Research

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Treatment outcome of primary Fibromyalgia Syndrome (FMS) using Duloxetine *versus* Pregabalin & Nortriptyline – An observational study

Mushtaq Ahmad*, BilalRather, Fayaz sofi & ZahoorAhmad

Department of Rheumatology, SKIMS Sours, Srinagar, India

***Author for correspondence:**

drmushtaq_01@yahoo.co.in

Introduction: The prevalence of FMS is about 2% as per ACR 2010 criteria. It is 5 times more common in women than in men. The etiology of FMS is presumptive and not clearly known as yet. Non-Pharmacological [Cognitive Behavioral Therapy (CBT)] and Pharmacological therapy is provided for mitigating somatic & psychological manifestations of FMS.

Aim of study: To know the effectiveness of Duloxetine and Pregabalin+Nortriptyline on FMS for Kashmiri patients and compare their magnitude of effectiveness.

Material and methods: It was 2 years observational study from July 2016 to June 2018. 50 patients fulfilling 2010 ACR classification criteria for FMS received the treatment. 26 patients received Duloxetine [Dose 20 mg-60 mg], 24 patients received Pregabalin [Dose 75 mg-150 mg] and Nortriptyline [Dose 25mg].

Results: Most of the parameters of FMS improved more in the Pregabalin+Nortriptyline group. However sadness improved more in the Duloxetine group.

Conclusion: In addition to CBT [Cognitive Behavioral Therapy], Pharmaco Therapy is helpful in mitigating various parameters of Fibromyalgia syndrome to improve the quality of life of FMS patients.

Keywords: fibromyalgia syndrome • pregabalin • duloxetine • nortriptyline

Introduction

Fibromyalgia syndrome manifests as non-inflammatory pain, stiffness, and tenderness emanating from muscles, tendons, and ligaments [1,2]. The prevalence of FMS is about 2% as per ACR 2010 criteria [3-7]. It is 5 times more common in women than in men [8]. The etiology of FMS is presumptive and not clearly known as yet. Non-pharmacological [CBT] and Pharmacological therapy is provided for mitigating somatic & psychological manifestations of FMS.

Material and methods

It was 2 years observational study from July 2016 to June 2018. Patients fulfilling 2010 ACR classification criteria for FMS received the treatment. 26 patients received Duloxetine (including one who did not responded to Pregabalin+Nortriptyline thus switched to Duloxetine after 3 months) [Dose 20 mg-60 mg]. Dose of Duloxetine was increased by 20 mg after every 4 weeks to 60 mg depending on scale of improvement. Dose of Pregabalin was increased from 75 mg to 150 mg after 4 weeks depending on response and continued at that dose. Pregabalin was given in morning and Nortriptyline in the evening.

Patients at initial presentation of dry mouth and hypertension were not given regimen including Nortriptyline (Pregabalin + Nortriptyline) and Duloxetine respectively for fear of worsening of Anticholinergic symptoms (due to Nortriptyline) and hypertension (Secondary to Duloxetine) respectively. Patients were followed for various features of FMS i.e, fatigue, concentration, insomnia, sadness, anxiety, rigidity and pain. The severity of above features were graded from 0-10 on problem scale (0=no problem,

10= severe problem). The improvement was graded from 0-10 on improvement scale (5 was taken as no change, 5→0 as improvement, 0 as complete improvement, 5-10 worsening). Patients were monitored for at least 3 months for a given regimen if no adequate response switched to another regimen. One patient did not respond to Pregabalin+Nortriptyline and thus switched to Duloxetine after 3 months and improved by Duloxetine (included in Duloxetine group). Informed consent from participating patients was taken.

Statistical methods

The recorded data was compiled and entered in a spreadsheet [Microsoft Excel] and then exported to the data editor of SPSS Version 20.0 (SPSS Inc. Chicago, Illinois, USA). Continuous variables were expressed as Mean ± SD and categorical variables were summarized as frequencies and percentages. Student's independent t-test was employed for intergroup analysis of data.

For intragroup analysis, a paired t-test was applied. A P-value of less than 0.05 was considered statistically significant. 26 patients received Duloxetine and 24 patients received Pregabalin+Nortriptyline. One patient did not respond to Pregabalin+Nortriptyline and switched to Duloxetine after 3 months and responded (included in Duloxetine group).

Results

Out of 50 patients who were recruited for study 48 were females and 2 were males. The mean age of patients was 34.1 ± 10.04. In the Duloxetine group, mean score of Fatigue was 7.5 before treatment & 1.7 after treatment [p value <0.001*]. Concentration/Memory mean of 5.7 before treatment & 1.7 after treatment [p value <0.001*]. Insomnia mean of 6 before treatment improved to 1.2 after treatment [p value <0.001*]. Sadness mean of 8.2 before treatment improved to 1.6 after treatment [p value <0.001*]. Anxiety mean of 7.5 before treatment improved to 1.7 after treatment [p value <0.001*]. Rigidity mean of 7.3 before treatment improved to 1.7 after treatment [p value <0.001*]. Pain mean of 7.3 before treatment improved to 1.2 after treatment [p value <0.001*] (Tables 1-4).

In Pregabalin+Nortriptyline group fatigue improved from a mean of 8.6 before treatment to 1.7 after treatment [p value <0.001*]. Concentration/Memory mean of 7.1 before treatment to 1.3 after treatment [p value <0.001*]. Insomnia mean of 6.3 before treatment improved to 1.3 after treatment [p value <0.001*]. Sadness mean of 7.9 before treatment improved to 1.3 after treatment [p value <0.001*]. Anxiety mean of 7.7 before treatment improved to 1.1 after treatment [p value <0.001*]. Rigidity mean of 7.0 before treatment improved to 1.3 after treatment [p value <0.001*]. Pain mean of 9.2 before treatment improved to 1.3 after treatment [p value <0.001*] (Table 5).

Among the two groups Fatigue, Concentration/

Table 1. Age distribution of study patients.

Age [years]	Frequency	Percentage
20-29	20	40
30-39	14	28
40-49	16	32
Total	50	100
Mean ± SD=34.1 ± 10.4		

Table 2. Gender distribution of study patients.

Age [years]	Frequency	Percentage
Male	2	4
Female	48	96
Total	50	100

Table 3. Table depicting change in parameters of FMS as per age group.

	20-29 Years		30-39 Years		40-49 Years	
Parameter	Mean	SD	Mean	SD	Mean	SD
Fatigue	7.7	2.72	7.6	2.82	8.9	1.36
Concentration	5.3	3.73	6.1	3.46	7.9	2.66
Insomnia	5.2	3.77	7.1	3.39	6.6	2.59
Sadness	7.6	3.49	8.2	1.92	8.7	1.23
Anxiety	6.9	3.57	8	2.08	8.2	1.47
Rigidity	6.6	2.61	7.9	1.49	7.2	2.34
Pain	9.1	1.07	8.9	1.07	8.5	1.36

Table 4. Comparison of various parameters in fibromyalgia syndrome scale before and after treatment [Duloxetine].

Parameter	Before Treatment [n=26]		After Treatment [n=26]		Difference	P-value
	Mean	SD	Mean	SD		
Fatigue	7.5	2.85	1.7	1.31	5.8	<0.001*
Concentration	5.7	3.47	1.7	2.09	4	<0.001*
Insomnia	6	3.48	1.2	2.12	4.8	<0.001*
Sadness	8.2	2.58	1.6	1.96	6.7	<0.001*
Anxiety	7.5	2.93	1.3	1.94	6.2	<0.001*
Rigidity	7.3	2.09	1.7	1.57	5.6	<0.001*
Pain	8.6	1.27	1.2	0.91	7.4	<0.001*
*Statistically Significant Difference (P-value<0.05)						

Table 5. Comparison of various parameters in fibromyalgia syndrome scale before and after treatment [Nortriptyline plus pregabalin].

Parameter	Before Treatment [n=24]		After Treatment [n=24]		Difference	P-value
	Mean	SD	Mean	SD		
Fatigue	8.6	1.75	1.7	1.29	6.9	<0.001*
Concentration	7.1	3.4	1.3	1.32	5.8	<0.001*
Insomnia	6.3	3.35	1.3	1.4	5	<0.001*
Sadness	7.9	2.55	1.3	0.97	6.6	<0.001*
Anxiety	7.7	2.46	1.1	1.32	6.5	<0.001*
Rigidity	7	2.51	1.3	1.29	5.7	<0.001*
Pain	9.2	0.98	1.3	1.11	7.9	<0.001*
*Statistically Significant Difference (P-value<0.05)						

Table 6. Showingeffectiveness of Duloxetine and Nortriptyline + pregabalin for various parameters on fibromyalgia syndrome scale.

Parameter	Duloxetine [n=24]		Nortriptyline+Pregabalin [n=24]		P-value
	Mean	SD	Mean	SD	
Fatigue	5.8	3.02	6.9	2.07	0.134
Concentration	4	3.47	5.8	3.1	0.054
Insomnia	4.8	3.49	5	2.95	0.837
Sadness	6.7	2.98	6.6	2.57	0.912
Anxiety	6.2	2.99	6.5	3.15	0.709
Rigidity	5.6	2.82	5.7	3.08	0.965
Pain	7.4	1.3	7.9	1.14	0.174

Memory, Insomnia, Anxiety, Rigidity & Pain improved more in the Pregabalin+Nortriptyline while as sadness improved more in Duloxetine group [p value not significant] (Table 6).

Discussion

No study has compared Duloxetine with Pregabalin + Nortriptyline to the best of our efforts to search about the same in online published literature. In our study, both regimes were effective for various parameters of Fibromyalgia syndrome. Most of the parameters improved more in the Pregabalin & Nortriptyline group. Sadness improved more in the Duloxetine group. Duloxetine, Pregabalin and Nortriptyline have been used separately in various published studies. Data from randomized controlled trials showed Duloxetine to be beneficial for FMS. These studies indicated a reduction of pain [48% in Duloxetine and 32% placebo receiving patients] [9,10]. In our study, it improved from 8.6 to 1.2 [74 % improvement]. In a multicenter double-blind randomized controlled trial of 750 patients using 300, 450 & 600 mg Pregabalin in 14 weeks revealed significant improvement in pain and other functional measures [11,12]. In our study using Pregabalin in the morning [75-150 mg] & Nortriptyline 25 mg in the evening revealed an improvement of 79%. Our study concludes that both regimens are effective for various components of FMS, but if depression is a predominant association with pain duloxetine scores over pregabalin and nortriptyline. In this study, nortriptyline was prescribed at bedtime to improve sleep also. All above 50 patients of both groups are following our facility and their symptoms are controlled on the above regimens. We have observed symptoms recur within weeks of their self withdrawal of drugs with their belief of permanent improvement. So answer for the duration of treatment is to be sought. In addition to pharmacological therapy, we assure patients of FMS, nonfatal but definitely troubling nature of illness. We stress on them that believing nonfatal outcomes and positive approaches will be the cornerstone of improvement (CBT) and pharmacotherapy augments the improvement of various parameters of FMS. Thus CBT is concluded to be augmented by pharmacotherapy.

Conclusion

From our study, we conclude that both Duloxetine & Pregabaline with Nortriptyline are helpful for fibromyalgia syndrome in our patient population. Pregabaline+Nortriptyline has an edge over Duloxetine in most parameters except sadness (Though not statistically significant). Thus, if the patient is having associated depressive features Duloxetine should be preferred.

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