



Efficacy and Safety Comparison Between Pregabalin and Thiocolchicoside in Acute Back Pain

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Abstract

Objective: The study conducted to compare safety and efficacy between thiocolchicoside, GABA mimetic centrally acting skeletal muscle relaxant and pregabalin, GABA mimetic anti-epileptic in treatment of acute non-specific low back pain.

Patient and Method: The study conducted out in Department of Neurosurgery and Spinal Surgery at Jinnah Hospital. Eighty patients were included during the study period of three months. Out of 80, 40 were given pregabalin 75 mg 1hs and rest were given thiocolchicoside 8 mg bd by the prescribing doctor. Patients, aged between 18-60 years having non-radiating low back pain for less than seven days were selected. Data was collected in manual format, which included the patient's details and prescribed drugs. Patients were also given notepads to record adverse effects. On day 1, the pain was measured on visual analogue scale. After a week, follow up was done and decrease in pain was also measured on same visual analogue scale.

Results: There was significant difference between pre and post visual analogue scale score in both groups with a p-value of less than 0.0001. However, difference between two groups was not statistically significant (p-value 0.0664). In both groups, patients did not report any adverse effects. Thiocolchicoside has better efficacy as compared to pregabalin. In Pakistan, drug abuse risk is much higher, thiocolchicoside is a safer choice as skeletal muscle relaxants and it should not be given for more than a week.

Conclusion: From the study, it can be shown that thiocolchicoside has better efficacy in treatment of acute non-specific low back pain as compared to pregabalin.

Keywords: Acute Non Specific; Low Back Pain; Thiocolchicoside; Pregabalin; Efficacy and Safety

Introduction

Non-specific acute low back pain is expressed as pain between the inferior gluteal folds and costal margins which is accompanied by limited painful movement, either influenced by posture or physical activities and also may be linked with referred leg pain [1]. Diagnosis of low back pain indicates that it is not related to conditions such as spondylitis, fractures, vascular, direct trauma, endocrine, metabolic, or infectious related processes. Therefore, it is referred as low back pain which is neither recognized by well-known or distinguishable pathology [2-4].

Among the middle aged group of people, this pain is a very common complaint which affects more than 90% of the population at least once in their lifespan [5]. It is mostly related to muscle spasm particularly when associated with persistent pain [6]. This is a significant socioeconomic as well as health related problem accompanied by huge healthcare cost, disablement and work absenteeism [7, 8]. Several treatment options are available such as antidepressants, acetaminophen, corticosteroids, anticonvulsants, topical analgesics, and opioids as well as muscle relaxants for mechanical back pain [8].

Despite availability and use of analgesic agents, pain relief may be insufficient and unpredictable. There are two drugs widely used for symptomatic relief of acute nonspecific low back pain. One is thiocolchicoside, which is pharmaceutically related to colchicine, and it is believed that it acts as a glycinergic and GABA mimetic medication. It can be combined with NSAIDs, which are widely used for the painful spasms of muscle such as backache, and sprains as well

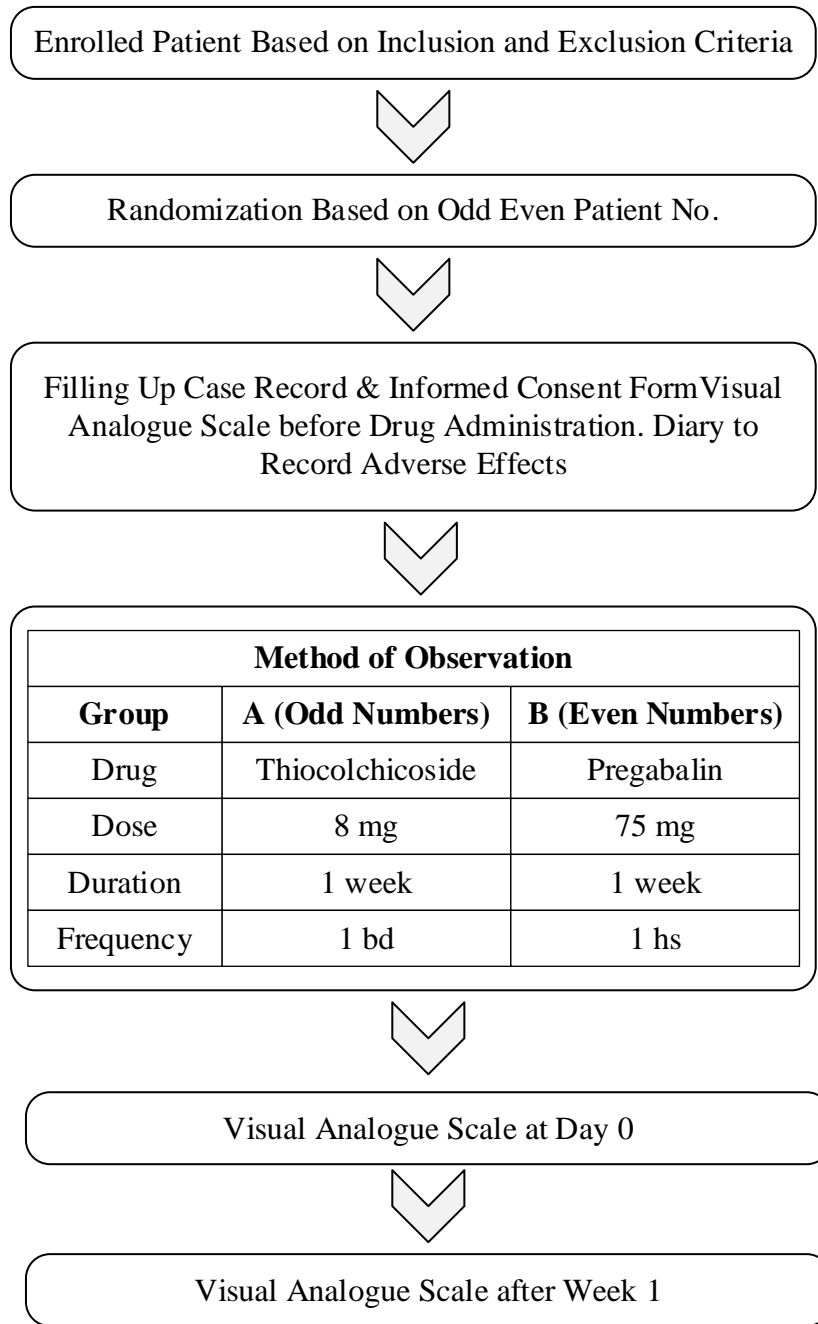
as torticollis. The second drug is pregabalin, which is a newer congener of gabapentin. It has been particularly used for neuropathic pain [7,9-10]. The sedative side effects of this drug are less prominent [3]. Hence this study was planned with two treatment groups, one receiving pregabalin and the other receiving thiocolchicoside. Their efficacies were compared with respect to pain relief and other symptoms of low back acute pain. The main purpose of the study is to compare the adverse effects and efficacy between pregabalin and thiocolchicoside in the medical management of non-specific acute low back pain.

Patients and Methods

It was an open labelled randomized study conducted in the Department of Neurosurgery and Spinal Surgery at Jinnah Hospital which is a tertiary care teaching hospital. The study was conducted for a period of six months. Patients were enrolled on the basis of inclusion and exclusion criteria. They were enrolled after obtaining their written consent. Different parameters were used to assess pain level such as visual analogue scale (VAS) score, sleep disturbances, amount of time the patient can sit, stand and walk without experiencing discomfort.

The analysis was performed by SPSS Version 24®. The difference between the thiocolchicoside and pregabalin group before and after administration of the respective drugs were compared using unpaired t-test. In each group, the VAS score was compared using the paired t-test at baseline as well after the administration of drug. The p-value of 0.05 was considered significant.

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Inclusion Criteria (Table 1)

- Patients of age range 18-60 years.
- Either of the gender.
- Patients with clinical history of non-specific low back pain of less than or equal to 7 days will be included in the study.
- Nonspecific low back pain with an acute episode of recent onset (less than 48 hours) defined by average pain within the last 24 hours equal or more than 5 on the visual analogue scale (VAS).
- Patients who were willing to take medications as directed, to come for follow up, to give written consent and comply with the protocol requirements.

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Table (1): Low Back Pain of Diagnostic Category

Category	Pain Type
1	Low back pain radiating no farther than the intergluteal fold
2	Low back pain radiating no farther than the knee

Table (2): Low Back Pain of Diagnostic Category

Category	Pain Type
3	Low back pain radiating beyond the knee with no neurologic signs
4	Low back pain radiating to a precise and entire leg dermatome with or without neurologic signs

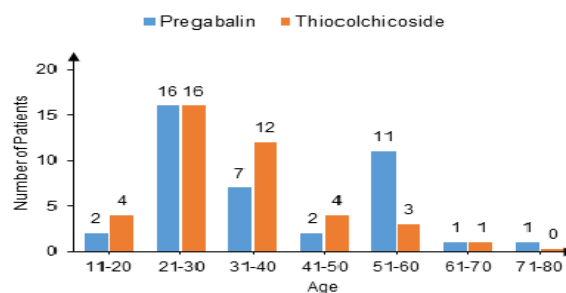
Exclusion Criteria (Table 2)

- Pregnancy
- Low back pain due to vertebral collapse or of mechanical origin (suspected by history taking and physical examination) such as neoplasm, infection or inflammatory disorders.
- History of Inflammatory arthritis of large joints, or any structural deformity. History of seizure disorder or any recent history of violent trauma, psychiatric or mental diseases or any widespread neurological symptoms.
- History of malignant tumor.
- Patient who have received other therapy [NSAIDs (including aspirin), muscle relaxant or opioid analgesics, physiotherapy, physical manipulations, invasive intervention, acupuncture therapy within last 48 hours].
- History of Immunosuppression, HIV or use of immunosuppressive drugs.
- Inclusion in another study in past 6 months or previous inclusion in this study.
- History of alcohol, drug or narcotics abuse.
- Constant progressive, non-mechanical pain (no relief with bed rest)
- Thoracic pain.
- Patient systemically unwell or having fever, or unexplained weight loss.
- Clinically significant renal dysfunction/hepatic dysfunction.
- Patient suffering from diarrhea.

Results

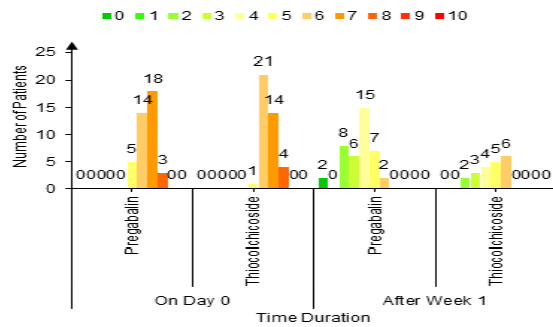
The total number of patients recruited in the study was 80. No patients discontinued the therapy prematurely. The total mean age was 36.25 years. The mean age group for pregabalin was 38.97 years, whereas mean age group for thiocolchicoside was 33.50 years (Figure 1).

Figure (1): Age Distribution



The ratio of males and females included in the study was 1.105:1. Most of the patients included in the study were either housewives (30%) or businessmen (16.25%). One patient had allergy to nimesulide. None of the patient suffered either from addiction or family history of back pain. On day 0, after administration of pregabalin, 18 patients had a visual analogue scale (VAS) score of 7 and after a week, 15 patients score had been decreased to 4. On day 0, after administration of thiocolchicoside, 23 patients had visual analogue scale (VAS) score of 7 and after a week, 18 patients score had been decreased to 3; which showed that thiocolchicoside is more efficacious as compared to pregabalin (Figure 2).

Figure (2): Visual Analogue Score Comparison

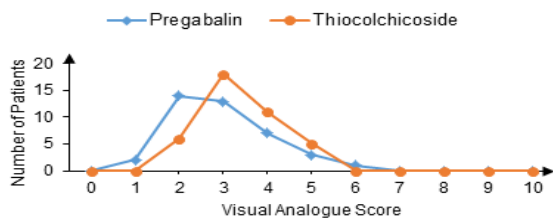


There was a significant difference between pre and post VAS score in both the groups at a p-value of less than 0.0001. But, the difference between the two groups was not statistically significant (p-value = 0.0664).

Sleeping Pattern

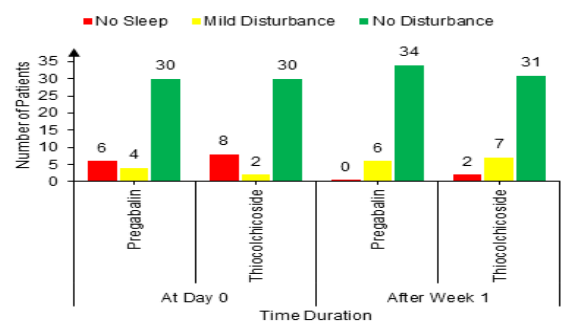
In our study, pregabalin shows onset of action from 2nd day and reaches a peak on the 3rd day, whereas in thiocolchicoside, effect starts from 1st day itself and reaches a peak on the 2nd day. The effect of both the drugs decrease gradually after the 3rd day. Therefore, thiocolchicoside has faster onset of action as compared to pregabalin (Figure 3).

Figure (3): Difference of Visual Analogue Score after Week 1



After one week of treatment with pregabalin, one patient had improvement in their sleeping patterns. Whereas for thiocolchicoside, only four patient had improvement in their pattern of sleep (Figure 4).

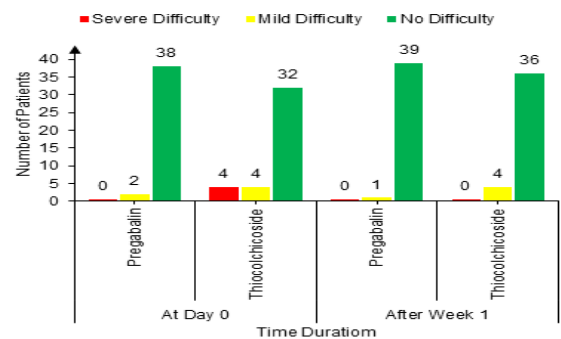
Figure (4): Difference in Sleep Pattern



Sitting Pattern Thiocolchicoside

When the patients came for the first consultation, 38 patients had no problems in sitting for longer duration, whereas 2 patient could not sit for more than 15-20 minutes due to pain. After one week of treatment, only one patient had mild disturbance, whereas the other 39 had no disturbances (Figure 5).

Figure (5): Difference in Sitting Pattern



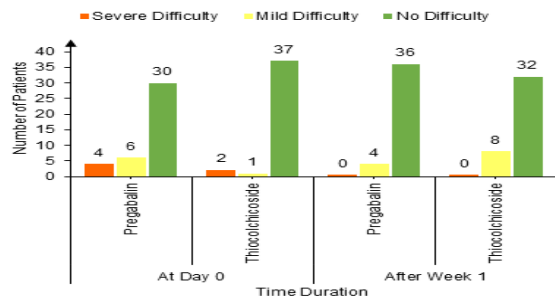
Pregabalin

When the patients came for the first consultation, 32 patients had no problems in sitting for longer duration, whereas 4 patient could not sit for more than 20 minutes and 4 patients not more than 30 minutes due to pain. After one week of treatment, only 4 patients had mild disturbance, whereas the other 36 had no disturbances (Figure 5).

Standing Pattern Thiocolchicoside

When the patients came for the first consultation, 30 patients had no problems in standing for longer duration, whereas 6 patient could not stand for more than 15-30 minutes and four patients for maximum 20 minutes due to pain. After one week of treatment, only 4 patients had mild disturbances, whereas the other 36 had no disturbances (Figure 6).

Figure (6): Difference in Standing Pattern



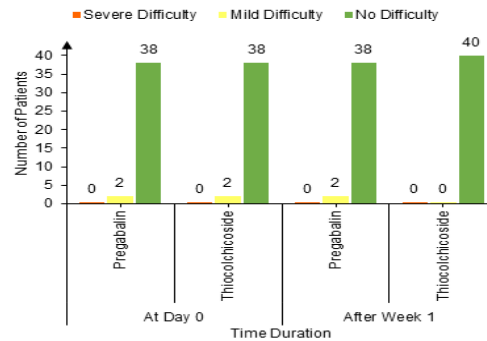
Pregabalin

When the patients came for the first consultation, 37 patients had no problems in standing for longer duration, whereas 2 patients could not stand for longer duration, whereas 1 patient cannot able to stand for more than 5-10 minutes due to pain. After one week of treatment, only 8 patients had mild disturbances, whereas the other 32 had no disturbances (Figure 6).

Walking Pattern Thiocolchicoside

When the patients came for the first consultation, 38 patients had no problems in walking for longer duration, whereas 2 patient could not walk for more than 5-10 minutes due to pain. After one week of treatment, all 40 patients had no disturbances (Figure 7).

Figure (7): Difference in Walking Pattern



Pregabalin

When the patients came for the first consultation, 38 patients had no problems in walking for longer duration, whereas 2 patient could not walk for more than 10 minutes due to pain. After one week of treatment, only 2 patient had mild disturbance, whereas the other 38 had no disturbances (Figure 7).

Comparison of Effects

The patients were given notepads to record the adverse effects. Patients complained sedation as an adverse effect after taking pregabalin. 16 patients out of the total 40 taking pregabalin complained of sedation. 6 patients complained of drowsiness. Patients taking thiocolchicoside did not complain of any adverse effects.

Discussion

Total numbers of patients enrolled from either sex were 80. Out of 42 males enrolled, 18 and 24 males were assigned to pregabalin and thiocolchicoside group respectively. Whereas, out of 38 females enrolled, 22 and 16 females were assigned to pregabalin and thiocolchicoside group respectively. Mean age of patients was 36.25 years and mean body weight was 65.60 kgs. In our study, none of the patients discontinued the therapy prematurely, whereas, in a study done by Freynhagen R et al, 3 and 2 patients respectively, discontinued the treatment prematurely [4].

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On evaluation of efficacy of pregabalin and thiocolchicoside-treated group of patients by visual analogue scale (VAS), it was found that, there was statistically significant difference between pre and post VAS score in both the group with the p-value < 0.0001. But the difference between the two group was not statistically significant (p-value = 0.0664) [5]. In our study, pregabalin shows onset of action from 2nd day and reaches a peak on the 3rd day, whereas in thiocolchicoside, effect starts from 1st day itself and reaches a peak on the 2nd day. The effect of both the drugs decreases gradually after the 3rd day. Thus, thiocolchicoside has faster onset of action as compared to pregabalin [7, 11].

On the contrary, one study reported that there was a decrease in the VAS score, however they did not mention the exact decrease [5]. Moreover, in the study done by Lahoti G et al, there was significant decrease in the VAS score, which is in accordance to our study [6]. It is documented that the efficacy of pregabalin is due to enhancement of GABA release [12]. Another theory states that, it modulates a subset of neuronal voltage sensitive calcium channels [13]. It is postulated that decreased entry of calcium into the presynaptic neuron through these channels could reduce glutamate release, lowering neuronal excitability [3].

On the other hand, action of thiocolchicoside is because of its GABA-mimetic and glycinergic properties [14]. It selectively depresses spinal and supraspinal polysynaptic reflexes involved in the regulation of muscle tone without significantly affecting monosynaptically mediated stretch reflex [15]. Polysynaptic reflexes in the ascending reticular formation are also depressed though to a lesser extent [3].

On assessment of sleep parameter in pregabalin and thiocolchicoside-treated patients during their first consultation, 30 patients had no sleep disturbances. After thiocolchicoside administration 2 patients had mild to moderate sleep disturbances and after pregabalin administration, 4 patients has mild sleep disturbances due to pain [7, 8]. However, after one week of treatment, only 7 patients

had mild sleep disturbances, while, remaining 31 had no sleep disturbances in pregabalin-treated group. Whereas, 6 patients had mild sleep disturbances, while remaining 34 had no sleep disturbances in thiocolchicoside-treated group [9].

In our study, patients taking pregabalin complained of sedation. However, the study showed that sedation helped the patients alleviate the sleep disturbances. Hence, instead of being a side effect, it actually helped the patients. In a study done by Freynhagen R et al, significant and rapid improvements were noted in the sleep interference score (p < 0.00001) [4].

In pain during sitting, standing and walking conditions, patients showed remarkable improvement throughout the study. In spite the small sample size, the greatest merit of our study was that it was a comparative study. Thiocolchicoside, has been proven effective for chronic neuropathic pain [16,17]. The fact that it works for low back pain without radiation for patients presenting in an orthopedic outdoor department possibly shows a correlation between even simple back pain and neurological involvement [9, 10].

Conclusion

We conclude that, pain management is the subject of many initiatives within the disciplines of medicine, ethics and law, we are at an “inflection point” in which unreasonable failure to treat pain is viewed worldwide as poor medicine, unethical practice, and an abrogation of a fundamental human right. Perhaps, the greatest challenge is the education of clinicians on the need to adjust our approach towards the management of pain.

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