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Comparative Efficacy of Gabapentin Monotherapy and Combination Therapy for the Management of Radiating Pain: A Randomized Controlled Trial

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Abstract: Radiating discomfort greatly affects life quality and presents challenges for effective management. Gabapentin, a primary drug used for neuropathic discomfort, is essential in controlling pain. Nevertheless, the relative effectiveness of gabapentin alone compared to combination therapy (Ultracet or Akilose P) in treating radiating pain is still undetermined. This observational study aimed to evaluate and compare the treatment outcomes of gabapentin monotherapy and combination therapy for the control of widespread pain.

A review was carried out on 100 individuals diagnosed with radiating discomfort, all of whom received treatment for four weeks at a specialized pain management facility. Information was gathered from the patients' files, covering initial pain ratings, weekly VAS scores, and demographic details. Statistical evaluations were conducted using Welch's t-test alongside descriptive statistics.

In the gabapentin-only group, the average pain rating fell from 11.11 (at the start) to 5.10 (by week 4), indicating a 54.05% improvement. Likewise, the combination therapy group experienced a decline from 10.34 to 6.00, showing a 42.03% improvement. The difference between both groups was not statistically relevant (t=0.6818, p=0.4590). However, gabapentin alone exhibited superior tolerability and fewer adverse effects.

The research emphasizes that gabapentin as a standalone treatment achieves significant pain reduction and is a more favorable long-term option due to its lower adverse effect profile. It is suggested that further studies with larger populations and longer timeframes are necessary to confirm these results and enhance treatment approaches.

Keywords: *Radiating Pain, Gabapentin, Monotherapy, Combination Therapy, Randomized Controlled Trial, Visual Analog Scale.*

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I. NTRODUCTION

Gabapentin is prescribed frequently for chronic back pain syndromes in both primary care and specialty pain clinics, particularly when there is a 'radicular' or neuropathic component with pain radiating into the upper or lower legs. [1]

Important elements related to radiating pain in the lower back within general medicine are not well understood, primarily because much of the research is carried out in hospital environments with brief follow-up periods. Differences in the populations studied and in the definitions used have led to varying rates of occurrence and prevalence across different investigations.[2]

Nerve pain occurs due to injury to the somatosensory nervous system and can stem from different pathological processes. It is often characterized by its location in the body or the reasons behind it. The conditions and the pathophysiological states that determine the onset of neuropathic pain mostly involved are metabolic disorders (e.g. peripheral diabetic neuropathy (PDN)), neuropathies associated with viral infections (e.g. post-herpetic neuralgia, HIV, leprosy), autoimmune disorders affecting the central nervous system (e.g. multiple sclerosis and Guillain–Barre syndrome), chemotherapy-induced peripheral neuropathies, damage to the nervous system of traumatic origin (e.g. spinal cord injury (SCI) and amputation), inflammatory disorders, hereditary neuropathies, and channelopathies.

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Radiating pain poses significant challenges in clinical management due to its complex etiology, variable presentation, and impact on patients' quality of life.

Among the myriad conditions giving rise to radiating pain, neuropathic disorders stand out as prominent contributors.[3]

Population-based estimates of neuropathic pain prevalence are important in order to determine resource requirements (clinical, financial, educational) for primary care, where most people with chronic pain are treated and managed, and to inform the targeting of treatment and prevention strategies.[4]

Disorders causing neuropathic pain include cervical or lumbar radiculopathy, diabetic polyneuropathy, post-traumatic neuropathy, and postherpetic neuralgia. Neuropathic pain impairs patients' mood, quality of life, daily activities, and occupational performance, and generates health-care costs three times higher than in matched controls.[5]

Gabapentin, a derivative of γ-aminobutyric acid with three alkyl groups, influences α-2-δ calcium channels that are crucial in the experience of neuropathic pain. It has received approval from the FDA for treating postherpetic neuralgia, partial seizures, and moderate to severe restless leg syndrome, and it is frequently used off-label for various issues like neuropathic pain, fibromyalgia, and anxiety. It also has an off-label use for neuropathic pain, fibromyalgia, bipolar disorder, postmenopausal hot flashes, essential tremors, anxiety, resistant depressant and mood disorders, irritable bowel syndrome (IBS), alcohol withdrawal, postoperative analgesia, nausea and vomiting, migraine prophylaxis, headache, interstitial cystitis, painful diabetic neuropathy, social phobia, generalized tonic-clonic seizures, pruritus (itching), insomnia, post-traumatic stress disorder (PTSD), and refractory chronic cough.[6]

PDPN-specific scores that are based on nerve fiber functioning should be assessed in prospective cohort studies to provide insight into the predictive value of the underlying pathophysiological process on long-term SCS outcome in PDPN. The Michigan Diabetic Neuropathy Score (MDNS), which is based on abnormal nerve conductions and neurological examination, is a validated assessment of the severity of neuropathy in patients with PDPN.[7]

Tramadol is a pain-relieving medication classified as an opioid, which has been accessible to the public since it was launched in 1977. It is frequently used in conjunction with acetaminophen (also known as paracetamol) to improve its pain-relieving capabilities, and there are options for both oral and injectable forms. [8]

Tramadol is available in both injectable and oral preparations. It is not recommended for use with children under 10 years old. It has T1/2 elimination half-life at 4-6 hours. Tramadol undergoes hepatic metabolism via the cytochrome P450 isozyme CYP2D6, being O- and N-demethylated to five different metabolites. Of these, M1 (O-Desmethyltramadol) is the most significant since it has 200 times the μ-affinity of (+)-tramadol and furthermore has an elimination half-life of nine hours, compared with six hours for tramadol itself. Phase II hepatic metabolism renders the metabolites water-soluble and they are excreted by the kidneys. Thus, reduced doses may be used in renal and hepatic impairment.[18]

Acetaminophen acts via at least two pathways. The main mechanism of action of acetaminophen is reducing the oxidized form of the COX enzyme, preventing it from forming proinflammatory chemicals, which are important mediators of inflammation, pain, and fever[7][8]. Acetaminophen is metabolized to AM404, a compound with several actions; most important, it inhibits the uptake of the endogenous cannabinoid/vanilloid anandamide by neurons. Furthermore, AM404 inhibits sodium channels, as do the anesthetics lidocaine and procaine. One theory holds that acetaminophen works by inhibiting the COX-3 isoform of the COX family of enzymes(10). Acetaminophen is metabolized primarily in the liver, into non-toxic products.[19]

ULTRACETTM (tramadol hydrochloride/ acetaminophen) combines two analgesics, tramadol 37.5 mg and acetaminophen 325 mg. Since ULTRACETTM contains only 37.5 mg of tramadol and 325 mg of acetaminophen, the use of 25% less tramadol in the combination product should reduce the incidence of tramadol-related adverse events while the addition of acetaminophen should reduce the onset time of analgesia and possibly improve the degree of analgesia[11]. It also has a synergistic effect whereas using it alone does not. The authors intend to prove the efficacy and effectiveness of ULTRACETTM and tramadol and acetaminophen in management of mild to moderate pain after upper extremity surgery.[20]

Gabapentinoids are medications that work on the central nervous system and provide pain relief for neuropathic and nociplastic types of pain. They could be especially effective in managing issues such as knee osteoarthritis (OA) and long-lasting pain linked to nociplastic processes. However, gabapentinoids carry risks of adverse events (AEs), including a 5% chance of drug abuse/misuse and 3% chance of overdose. Screening for nociplastic pain could help identify patients most likely to benefit while sparing others of gabapentinoids' serious AEs.[9]

- *There are Several Aspects that Define Pain and its effects:-*

The seriousness of pain encompasses both how strong the pain feels and how much it disrupts everyday tasks (disability). These two elements can be evaluated with a two-dimensional or single-dimensional scale, based on the assessment method used. [11] High intercorrelations between pain-intensity measures and pain-related disability measures support the concept of using them as a unitary construct of pain severity. Moreover, disability is seen as a major indicator for the severity of a pain condition and several

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tools have been developed to assess the pain-related disability. Some of the most frequently used tools in the field of spinal surgery are the Oswestry Disability Index (ODI) and the Roland & Morris Disability Questionnaire. These tools assess the limitations in different activities of daily living such as dressing, walking, family life, etc.[5]

Chronicity. Different definitions of chronic back pain are in use. In 1984, Nachemson and Bigos defined it as a period of at least 3 months with persisting pain. In 1996, Von Korff and Saunders defined it as the back pain that lasts at least for half of the days during an year. Raspe et al.[12] investigated 40 epidemiologic/therapeutic studies between 1998 and 2000 with regard to the definitions of chronic back pain that were used. Between 4 weeks and more than 1 year of persisting pain, he showed that there is no consensus on the above definition of chronicity. Von Korff and Miglioretti[13] recently presented a prognostic approach to define chronic pain by defining it as a 'clinically significant pain likely to be present for one or more years in the future'. A 50–79% probability of future clinically significant pain was defined as 'possible chronic back pain' and an 80% or larger probability as 'probable chronic back pain'. Using a depression scale of pain intensity during the past 6 months, the number of days with back pain and the number of days with pain from other pain sites as prognostic factors they were able to predict which patients would surpass the aforementioned thresholds of 50 and 80%.

Pain experience. This contains pain intensity and pain affect. Pain intensity describes how much a patient is in pain whereas pain affect describes the 'degree of emotional arousal or changes in action readiness caused by the sensory experience of pain'. It has been shown that pain intensity may quite easily be declared by most patients and that different methods of measuring pain intensity showed high intercorrelation. Contrary to these findings, alternative methods of pain affect-assessing did not intercorrelate as high as those of pain intensity, making the utilisation of this part of pain characterisation more complicated. A lot of factors such as social situation, work situation and setting and history of prior injury may influence pain perception and show large inter-individual differences. As perception of pain may differ within a time-period, recent studies have mentioned that it is more valuable to ask patients to rate their 'usual' pain on average over a past short period of time, e.g. 1 week, than to ask for 'current' pain at the specific time of fulfilling a questionnaire.[14] Posing such questions relies on the assumption that patients are able to accurately recall their pain levels of a past period of time. Whether or not this is reliable is discussed controversially. Whereas some studies find it to be unreliable to assess pain retrospectively others report acceptable levels of validity up to a 3-months recall period. It has been found that pain is usually overestimated when actual intensity of pain is higher and underestimated when it is lower. [15] Moreover, Haas et al. found that pain and disability recall become more and more influenced by the present pain and disability during a period of 1 year while the influence of actual relief and pain and disability reporting at the initial consultation decreased. On the other hand, Von Korff et al stated that recall of chronic pain in terms of its average intensity, interference with activities (disability due to pain), number of days with pain and number of days with activity limitation, lead to acceptable validity levels. As mentioned in the beginning, assessment of pain is broadly used in spinal surgery. In the setting of pre-/postoperative follow-up investigations, it is unavoidable to use some kind of pain recall when 'current pain' as a test-parameter (as recommended above), is not used. With regard to the current literature, it seems to be justifiable to use short time-periods of pain and disability recall for comparison of pain status of patients in the course of back disease. The interpretation whether or not a statistically significant change corresponds to a significant clinical change as well or defining a threshold remains challenging and needs further research. It must also be kept in mind that the same method of assessing pain may have different thresholds of clinical significance, depending on the setting for example acute or chronic pain.

The use of this scale for comparative purposes is limited by its lack of sensitivity for detecting relatively small changes. Improvement in discrimination can be achieved by using a numerical rating scale (NRS), eg, marked 0-10 or 0-20, or by the introduction of the visual analogue scale (VAS). This last technique utilises a straight line, conventionally 10 cm long, whose extreme limits are marked by perpendicular lines. The ends of the scale carry a verbal description of each extreme of the symptom to be evaluated, and the patient is asked to mark the line at a position between the two extremes which represents the level of pain. The present study was designed to investigate the degree of correlation between pain scores registered on 4 different rating scales.[10]

Independent samples t test:- The independent t test, also called unpaired t test, is an inferential statistical test that determines whether there is a statistically significant difference between the means in two unrelated (independent) groups?

To apply this test, a continuous normally distributed variable (Test variable) and a categorical variable with two categories (Grouping variable) are used. Further mean, SD, and number of observations of the group 1 and group 2 would be used to compute significance level. In this procedure, first significance level of Levene's test is computed and when it is insignificant ($P > 0.05$), equal variances otherwise ($P < 0.05$), unequal variances are assumed between the groups and according P value is selected for independent samples t test. In SPSS [Analyze – compare means – independent samples t test].[16]

One such combination drug tramadol 37.5 mg/paracetamol 325 mg is an ideal combination analgesic because first, these are the most frequently used combination analgesics and second these are combination for which there is most evidences published.[17] However their adverse effects such as nausea, vomiting, itching and respiratory depression are a concern for the patient particularly due to opioid component.4 Studies shows

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nausea, vomiting, dizziness and somnolence were most prominent in the tramadol group.

II. MATERIAL AND METHODOLOGY

➢ *Type of Study:*

This was a prospective observational and comparative study designed to evaluate the efficacy of gabapentin monotherapy versus combination therapy (using either Ultracet or Akilose P) in the management of widespread pain. The study was approved by the institutional review board and complied with the ethical principles outlined in the Declaration of Helsinki.

➢ *Study Population:*

- Prevalence:

Studies have shown that a significant proportion of patients have radiating pain, including sciatica, lumbar radiculopathy, and cervical radiculopathy. Based on previous literature, the response rate was estimated to be 50% (p = 0.5).

$$n = \frac{4pq}{E^2}$$

Where,
n = required sample size,
p = estimated proportion of patients responding to treatment (assumed to be 0.5 based on previous literature),
q = complementary probability (1 - p), and
E = desired margin of error (set at 0.1)

Based on previous literature and clinical experience, an estimated response rate of p=0.5 was assumed. With a desired margin of error of e=0.1 and a confidence level of 90%.
Then, we get

$$n = \frac{4(0.5)\ (1 - \ 0.5)}{(0.10)^2}$$

Total sample size: 100 **n = 100**

➢ *Study Procedure:*

Patients with diffuse pain, including sciatica, arm pain, and lumbar radiculopathy, were evaluated according to specific criteria. A visual analog scale (VAS) was used to measure pain intensity. Participants were divided into two treatment groups: gabapentin monotherapy and combination therapy (gabapentin with Ultracet or Akilose P).

Pain score data were collected at baseline (week 0) and after 4 weeks of treatment, and results were compared statistically.

➢ *Inclusion Criteria:*

- Age:- Participants were 18 years of age or older.
- Diagnosis:- Patients had a confirmed diagnosis of radiating pain, including sciatica, arm pain, cervical radiculopathy, lumbar radiculopathy, or postherpetic neuralgia.
- Duration of pain:- The radiating pain had lasted at least four weeks prior to enrollment.
- Informed consent:- Patients agreed to participate after providing informed consent.
- Cognitive ability:- Ability to understand study procedures and complete questionnaires.
- Communication:- Effective communication skills to report pain and response to treatment.
- Stable medical condition: - Stable medical condition, no acute exacerbations.
- Compliance:- Willingness to comply with study protocols, including follow-up visits and treatment.
- No contraindications:- No known allergies or contraindications to study drugs (gabapentin, Ultracet or Akilose P).
- Legally authorized representative:- In case of cognitive impairment, consent may be obtained from the legal representative.

➢ *Exclusion Criteria:*

- Age:- Patients under 18 years of age.
- Pregnant/lactating women: - Pregnant or lactating women were excluded due to potential risk. Cognitive impairment: - Individuals unable to understand or consent to study procedures. Terminal illness:- Patients with a life expectancy shorter than the duration of the study. Contraindications to the drug:-History of allergy or contraindication to gabapentin, Ultracet, or Akilose P.
- Drug addiction:-Patients with a history of drug addiction or dependence.
- Serious psychiatric disorders:-Conditions such as schizophrenia, bipolar disorder or psychosis.
- Uncontrolled medical conditions:-Uncontrolled hypertension, diabetes or cardiac arrhythmia.
- Previous research participation:-Those who have participated in similar research.

➢ *Data Collection Form:*

The data collection form was structured as follows:

- Patient demographics:- age, BMI, weight, and height.
- Clinical history:- Details of pain type, duration, medical history, and medications.
- Treatment data:- Dose and duration of treatment with gabapentin or combination.
- Outcome measures:- Pain intensity scores at baseline and after 4 weeks.

➢ *Statistical Analysis:*

Data were analyzed using Microsoft Office 2010, GraphPad Prism 5.0, and Windows 8 tools. Results were presented as mean, percentage, and graph. A t-test was used to compare pain scores between treatment groups to determine statistically significant differences.

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III. RESULTS

The primary aim of this investigation was to meticulously examine and juxtapose the therapeutic efficacy of Gabapentin monotherapy against a combination regimen comprising Ultracet and Akilose P. in radiating pain scores over a comprehensive four-week duration. Our investigation encompassed a diverse sample pool consisting of 100 individuals, meticulously divided into two distinct cohorts: 59 subjects were assigned to the Gabapentin monotherapy group, while the remaining 41 participants were allocated to the combination treatment arm.

Throughout the duration of the study, pain scores were meticulously assessed using the universally recognized Visual Analog Scale (VAS), supplemented by a series of meticulously designed questionnaires administered at weekly intervals, specifically at 0, 1, 2, and 4 weeks post-initiation of treatment. This rigorous assessment regimen aimed to capture any potential shifts or alterations in pain perception and management over the course of the study period.

Analysis of the collected data revealed intriguing insights into the dynamics of pain management within each treatment group. For participants receiving Gabapentin monotherapy, the initial mean pain score at baseline (0 weeks) stood at 11.11 on the VAS, indicating a substantial degree of discomfort and distress associated with radiating pain. However, as the study progressed, a notable downward trend in pain scores was observed, with the mean score plummeting to 5.10 by the conclusion of the four-week period.

Similarly, participants enrolled in the combination treatment arm, comprising Ultracet and Akilose P., commenced the study with a mean pain score of 10.34 at baseline, reflecting a comparable level of radiating pain severity to their counterparts in the Gabapentin monotherapy group. As the study unfolded, these individuals also experienced a discernible reduction in pain intensity, with the mean pain score diminishing to 6.00 by the conclusion of the four-week assessment period.

A pivotal aspect of our investigation entailed subjecting the data to rigorous statistical scrutiny, culminating in the application of a t-test to discern any significant disparities in pain scores between the Gabapentin monotherapy and combination treatment cohorts at the critical four-week juncture. The resultant t-value of 0.6818, accompanied by a corresponding p-value of 0.4590, indicated a lack of statistically significant divergence in pain scores between the two treatment modalities. This intriguing finding underscores the notion that both Gabapentin monotherapy and the combination of Ultracet and Akilose P. exert comparable efficacy in mitigating radiating pain over the course of a four-week treatment regimen.

Notably, the inherent limitations inherent in our study, including the relatively modest sample size and the abbreviated four-week duration, underscore the need for further investigation and validation of these findings in larger, more protracted clinical trials.

Patient receives Gabapentin Monotherapy

The pain score according to Visual Ananlouge Scale (VAS) and Patient Questionnaire for 0^{th} , 1^{st} ,2^{nd} , 3^{rd} and 4^{th} week of treatment of gabapentin monotherapy.

Table for 0^{th} week

Sr. No	At 0 week
1	10
2	10
3	12
4	9
5	14
6	9
7	10
8	12
9	13
10	9
11	9
12	12
13	9
14	13
15	8
16	10
17	14

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18	12
19	12
20	11
21	14
22	9
23	8
24	11
25	14
26	9
27	8
28	8
29	13
30	13
31	13
32	8
33	9
34	12
35	9
36	11
37	10
38	13
39	10
40	13
41	13
42	12
43	9
44	10
45	13
46	12
47	10
48	14
49	11
50	11
51	14
52	10
53	14
54	13
55	10
56	10
57	15
58	9
59	13
TOTAL	656
MEAN	11.11

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For 0th week

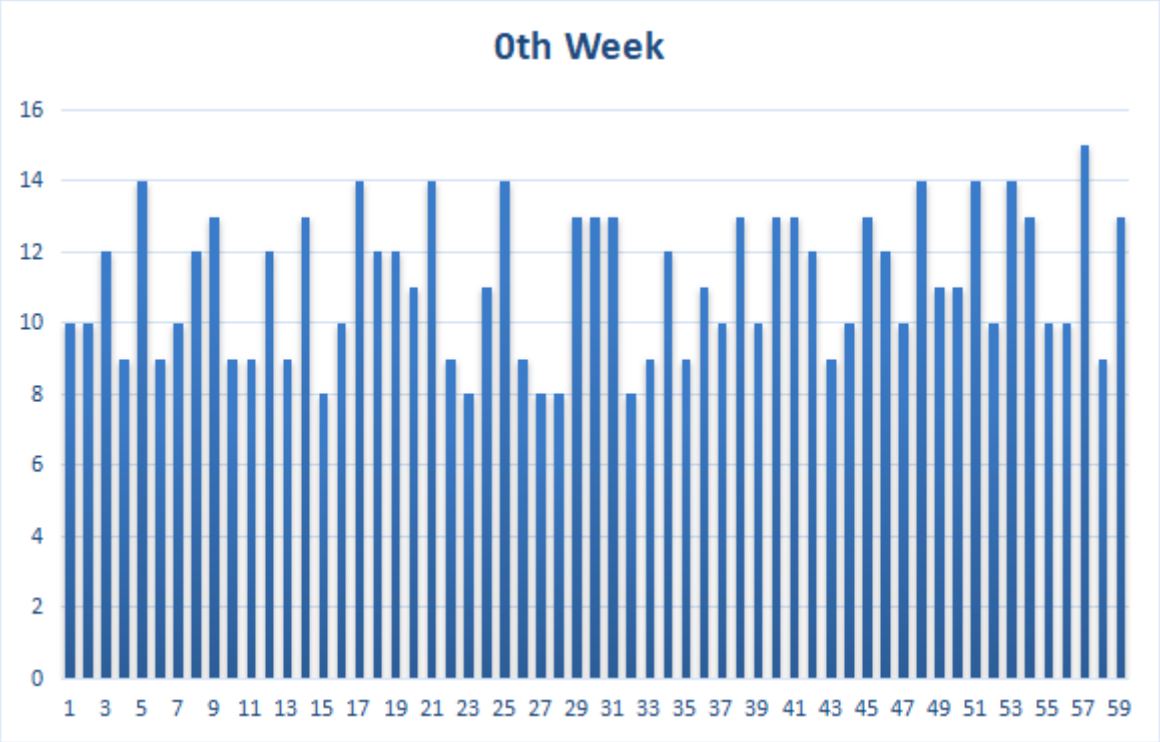

Table for 1st week

Sr. No	1st week
1	10
2	8
3	7
4	5
5	8
6	10
7	7
8	9
9	8
10	7
11	7
12	10
13	7
14	10
15	5
16	8
17	12
18	10
19	8
20	7
21	10
22	5

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23	5
24	8
25	8
26	5
27	5
28	5
29	7
30	10
31	7
32	6
33	7
34	8
35	7
36	7
37	7
38	7
39	7
40	5
41	11
42	9
43	7
44	7
45	8
46	9
47	7
48	7
49	10
50	7
51	8
52	5
53	8
54	8
55	7
56	5
57	8
58	5
59	7
TOTAL	442
MEAN	7.49

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For 1st week

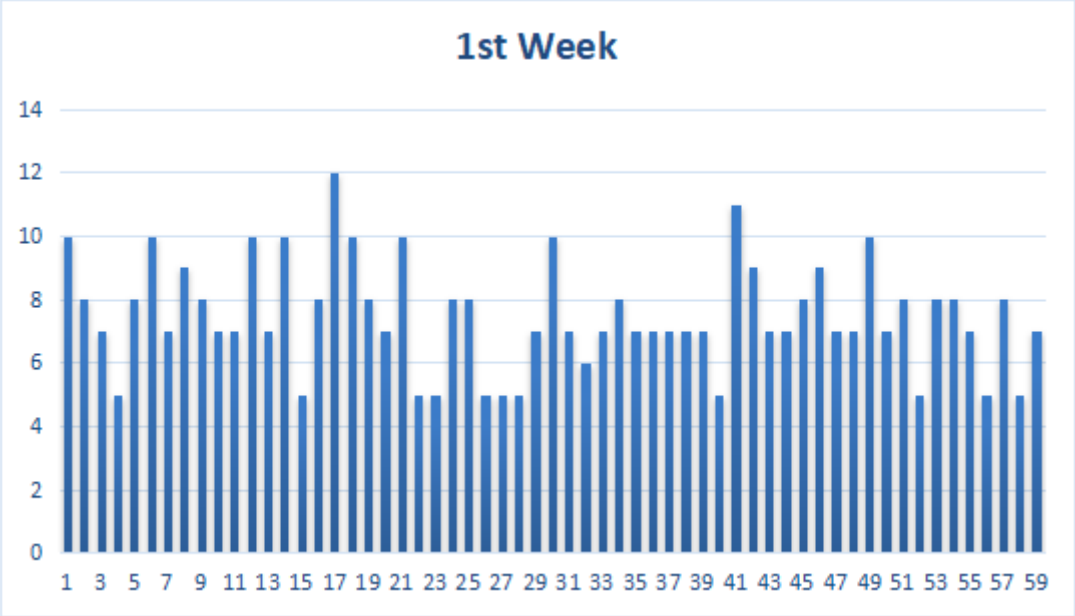

Table for 2nd week

Sr. No	2nd week
1	7
2	6
3	5
4	5
5	8
6	9
7	5
8	7
9	6
10	5
11	6
12	9
13	5
14	7
15	5
16	6
17	6
18	9
19	5
20	7
21	6
22	5
23	5
24	5

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25	8
26	5
27	5
28	5
29	5
30	6
31	7
32	5
33	5
34	6
35	5
36	5
37	5
38	5
39	5
40	5
41	7
42	5
43	5
44	5
45	7
46	5
47	5
48	6
49	6
50	5
51	7
52	7
53	7
54	5
55	5
56	5
57	7
58	5
59	7
TOTAL	347
MEAN	5.88

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For 2nd week

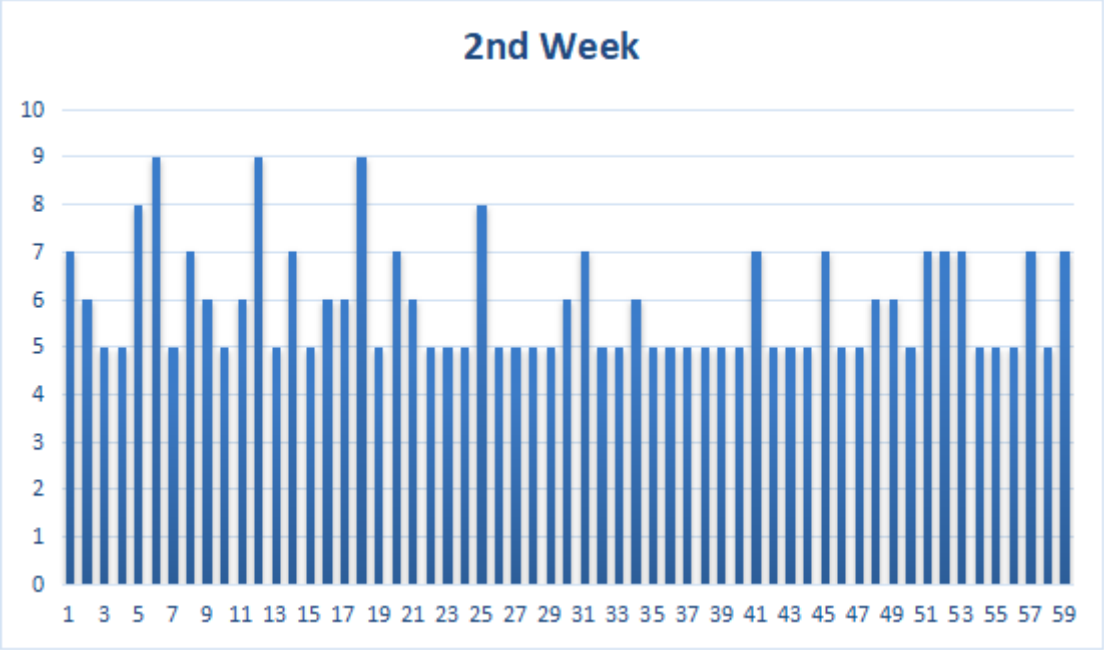

Table for 4th week

Sr. No	4th week
1	3
2	5
3	4
5	5
4	6
5	7
6	5
7	5
5	6
5	5
6	5
5	8
5	5
8	5
5	6
5	5
6	8
5	9
8	6
9	5
6	6
5	3
6	3
3	3
3	6

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3	3
6	4
3	3
4	4
3	6
4	5
6	5
5	5
5	5
5	5
5	5
5	6
5	5
6	5
5	5
5	6
5	5
6	5
5	5
5	5
5	3
5	5
3	5
5	6
5	5
6	6
5	5
6	6
5	5
6	4
5	5
4	7
5	3
7	5
TOTAL	301
MEAN	5.10

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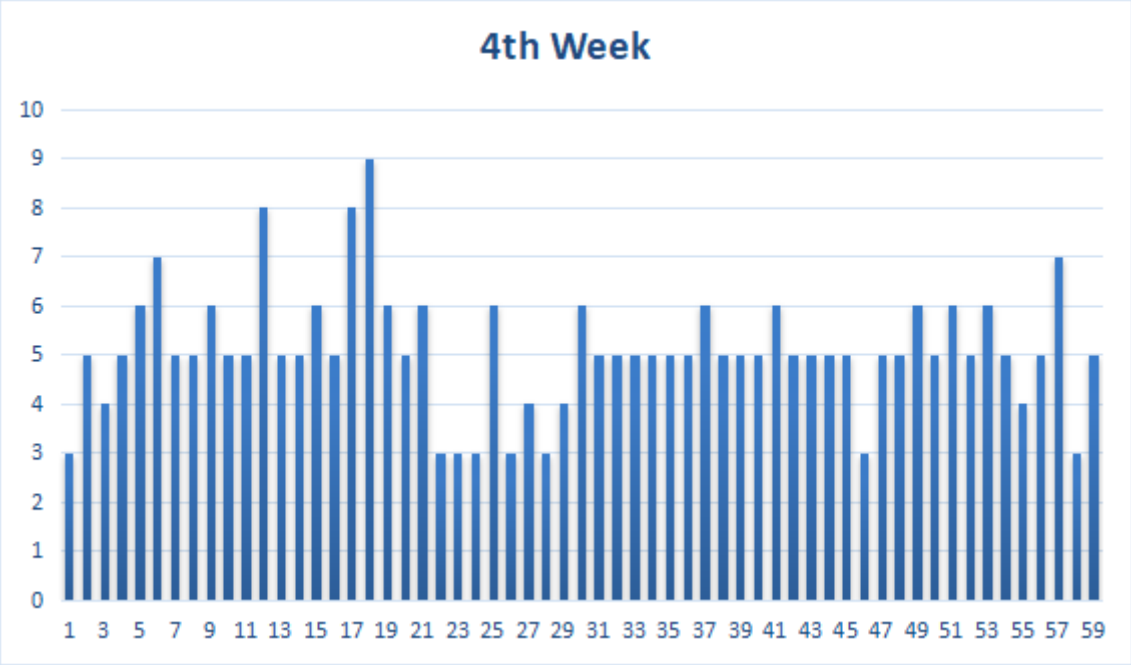
For 4th week



➢ *Mean Pain Difference*

The mean pain score difference between 0th , 1th , 2nd and 4th week are show in the the fig 1 and 2.

MEAN	VALUES
0TH Week	11.11
1st Week	7.49
2nd Week	5.88
4th Week	5.10

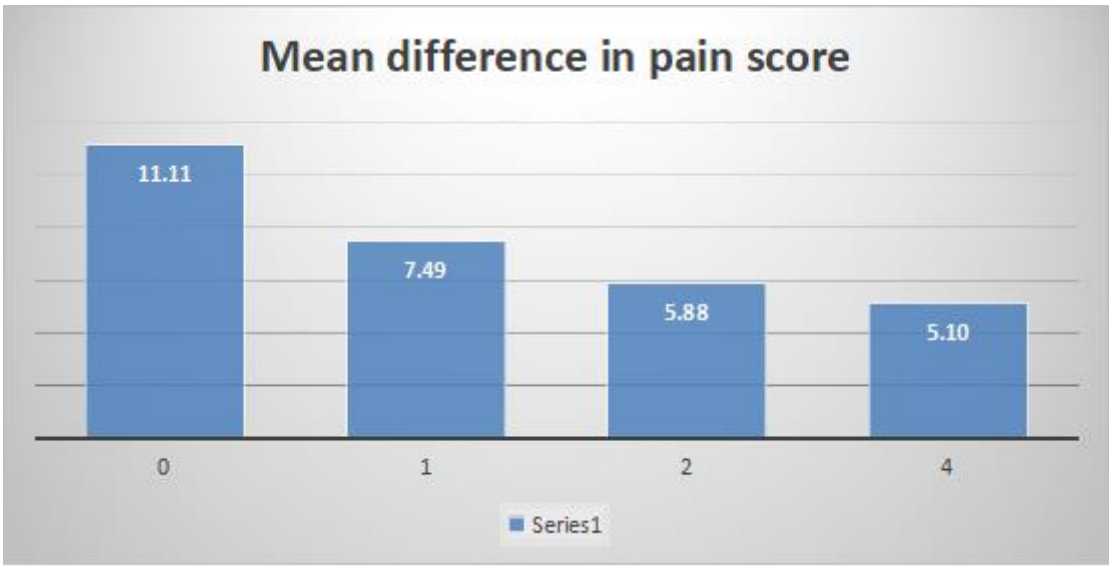


Fig 1. Mean difference in pain score

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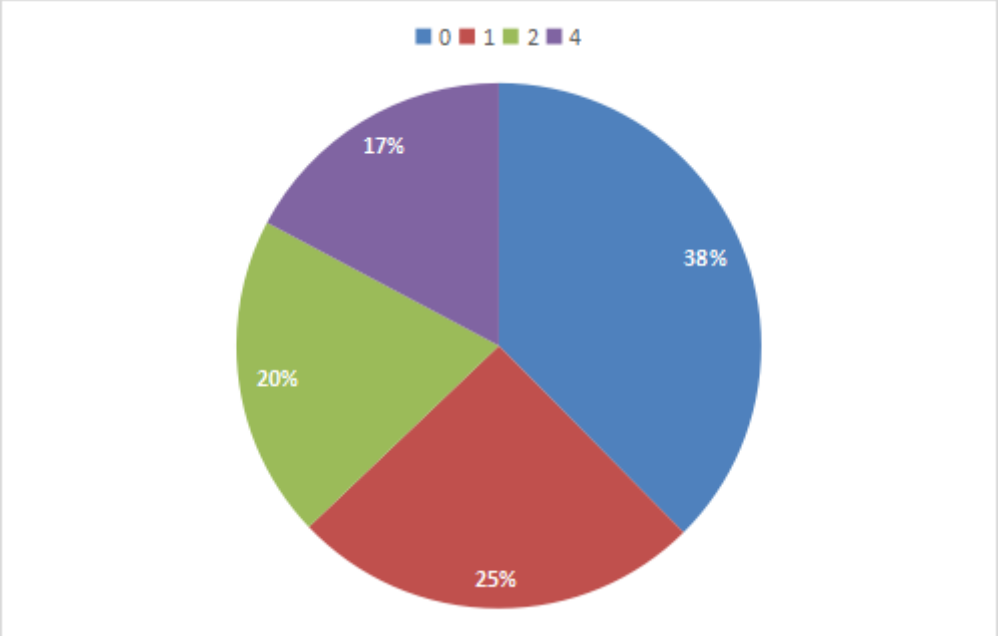

Fig 2. Pie chart representation of mean difference in pain score

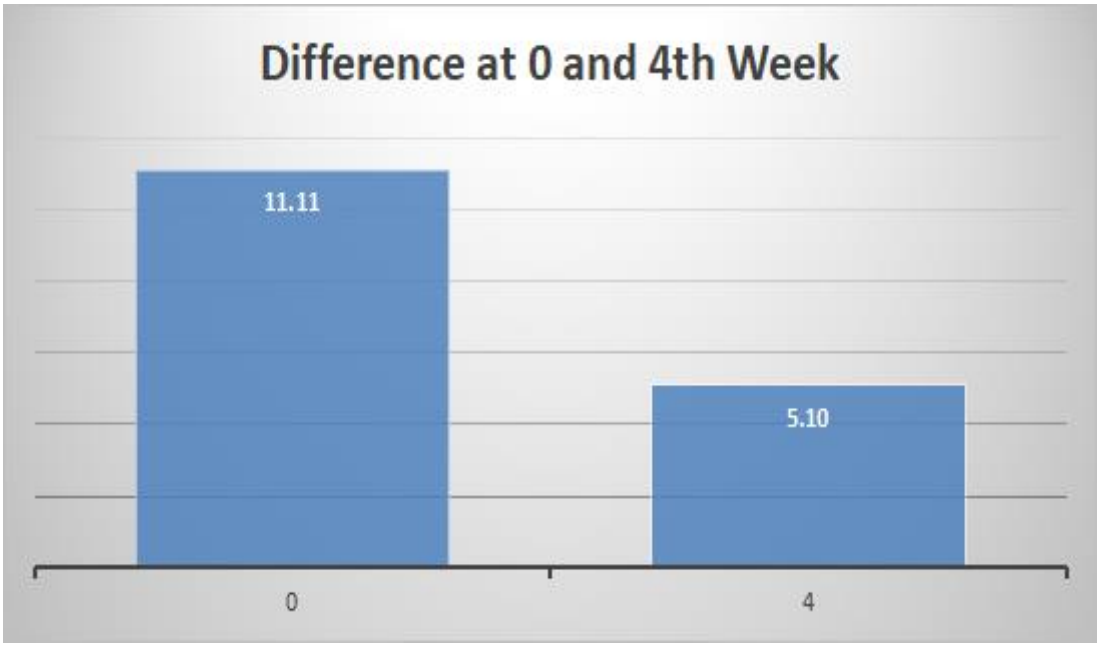

Fig 3: Difference at 0 and 4th Week

➢ *Patient reciving Gabapentine Combination therapy*
(Ultracet or Akilose P)

The pain score according to Visual Ananlouge Scale (VAS) and Patient Questionnaire for 0^{th} , 1^{st} ,2^{nd} , 3^{rd} and 4^{th} week of treatment of gabapentin combination therapy.

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Table for 0th week

Sr. No	0 Week
1	14
2	9
3	9
4	10
5	10
6	8
7	13
8	9
9	13
10	12
11	13
12	15
13	12
14	11
15	11
16	8
17	12
18	11
19	14
20	8
21	11
22	8
23	8
24	8
25	11
26	8
27	8
28	8
29	9
30	11
31	10
32	10
33	9
34	12
35	8
36	13
37	8
38	11
39	10
40	8
41	13
TOTAL	424
MEAN	10.34

For 0 week

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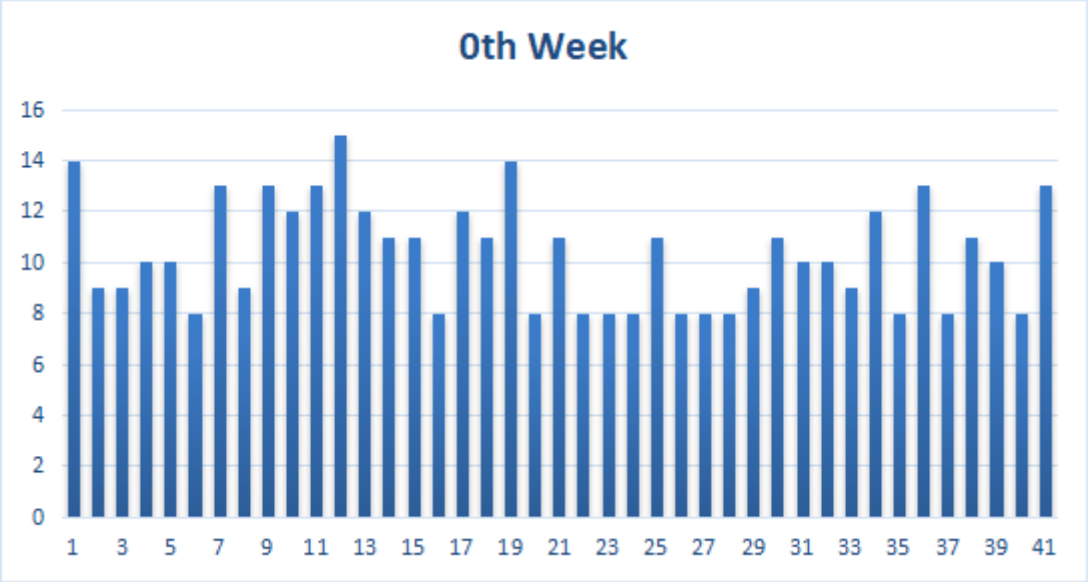

Table for 1st week

Sr. No	1st week
1	10
2	10
3	7
4	9
5	9
6	7
7	10
8	7
9	9
10	10
11	9
12	8
13	10
14	7
15	7
16	7
17	9
18	7
19	9
20	7
21	7
22	7
23	7
24	7

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25	7
26	7
27	7
28	7
29	7
30	7
31	7
32	9
33	7
34	7
35	7
36	9
37	5
38	9
39	7
40	7
41	11
TOTAL	323
MEAN	7.87

For 1st week

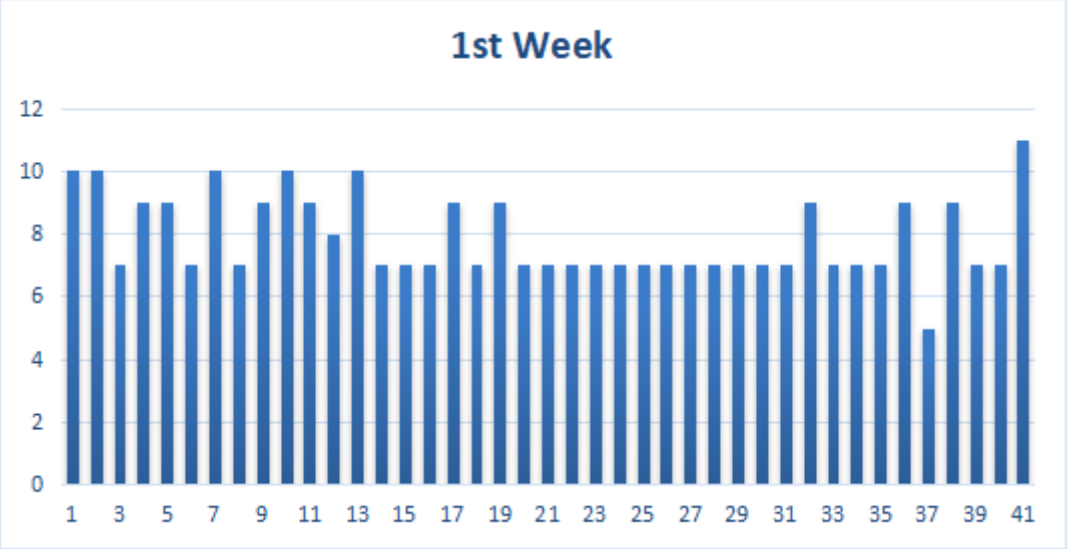

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Table for 2nd week

Sr. No	2nd week
1	9
2	8
3	5
4	7
5	7
6	5
7	8
8	5
9	8
10	8
11	9
12	8
13	8
14	7
15	7
16	5
17	7
18	7
19	7
20	5
21	7
22	5
23	6
24	5
25	7
26	5
27	5
28	5
29	5
30	6
31	5
32	7
33	7
34	6
35	5
36	7
37	5
38	7
39	7
40	5
41	8
TOTAL	265
MEAN	6.46

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For 2nd week

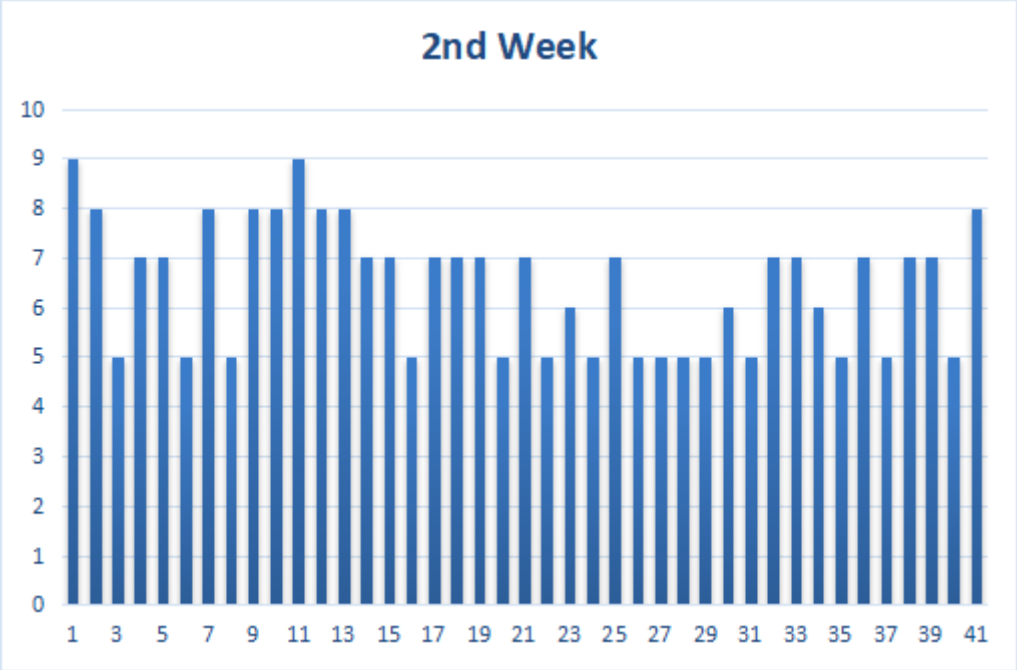

Table for 4th week

Sr. No	4th week
1	8
2	8
3	5
4	7
5	7
6	5
7	8
8	5
9	7
10	7
11	7
12	6
13	8
14	7
15	7
16	5
17	5
18	5
19	7
20	5
21	5
22	5
23	6

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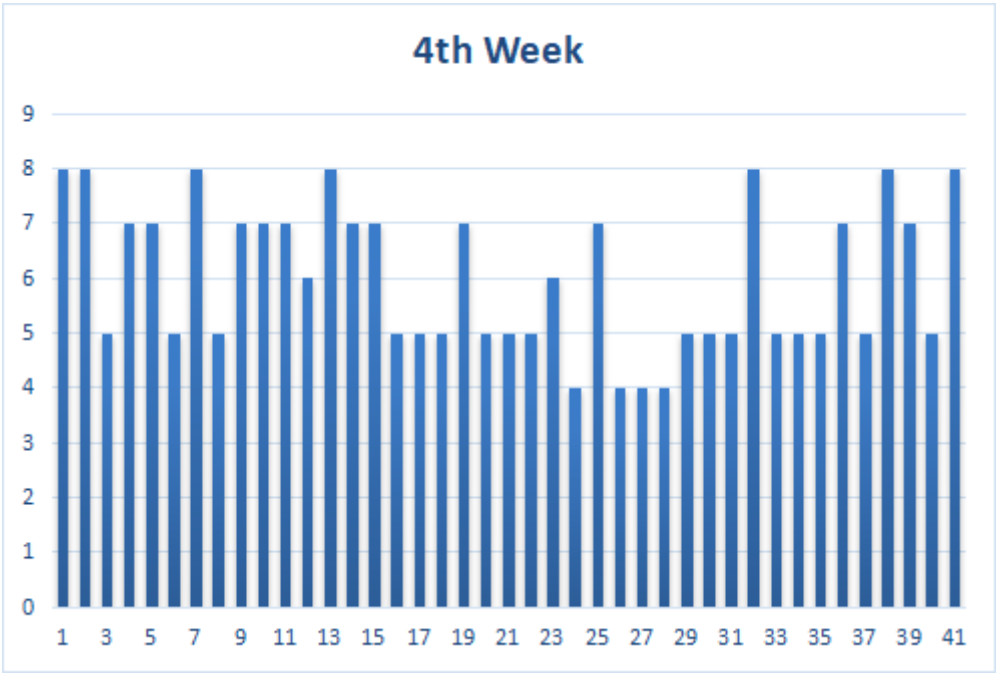
24	4
25	7
26	4
27	4
28	4
29	5
30	5
31	5
32	8
33	5
34	5
35	5
36	7
37	5
38	8
39	7
40	5
41	8
TOTAL	246
MEAN	6

For 4th Week



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➢ *Mean Pain Difference*

The mean pain score difference between 0th , 1th , 2nd and 4th week are show in the the fig 4 and 5.

MEAN	VALUES
0TH Week	10.34
1st Week	7.87
2nd Week	6.46
4th Week	6

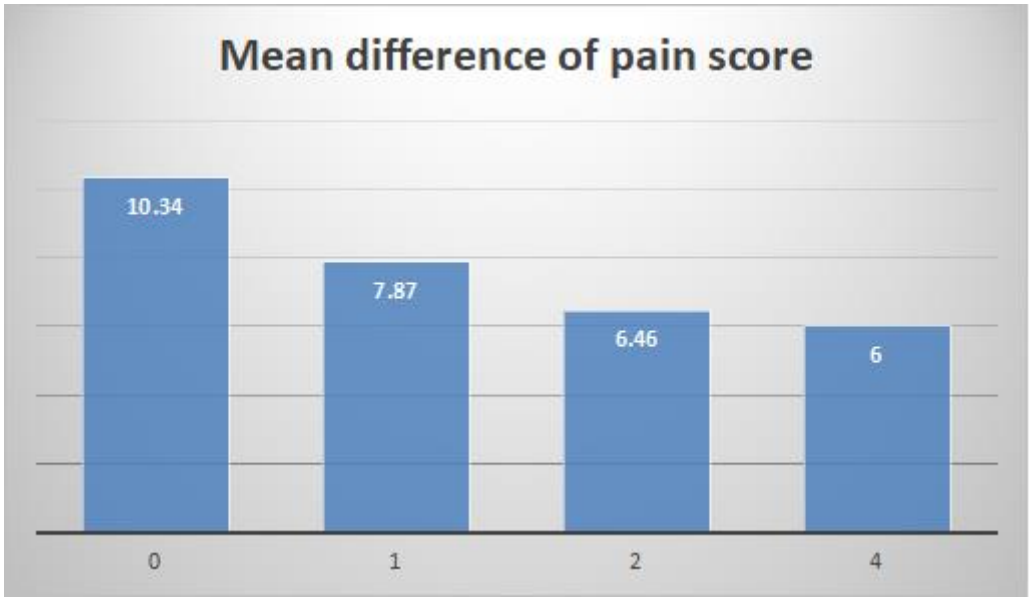

Fig 4. Mean difference of pain score

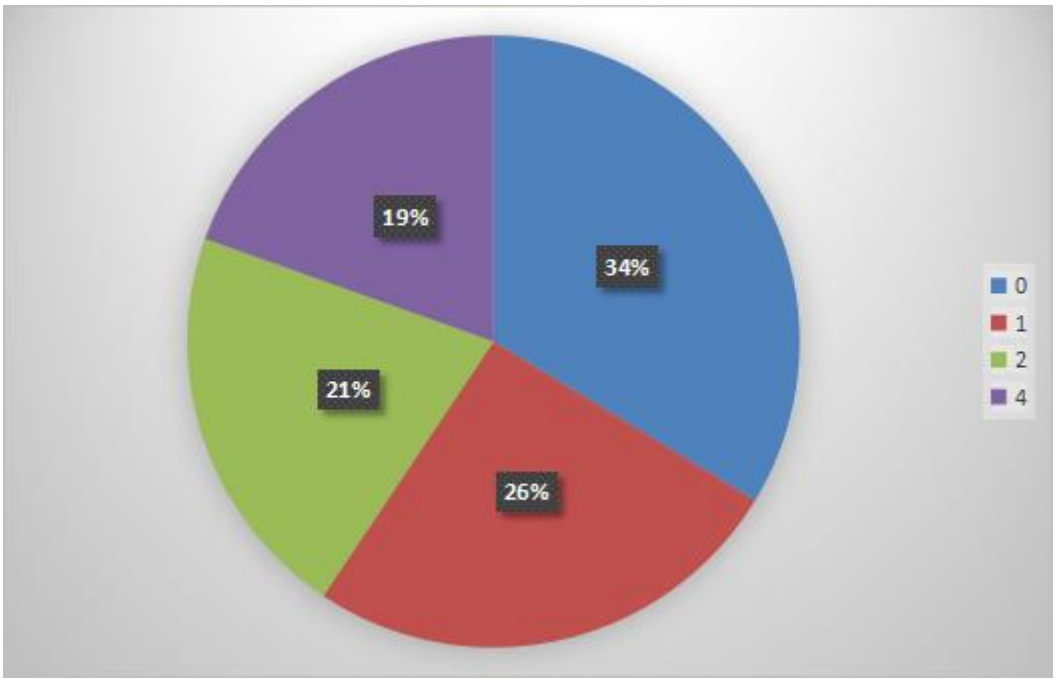

Fig 5. Pie chart representation of mean difference of pain score

The Difference in pain intensity at 0th and 4th week are reduce by 4.34 as shown in the fig 6 .

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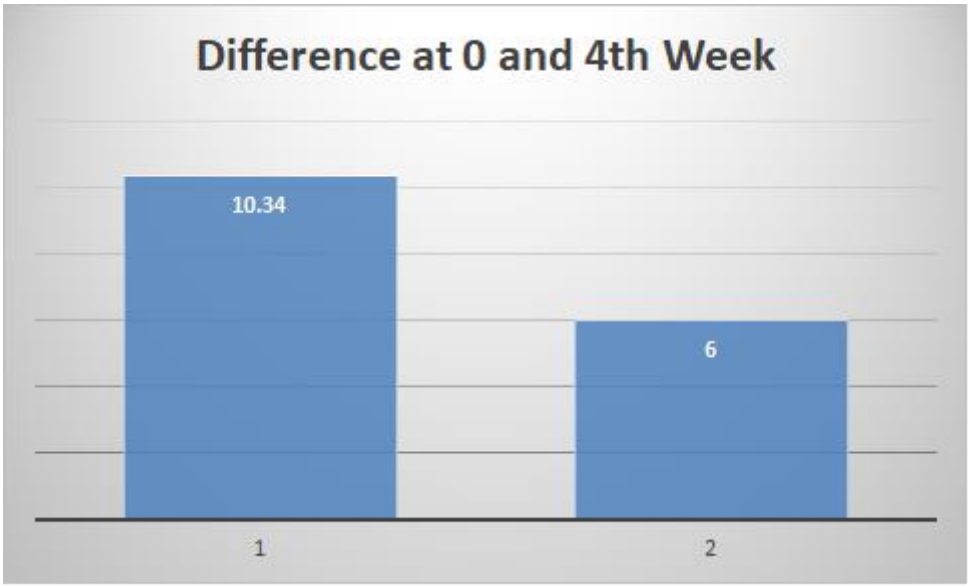

Fig 6. Difference at 0 and 4th Week

- *Gabapentin Monotherapy Group:*

✓ At the commencement of the study (0 weeks), the Gabapentin monotherapy group, comprising 59 patients, exhibited a mean pain score of 11.11 on the Visual Analog Scale (VAS).
✓ Over the four-week intervention period, a notable decline in pain severity was observed, with the mean pain score decreasing to 5.10 by the conclusion of the study.
✓ This reduction of 6.01 points between the baseline and four-week assessments represents a substantial improvement, underscoring the efficacy of Gabapentin monotherapy in managing radiating pain.
✓ In percentage terms, this reduction translates to approximately 54.05%, reflecting a significant alleviation of pain burden among participants.

- *Combination Treatment Group (Ultracet and Akilose P.):*

✓ In contrast, the combination treatment group, comprising 41 patients, commenced the study with a slightly lower mean pain score of 10.34 at baseline (0 weeks).
✓ Throughout the four-week intervention period, a discernible decrease in pain severity was observed, with the mean pain score diminishing to 6.00 by the conclusion of the study.
✓ While this reduction of 4.34 points from baseline to the four-week assessment reflects an improvement in pain management, it is notably lower than the reduction observed in the Gabapentin monotherapy group.
✓ In percentage terms, this reduction corresponds to approximately 42.03%, indicating a substantial but comparatively less pronounced alleviation of pain compared to the monotherapy group.

The difference in pain score at 4th week in Gabapentin monothereapy and Gabapentin combination therapy are shown in fig 7.

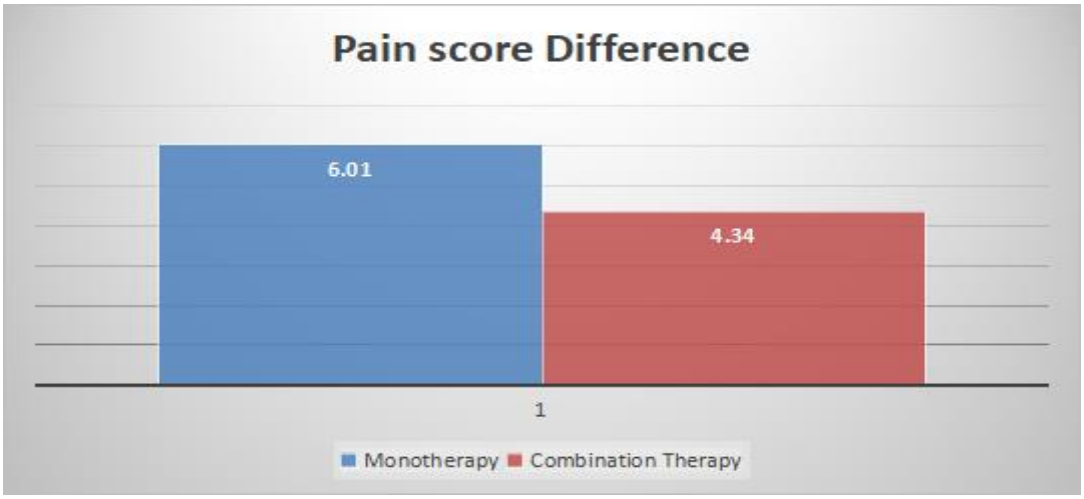

Fig 7. Pain score Difference

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➢ *Statistical Analysis*

Welch's t-test was used to compare the effectiveness of gabapentin monotherapy versus combination therapy (Ultracet or Akilose P) in reducing pain intensity, taking into account the unequal sample sizes and differences between groups. Unlike the traditional independent samples t-test, Welch's t-test takes these differences into account, providing a more precise assessment of the statistical significance of the observed differences.

The formula for the t-statistic in Welch's t-test is:

$$t = \frac{\overline{X}_1 - \overline{X}_2}{\sqrt{\frac{s_1^2}{N_1} + \frac{s_2^2}{N_2}}}$$

Where:

- $\bar{X}_1$ and $\bar{X}_2$: Sample means of the two groups,
- s_1^2 and s_2^2: Sample variances of the two groups,
- n1 and n2: Sample sizes of the two groups.

➢ *Calculation Details:*

$\bar{X}_1$ =5.10
$\bar{X}_2$ =6
s_1 =6.31
s_2 =7.8
n1 =59
n2 =41

By putting all the values in the formula we obtained **t value** as **0.6818.**

- **One-sided p-value**: 0.271.
- **Two-sided p-value**: 0.542.

Since both p-values exceed the significance level (**α=0.1**), the null hypothesis (H_0) cannot be rejected. This indicates that there is no statistically significant difference in pain improvement between gabapentin mono-therapy and combination therapy.

➢ *Interpretation and Clinical Implications:-*

Although both treatments showed pain relief, there was no significant difference in efficacy. However, factors beyond efficacy, such as tolerability and risk of side effects, must be considered when choosing a treatment.

Combination therapy (including Ultracet or Akilose P) may have a higher risk of side effects due to the use of multiple drugs. On the other hand, gabapentin monotherapy may offer the benefit of reduced side effects and improved tolerability, making it the preferred option for long-term pain control.

This study highlights the importance of comprehensively evaluating treatment options, taking into account both efficacy and patient safety. Further studies with larger samples and longer follow-up periods are needed to confirm these results.

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IV. DISCUSSION

Gabapentin, an anticonvulsant originally developed as a muscle relaxant and antispasmodic, has been shown to be effective in the management of neuropathic pain and some neuropathic conditions. Although chemically similar to the neurotransmitter GABA, gabapentin does not bind to the GABA receptor and does not affect its synthesis or uptake. Instead, gabapentin modulates voltage-gated calcium channels, reducing neurotransmitter release and thereby reducing pain.

Gabapentin is well tolerated, with relatively few serious side effects, making it a preferred choice for neuropathic pain. Common side effects associated with other anticonvulsants, such as sedation, ataxia, and gastrointestinal upset, are less common with gabapentin. Despite its favorable safety profile, gabapentin is contraindicated in pregnancy and lactation unless the potential benefits outweigh the risks, as there have been no well-controlled studies in these populations.

The primary objective of this study was to compare the efficacy of gabapentin monotherapy versus combination therapy consisting of Ultracet (tramadol + paracetamol) and Akilose P (aceclofenac + paracetamol) in reducing pain intensity in patients with diffuse pain. Pain intensity was assessed using a visual analog scale (VAS), a reliable and widely accepted tool for quantifying pain.This observational study provides insight into the comparative efficacy of gabapentin monotherapy and combination therapy in the management of widespread pain, filling an important gap in clinical practice.

➢ *Key Findings:-*

Our study recruited 100 participants, divided into two groups:

- **Gabapentin Monotherapy Group** (n = 59).
- **Combination Therapy Group** (n = 41).

Baseline VAS scores were comparable between groups, with mean pain scores of **11.11** in the gabapentin monotherapy group and **10.34** in the combination therapy group. Over the four-week treatment period, both groups exhibited a significant reduction in pain intensity:

- **Gabapentin Monotherapy Group**: Mean pain score reduced to **5.10** (54.05% reduction).
- **Combination Therapy Group**: Mean pain score reduced to **6.00** (42.03% reduction).

Statistical analysis using Welch's t-test revealed a **t-value of 0.6818** and a **p-value of 0.4590**, indicating no statistically significant difference in pain reduction between the two treatment modalities at a significance level of 0.1.

➢ *Interpretation:-*

The study findings suggest that gabapentin monotherapy and combination therapy provide comparable efficacy in managing radiating pain over a four-week treatment regimen. The null hypothesis, positing no significant difference in pain improvement between the two groups, could not be rejected based on the observed t- and p-values.

However, treatment selection should extend beyond efficacy to consider factors such as side effects, tolerability, and patient compliance. Gabapentin monotherapy offers notable advantages in these areas, particularly in long-term treatment scenarios. Combination therapies, while effective, carry an elevated risk of adverse effects associated with the opioid and non-steroidal anti-inflammatory components. These risks may outweigh the benefits for certain patient populations, emphasizing the need for individualized treatment approaches.

➢ *Clinical Implications*

Although both treatment regimens have demonstrated efficacy, gabapentin monotherapy may be preferred for the management of persistent pain due to:

- Lower risk of adverse events compared with combination therapy.
- Favorable safety profile, which may improve patient adherence.
- Reduced risk of complications associated with polypharmacy.

This study highlights the importance of balancing efficacy with safety and tolerability in the management of chronic widespread pain. Further studies with larger samples and longer follow-up are warranted to confirm these findings and explore other factors influencing treatment outcomes.

V. CONCLUSION

This study provides a comprehensive analysis of treatment modalities for the management of diffuse pain, focusing on the reduction of pain scores from baseline (week 0) to end point (week 4). The reduction in pain scores served as the primary measure of treatment efficacy. Gabapentin monotherapy was shown to significantly reduce the mean pain score, improving by 54.05% after four weeks (mean reduction: 6.01 points, from 11.11 to 5.10). This highlights its potential as an effective solution for long-term pain relief in patients with diffuse pain.

Compared to the combination treatment group (Ultracet and Akilose P), pain scores improved by 42.03% (mean reduction:4.34 points, from 10.34 to 6.00). Although this reduction was significant, it was not as pronounced as the improvement seen with gabapentin monotherapy.

Statistical analysis using Welch's t test showed no significant difference between the two groups at the four-week assessment (t value = 0.6818, p = 0.4590). Although gabapentin monotherapy appeared to provide numerically greater pain relief, the lack of statistical significance suggests that the two treatments were equally effective over the observation period.

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Gabapentin monotherapy has several advantages beyond efficacy, including safety and tolerability, making it a strong candidate for long-term pain management. In contrast, combination therapy with Ultracet and Akilose P may be more suitable for short-term use, due to the increased risk of side effects associated with long-term use of multiple drugs.

Clinicians are encouraged to consider gabapentin monotherapy as a preferred option for patients requiring long-term pain relief, particularly those at high risk of adverse effects from combination therapies. However, the choice of treatment should always take into account the individual patient's needs, preferences, and tolerance.

These results provide valuable information on the comparative efficacy of gabapentin monotherapy and combination therapy, supporting evidence-based decision-making in the management of widespread pain. Further studies with larger sample sizes and longer follow-up periods are needed to validate these findings and explore long-term outcomes.

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