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To evaluate the efficacy and safety of Eperisone in patients with acute lower backache associated with muscle spasm.

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Abstract: *Eperisone hydrochloride is a newly introduced muscle relaxant used for treatment of backache associated with muscle contracture, supposed to be better in adverse effect profile.*

Objectives: *To evaluate the efficacy and safety of eperisone in patients of acute lower back pain associated with muscle spasm.*

Methods: *Hundred patients between age of 18 to 55 years having low back pain of ≤ 7 days duration were prescribed eperisone orally twice a day for 7 days. Severity of pain at rest and on movement was recorded using Visual Analogue Scale. Muscle spasm was evaluated by hand-to-floor distance using a simple graduated bar (0 value at floor) and Lasegue's manoeuvre.*

Results: *There was statistically significant reduction in severity of pain and muscle spasm on day 3 and day 7($p < 0.001$). None of patient reported with sedation or any other central nervous side effects. Tolerability and efficacy was evaluated based on the global assessment by the investigator based on a 4-point scale marked a excellent/good/average/poor. As per investigators' assessment about efficacy of trial drug, 70 % of patients reported excellent, 26 % good, 3 % average and 1% poor efficacy. As per investigators' opinion about tolerability, 78% of patients reported excellent, 18 % good, 2% average and 2 % reported poor.*

Conclusion: *Eperisone significantly reduces the intensity of pain and improves the mobility without causing side-effects, preferred option for patients with lower backache pain associated with muscle spasm.*

Keywords: *Eperisone, Low backache (LBP), non-steroidal inflammatory drugs (NSAIDs), Visual Analogue Scale (VAS)*

I. Introduction

Low back pain (LBP), a very commonly observed complaint among middle aged population, affecting 90% of all adults at least once in lifetime and is usually associated with 'muscle spasm'.[1] Higher incidence of low back pain is reported in Indian population in younger patients due to sedentary lifestyle, occupational exposure and lack of exercise. It is a major health and socioeconomic problem[2] and is associated with high costs of healthcare, work absenteeism and disablement.[3] Generally, low back pain is managed with short term use of non-steroidal anti inflammatory drugs (NSAIDs) and centrally acting skeletal muscle relaxants[4] However, it is difficult to find which medication is offering a clear overall net advantage between benefits and harms. Therefore, it is important to understand the mechanism underlying the pain for physician who treats patients with acute low back pain.

The rationale for use of centrally acting muscle relaxants in back pain is supported by evidence of a spinal muscle spasm in these patients.[5] In fact, nociception usually results from a secondary inflammation and muscle spasm after acute injury of different structures of the spine, such as muscle, tendon, ligament, disc or bone.[6]

Eperisone hydrochloride is widely used for treatment of muscle stiffness and pain. It is marketed in India and other countries under the brand name myonal. It acts by reducing alpha & gamma afferent activities and inhibits spinal cord activities by acting on the spinal cord and supraspinal structures along with muscle relaxant activity by acting on skeletal muscles. It has reported that it increases blood flow and causes vasodilatation by also acting on vascular smooth muscles. Also it differs from other muscle relaxants by not showing sedative property. [7] .The present study was undertaken to evaluate the efficacy and safety of this recently introduced drug available in the market and prescribed by orthopedicians, i.e., eperisone in patients with acute lower backache associated with muscle spasm.

II. Material And Methods

Study Design: This prospective, open, non-comparative, non-randomized drug study was undertaken in outpatient department of orthopaedics, in one of north Indian government medical institute. The study protocol was approved by institutional ethical committee. Patients attending the outpatient department were screened and assessed according to the specified inclusion and exclusion criteria. A total of 60 eligible patients of both sexes having acute low back pain, of moderate to severe intensity with muscle spasm, willing to take medications as directed and come for the follow-up were enrolled in the study. The written consent of patients was taken on informed consent form in the local language.

Inclusion criteria: Patients of either sex in the age range of 18 to 55 years with a history of low back pain and muscle spasm of ≤ 7 days were included in the study.

Exclusion criteria: Patients with back pain due to malignancy, infection, abnormal metabolism, osteoarthritis of hip or any other disease, back pain referred from other organs, patients with a history of presence of peptic ulceration or gastrointestinal tract bleeding or severe dyspepsia, patients allergic to Non steroidal anti inflammatory drugs (NSAIDS) and skeletal muscle relaxants or suffering from asthma or other allergic disorders, patients treated with Non steroidal anti inflammatory drugs (NSAIDS) or skeletal muscle relaxants for 3 days prior to study, patients with severe concurrent systemic disease including bleedings diathesis, patients on anticoagulation therapy, patients suffering from hepatic or renal impairment and pregnant or lactating women were excluded from the study.
Treatment Procedure: Demographic data and relevant medical history was obtained from all patients prior to initiation of therapy. Patients received eperisone (100mg) thrice a day orally for 7 days. Commercial available preparations were used. Patients were evaluated on day 3, and day 7 for severity of pain and muscle spasm. At each visit patients were asked to report if any adverse effect present.

Criteria for evaluation:
Primary efficacy measures:
Pain assessment scale: Assessment of intensity of pain at rest and pain on movement was carried out on day 0 (visit 1, baseline), day 3 (visit 2) and day 7 (visit 3) by means of a 10 cm visual analogue scale (VAS)[8] as reported by a patient between 0 (no pain) to 10 (unbearable pain). The patients were asked to score by ticking off the scale between 0 (no pain) and 10 (unbearable pain).

Muscle spasm assessment –
Finger-to floor distance (FFD): It was measured by flexion at hip joint in standing position. The patients were told to bend down as far as possible without bending the knees and try to touch the floor with their fingers. The remaining distance between the floor and fingertips was measured by ruler in centimetres.[7]

Lasegue's manoeuvre: In this test, articular excursion of the hip in degrees on performing lasegue's manoeuvre before inducing pain in supine position which involved gradually raising of lower extremity by flexing the hip with the knee in extension passively. The angle between the raised limb and tabletop was measured. [7]

Secondary efficacy measure: .Global efficacy evaluation was evaluated based on the global assessment based on a 4-point scale marked as excellent/good/ average/poor.

Safety measures: Side effects like tiredness, drowsiness, dizziness, and alertness were noted based on history, observations of adverse reactions. Also global assessment of tolerability to therapy was assessed on a four-point scale of excellent/ good/ average / poor.

Statistical Analysis: Comparison was done both inter and intra group between baseline, day 3 and day 7 values and expressed in mean ± standard deviation. Then the data was pooled and analyzed by unpaired t-test and one-way ANOVA using SPSS 16 software.

III. Observations And Results

Efficacy assessment:

A total of 60 patients were enrolled in the study. During the study period, 5 patients did not come for follow-up, so data of these 6 patients were not included in the statistical analysis. The effects of the eperisone and placebo on pain on rest were shown in figure 1 and pain on movement was shown in figure 2. Severity of pain on rest was reduced from 100% to 62.5% on day 3 ($p< 0.001$) and 6.9% on 7th day ($p< 0.001$) (figure 1). There was statistically significant decline in the pain intensity on day 3 and at the end of the treatment (Day 7). Similar results were obtained in the evaluation of pain on movement i.e. severity of pain on movement was reduced from 100% to 71.7% on day 3 and 15.2% on 7th day (figure 2). There was statistically significant decline in the pain intensity on movement on day 3 ($p< 0.001$) and at the end of the treatment i.e. on day 7($p< 0.001$). The hand to floor distance decreased from 46.3± 2.32 cm on day 1 to 25.8 ± 1.64 cm on day 3 (- 44.2%)($p<0.0001$) and 15.2 ± 0.54 cm (- 67.2%)($p<0.0001$) on day 7 (figure 3). There was a decrease in muscle spasm on day 3 and on day 7. The articular excursion performed before inducing pain, was on average 70.7° at baseline and increased to 78.5° on day 7 ($p < 0.01$vs basal) (figure 4).

Safety assessment: None of patient reported with sedation, drowsiness or dizziness and only 3 patients out 55 (5.4%) manifested gastrointestinal side effects during the study. No serious adverse events were reported which led to withdrawal of patient from the study.

Global efficacy and tolerability evaluation: As per investigators' assessment about efficacy, 70 % of patients reported excellent, 26% good, 3 % average and 1 % reported poor efficacy. As per investigators' opinion about tolerability, 78% of patients reported excellent, 18 % good, 2% average and 2 % reported poor tolerability.

IV. Discussion

Skeletal muscle relaxants are effective in acute low back pain for short-term pain relief. These drugs provide relief from acute muscle spasm by blocking the spasm-pain-spasm cycle associated with low back pain. Unfortunately, most of central muscle relaxants are associated with central nervous system and gastrointestinal upset as major side-effect. Our study reported that eperisone is an effective muscle relaxant agent with good efficacy which are currently used in the management of low back pain due to a contraction of spinal muscles with better adverse effect profile .

Eperisone is a new muscle relaxant compound with slightly different pattern of activities. Actions of eperisone on several organs have been characterized by an inhibition of mono- and multisynaptic reflexes in relation to the inhibitory action on α- and γ – efferent neurons in the spinal cord and supra-spinal structures.[9] Eperisone suppresses the static and dynamic activities of muscle spindle in man, as a consequence of modifications of descending influences from central structures on the static and dynamic gamma motor neurons that innervate the muscle spindle. [10] Eperisone increases

the local blood flow by its effect on elevation of the electrical threshold required for generation of the action potential and a Ca2+ antagonistic activity in the smooth muscle cells of the basilar artery. [11] Eperisone may block the post junctional α1- and α2-adrenergic, muscarinic, serotonergic receptors and pre junctional α2 adrenoceptors, and reduce the prostacyclin synthesis via a mechanism other the cyclooxygenase inhibition.[12] Since the deep tissue pain can be related to reduced muscle blood flow, which comprises the metabolic demand under muscle work,[13] it has been suggested that one factor leading to low back pain in some cases might be various degrees of ischemia of the extensor muscles in the lumbar spine[14] In these conditions, because of its effects on local blood flow, eperisone supposed to be a valuable and better alternative to other muscle relaxant agents in the treatment of low back pain.[15] Sakai et al in 2008 have reported the improvement in intramuscular oxygenation and increased paraspinal muscle blood flow after oral administration of the eperisone hydrochloride during lumbar extension and flexion in patients with chronic Lower back pain during four weeks of therapy.[16] Chandanwale et al in 2011 concluded that Eperisone hydrochloride was effective and well tolerated option for the treatment of patients with acute musculoskeletal spasm with LBP with an added advantage of intrinsic analgesic activity[17]

In the present he efficacy and safety of eperisone was evaluated in patients with acute lower backache associated with muscle spasm. Severity of pain at rest was assessed using Visual analogue scale between two groups. The scores decreased significantly as compared to baseline score on day 3 and day 7 within the two groups of patients. However the decrease in severity of pain at rest was more pronounced within group A as compared to group B patients, This result is in accordance with the result reported by previous studies.

Present study confirms efficacy of eperisone patients with acute lower backache associated with muscle spasm. The study reported a statistically significant improvement in hand-to floor distance on the 3rd ($p<0.0001$) and 7th day ($p<0.0001$) as compared to baseline in treatment group.

V. Conculsion

The incidence of acute backache is increasing in the present scenario due to modernisation, lack of exercise and postural problems. Although currently used central muscle relaxants provide relief from back pain associated spasm have central nervous system side-effects like sedation, tiredness, weakness etc. Today, patients look for speedy recovery and returning back to daily activities without any compromise on quality of life.

In this randomised study, eperisone in patients with acute lower backache associated muscle spasm was found to be effective and without any sedation. Additionally eperisone showed effective pain control with no effect on psychomotor parameters. This favourable therapeutic profile in terms efficacy, better quality of life and speedy recovery makes eperisone as a preferred option for clinicians in treatment of painful muscle spasm. In conclusion, eperisone for the treatment of LBP significantly reduces the intensity of pain and improves the mobility without causing side-effects.

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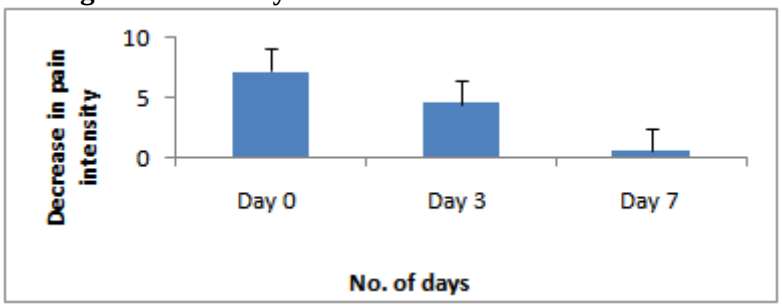
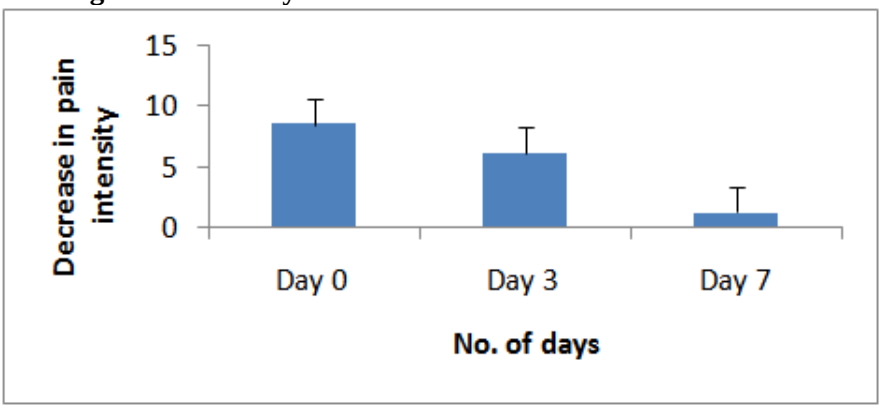
Figure 1- Intensity Of Pain Relief On Rest As Per Vas



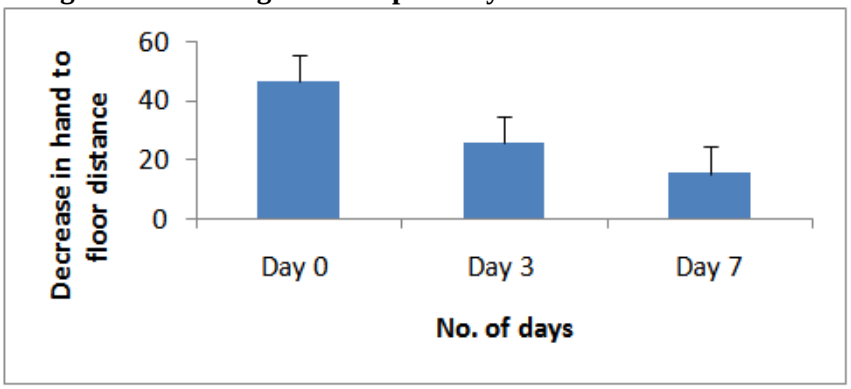
Effects of a 7 day treatment with eperisone (100mg) thrice daily on pain at rest in patients with acute low back pain; pain was evaluated by means of 10-cm VAS. Statistically significant (p< 0.001) difference was observed on day 3 and on day 7.

Figure 2- Intensity Of Pain Relief On Movement As Per Vas



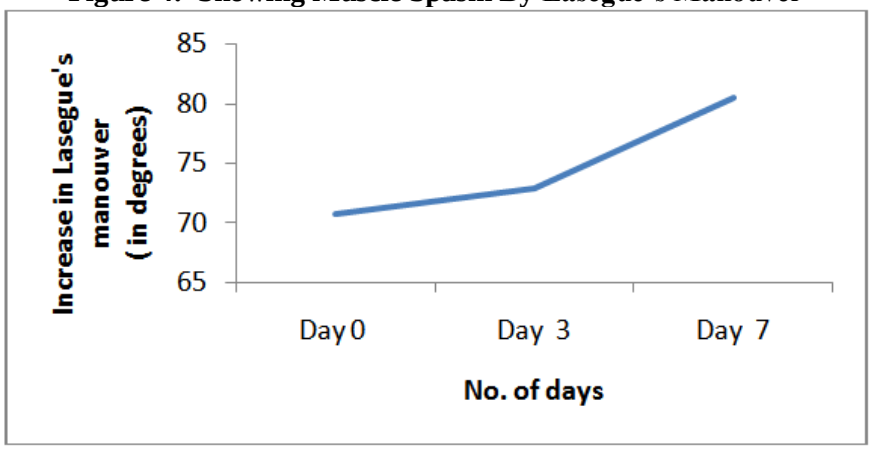
Effects of a 7 day treatment with eperisone (100mg) thrice daily on pain at movement in patients with acute low back pain; pain was evaluated by means of 10-cm VAS. Statistically significant (p< 0.001) difference was observed on day 3 and on day 7.

Figure 3 - Showing Muscle Spasm By Hand-To-Floor Distance



Effects of a 7 day treatment with eperisone (100mg) thrice daily on the "hand-to floor" distance (cm); Statistically significant (p< 0.05) difference was observed on day 3 and on day 7.

Figure 4: Showing Muscle Spasm By Lasegue's Manouver



Effects of a 7 day treatment with eperisone (100mg) thrice daily on the Lasegue' manoeuvre (expressed as degrees); Statistically significant (p< 0.05) difference was observed on day 3 and on day 7.