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A COMPARATIVE STUDY ON THE EVALUATION OF PREGABALIN VERSUS DULOXETINE AND THE PRESCRIBING TRENDS IN PATIENTS WITH FIBROMYALGIA SYNDROME

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ABSTRACT

Objective: To determine and compare the safety, effectiveness and tolerability of Pregabalin and Duloxetine, to assess the quality of life among patients under this study along with assessing the medication adherence of drugs under study and to analyse the prescribing pattern of drugs in patients with fibromyalgia syndrome. **Methods:** A prospective, observational study was conducted. Patients who have been recently diagnosed and treated with pregabalin or duloxetine monotherapy were identified. The patients were then reviewed after 4 weeks to assess the effectiveness of the drugs under study using the Short Form McGill Pain Questionnaire (SF –MPQ). The tolerability was assessed and recorded at clinical visit by asking the patient about whether they had discontinued the drug or not by using Global Assessment Scale of Tolerability. The safety was assessed using Standard Adverse Reaction Questionnaire. The Fibromyalgia Impact Questionnaire (FIQ) was used to assess quality of life in fibromyalgia patients receiving monotherapy of pregabalin or duloxetine. The adherence was examined using 8-scale Morisky Medication Adherence Scale (MMAS). The prescription pattern of drugs used in fibromyalgia was also analysed. **Results:** Since the P value is less than 0.01, the difference in mean scores of effect, before and after are statistically highly significant in both the groups. Since the P value is less than 0.01, the difference in mean scores of quality of life before and after are statistically highly significant in both the groups. Since P value obtained is more than 0.05, there is no significant difference in safety among the groups. Since P value is less

than 0.01, there is a highly significant association between tolerability and the groups. Among 35 patients on Pregabalin, monotherapy of Pregabalin (0-0-1) OD was mostly prescribed (38.71%). Among another 35 patients on duloxetine, 42.86% patients were on monotherapy of Duloxetine (0-0-1) OD. Most people were low and medium adherent to medications. **Conclusions:** Pregabalin was found to be more effective in reducing the pain compared to Duloxetine therapy. Constipation was the most common ADR observed in Duloxetine therapy. Thus, it can be concluded that Pregabalin therapy is more safer compared to Duloxetine therapy. Pregabalin was well tolerated compared to that of Duloxetine. It is observed that most of the patients on mixed diet had experienced Fibromyalgia. Thus it can be concluded that mixed diet and weight gain is associated with development of Fibromyalgia. The post menopausal were more prone to Fibromyalgia due to estrogen imbalance. Eventhough, PGN is found to be more effective than Duloxetine, cost is higher with pregabalin. So, cost reversal must be done for better therapy.

KEYWORDS: Pregabalin, Duloxetine, Safety, Effectiveness,Tolerability, Quality of life.

INTRODUCTION

Fibromyalgia

The term ‘fibro’ in Fibromyalgia is derived from the latin word ‘fibra’ meaning fibrous tissues, ‘myo’ from the greek word ‘myo’ meaning muscles and ‘algia’ (greek) denotes pain. Fibromyalgia is a chronic clinical syndrome which is characterised by widespread chronic pain at tender points.[1] One out of every 25 persons is affected with Fibromyalgia. In early days, different terms like muscular rheumatism and fibrositis were used. Fibromyalgia was also misdiagnosed as degenerative joint diseases. Fibromyalgia is not an autoimmune disease, but more common than any other conditions.[2]

The significant features of this disorder are fatigue, sleep disturbances and joint stiffness. People may also experience a range of other symptoms including multiple body systems.[3] Fibromyalgia is a heterogenous disorder. Fibromyalgia affects an estimated 3% to 6% of the total world population, with greatest prevalence rate in women (90%).[4,5]

There are almost (9 pairs) that is 18 points known as tender points in Fibromyalgia syndrome.

- Occiput
- Low cervical
- Trapezius

- Second rib
- Supraspinatus
- Gluteal
- Lateral epicondyle
- Knee
- Trochanter

Epidemiology

There are a number of epidemologic studies to identify patients with FMS. The first study was conducted in Wichita, Kansas by population screening.[6] The overall prevalence was found to be 2%, with 3.4% of women and 0.5% of men diagnosed with FMS. The prevalence is generally greater in clinical setting rather than in epidemiological studies. The determination of incidence of FM is not very easy.[7] The ICD -9 coding insurance claim database found an incidence of FMS in 11.28 per 1000 person years for females and 6.88 per 1000 person years in male population.[8,9]

Etiology and Pathogenesis

The etiopathogenesis of FMS is not certain. The suggestions are:

(A). Genetic and Familial Predisposition

The polymorphism of serotonergic, catecholaminergic, dopaminergic pathways are involved in FM pain transmission.[10] The disorder is expressed more in the presence of environmental triggers including acute illness, physical trauma, emotional feelings etc. These triggering factors can amplify pain perception in pathways of processing of pain due to FMS.[11] It is suggested that the first degree relatives of patients with FMS are more likely to have this disorder than normal population.

(B). Autonomic Nervous System Dysfunction

The Hypothalamic–Pituatory–Adrenal Axis is activated by emotional as well as physical trauma. FM patients have hyperactive HPA axis and thus makes a causal relationship of ANS with FMS.

(C). Infections and Inflammation

Inflammation can trigger central sensitization. Such patients have increased level of Substance P and increased threshold of pain.[12]

(D). Psychological Factors

Anxiety, depression, mood disorders, stress disorders can also cause FMS.[13] There is an important relationship between psychological and physiological pathways in persons with FMS. Recent studies show that psychophysiological responses of BP, heart rate etc are associated with psychological coping.[14,15]

Signs and Symptoms

- Chronic widespread muscle pain
- Headache
- Sleep disorders
- Fatigue
- Prolonged muscle spasm
- Bowel disturbances

Many patients experience cognitive dysfunction called fibro fog or brain fog, involving poor concentration, memory loss, anxiety, depression etc.

Diagnosis

The American College of Rheumatology has identified nine paired (18) tender points criteria for diagnosing FMS. The criterias are the following:

- A history of chronic widespread muscular and joint pain for more than 3 months.
- Tender points – if patients feel pain at 11 or more points, FMS can be confirmed.

It is very difficult to diagnose FMS because most of the laboratory testing appears to be normal and many of the symptoms are similar to that of other orthopaedic conditions.[16]

Differential Diagnosis of Fms

- Hypothyroidism
- Metabolic insufficiencies
- Myofacial pain syndrome
- Rheumatic disease
- Psychological diagnosis
- Hypermobility syndrome
- Whiplash syndrome
- Widespread burns[17]

New Diagnostic Criteria

According to recent studies of ACR, tender point test is being replaced by widespread pain index and symptom severity score. Instead of tender point count, patients may claim 19 body regions where pain is experienced during the last week. One point is given for each area, so scoring is between 0-19. This numbering is called as WPI (Widespread Pain Index). Another part of the score is used to assess the diagnosis of FM by evaluating person's symptoms. The scaling is made between 0-3.[18]

Risk Factors

Common risk factors include:

- Gender; The syndrome appears to be more prominent in women (between the ages of 25 and 60) than in men. But genetics are suspected as a possible reason.
- Family history; Relatives with similar symptoms or who have been diagnosed with Fibromyalgia themselves are more prone to this condition.
- Related or similar health conditions; Conditions such as rheumatoid arthritis or osteoarthritis, and even lupus can sometimes lead to the development of Fibromyalgia

Complications

The constant pain, fatigue, and sleep disturbances associated with Fibromyalgia can interfere with daily life. Many people are unable to function at work or at home, and become frustrated because this condition is often misunderstood. Specific complications of Fibromyalgia may include:

- **Mental Fog**; Some people with Fibromyalgia experience memory and cognitive problems that may interfere with their ability to concentrate. This is often known as "fibro fog.".
- **Hospitalization;** People with Fibromyalgia are about twice as likely as others to be hospitalized for any reason, according to the Center for Disease Control and Prevention (CDC).
- **Depression and mood disorders;** People with Fibromyalgia are more likely to have major depression**.**
- **Death From Suicide or Injury**; The risk of death is higher than in the general population.[19]

Fibromyalgia Associated Pain Amplification Syndrome

- Temperomandibular disorder

- Tension headache
- Irritable bladder
- Irritable bowel syndrome
- Dysmennorhea
- Vulrodynia.[6]

Management

Treatment mainly aims at symptom reduction through behavioural therapy, physical therapy, exercise and pharmacological therapy.

Non Pharmacological Therapy

(A) Education and Self Management

Patient education about physiology of chronic pain in FMS and the role of non pharmolocological treatment is very beneficial. Comparison of different meta-analyses found that pharmacological treatment with aerobic exercise and CBT (Cognitive Behavioural Therapy) is very useful in FMS treatment.[20]

(B). Exercise and Body Based Therapies

The patient must find the suitable exercises for which he / she will be more comfortable is the most important factor. Massage therapy provides a good evidence for relieving myofascial pain in FM symptoms. Neurostimulation therapies, including central neurostimulatory therapies and electrical nerve stimulation therapies are also beneficial.[22]

(C). Cognitive Behavioral Therapy

It includes cognitive restructuring and behavioural training, such as relaxation and social skill training. CBT helps in pain reduction.[21,22]

Pharmacotherapy

The various classes of medicines used are analgesics, antidepressants, opioids etc. The US Food and Drug Administration (FDA) has approved three drugs for use in Fibromyalgia: Pregabalin (Lyrica), Duloxetine (Cymbalta), And Milnacipran (Savella).

- **Pregabalin:** It is an anticonvulsant drug. It is used to reduce pain and improves daily function and sleep.

- **Duloxetine:** It is an antidepressant, also belonging to the class SNRI. It is used to relieve pain, fatigue, and sleep problems, are generally prescribed at lower doses than for treatment of depression.
- **Milnacipran:** It is a SNRI used in the Fibromyalgia. It has been shown to reduce pain, improve physical function and brings overall Fibromyalgia improvement. The most common side effects are nausea, constipation, dizziness.
- **Amitryptiline:** Amitriptyline is a tertiary amine tricyclic antidepressant. The mechanism of action is to inhibit NET (nor – epinephrine transporter) and SERT (serotonin transporter) located at neuronal / platelet membrane. It has potent anticholinergic effect including dry mouth, blurring of vision, constipation and urinary hesitancy. It increases the restful sleep, may help treat FM. It is taken at lower doses at bedtime.
- **Analgesics:** NSAIDs and acetaminophen are of limited efficacy in reducing pain due to Fibromyalgia. Tramadol, a weak opioid agonist with additional effects on serotonin and norepinephrine receptors, improves pain associated with Fibromyalgia.
- **Tramadol:** Centrally acting opioid analgesic. It has affinity for μ opioid receptor. It inhibits reuptake of noradrenaline and 5-HT. It activates monoaminergic spinal inhibition of pain.[27]
- **Muscle relaxants:** Such as cyclobenzaprine. It provides relief of muscle pain especially when taken at bedtime.
- Topical capsaicin, obtained from red chili peppers, is essentially free of toxicity, other than mild burning at the site of application, and can be a useful adjuant in combination with gentle massage.

SNRIs (Serotonin and Norepinephrine Reuptake Inhibitor)

Fibromyalgia is associated with CNS processing of pain. Serotonergic and noradrenergic neurons are implicated in medications of endogenous pain inhibitory mechansims through descending inhibitory pain pathways in CNS. The SNRIs may correct functional deficit of serotonin and norepinephrine in these inhibitory pathways and this reduces the pain.[23]

Duloxetine

Duloxetine was introduced in the United States in the year 2004.

Therapeutic category: Antidepressant, serotonin and norepinephrine reuptake inhibitor

Dosage forms: Capsule 20 mg, 30 mg, 60 mg

Use: Duloxetine is used for the treatment of depression, generalized anxiety disorder, pain associated with diabetic peripheral neuropathy, fibromyalgia, and chronic musculoskeletal pain.

Mechanism of Action

Duloxetine has potent serotonin and norepinephrine and weak dopamine reuptake inhibition. It works by preventing the reuptake of serotonin and nor epinephrine by nerves after they have been released. Since uptake is an important mechanism for removing released neurotransmitters and terminating their actions on adjacent nerves, the reduced uptake caused by Duloxetine increases the effect of serotonin and norepinephrine in the brain. The mechanism responsible for its effectiveness treating pain is not known but is thought to involve its effects on serotonin and norepinephrine in the brain.

Pharmacokinetics

Duloxetine is well absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 6 hours after an oral dose. Food delays the time to reach peak concentrations to 10 hours. Protein binding is about 96%, primarily to albumin and alpha-1-acid glycoprotein. Duloxetine is extensively metabolised by the Cytochrome P450 isoenzymes CYP1A2 and CYP2D6; two major, but inactive, metabolites are formed, 4-hydroxy duloxetine glucuronide and 5-hydroxy-6-methoxy duloxetine sulfate. These and other metabolites are principally excreted in the urine; about 20% is excreted in the faeces. Less than 1% of a dose is excreted in the urine as unchanged Duloxetine. The elimination half life of Duloxetine is 8 to 17 hours with an average of about 12 hours.

Precautions

Antidepressants increase the risk of suicidal tendency. Close monitoring for clinical worsening suicidality or unusual changes in behaviour. It must not be used in patients with hepatic failure as it may cause hepatotoxicity. Use caution with renal impairment.

Interactions

- Duloxetine can inhibit metabolism of agents such as desipramine that are metabolised extensively through CYP2D6.
- Serum levels of tricyclic antidepressants may be increased by Duloxetine

Adverse Reactions

- Insomnia, somnolence, dizziness, headache, constipation, urinary obstruction, myalgia, blurred vision, diaphoresis, weight loss.
- SSRIs and SNRIs may induce nausea, but it is a transient effect which subsides after first week of therapy.[26]

Pregabalin

Pregabalin is an alpha-2delta-1ligand. It is an anticonvulsant drug and a structural analogue of GABA, but doesnot seem to affect transmitter response.

Therapeutic category: anticonvulsant

Dosage forms: Pregabalin is normally started at 50 mg or 75 mg twice daily and increased in incremental steps of 50 mg every 2 weeks upto 600 mg.

Use: for analgesic, anxiolytic as well as antiepileptic action.

Mechanism of Action

Pregabalin binds with high affinity to the $\alpha_2\delta$ subunit-containing Voltage-Gated Calcium Channels (VDCC). It increases extracellular GABA concentrations in the brain by producing a dose-dependent increase in L-Glutamic acid decarboxylase (GAD), the enzyme responsible for making GABA.

Pharmacokinetics

Pregabalin is rapidly absorbed after oral doses and peak plasma concentrations are achieved within 1.5 hours. Oral bioavailability is about 90%. The rate but not the extent of absorption is reduced if given with food but this is not clinically significant. Steady state is achieved after 1 to 2 days. Pregabalin is not bound to plasma proteins and undergoes negligible metabolism. About 98% of a dose is excreted in the urine as unchanged drug. The mean elimination half-life is 6.3 hours. Pregabalin is removed by haemodialysis. Oral clearance decreases with age. So, dose must be reduced in elder patients

1.3.3 Adverse Effects

The most common side effects are dizziness and somnolence. Weight gain and peripheral edema are also found. Central adverse effects found with Pregabalin therapy includes blurred vision, vertigo, confusion, impaired attention.

Precautions

Pregabalin should not be stopped suddenly. Since, it can cause syndrome similar to alcohol / benzodiazepine withdrawal.[25] Patients with creatinine clearance less than 30ml/min are at greater risk of adverse effects. So, dosing must be adjusted in such patients.

Fibromyalgia Impact Questionnaire

The Fibromyalgia Impact Questionnaire (FIQ) was developed in 1980s and was first published in 1991.[28] Minor revisions were made in 1997 and 2002.[29] Recently, It has become one of the most frequently used tools in the evaluation of Fibromyalgia patients. The original questionnaire used a visual analogue scale (VAS) that required patients to mark a 100-mm line and was scored with a ruler. The scoring was made complicated by the need to reverse scores in one question and the use of constants to convert the first 13 questions to a standardized scale of 0 to 10.[30] The functional questions in the first part of the FIQ were originally intended for women living in wealthy background and assumed the possession of a car, a vacuum cleaner, and a washing machine.[31]

Short Form –Mcgill Pain Questionnaire

The publication of the McGill Pain Questionnaire (Melzack, 1975) made a major impact in pain research. Pain was mainly described and measured in terms of intensity, but in MPQ, the qualitative aspect of pain was included and has become important in pain research.[32] The MPQ is used for evaluation of the complaints of pain in a patient. Furthermore, it can also be used for diagnostics and to control the effects of therapies and/ or pain relief in individual patients.[33] The short-form McGill Pain Questionnaire (SF-MPQ) is a shorter version of the original MPQ, and was developed later in 1987. The pain rating index has 2 subscales:

1. Sensory subscale with 11 words, and
2. Affective subscale with 4 words from the original MPQ.

These words or items are rated on an intensity scale as 0 = none, 1 = mild, 2 = moderate and 3 = severe. There's also one item for present pain intensity and one item for a 10 cm visual analogue scale (VAS) for average pain.[34] The SF-MPQ was further revised in 2009 for the use in neuropathic and non-neuropathic pain conditions (SF-MPQ-2). This new version includes 7 additional symptoms related to neuropathic pain, for a total of 22 items with 0-10 numerical response options.

METHODOLOGY

Study Design: A prospective observational study.

Sample Size and Population

- $n = 1.96 \times 2PQ / d^2$

n = sample size

P = prevalence

Q = 1-P

d = precision

- n = 70
- Patients reported to the Department of Neuro medicine

Study Setting: Neuro medicine department of Pushpagiri Medical College hospital, Thiruvalla.

Study Period: 6 months

Study criteria

Inclusion criteria

- OP patients in Neuromedicine department.
- Both female and male patients with pure Fibromyalgia (including diabetic neuropathic pain).
- Patients with age greater than 18 years.
- Those who give consent voluntarily to participate in the study.
- Patients receiving either Pregabalin or Duloxetine.

Exclusion Criteria

- Patients who are not willing to give consent.
- Pregnant or lactating women.
- Patients with inflammatory rheumatic disease and psychiatric illness.
- Patients with other pain syndromes, joint pain and osteoarthritis.

Brief Procedure

A prospective, observational study was conducted in the Department of Neuromedicine at Pushpagiri Medical College Hospital, Thiruvalla on the topic "A comparative study on evaluation of Pregabalin versus Duloxetine and the prescribing trends in patients with Fibromyalgia syndrome". The entire study was conducted only after getting approval from

Institutional Ethics Committee. The selection of patients was based on inclusion and exclusion criteria. All patients were provided with a brief introduction regarding the study and confidentiality of the data. A written informed consent was obtained from the patient or caregiver.

Patients who have been recently diagnosed and treated with either Pregabalin or Duloxetine monotherapy were identified. The demographic details of patients were collected and recorded. The patients were then reviewed after 4 weeks to assess the effectiveness of the drugs under study using the Short Form McGill Pain Questionnaire (SF –MPQ). The tolerability was assessed and recorded at clinical visit by asking the patient about whether they had discontinued the drug or not by using Global Assessment Scale of Tolerability. The safety was assessed using Standard Adverse Reaction Questionnaire. The Fibromyalgia Impact Questionnaire (FIQ) was used to assess quality of life in fibromyalgia patients receiving monotherapy of pregabalin or duloxetine. The adherence was examined using 8-scale Morisky Medication Adherence Scale (MMAS).The prescription pattern of drugs used in fibromyalgia was also analysed.

RESULTS

Table No. 1: Distribution of Sample According To Age.

Age	PREGABALIN (50 mg)	DULOXETINE (20mg)	Chi square	df	P value
Below 50	7	8	2.703	3	0.44
	20.0%	22.9%			
50-59	14	8			
	40.0%	22.9%			
60-69	10	12			
	28.6%	34.3%			
70 and above	4	7			
	11.4%	20.0%			
Total	35	35			
	100.0%	100.0%			

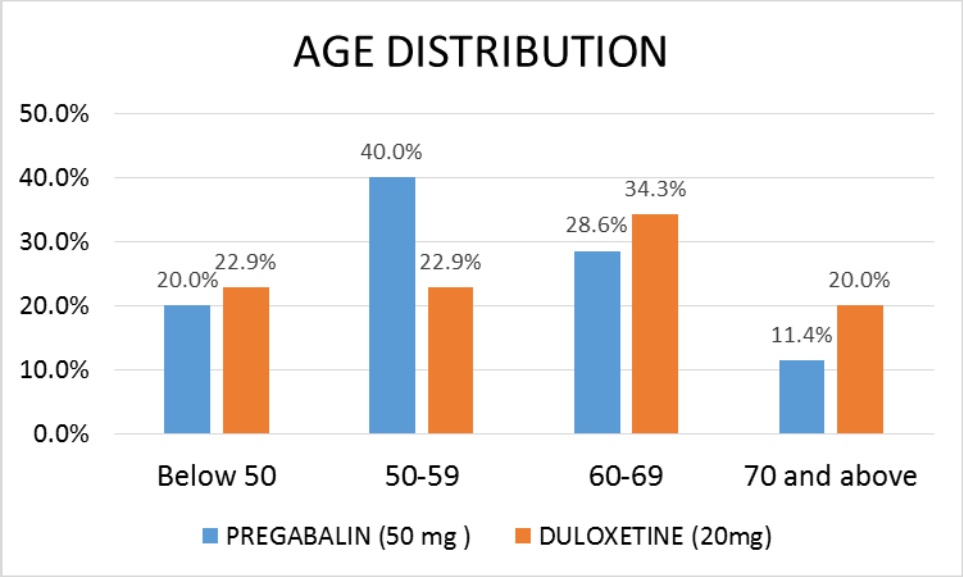

Figure No. 1: Distribution of Sample According To Age.

- The results shows that highest number of pregablin users are under 50-59 age group (40%), whereas highest number of duloxetine users are in 60-69 age group (34.3%).

Table No. 2: Distribution of Sample According To Gender.

GENDER	PREGABALIN (50 mg)	DULOXETINE (20mg)	Chi square	df	P value
FEMALE	28	16	8.811	1	0.003
	80.0%	45.7%			
MALE	7	19			
	20.0%	54.3%			
TOTAL	35	35			
	100.0%	100.0%			

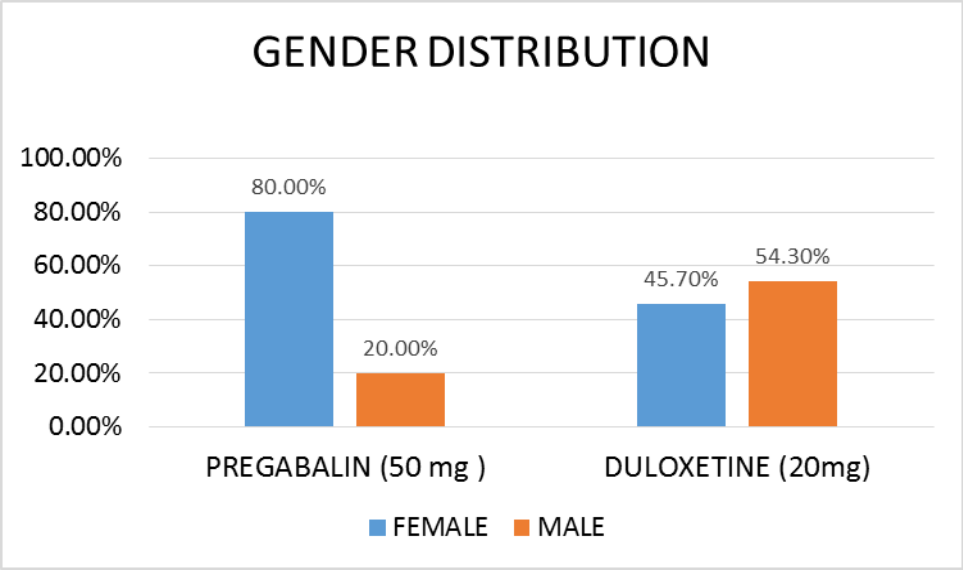

Figure No. 2: Distribution of Sample According To Gender.

- In the study, it was found that 80% patients under pregabalin therapy and 45.7% patients under duloxetine therapy were females. Thus in this study, fibromyalgia syndrome was more observed in female population.

Table No. 3: Distribution of Sample According To Weight.

Groups	Mean Weight (in Kg)	Std. Deviation	Mean difference	Independent t value	df	P value
PREGABALIN (50 mg)	55.43	7.68	1.51	0.818	68	0.416
DULOXETINE (20mg)	56.94	7.81				

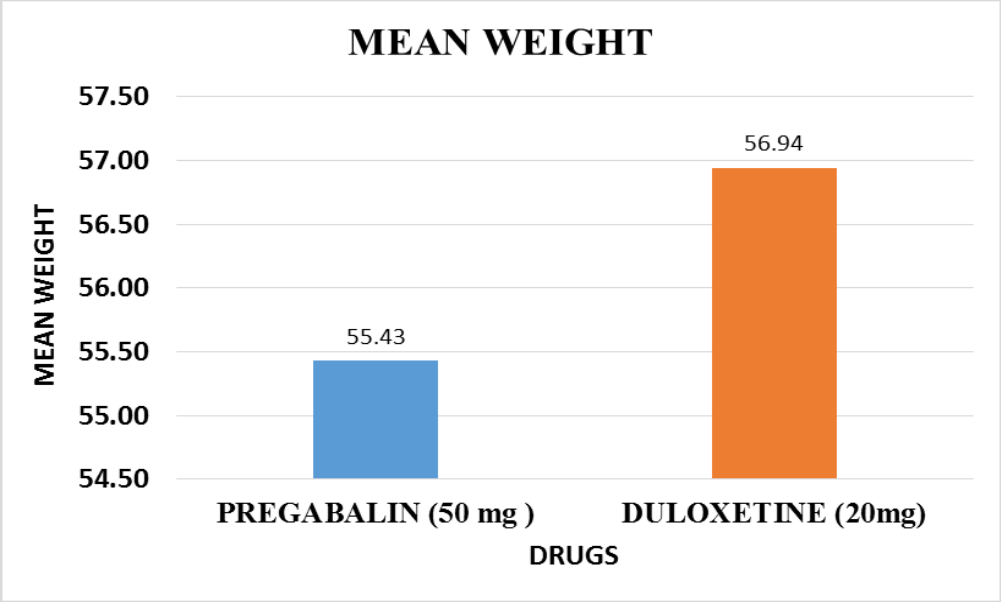

Figure No. 3: Distribution of Sample According To Weight.

- The mean weight for patients under pregabalin therapy was found to be 55.43 kg and that of patients under duloxetine therapy was found to be 56.94 kg.

Table No. 4: Distribution of Sample According To Family History.

FAMILY HISTORY	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
No	32	29	1.148	1	0.284
	91.4%	82.9%			
Yes	3	6			
	8.6%	17.1%			
TOTAL	35	35			
	100.0%	100.0%			

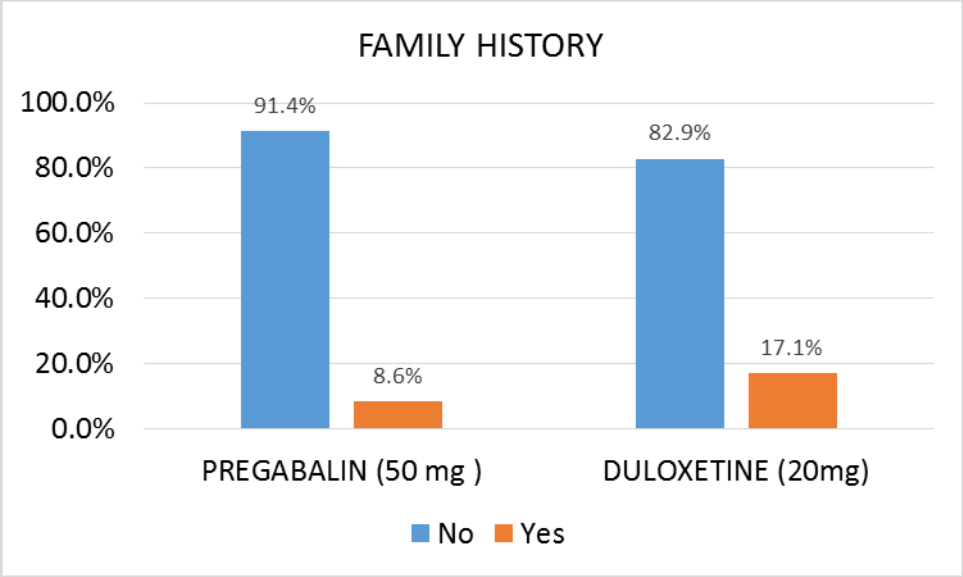

Figure No. 4: Distribution of Sample According To Family History.

- 91.4% patients on Pregabalin and 82.9% patients on Duloxetine had no family history. Most patients had no family history.

Table No. 5: Distribution of Sample According To Social History.

SOCIAL HISTORY	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	Df	P value
No	32	29	1.148	1	0.284
	91.4%	82.9%			
Yes	3	6			
	8.6%	17.1%			
TOTAL	35	35			
	100.0%	100.0%			

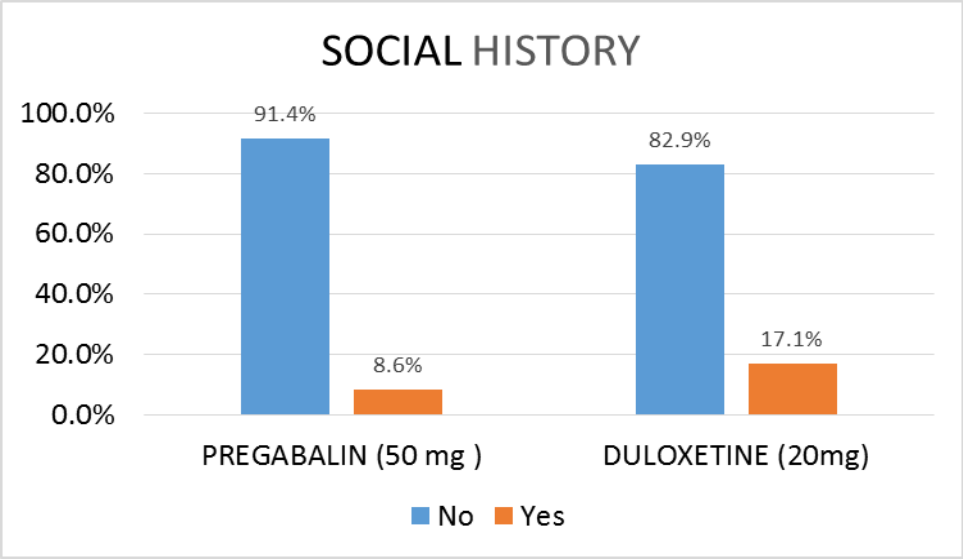

Figure No. 5: Distribution of Sample According To Social History.

- 8.6% patients with social history was administered with pregabalin and 17.1% of patients was administered with duloxetine.

Table No. 6: Distribution of Sample According To Allergic History.

ALLERGIES	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
No	31	29	0.467	1	0.495
	88.6%	82.9%			
Yes	4	6			
	11.4%	17.1%			
TOTAL	35	35			
	100.0%	100.0%			

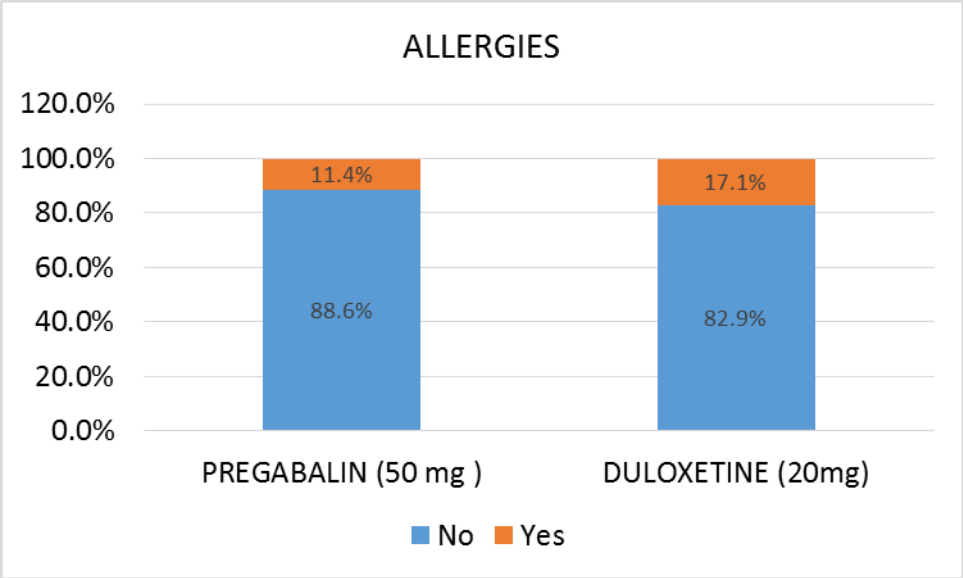

Figure No. 6: Distribution of Sample According To Allergic History.

- 11.4% patients on Pregabalin therapy and 17.1% patients on Duloxetine therapy has shown allergic history.

Table No. 7: Distribution of Sample According To Intake of Alternative Medicine.

ALTERNATIVE MEDIICINE	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
No medicine	31	35	4.242	1	0.039
	88.6%	100.0%			
With Medicine	4	0			
	11.4%	0.0%			
TOTAL	35	35			
	100.0%	100.0%			

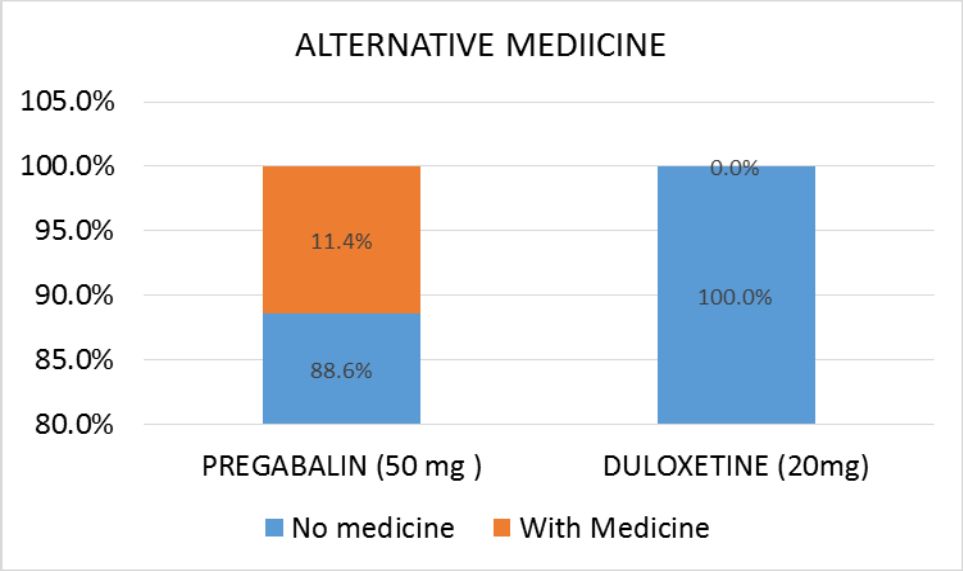

Figure No. 7: Distribution of Sample According To Intake of Alternative Medicine.

- Patients upon pregabalin, 11.4% had alternative medicines. Patients on duloxetine therapy had no alternative medicines.

Table No. 8: Distribution of Sample According To Diet Intake.

DIET	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
Veg	2	1	0.348	1	0.555
	5.7%	2.9%			
Mixed	33	34			
	94.3%	97.1%			
TOTAL	35	35			
	100.0%	100.0%			

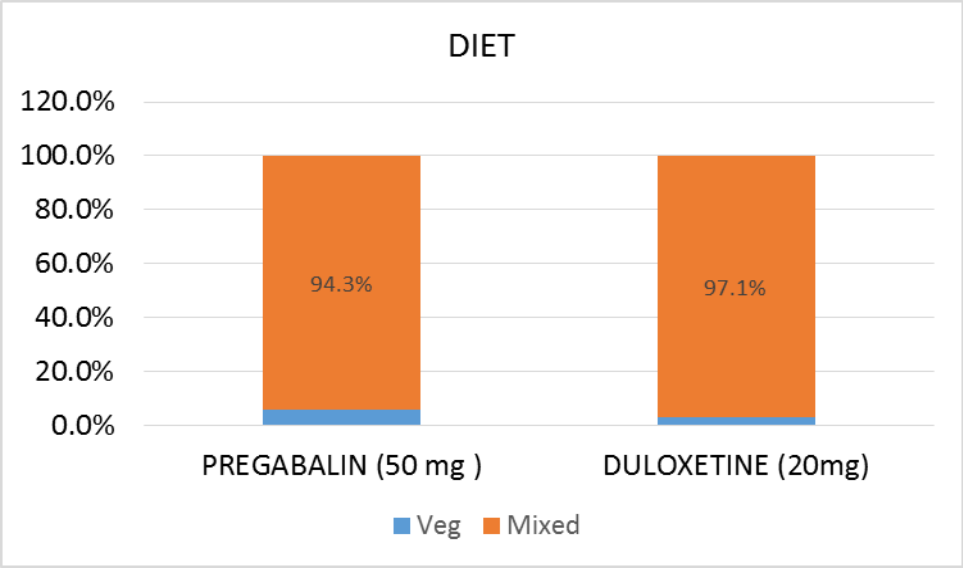

Figure No. 8: Distribution of Sample According To Diet Intake.

- 94.3% patients on Pregabalin therapy and 97.1% patients on Duloxetine therapy were following mixed.

Table No. 9: Distribution of Sample According To Menstrual Status.

MENSTRUAL STATUS	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
Post menopausal	21	10	0.764	1	0.382
	75.0%	62.5%			
Pre menopausal	7	6			
	25.0%	37.5%			
TOTAL	28	16			
	100.0%	100.0%			

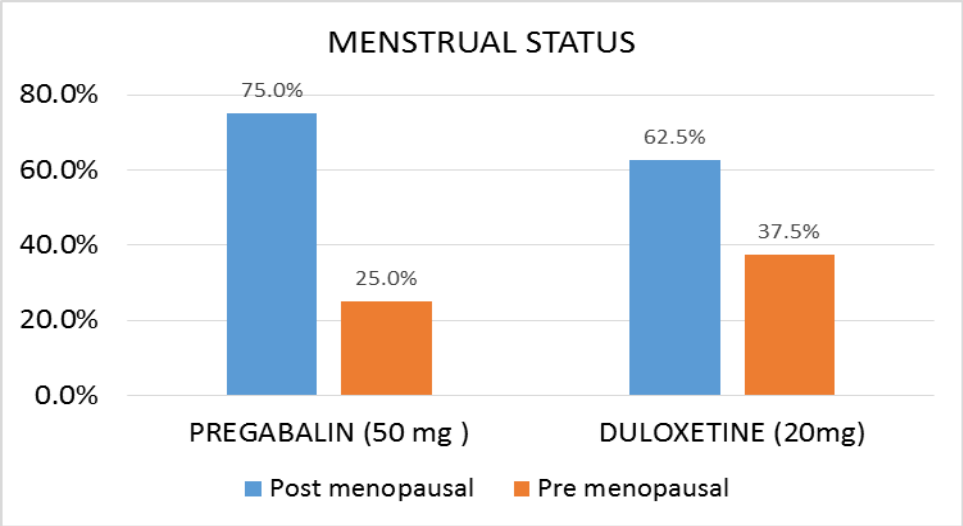

Figure No. 9: Distribution of Sample According To Menstrual Status.

- Among the study population, 75% of post menopausal patients were on pregabalin therapy and 62.5% on duloxetine therapy. While 25% of pre-menopausal patients were on duloxetine therapy. The results shows that most of the patients were post-menopausal.

Table No. 10: Distribution of Sample According To Quality of Life.

Group	QUALITY OF LIFE	Mean	Std. Deviation	Mean difference	95% confidence interval	Paired t value	Df	P value
PREGABALIN (50 mg)	BEFORE	60.31	12.09	21.11	17.32-24.89	11.315	34	0.001
	AFTER	39.20	15.98					
DULOXETINE (20mg)	BEFORE	50.97	8.49	6.31	3.89-8.73	5.312	34	0.001
	AFTER	44.65	10.03					

- Since the P value is less than 0.01, the difference in mean scores of quality of life before and after are statistically highly significant in both the groups.

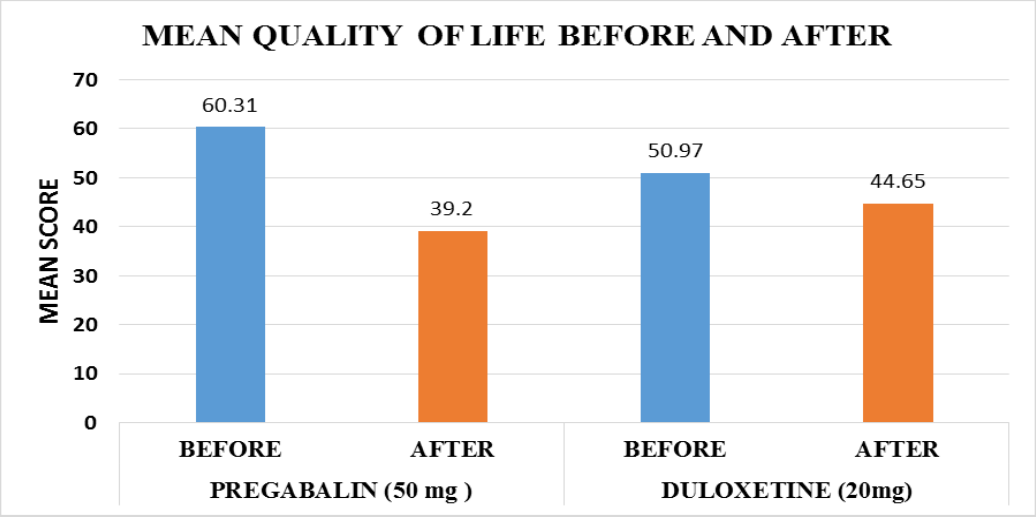

Figure No. 10: Distribution of Sample According To Quality of Life.

- The following table shows the comparison of difference of scores of the two groups.

Table No. 10(A): Distribution of Sample According To Quality of Life – Mean Difference.

Group	Mean	Std. Deviation	Mean difference	95% confidence interval	Independent t value	Df	P value
PREGABALIN (50 mg)	21.11	11.04	14.79	10.38-19.21	6.687	68	0.001
DULOXETINE (20mg)	6.31	7.03					

- Since the P value obtained is less than 0.01, it is concluded that the mean difference in Pregabalin group is significantly higher than the Duloxetine group.

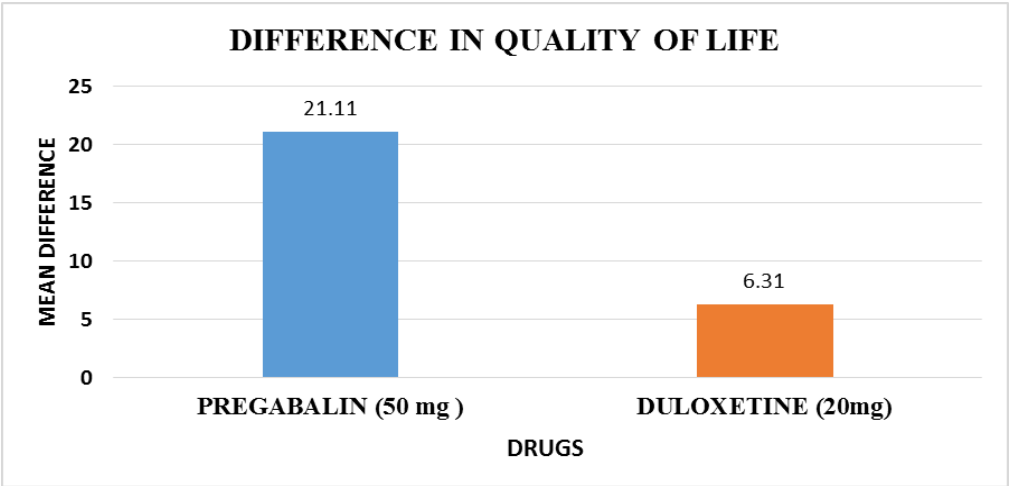

Figure No 10(A): Distribution of Sample According To Quality of Life- Mean Difference.

Table No. 11: Distribution of Sample According To Effectiveness.

Group	EFFECTIVENESS	Mean	Std. Deviation	Mean difference	95% confidence interval	Paired t value	Df	P value
PREGABALIN (50 mg)	BEFORE	22.71	4.92	9.2	7.72-10.68	12.648	34	0.001
	AFTER	13.51	3.97					
DULOXETINE (50mg)	BEFORE	19.60	4.65	2.77	1.69-3.84	5.23	34	0.001
	AFTER	16.83	4.48					

- Since the P value is less than 0.01, the difference in mean scores of effect, before and after are statistically highly significant in both the groups.

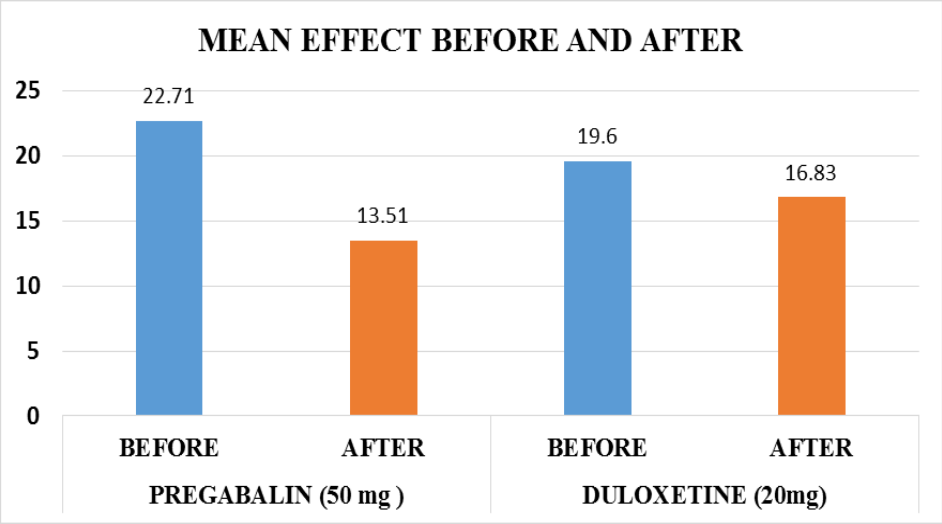

Figure No. 11: Distribution of Sample According To Effectiveness.

- The following table shows the comparison of difference of scores of the two groups.

Table No. 11(A): Distribution of Sample According To Effectiveness – Mean Difference.

Group	Mean	Std. Deviation	Mean difference	95% confidence interval	Independent t value	df	P value
PREGABALIN (50 mg)	9.20	4.30	6.43	4.63-8.22	7.143	68	0.001
DULOXETINE (20mg)	2.77	3.14					

- Since the P value obtained is less than 0.01, it is concluded that the mean difference in Pregabalin group is significantly higher than the Duloxetine group.

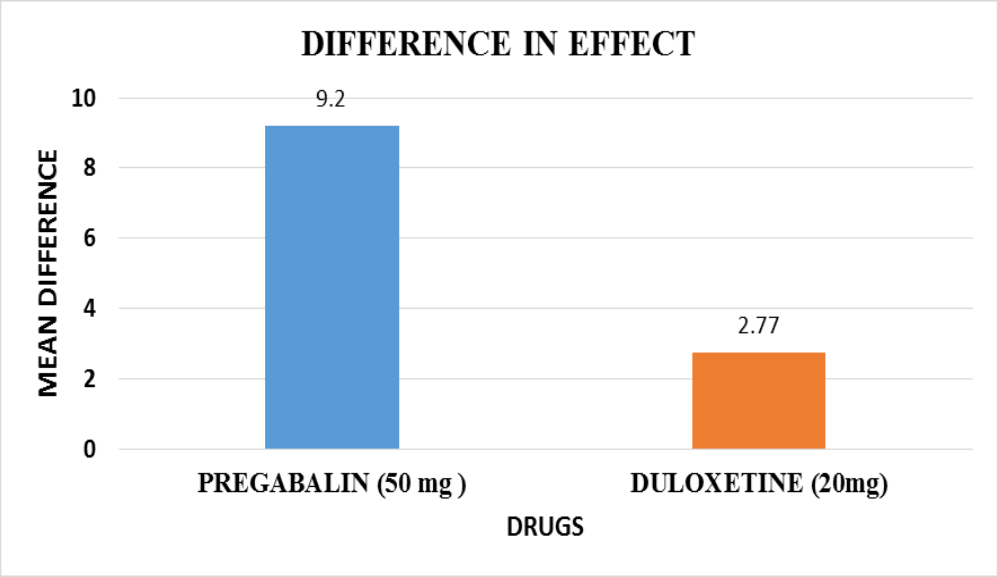

Figure No. 11(A): Distribution of Sample According To Effectiveness- Mean Difference.

Table No. 12: Distribution of Sample According To Medication Adherence Scale.

MEDICATION ADHERENCE SCALE	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
Low adherence	28	22	2.52	1	0.112
	80.0%	62.9%			
Medium adherence	7	13			
	20.0%	37.1%			
TOTAL	35	35			
	100.0%	100.0%			

- Since P value is greater than 0.05, the medication adherence of patients in the both groups are not significant.

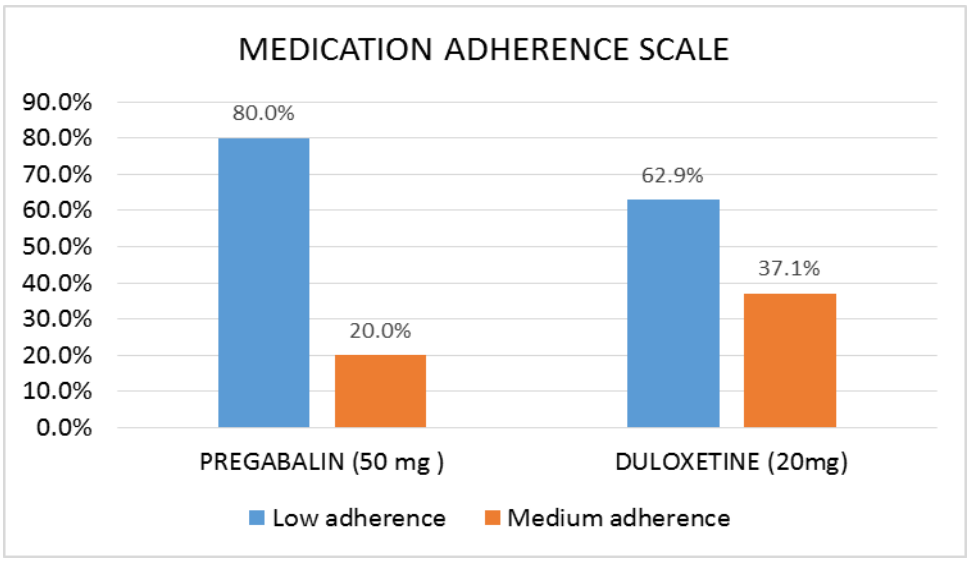

Figure No. 12: Distribution of Sample According To Medication Adherence Scale.

Table No. 13: Distribution of Sample According To Tolerability Scale.

TOLERABILITY SCALE	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
Poor	0	1	56.133	4	0.001
	0.0%	2.9%			
Moderate	0	11			
	0.0%	31.4%			
Medium	0	19			
	0.0%	54.3%			
Good	26	4			
	74.3%	11.4%			
Very good	9	0			
	25.7%	0.0%			
TOTAL	35	35			
	100.0%	100.0%			

- Since P value is less than 0.01, there is a highly significant association between tolerability and the groups. For Pregabalin 100% cases shows Good and Very good tolerability whereas in the Duloxetine group 88.6% cases are below Good tolerability.

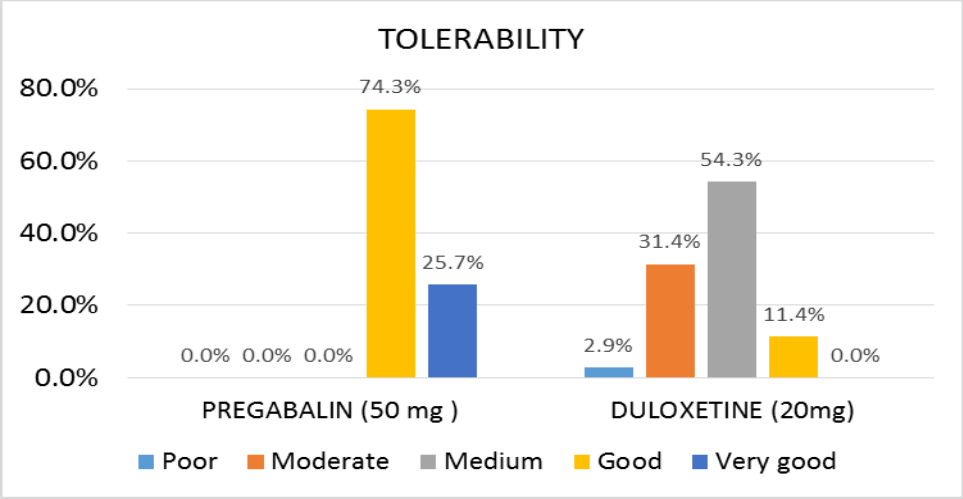

Figure No. 13: Distribution of Sample According To Tolerability Scale.

Table No. 14: Distribution of Sample According To Safety.

SAFETY	PREGABALIN (50 mg)	DULOXETINE (50mg)	Chi square	df	P value
NIL	35	33	2.059	1	0.151
	100.0%	94.3%			
constipation - ADR	0	2			
	0.0%	5.7%			
TOTAL	35	35			
	100.0%	100.0%			

Since P value obtained is more than 0.05, there is no significant difference in safety among the groups.

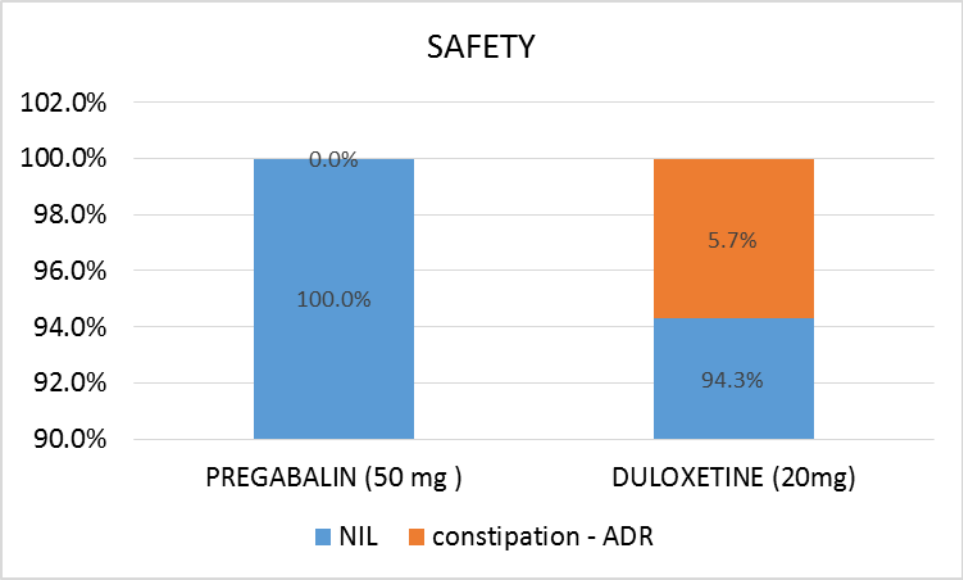

Figure No 14: Distribution of Sample According To Safety.

Table No. 15: Prescription Pattern of Pregabalin.

Drugs	Number of patients	Percentage
PREGABALIN (only) 0-0-1	12	38.71
PREGABALIN (only) 1-0-1	6	19.35
PREGABALIN + NSAID-OPIOID COMBINATION + ANTIDEPRESSANT	5	16.13
ANTIDEPRESSANT + PREGABALIN	5	16.13
ANTIHYPERLIPIDEMIC + NSAID- 0PIOID COMBINATION + PREGABALIN	1	3.23
ANTIHYPERLIPIDEMIC + ANTIHYPERTENSIVE + PREGABALIN	1	3.23
ANTIHYPERTENSIVE + PGN	1	3.23

- Out of 70 patients on pregabalin, monotherapy of pegabalin (0-0-1) OD was mostly prescribed. (38.71%), followed by monotherapy of pregabalin (1-0-1) BD (19.35%), pregabalin + Nsaid –opioid combination + antidepressant (16.13%), antidepressant + pregabalin 916.13%), antihyperlipidemic + NSAID –opioid + pregabalin (3.23%), antihypertensive + antihyperlipidemic + pregabalin (3.23%) and antihypertensive + pregabalin (3.23%).

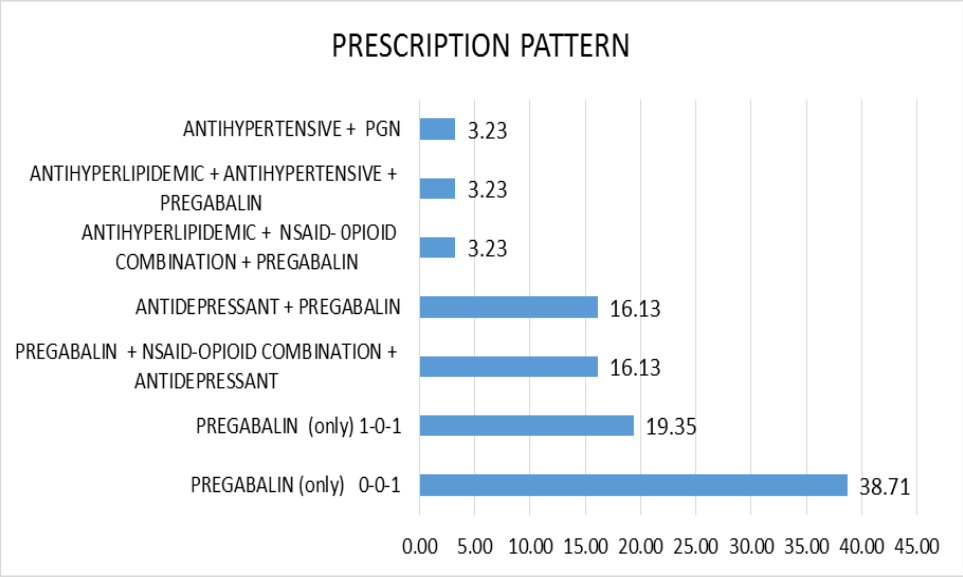

Figure No. 15.

Table No. 16: Prescription Pattern of Duloxetine.

DRUG	Number of patients	Percent
DULOXETINE (ONLY) 0-0-1	15	42.86
DULOXETINE (ONLY) 1-0-1	9	25.71
DULOXETINE + GABAPENTIN	5	14.29
(NSAID +OPIOID COMBINATION) + DULOXETINE	6	17.14

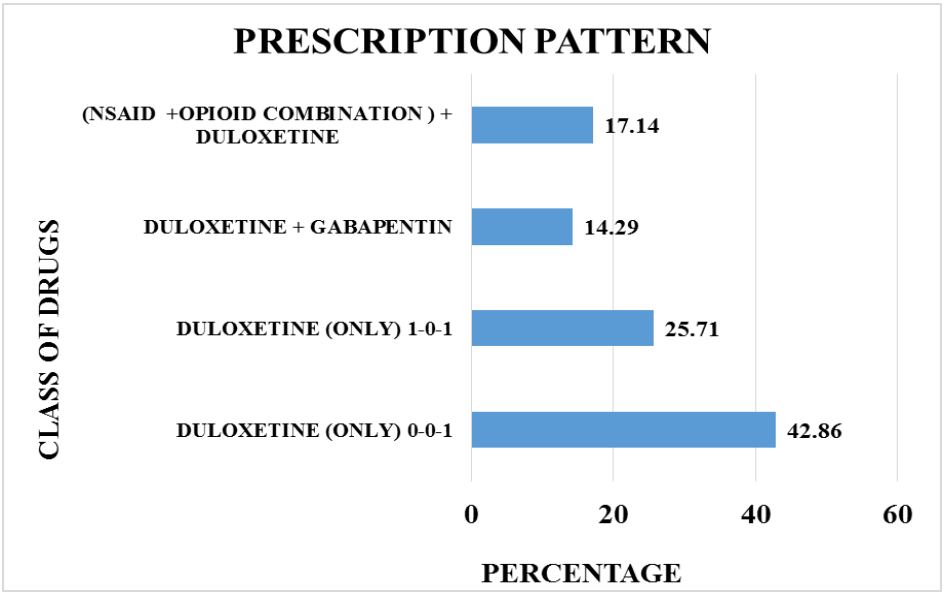

Figure no. 16

- Out of another 35 patients on duloxetine, 42.86% patients were on monotherapy of duloxetine (0-0-1) OD, followed by duloxetine (1-0-1) BD (25.71%), duloxetine + gabapentin(17.14%) and NSAID -opioid +duloxetine (14.29%).

CONCLUSION

The study was a prospective observational study using 70 patients recently diagnosed with Fibromyalgia syndrome. The study demonstrates that Pregabalin was more statistically significant in improving Quality of Life of Fibromyalgia patients compared to that of Duloxetine. The difference in mean scores of Quality of Life before and after therapy were statistically highly significant in both groups. It was concluded that mean difference of Quality Of Life score in Pregabalin group was significantly higher than the Duloxetine group.

In addition, Pregabalin was found to be more effective in reducing the pain compared to Duloxetine therapy. There were no ADR observed with Pregabalin. Constipation was the most common ADR observed in Duloxetine therapy. Thus, it can be concluded that Pregabalin therapy is more safer compared to Duloxetine therapy. Pregabalin was well tolerated compared to that of Duloxetine.

From this study, it is observed that most of the patients on mixed diet had experienced Fibromyalgia. Thus it can be concluded that mixed diet and weight gain is associated with development of Fibromyalgia. The post menopausal women were more prone to Fibromyalgia due to estrogen imbalance. Eventhough, PGN is found to be more effective than Duloxetine, cost is higher with pregabalin. So, cost reversal must be done for better therapy.

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