To compare the efficacy and safety of eperisone with thiocolchicoside in patients with acute lower backache associated with muscle spasm

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Abstract

Background & Objectives: Eperisone hydrochloride is a new drug came in market with centrally acting muscle relaxant, having additional vasodilator effect and used for treatment of backache associated with muscle stiffness like thiocolchicoside but supposed to be slightly better in efficacy and adverse effect profile. The aim of this study was to compare the efficacy and safety of eperisone with thiocolchicoside in patients with acute lower backache associated with muscle spasm.

Methods: 100 eligible subjects were taken and assessment of severity of pain and muscle spasm was done by using Visual Analogue Scale, finger-to-floor distance (FFD), Lasegue's maneuver and modified Schober's test.

Results: No statistically significant difference in pain relief and muscle spasm among both the treatment groups but clinically pain relief is slightly better in eperisone group. The adverse drug reactions occurring during study showed a slightly better safety profile in patients on eperisone than on thiocolchicoside.

Conclusion: These findings confirm that eperisone represents a valuable and safer alternative to thiocolchicoside for treatment of low back pain associated with muscle spasm.

Keywords: Eperisone, Low backache (LBP), Muscle relaxants, Visual Analogue Scale (VAS), Thiocolchicoside

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Introduction

The use of centrally acting muscle relaxants for low backache continues to be source of controversy among orthopaedicians because of their side effects. Generally, short term use of non-steroidal inflammatory drugs (NSAIDs) and centrally acting skeletal muscle relaxants are used in the management of Low back pain[1]. Both groups are beneficial in acute stage but these drugs have their own adverse effect profile. NSAIDs are unfit for gastrointestinal tract i.e. showing gastric upset and centrally acting muscle relaxants have central nervous system side effects like drowsiness, which show non-compliance from patient side. It is also not very justified which group of medications is offering overall net advantage between benefits and harms. Therefore, it is need for the day that orthopaedician should clearly know the mechanism behind backache for orthopaedician who treats patients with acute low back pain.

The use of centrally acting muscle relaxants is justified as it is reported that there is a spasm of spinal muscles occur in back pain[2]. It is clear that nociception usually occurs after a secondary inflammation and muscle spasm after acute injury of spine structures such as muscle, tendon, ligament, disc or bone[3].

Eperisone hydrochloride is a recently introduced centrally acting muscle relaxant, beta-amino propiophenone derivative. It reduces muscle ischemia and pain by acting on skeletal muscles as well as on vascular smooth muscles[4]. Eperisone causes vasodilatation and facilitates blood flow by acting on vascular smooth muscles[5]. It reduces alpha & gamma afferent activities and inhibits spinal cord activities as it shows its action on the spinal cord and supraspinal structures. Muscle relaxant activity occurs as eperisone acts on skeletal muscles. It is unique from other muscle relaxants as sedation is not observed with this drug[6]. Eperisone hydrochloride is widely prescribed now days for treatment of muscle stiffness and pain.

Thiocolchicoside is a synthetic derivative of colchicines, derived from flower seeds of superba gloriosa[7]. It has affinity for the GABA-A and glycine receptors which are inhibitory in nature therefore muscle relaxant action is reported. Analgesic activity is also reported because of its GABA-mediated action. Thiocolchicoside proved its clinical efficacy and tolerability in many recent clinical trials[7-11].

Both drugs are newer in market hence the present study was undertaken to compare the efficacy and safety of these two drugs prescribed by orthopedicians, i.e., thiocolchicoside versus eperisone in patients with acute lower backache associated muscle spasm in Indian population.

Material and Methods

Study Design: This prospective, open labelled, randomized, comparative drug study was undertaken in outpatient department of orthopaedics, in Bhagat Phool Singh Govt. Medical College, Khanpurkalan, Haryana, India. The study protocol was approved by the Indian council of medical research (ICMR) and institutional ethical committee.

Selection criteria: Patients coming with low backache to Orthopaedics outpatient department at BPS Govt medical college for women, Khanpuralan were selected after screening according to the well-defined inclusion and exclusion criteria. Total 100 patients of either sex having acute low backache of moderate to severe intensity between 18 to 45 years of age were enrolled for study after taking written informed consent.

Patients having chronic spine diseases such as osteoporosis, severe arthritis, spondylitis, muscular diseases such as myositis, myotonia, poliomyositis fracture, cancer and muscular dystrophy and other diseases affecting the neurological or cardiovascular systems, liver and kidneys were not included in the study. Patients who had taken muscle relaxants by any route in previous 7 days and those with hypersensitivity to muscle relaxants were not recruited in the study. Pregnant and lactating women were also excluded from the study.

Treatment Procedure: Eligible patients were randomly divided into 2 groups: Group A and group B, 50 each. Group A was receive deperisone (100mg) thrice a day and Group B received thiocolchiocoside (8 mg) twice daily orally for 7 days. Patients were evaluated on1st day, day 3, and day 7 for severity of pain and muscle spasm. Patients were asked about adverse effect if present at each treatment visit. Diclofenac sodium was give as concomitant medicine for pain relief in patients who did not get relief.

Efficacy assessment

Assessment of pain: Intensity of pain at rest and pain on movement was assessed with visual analogue scale (VAS) i.e. 0-10 cm scale, on day 0 (visit 1, baseline), day 3 (visit 2) and day 7 (visit 3). The patients were asked to mark between 0 (no pain) and 10 (unbearable pain) on the given scale[12].

Assessment of Muscle spasm

Finger-to floor distance (FFD): Finger-to floor distance is assessedby flexing the hip joint in standing. The patients were asked to bend forward and try to touch the floor with their fingers without bending the knees. The remaining distance between the fingertips and floor was measured in centimetres with the help of ruler[13].

Lasegue's manoeuvre: In this test, the angle between the raised limb and table top was measured. Lasegue's manoeuvre was performed in a supine position while gradually raising the leg by flexing the hip with the knee in extension passively. The degree of articular excursion before and at the end of treatment was measured[13].

Safety measures: Patients were monitored for adverse events based on the history like asking about tiredness, drowsiness, dizziness etc. and observations of adverse reactions on every visit.

Statistical Analysis: Both inter and intra group comparison was done between baseline, day 3 and day 7. The results were expressed in form of mean±standard deviation. After that the data was analyzed by unpaired t-test and one-way ANOVA using Statistical software's SPSS 16 version. P- Value < 0.05 was considered to be significant statistically.

Results

Two patients from both groups did not come for follow during the study period, so data of 96 patients were applied for the statistical analysis. The effects of the drugs on pain on rest were shown in Fig. 1 and pain on movement was shown in Table 1. In group A, pain intensity at rest was decreased from 100% to 62.5% on day 3 and 34.7% on 7th day whereas in Group B it was decreased from 100% to 73.9% on day 3 and 40.5% on day 7 (Fig. 1). Pain intensity at rest was statistically significant declined on day 3 and on day7 of the treatment i.e. At the end of treatment in both groups i.e. A and B while using one- way ANOVA (P< 0.001 in both groups).

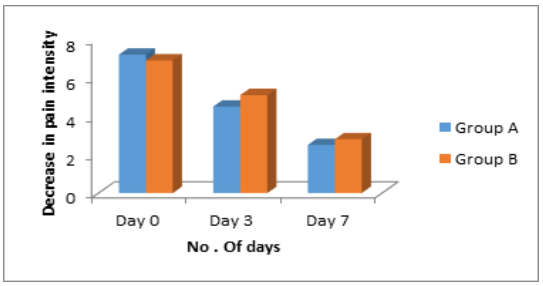

Fig. 1. Effects of 7-days treatment with eperisone 100 mg t.i.d. or thiocolchicoside 8 mg b.i.d. on the spontaneous pain in patients with acute low back pain using VAS scale. No statistically significant difference was observed between the two groups of patients at any time

Table 1: Intensity of Pain Relief on movement as per VAS

Pain intensity	Baseline	Day 3	P value	Day 7	P value
Group A	8.9(100%)	6.7 (75.3%)	0.001	2.1(23.6%)	0.001
Group B	8.6(100%)	6.5(75.6%)	0.001	2.6(30.2%)	0.001

Table 1: Effects of 7-days treatment with eperisone 100 mg t.i.d. or thiocolchicoside 8 mg b.i.d. on pain at movement in patients with acute low back pain using VAS scale. No statistically significant difference was observed between the two groups of patients at any time.

There was slightly more clinically improvement during pain on rest was observed in group A as compared to group B while using independent student t – test (p>0.05). Similar results were seen when pain on movement was assessed i.e. in group A, intensity of pain on movement was decreased from 100% to 75.3% on day 3 and 23.6% on 7th day whereas in Group B it was decreased from 100% to 75.6% on day 3 and 23.2% on day 7 (Table 1). Pain intensity on movement was statistically significant declined on day 3 and on day7 of the treatment i.e. at the end of treatment in both groups i.e. A and B while using one- way ANOVA (P<0.001 in both groups). There was slightly more clinically improvement but no statistically significant difference was observed during pain on movement in group A as compared to group B while using independent student t – test (p >0.05).

The distance decreased from 38.3cm to 27.8 cm on day 3 (-27.4%) and 15.2 cm (-60.3%) on day7 in group A and from 36.7 cm to 28.5 cm (-22.3%) on day 3 and 17.9 cm (-51.2%) on day 7 in group B (Fig. 2).

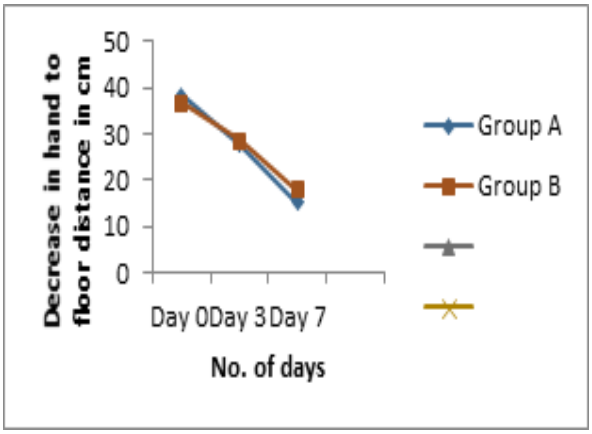

Fig. 2: Effects of a 12-day treatment with eperisone 100 mg t.i.d. or thiocolchicoside 8 mg b.i.d. on the "hand-to floor" distance (cm); no statistically significant difference was observed between the two groups of patients at any time

There is statistically significant reduction in muscle spasm was noted in both the groups using one- way ANOVA (P< 0.001). Although the results achieved in group A were slightly better than those in group B, no statistically significant difference was observed between the two groups at any time using independent student t – test (p>0.05).

The articular excursion performed before inducing pain, was on average 72.7° at baseline and increased to 80.5° on day 7 (p < 0.01vs basal) in group A, while in the group B patients the excursion increased from 74.5° at baseline to 82.9° at the end of the treatment (p < 0.01 vs. basal) (Fig. 3).

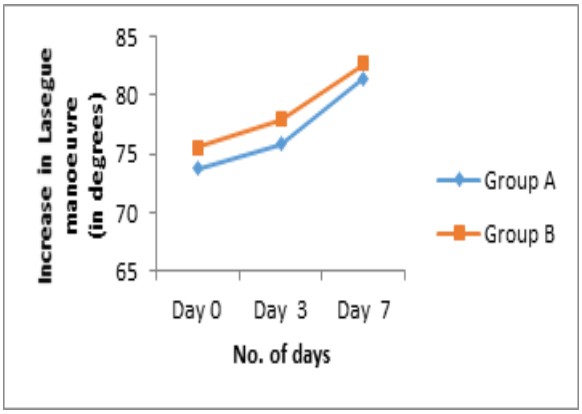

Fig. 3: Effects of 7days treatment with eperisone 100 mg t.i.d. or thiocolchicoside 8 mg b.i.d. on the Lasegue' manoeuvre (expressed as degrees); no statistically significant difference was observed between the two groups of patients at any time

The adverse drug reactions occurring during study showed a statistically significant better safety profile in Group A than group B. Only 4 patients out 48 (8.3%) manifested gastrointestinal side effects during the study treated in group A, while in group B, 10 out of 48 (21%) patients reported with gastrointestinal side effects. None of patients reported with sedation in group A while 1out of 48 (2%) patients reported with sedation in group B.

As per investigators' assessment about efficacy, 68% of patients reported excellent, 25% good, 7% average and 1% reported poor efficacy in group A. 65% of patients reported excellent, 28% good, 4% average and 3% reported poor efficacy in group B.

As per investigators' opinion about tolerability, 67% of patients reported excellent, 28% good, 4% average and1% reported poor in group A. In group B, 60% of patients reported excellent, 35% good, 3% average and 2% reported poor.

Discussion

Centrally acting 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[14,15]. Unfortunately, most of central muscle relaxants are associated with CNS and gastrointestinal upset as major side-effects[16]. Our study showed that eperisone is an effective muscle relaxant both in efficacy and tolerability slightly better as compared to thiocolchicosidewhich are currently used in the management of acute Low back pain.

Many randomized trials reported the efficacy of thiocolchicoside a spinal gabamimetic dug in the treatment of acute low-back pain[5,8,10,13]. Within a week of treatment, pain at rest was improved with thiocolchicoside as seen with VAS score. There was also significant improvement in spinal muscle spasm as demonstrated by hand-to-floor distance.

Eperisone is having a pattern of activities slightly different from that of thiocolchicoside. Tanka et al reported that eperisone causes 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[17]. Eperisone enhances the local blood flow by its effect calcium blocking property in basilar artery[18].

Inoue S et al reported that eperisone inhibit angiotensin II-induced relaxations that is supposed to be mediated by endogenous prostacyclin. 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[19]. In healthy volunteers, a single dose of 300 mg of eperisone has shown a sympatho-suppressive action in resting skeletal muscles, without any effect on the microneurographically recorded muscle sympathetic nerve activity in actively contracting muscles[4]. Since the deep tissue pain can be related to reduce muscle blood flow, which comprises the metabolic demand under muscle work[20]. 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[2]. 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. Sakai et al demonstrated enhanced paraspinal muscle blood flow after eperisone taken orally in chronic lower backache patients during treatment[21].

None of patient reported with sedation, drowsiness or dizziness in both the groups. In eperisone group, there were mild gastrointestinal side effects in the form of nausea (5%) abdominal pain (3%) and gastirits(2%) while in thiocolchicoside group, nausea in 7% and 4% reported with gastiritis. Cabitza et al reported the adverse effects seen with eperisone were restricted to the gastrointestinal tract, their severity was moderate and the total incidence of side effects was lower than 5% of the treated patients[5].

Conclusion

According to the results of this prospective randomized study, we conclude that eperisone and thiocolchicoside both are effective in acute Low back pain with spasm. Eperisone is an effective centrally acting skeletal muscle relaxant agent with slightly better efficacy and safety than thiocolchicoside, so may be alternative option for treatment of patients with Low back pain associated with muscle spasm.

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