years, diagnosed with somatoform pain disorder according to ICD-10, and either patients themselves or their relatives willing to give informed consent to participate in the study.

Exclusion criteria

This study excluded patients who had a history of bipolar disorder, major depressive disorder, schizophrenia, current suicidal behaviour, pregnancy or lactation, as well as individuals with organic dysfunction. Those who were taking any other medications were also excluded from our study.

Study tool and data collection

Patients who met specific criteria were enrolled and divided into two groups: Group A received amitriptyline 75 mg once daily, while Group B received duloxetine 40 mg once daily for 3 months.

At the initial visit, patient demographic data were collected. They were subjected to PHQ 15 score, SOFAS scores at baseline. Follow-up evaluations were done at weeks 4, 8, and 12. The effectiveness was measured using the patient health questionnaire-15 (PHQ-15) and social and occupational functional assessment score (SOFAS). Treatment adherence was assessed by using the medication adherence rating scale (MARS). Side effects were monitored at regular intervals.

The PHQ-15 assesses somatic symptoms on a scale from 0 to 2, with total scores ranging from 0 to 30. These scores are categorized as minimal (0-4), low (5-9), medium (10-14), and high (15-30). The SOFAS evaluates social and occupational functioning from 0 (inadequate information) to 100 (excellent functioning).

The medication adherence rating scale (MARS) assesses how well patients follow their prescribed medication regimen with ten yes-or-no questions. Scores range from 0 to 10, where higher scores reflect better adherence and lower scores indicate poor adherence.

Statistical analysis

Data was analyzed by using Social Package for Statistical Sciences (SPSS) version 20. Continuous variables were compared using the student t-test, and categorical variables like frequency and proportion were analyzed using the Chi-Square test. Paired t-tests were used for within-group comparisons before and after treatment, while independent samples t-test compared treatment groups. P value < 0.05 was considered as statistically significant.

RESULTS

A total of 100 patients included in the study were divided into two treatment groups. The demographic data and baseline characteristics of the patients were recorded and compiled (Table1).

Effectiveness of treatment

The study evaluated two treatment groups for somatoform pain disorders over a 12-week period. The participants were 69% female and 31% male, with 54% being housewives and most belonging to the lower middle class. In Group A, the mean PHQ-15 score decreased from 14.72±6.13 at the start to 3.16±0.97 by the 12th week, showing a significant improvement within the group ($p<0.05$).

Group B also experienced a significant improvement, with the PHQ-15 score decreased from 17.12±5.45 at baseline to 7.22±2.46 at 12 weeks. ($p<0.05$) There was no significant difference at the 4th week (p=0.85), but there was significant difference at 8th (p=0.001) and 12th weeks (p=0.001) between the two groups (Table 2).

In the SOFAS scores, Group A showed improved from 48.7±6.27 at baseline to 85.9±5.06 at 12 weeks. Group B also showed improvement, with scores rising from 50.8±5.99 at baseline to 82.6±6.1 at 12 weeks. Comparing the groups for SOFAS scores, there were no significant differences at the 4th (p=0.386) and 8th weeks (p=0.876), but a significant difference was observed at the 12th week (p=0.003) (Table 3).

Assessment of treatment adherence

Medication adherence was evaluated using the Medication Adherence Rating Scale. At baseline, 56% of patients in Group A and 58% in Group B were adherent. In Group A, adherence increased to 82%, 92%, and 96% at the 4th, 8th, and 12th weeks respectively.In Group B, adherence rates were 76%, 80%, and 90% at similar time period. However, the p-values for adherence rates between the groups were 0.462, 0.083, and 0.24, respectively, indicating no statistically significant differences (Table 4).

Comparison of adverse effects

Adverse effects were monitored at each follow-up visit. In Group A, the most common adverse effects were dry mouth, followed by drowsiness, fatigue, and nausea. In Group B, fatigue was the most frequently reported adverse effect, followed by anorexia and dry mouth (Table 5).

Table 1: Demographic characteristics of the patients in the two treatment groups.

Parameters	Group A	Group B	P value
Mean age (years)	46.2±9.09	48.2±7.42	0.089
Sex (male/female)	14/36	17/33	0.418
Rural/ urban	17/33	24/26	0.157
Occupation (Employee/ farmer/ house wife/ laborer)	9/5/33/3	22/4/21/3	0.041
Education (Degree/ Illiterate/ PUC/ School)	4/13/8/25	3/12/18/17	0.135
Socioeconomic status (lower/ middle/ upper)	38/6/6	41/6/3	0.541

Table 2: Effectiveness of treatment between two groups based on PHQ 15 score.

Group	PHQ 15 score (mean±SD)			
	Baseline	**4th week**	**8th week**	**12th week**
A	14.72±6.13	11.06±4.18	6.98±2.83	3.16±0.97
B	17.12±5.45	12.26±2.49	10.2±2.4	7.22±2.46
P value	0.041	0.85	0.001	0.001

Table 3: Effectiveness of treatment between two groups based on SOFAS Score.

Group	SOFAS score (mean±SD)			
	Baseline	**4th week**	**8th week**	**12th week**
A	48.7±6.27	62.2±5.42	71.7±5.6	85.9±5.06
B	50.8±5.99	61.2±5.81	71.8±5.8	82.6±6.1
P value	0.081	0.386	0.876	0.003

Table 4: Treatment adherence between two groups based on MARS score.

Group	MARS score Adherent/Non adherent			
	Baseline	4th week	8th week	12th week
A	28/ 22	41/9	46/4	48/2
B	29/ 21	38/12	40/10	45/5
P value	0.841	0.462	0.083	0.24

Table 5: Comparison of adverse effects between two treatment groups.

Adverse effects	Amitriptyline (n=50)	Duloxetine (n=50)
Dry mouth	15	5
Drowsiness	4	2
Fatigue	4	8
Nausea	3	2
Anorexia	3	5
Constipation	3	2
Insomnia	2	2
Diarrhoea	2	4

DISCUSSION

Somatoform disorders are highly prevalent in general medical settings, affecting 10% to 15% of primary care patients. The level of functional impairment caused by these disorders is comparable to that of depressive and anxiety disorders. Somatoform disorders are particularly challenging for clinicians to manage and frequently lead to high levels of patient dissatisfaction. There is also a notable uncertainty about the effectiveness of treatments for somatoform disorders compared to the more established treatments for depression and anxiety.[13]

The five main pharmacological classes include tricyclic antidepressants (TCAs), certain SSRIs, SNRIs, atypical antipsychotics, and herbal medicines. Data show that each of these categories is effective in treating a range of conditions. All classes of antidepressants seem to be effective in managing somatoform disorders and associated conditions.[14]

Tricyclic antidepressants were more effective than SSRIs in treating somatoform pain disorders. Amitriptyline was helpful in reducing tender point scores, alleviating functional symptoms, and improving pain, morning stiffness, overall well-being, sleep quality, and fatigue.[15]

A review of 34 randomized clinical trials involving 3922 patients found that 4 trials studied antidepressants for SFD. Three of these trails showed that antidepressants were beneficial for treating SFD.[13] A meta-analysis of 94 randomized controlled trials on antidepressants found significant benefits for treating SFD, with patients showing improvement more than three times than those receiving placebo (odds ratio 3.4, 95% CI 2.6–4.5). Additionally, the analysis revealed that tricyclic antidepressants were beneficial in a greater proportion of studies compared to SSRIs, with 76% of studies showing positive results for tricyclics versus 47% for SSRIs.[3] In a study done by Joshi S et al, both amitriptyline and fluoxetine significantly reduced PHQ-15 scores. However, fluoxetine worked faster than amitriptyline between weeks 2 and 4. Amitriptyline also had more side effects compared to fluoxetine. Our study showed similar side effects with amitriptyline.[16]

Duloxetine is a serotonin-norepinephrine reuptake inhibitor that primarily inhibits serotonin reuptake more than norepinephrine. The FDA has approved duloxetine for the treatment of fibromyalgia, diabetic neuropathic pain, major depressive disorder, and generalized anxiety disorder. In a study done by Pokhrel R et al, early-stage somatic symptom disorder (SD) was treated with duloxetine, ranging from a low dose of 20 mg to a higher dose of 60 mg. At 6-weeks 21 out of 50 patients had recovered, while 22 out of 50 patients had recovered by 12 weeks.[17]

In a double-blind, placebo-controlled trial, it was demonstrated that a dosage of 60 mg duloxetine was more effective than placebo from week three to week eleven, showing significant improvement during this period.[18] However, a report on two cases of SD in adolescents indicated significant improvement in symptoms, with greater benefits observed with 60 mg and 120 mg of duloxetine starting from 3rd week.[19]

In a single-blind placebo trial done by Sullivan et al. administered placebo for 2 weeks followed by 10 weeks of duloxetine at doses of 60-90 mg. They found that duloxetine significantly improved pain intensity and self-reported function after 3 weeks of treatment, demonstrating good drug tolerability.[20] In our study, improvement was observed at a dose of 40 mg from 8th week onwards. Previously no studies have evaluated the effectiveness and safety of amitriptyline and duloxetine in patients with somatoform pain disorders.

As observed in previous research, dry mouth was more commonly reported with Amitriptyline compared to Duloxetine.[21] According to Sumedhan et al, the incidence of dry mouth in the amitriptyline group was 16%, whereas our study found it to be 30%.[22] In contrast, the Duloxetine group reported no cases of dry mouth in their study, but we observed a 10% incidence of dry mouth among our patients. In a study done by Kamal MM et al, dry mouth was significantly more frequent in the amitriptyline group than in the duloxetine group ($p<0.013$).[23] These findings align with the results of our study.

There were few limitations in the study which may affect the generalizability of the findings. First, the sample size of 100 participants (50 per group) is relatively small, which

could limit the statistical power of the results and may not fully capture the variability in treatment responses. A larger sample size might provide more robust data on the effectiveness and safety of amitriptyline and duloxetine.

Second, the follow-up duration of 12 weeks may not be sufficient to assess the long-term effects and sustainability of the treatments. Both medications are often used for extended periods in chronic pain management, and a longer study duration would provide more insight into how well these drugs perform over time, especially regarding long-term adherence and the persistence of adverse effects.

Another potential limitation is the possibility of underreporting of adverse effects. Additionally, confounding variables, such as patient comorbidities, concurrent medication use, or psychological factors, may have impacted the outcomes. These variables were not fully controlled in the study, which could have influenced both the efficacy and safety data.

CONCLUSION

This study shows that both amitriptyline and duloxetine were effective for treatments of somatoform pain disorders. However, amitriptyline was more effective than duloxetine. Adherence was equal in both the groups though amitriptyline caused dry mouth more frequently than duloxetine.

Recommendations

Future research should focus on conducting long-term studies to better understand the efficacy and safety of amitriptyline and duloxetine in managing somatoform pain disorders over extended periods. long-term studies could also help in identifying whether side effects such as dry mouth, fatigue, and gastrointestinal issues diminish over time or if they persist, potentially impacting patient adherence and quality of life.

Another important area of research is the exploration of alternative therapies, such as newer pharmacological options or non-drug treatments like cognitive-behavioural therapy (CBT), mindfulness-based stress reduction, or physical therapy. These approaches could be studied either as standalone treatments or in combination with medications like amitriptyline and duloxetine to determine if a multimodal approach provides better outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Agarwal V, Nischal A, Praharaj SK, Menon V, Kar SK. Clinical practice guideline: psychotherapies for somatoform disorders. Ind J Psychi. 2020;62(2):263-71.
2. Simon GE, VonKorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. N Engl J Med. 1999;341(18):1329-35.
3. O'Malley PG, Jackson JL, Santoro J, Tomkins G, Balden E, Kroenke K. Antidepressant therapy for unexplained symptoms and symptom syndromes. J Fam Pract. 1999;48(12):980-90.
4. Volz HP, Murck H, Kasper S, Möller HJ. St John's wort extract (LI 160) in somatoform disorders: results of a placebo-controlled trial. Psychopharmacol (Berl). 2002;164(3):294-300.
5. Müller T, Mannel M, Murck H, Rahlfs VW. Treatment of somatoform disorders with St. John's wort: a randomized, double-blind and placebo-controlled trial. Psychosom Med. 2004;66(4):538547.
6. Liu Y, Zhao J, Fan X, Guo W. Dysfunction in serotonergic and noradrenergic systems and somatic symptoms in psychiatric disorders. Front Psychiatry. 2019;10:286.
7. Richardson BP. Serotonin and nociception. Ann N Y Acad Sci. 1990;600:511-9.
8. Jones SL. Descending noradrenergic influences on pain. Prog Brain Res. 1991;88: 381-394.
9. Stahl SM. The psychopharmacology of painful physical symptoms in depression. J Clin Psychiatry. 2002;63(5):382-3.
10. Dinan TG, Barry S, Ahkion S, Chua A, Keeling PW. Assessment of central noradrenergic functioning in irritable bowel syndrome using a neuroendocrine challenge test. J Psychosom Res. 1990;34(5):575-80.
11. Detke MJ, Lu Y, Goldstein DJ, Hayes JR, Demitrack MA. Duloxetine, 60 mg once daily, for major depressive disorder: a randomized double-blind placebo-controlled trial. J Clin Psychiatry. 2002;63(4):308-15.
12. Detke MJ, Lu Y, Goldstein DJ, McNamara RK, Demitrack MA. Duloxetine 60 mg once daily dosing versus placebo in the acute treatment of major depression. J Psychiatr Res. 2002;36(6):383-90.
13. Kroenke K. Efficacy of treatment for somatoform disorders: a review of randomized controlled trials. Psychosom Med. 2007;69(9):8818-81.
14. Somashekar B, Jainer A, Wuntakal B: Psychopharmacotherapy of somatic symptoms disorders. Int Rev Psychiatry. 2013:25:107-15.
15. Sardesai A, Muneshwar K N, Bhardwaj M, et al. The importance of early diagnosis of somatic symptom disorder: a case report. Cureus 2023;15(9):44554
16. Joshi S, Pandey AK, Sapkota N. Efficacy and tolerability of Amitriptyline versus Fluoxetine in the treatment of patients with somatoform disorder: A randomized comparative trial. J Psyc Asso of Nepal. 2015;4(2):10-5.
17. Pokhrel R, Rajbhandari N, Sah S, Kathet R, Sah P, Karn S. Effectiveness of duloxetine in treating early stage of somatoform disorder at Koshi zonal hospital. BJHS. 2019;4(1)8:602-6.

18. Skljarevski V, Ossanna M, Liu-Seifert H. A double-blind, randomized trial of duloxetine versus placebo in the management of chronic low back pain. Eur J Neurol. 2009;16(9):1041–8.
19. García-Marn I, Miranda-Vicario EM, Soutullo CA. Duloxetine in the treatment of adolescents with somatoform disorders: a report of two cases. Actas Esp Psiquiatr. 2012;40(3):165-8.
20. Sullivan MD, Bentley S, Fan MY, Gardner G. A single-blind, placebo run-in study of duloxetine for activity-liming osteoarthritis pain. J Pain. 2009;10(2):208-13.
21. Kaur H, Hota D, Bhansali A, Dutta P, Bansal D, Chakrabarti A. A comparative evaluation of amitriptyline and duloxetine in painful diabetic neuropathy: a randomized, double-blind, cross-over clinical trial. Diabetes Care. 2011;34(4):818-22.
22. Sumedhan SV, Wilson V, Manoj P, Rajamony PN. Effectiveness and safety of amitriptyline, duloxetine, and pregabalin in painful diabetic neuropathy: An observational study. Natl J Physiol Pharm Pharmacol. 2023;13(7):1374-9.
23. Kamal MM, Rahman MM, Sharmin S, Bhowmick DK, Islam MS, Akhtaruzzaman AKM. Efficacy of amitriptyline and duloxetine in post-chikungunya neuropathic pain; a randomized, open-label, cross-over clinical trial. Anaesth Pain Intensive Care. 2021;25(5):647–52.

Cite this article as: Nagabushan H, Monika P, Bhagyavathi HD. A prospective observational comparative study of effectiveness and adverse effects of amitriptyline versus duloxetine in the treatment of somatoform pain disorders in a tertiary care hospital. Int J Basic Clin Pharmacol 2025;14:6-11.