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Efficacy and Safety of Duloxetine for Pain in Fibromyalgia in Adults

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ABSTRACT

Objective: To assess efficacy and safety of Duloxetine for pain in adult patients diagnosed with fibromyalgia in our tertiary care hospital.

Study Design: Quasi-experimental study.

Place and Duration of Study: Medicine and Rheumatology Department, Pak Emirates Military Hospital Rawalpindi, Pakistan from Oct 2021 to Jun 2022.

Methodology: 500 patients of fibromyalgia diagnosed by consultant medical specialist or rheumatologist were included in the study. They were divided into two Groups. Group A received routine analgesics as per local protocol while Group B received Duloxetine in standard dose. Patients were evaluated with Brief pain inventory at the time of diagnosis and at end of two week of treatment for resolution of pain symptoms. Adverse effects experienced by patients were also recorded with in these two weeks.

Results Out of five hundred patients randomized into two Groups, 257(51.4%) were categorized into Group A (routine analgesics) and 253(48.6%) were categorized into Group B (Duloxetine). 390(78.0%) were female while 110(22.0%) were male. Mean age of patients put who were diagnosed with fibromyalgia in our study was 39.84 ±7.96 years. Patients who received Duloxetine had better response in pain symptoms as compared to those who took routine analgesics (*p*-value-0.001). No significant difference was observed in adverse effects in both the Groups (*p*-value>0.005).

Conclusion Patients of fibromyalgia who were managed with Duloxetine had better response to pain symptoms after two weeks as compared to patients managed with routine analgesics. No significant difference was found in adverse effect profile of patients in both the Groups.

Keywords: Analgesics, Duloxetine; Fibromyalgia; Pain.

How to Cite This Article: *Ain QU, Manzar A, Zafar Z, Tahir R, Zaheer MH, Hassan F. Efficacy and Safety of Duloxetine for Pain in Fibromyalgia in Adults. Pak Armed Forces Med J 2026; 76(Suppl-1): S13-S16. DOI: https://doi.org/10.51253/pafmj.v76iSUPPL-1.8937*

INTRODUCTION

Rheumatology has evolved as a field in Pakistan in last few years and experts are dealing with diseases in a more scientific and equipped manner.[1] Still a lot of burden of rheumatological or pain related disorders is shared by medical specialists and general physicians. Fibromyalgia is a similar disorder with high prevalence in all parts of the world.[2] Decline in different domains of health related quality of life is markedly reported by these patients and multiple treatment options are used by treating team to overcome different symptoms of this chronic condition.[3]

Pain is usually the most frequently encountered symptoms in all the specialties and affects overall quality of life of individuals.[4] Pain may be part of number of medical and surgical conditions and require immediate management and attention to restore normal wellbeing of individual.[5] Fibromyalgia is a pain related condition in which multiple modalities and medications have been used to manage the pain effectively.[6]

Clinicians have been in constant search for most suitable option to manage pain symptoms of fibromyalgia. Acuna *et al*., studied role of Duloxetine in these patients and came up with the idea that most of the pain relief in these patients is due to analgesic effect of Duloxetine and not antidepressant effect.[7] Lian *et al.*, published a systematic review and meta-analysis in 2020 with an aim to look for role of Duloxetine in managing pain among patients suffering from fibromyalgia.[8] They included seven studies with around 2500 patients and revealed that Duloxetine is an effective option for managing pain in patients of fibromyalgia and dose of 60mg is associated with minimum withdrawal symptoms. Welsch *et al*., in 2018 studied role of selective nor adrenaline reuptake inhibitors in management of fibromyalgia. They studied efficacy as well as tolerability. It was concluded that Duloxetine and Milnacipran were slightly effective for pain symptoms but no significant impact was seen in overall health related quality of life when compared with placebo. Adverse effects were

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Received: 22 Jun 2022; revision received: 04 Aug 2023; accepted: 25 Aug 2023

also seen more in medication Group as compared to placebo Group.[9]

Diagnosis of fibromyalgia is seen more in medical and rheumatology outpatients in last few years. Pain is most frequently reported symptoms in these patients and treating teams use various routine and neuropathic analgesics in order to cater for these symptoms among these patients. A recent local studied performed in biggest city of Pakistan Karachi concluded that more than 55% of patients coming to outpatients with chronic pain were diagnosed with fibromyalgia.[10] Limited local data has been available regarding use of selective nor adrenaline reuptake inhibitors for pain in management of fibromyalgia patients. We therefore planned this study with the rationale to assess efficacy and safety of Duloxetine for pain in adult patients diagnosed with fibromyalgia in our tertiary care hospital.

METHODOLOGY

This Quasi-experimental study was conducted at the medicine/Rheumatology department of Pak Emirates Military Hospital Rawalpindi from October 2021 to June 2022. Sample size was calculated by WHO Sample Size Calculator by using population prevalence proportion of response in pain symptoms of fibromyalgia with Duloxetine as 46.9% and treated with routine option as 32.1%.[11] Non probability Consecutive sampling technique was used to gather the sample and then all the patients were randomized into two Groups via lottery method.

Inclusion Criteria: All patients between the age of 18 and 65 years who were diagnosed with fibromyalgia in our department by consultant medical specialist or neurologist.

Exclusion Criteria: Patients who had history of allergic reaction or serious adverse effects with Duloxetine in the past were excluded. Those whose diagnosis was unclear or had other rheumatological or immune mediated illnesses were also excluded from the study. Patients with any uncontrolled metabolic diseases or acute or chronic infections at the time of diagnosis were also made part of exclusion criteria. Those who could not follow up after two weeks or refused to participate in the study were not included. Pregnant or lactating women or those with any mental health problems were also not included.

IREB committee granted ethical approval for this study via letter no A/28/177(2). After application of criteria laid down for the study patients of fibromyalgia were included in the analysis. Diagnosis of fibromyalgia was made according to ACR 2016 criteria.[12] Brief pain inventory was administered to all the patients at the time of diagnosis.[13] After that patients were divided into two Groups. Group A received the routine analgesics (NSIADs) while Group B received the Duloxetine in standard dose recommended by the treating physician.[14] Patients were followed up for two weeks and observed for any side effects though out this period. At the end of two weeks' brief pain inventory was administered again to all the study participants. Person who administered pain inventory did not know about the medications patient was taking. Response at the end of two weeks was defined as >30% reduction in brief pain inventory score during the course of two weeks' treatment with the mediations in both the Groups.[15] All the details during the study were entered in a proforma designed by research team for this study at the time of conception of study.

All statistical analysis was performed by using the Statistics Package for Social Sciences version 24.0 (SPSS-24.0). Frequency and percentages were calculated for all the qualitative variables. Mean±SD for age in both the Groups was also calculated for the study participants. Pearson Chi-square test was applied to look for significant difference in response to treatment and adverse effects in both the Groups. *p*-value less than or equal to 0.05 was considered as significant.

RESULTS

A total of 500 patients of fibromyalgia were included in the study. Out of five hundred patients randomized into two Groups, 257(51.4%) were categorized into Group A (routine analgesics) and 253(48.6%) were categorized into Group B (Duloxetine). 390 (78.0%) were female while 110(22.0%) were male. Table-I summarized the general characteristics of study participants. Mean age of patients put who were diagnosed with fibromyalgia in our study was 39.84±7.96 years. Out of total patients 310(62%) did not have >30% response to pain while 190(38%) patients achieved this response. Nausea 60(12%) was the commonest side effect experienced by study participants followed by vomiting 15(3%).

Table-II summarized the results of comparison among the two study Groups. Patients who received Duloxetine had better response in pain symptoms as compared to those who took routine analgesics (*p*-value-0.001). No significant difference was observed in

adverse effects when comparison was made in both the Groups (nausea (*p*-value>0.154), vomiting (*p*-value-0.369), headache (*p*-value-0.194)).

Table-I: Characteristics of Study Participants Diagnosed with Fibromyalgia (n=500)

Study Parameters	Values
Age (years)	
Mean+SD	39.84 ±7.96 years
Range (min-max)	20 years - 54 years
Gender	
Female	390(78%)
Male	110(22%)
Type of medication	
Routine analgesics	257(51.4%)
Duloxetine	243(48.6%)
>30% reduction in pain score	
No	310(62%)
Yes	190(38%)
Adverse effects in both Groups	
Nausea	60(12%)
Vomiting	15(3%)
Headache	19(3.8%)
Loss of appetite	10(2%)
Others	4(0.8%)

Table-II: Difference in Reduction in Pain and Adverse Effects in Both the Groups n=500)

Parameters	Routine Analgesics (n=257)	Duloxetine (n=243)	*p*-value
>30% reduction in pain score			
No	178(69.2%)	132(54.3%)	
Yes	79(30.8%)	111(45.7%)	0.001
Nausea			
No	221(85.9%)	219(90.1%)	
Yes	36(14.1%)	24(9.1%)	0.154
Vomiting			
No	251(97.6%)	234(96.3%)	0.369
Yes	06(2.4%)	09(3.7%)	
Headache			
No	250(97.2%)	231(95.1%)	
Yes	07(2.8%)	12(4.9%)	0.194

DISCUSSION

Duloxetine is a selective nor adrenaline reuptake inhibitor used mainly as antidepressant, anti-anxiety and neuropathic pain killer for years now. It is considered a relatively safe medication with limited adverse effects. Its analgesic property is unique and is used by clinicians in various conditions. Fibromyalgia is a condition with symptoms of pain in different parts of the body responding usually inadequately to routine analgesics. This disorder lies in domain of medical specialist, rheumatologist and psychiatrist. General physicians also deal with a lot of burden related to this condition. Due to remarkable analgesic properties of Duloxetine, we tried to generate local data and conducted this study with an aim to assess efficacy and safety of Duloxetine for pain in adult patients diagnosed with fibromyalgia in our tertiary care hospital in Rawalpindi. Lunn *et al.,* in 2014 studied role of Duloxetine in management of neuropathic pains and fibromyalgia. They revealed that dose of 60 mg or 120 mg is efficacious for managing pain related to diabetic neuropathy. Evidence was similar in patients of fibromyalgia on same doses but effect was slightly less as compared to patients of diabetic neuropathy pains. Serious side effects were rarely seen in their data set.[16] Our results were not very different in fibromyalgia patients and Duloxetine was found better than routine analgesics. A pragmatic trial was conducted by Mehta *et al.*, in 2022 regarding comparison of Duloxetine and Mirtazapine for effectiveness and side effects among patients suffering from fibromyalgia. They came up with the conclusion that mirtazapine was an inferior choice on the basis of effectiveness and adverse effects as compared to Duloxetine for management of pain in fibromyalgia.[17] We compared Duloxetine with routine analgesics and found similar results regarding effectiveness of Duloxetine.

Patients of Juvenile fibromyalgia in India were targeted for a placebo controlled trial of Duloxetine for management of pain symptoms. This trial was published in 2019 and concluded that patients on Duloxetine had significant reduction in pain scores at 13 weeks with no major side effects as compared to patients who were put on placebo.[18] Our study revealed that patients of fibromyalgia who were managed with Duloxetine had better response to pain symptoms after two weeks as compared to patients managed with routine analgesics. No significant difference was found in adverse effect profile of patients in both the Groups. Farias *et al.,* in 2002 published an overview of systematic reviews regarding comparison of Duloxetine and Amitriptyline for management of fibromyalgia. They inferred that both options were effective in fibromyalgia, Duloxetine being better tolerated in elderly patients. We studied patients between age Group of 18 and 60 years and found duloxetine as an effective and safe option when compared with routine analgesics.

LIMITATIONS OF STUDY

There were few limitations in this study. Fibromyalgia is a complex condition with multiple dimensions and only one dimension was covered. Moreover, pain is a

phenomenon caused and affected by number of factors and Duloxetine may not over all of these therefore it cannot be concluded that pain relief was due to Duloxetine only. Double blind placebo controlled randomized controlled trial may have been best design to evaluate efficacy and safety of Duloxetine for pain management in patients suffering from fibromyalgia.

CONCLUSION

Patients of fibromyalgia who were managed with Duloxetine had better response to pain symptoms after two weeks as compared to patients managed with routine analgesics. No significant difference was found in adverse effect profile of patients in both the Groups.

Conflict of Interest: None.

Funding Source: None.

Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

QUA & AM: Conception, study design, drafting the manuscript, approval of the final version to be published.

ZZ & RT: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

MHZ & FH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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