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Research Paper

A SUPERIOR DRUG IN TREATING SPORTS INJURY: A COMPARATIVE STUDY OF FLUPIRITINE WITH COMBINATION OF ACECLOFENAC AND TIZANIDINE IN MUSCULOSKELETAL PAIN

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Wrist, ankle and knee sprains are most commonly encountered problems in sports. In these cases pain relief and functional restoration at the earliest are the management goals. One of the most preferred drug treatment for pain control by Orthopedician in our area is a combination of Aceclofenac and Tizanidine despite their intolerable ADR profile. Flupiritine is a relatively newer class of drug having excellent analgesic and musculoskeletal relaxant property and with an excellent safety profile. This prospective, randomized, open label, active control trial was conducted with 200 participants having sprain who were prescribed either a combination of Aceclofenac 100 mg and Tizanidine 2 mg twice daily or Flupiritine 100 mg twice daily orally. Follow up was done on day 2, 4 and 7 with numeric rating scale, verbal descriptor scale and faces pain scale. Participant receiving Flupiritine experienced better pain relief and less disability (36%) than that of those receiving a combination of Aceclofenac and Tizanidine (11%) on day 2. After a week therapy 88% of participants reported complete pain relief with Flupiritine compared to only 51% with a combination of Aceclofenac and Tizanidine (p value < 0.001). ADR was much less in Flupiritine group (1%) compared to combination of Aceclofenac and Tizanidine (7%).

Keywords: Sprain, Flupiritine, Analgesic, Muscle relaxant

INTRODUCTION

A sprain is when ligamentous attachment of bones with muscle is disrupted around the joint. Commonly affected areas for sprains are ankle, knee and wrist caused by twist, fall or overstretching of involved tissue. These are usually graded on scale of I to III (American Medical Association Ligament Injury Classification).

Grade I: There is stretching of ligaments or mild tear with no or little instability of the joint.

Grade II: There is incomplete tear.

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Grade III: Ligament is completely torned or ruptured which feels almost like broken bone.

The sign of sprain includes bruising, swelling, tenderness, instability and immobility (*functio laesa* of Galen). The first step in management of these cases is four steps RICE therapy- Rest, Ice pack, compression and elevation (Harvey, 1997). Immobilization (with slings or splints), electrostimulation, cryotherapy, thermotherapy, ultrasound (high frequency sound wave) and massage for affected part are also tried. However for relief of pain and muscular soreness NSAIDs with muscle relaxant is usually offered (Mc Griff, 2003; Stanley and Weaver, 1998).

Orthopaedician in our tertiary care hospital usually prescribe an analgesic with muscle relaxant in these conditions. The most preferred is a combination of Aceclofenac and Tizanidine.

Aceclofenac is a phenyl acetate glycolic acid ester exactly similar to its predecessor, Diclofenac, an excellent analgesic and anti-inflammatory drug, having increased selectivity for COX-2 and thus considered GI friendly (Hinz *et al.,* 2003). Tizanidine is a clonidine congener, a centrally acting α_2 adrenergic agonist used in treatment of various muscular spasms (Wagstaff and Bryson, 1997). Aceclofenac lacks muscular relaxant properties, Tizanidine lacks analgesic power, so a combination of these two is usually prescribed for synergistic action at a dose of 100 mg and 2 mg twice daily.

Flupiritine is a centrally acting non-opioid analgesic having antinocipeptive and muscle relaxant properties comparable to opioids but having none of its ADR. It is usually prescribed in dose of 100 mg twice daily to alleviate various painful conditions (Klawe and Maschke, 2009).

Present study was to compare the efficacy and ADR profile of Flupiritine vs. a combination of Aceclofenac and Tizanidine in musculoskeletal pain of sprain.

MATERIALS AND METHODS

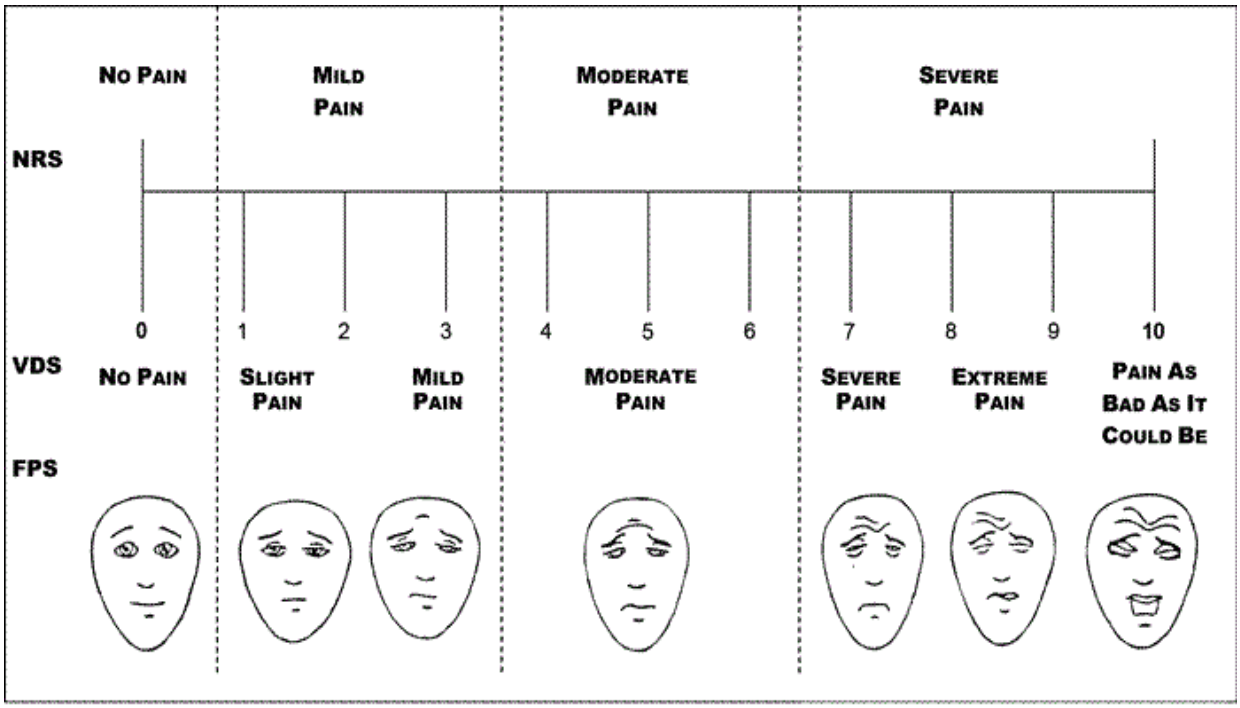
The orthopedic department of the tertiary care hospital where this study was performed from January 20, 2013 to March 13, 2014, treats more than 100 participants in its OPD every day, at least 5 of them are related to sports related injury. The university to which this medical hospital belongs has a vast campus and even vaster number of students who apart from pursuing various courses of study, also indulge in many sports activity resulting invariably to one or another sports related injury (Fong *et al.,* 2009).

With due permission of Institutional ethical committee and informed consent of participants this study was performed on students of both sexes between the age group of 18 to 35 years requiring analgesic and muscle relaxants following sports injury.

Exclusion criteria were any concomitant disease or regular use of any drug. After a thorough clinical examination, 200 such participants (100 in each group) were randomly assigned to take either Flupiritine 100 mg BID (Hummel *et al.,* 1991) (F group) or a combination of Aceclofenac (100 mg BID) and Tizanidine (2 mg BID) (C group) for this prospective, randomized, open label and active control trial. Prior to administration of these medications their blood sample was collected for CBC and liver function test.

Participants were asked for symptoms and were helped to grade the severity using the NRS

Figure 1: Numeric Rating Scale (NRS) Verbal Descriptor Scale (VDS) and Faces Pain Scale (FPS



(numeric rating scale), VDS (Verbal Descriptor Scale) and FPS (Faces Pain Scale) below (Figure 1).

They were asked to report on day 2 and 4 for review and reassessment and finally on day 7 when blood sample was again taken out.

STATISTICAL ANALYSIS

The data thus obtained was evaluated by using the statistical Package for Social Science (IBM SPSS v. 20). A Wilcoxon Signed and sum ranks test was used to analyze the percentage change in and between groups.

RESULTS

100 participants having almost similar baseline pain intensity (p value >0.67) were randomly assigned to either Group F or Group C. 94 participants in F group and 87 in group C completed the study. On day 2, 36 participants had appreciable pain relief in F group compared to only 11 in group C. On day 4, 73 participants had appreciable pain relief in group F. In group C this number was 48. Three participants in group C complain of dyspepsia and abdominal discomfort. (They were given PPI and were dropped from the study). One more participant in this group complained of giddiness and vertigo. (This participant too was dropped from the study). None in group F complained of any associated problem.

On day 7, 88 participants in group F were pain free and were able to perform normal activities. Rest had appreciable pain relief (Table I). One of the participant in this group complained of giddiness, nausea and undue fatigue. 51 participants in group C were pain free and had negligible disability rest had some improvement (Table 1). Two more participants in this group

Table 1: Change in Pain Severity During Treatment in Flupiritine and Combination Groups

Change in pain severity ↓	Flupiritine (n=94)				Combination (n=87)			
	At baseline	After1 week	Z value	p-value	At baseline	After1 week	Z value	p-value
Intensity	8.48±1.13	0.09±0.35	-8.49	<0.001	8.55±1.09	1.38±1.9	-8.15	<0.001

Table 2: ADR Profile During Treatment in Flupiritine and Combination Groups

	Flupiritine	Combination
Participants reporting adverse events (%)	1	7
No. of adverse events reported	1	7
Severity of adverse events		
Mild	1	7
Moderate	-	-
Severe	-	-
Relationship to study medication		
Unlikely	-	-
Possible	Yes	Yes

complained of GI related problem and one participant complained of postural giddiness which was due to hypotension (Table 2). In both groups there was no appreciable change in CBC and LFT after one week of therapy.

After a week therapy, Pain relief was significant in both groups. However Flupiritine was much more effective than combination of Aceclofenac and Tizanidine (p value < 0.001)

DISCUSSION

A sprain may be a very trivial problem for healthcare providers but the pain and disability associated with them is a cause of great concern for the sufferer. Consider the plight of a daily wage earner who because of this 'simple malady' can't earn his daily bread. To alleviate this problem at the earliest and without any untoward ADR should be the clinician's goal.

Flupiritine is a unique new class of drug which is denoted as Selective Neuronal Potassium Channel Opener (SNEPCO) (Kornheuber *et al.,* 1999) and this class of drug is associated with a variety of potential therapeutic benefit in the treatment of pain and muscle spasms. It's muscle relaxant potency is considered at par or even better than chlormezanone (Worz *et al.,* 1996). Since any disruption around the joint may produce nerve injury, Flupiritine's a neuroprotective property is of immense benefit as it limits neuronal excitability (Sattler *et al.,* 2008).

In comparison Aceclofenac is a NSAID, exerts its action through inhibition of COX enzyme (both

1 and 2, although more specifically COX-2) thus may predispose to GI problems. In our study 5 participants had GI problems. It is also known to produce anaphylactic reaction (Rojas *et al.,* 2006).

Tizanidine is a clonidine congener, an α_2 adrenergic agonist (clonidine is primarily used for hypertension), helpful in muscle spasm but can produce postural hypotension. Two participants encountered this problem in our study. More ever Tizanidine's therapeutic range is narrow and is known to produce deleterious effects if used with P450 isoenzyme inhibitors like Ciprofloxacin and oral contraceptive pills (Granfors *et al.*, 2004).

CONCLUSION

Prescribing NSAID with or without muscle relaxant is a knee jerk response of physicians whenever they encounter any patient with musculoskeletal pain. They now better take a pause and think of Flupiritine, which has proved its worth in this study.

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