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Original Article

Phonophoresis with Acelofenac has Significant Effect in the Reliving Pain in Upper Trapezius Tender Point

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Abstract

Purpose: The aim of this study was to find the immediate effect **acelofenac** gel on pain threshold and range of motion which follows a single treatment of tender points in the upper trapezius muscle. **Methods:** 30 subjects presenting with upper trapezius muscles spasm, aged 20-30 years old, participated in this study. Subjects underwent a screening process to establish the presence of tender points in upper trapezius muscle. Subjects were divided randomly into 2 groups.

Group A = Acelofenac gel and ultrasonic gel as coupling medium

Group B = ultrasonic gel as coupling medium

Visual Analogue Scale and Range of Motion is assessed pre treatment and immediately post treatment.

Result: The p value of VAS (post treatment) and ROM (post treatment) in Group A 0.000. **Conclusion:** ultrasound with acelofenac gel was better for immediate pain relive as compared to aqua sonic gel only

Keywords: Tender point; Phonophoresis; Ultrasound; Acelofenac gel.

Introduction

Neck pain/back pain is common and can limit individual's ability to participate in normal daily activities. Neck/back pain frequently becomes chronic.[1] Leading to difficulty in performing adls else can lead to repeated stress injuries Topical NSAIDs can provide good levels of pain relief; topical Aceclofenac solution is equivalent to that of oral NSAIDs.[1]

Topical NSAIDs can provide good levels of pain relief, without the systemic adverse events associated with oral NSAIDs, when used to treat acute musculoskeletal conditions.[2]

Study done by Pattanittum P *et al* in 2013 reveals that there remains limited evidence from which to draw firm conclusions about the benefits or harms of topical or oral NSAIDs in treating lateral elbow pain. Although data from five placebo-controlled trials suggest that topical NSAIDs may be beneficial in improving pain (for up to 4 weeks), non-normal distribution of data and other methodological issues precluded firm conclusions. Some people may expect a mild transient skin rash. Evidence about the benefits of oral NSAIDs has been conflicting, although oral NSAID use may result in gastrointestinal adverse effects in some people. No direct comparisons between oral and topical NSAIDs were available. Some trials demonstrated greater benefit from glucocorticoid injection than from NSAIDs in the short term, but this was not apparent in all studies and was not apparent by 6 months in the only study that included longer-term outcomes.[2,3]

Topical gel preparation has remains one of the most popular and important pharmaceutical dosage forms. As a result, the therapeutics effects of the drugs are achieved effectively whereas the systemic side effects can be avoided or minimized. The Non-

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Steroidal Anti-Inflammatory Drugs (NSAIDs) have been widely used in the treatment of rheumatoid arthritis and other related condition Aceclofenac, a non-steroidal anti-inflammatory drug, has been used in the treatment of rheumatoid arthritis and osteoarthritis. In order to decrease the gastric ulcerogenic effects, aceclofenac gels have been developed. This study was conducted to develop a gel formulation of aceclofenac using four types of gelling agents: carbopol,

hydroxypropylmethylcellulose (HPMC), carboxymethylcellulose sodium (Na CMC) and sodium alginate. Effect of penetration enhancer (propylene glycol) on the release has been studied. The gels were evaluated for physical appearance, rheological behavior, drug release and stability. The drug release from all gelling agents through a standard cellophane membrane was evaluated using Keshary-Chien diffusion cell. All gels showed acceptable physical properties concerning color, homogeneity, consistency, spreadability and pH value. Among all the gel formulations, carbopol showed superior drug release than followed by Na CMC, HPMC and sodium alginate. Drug release decreased with increase in polymer concentration. Drug release was not linearly proportional with the concentration of penetration enhancer or co-solvents.

Stability studies showed that the physical appearance, rheological properties, and drug release remained unchanged upon storage for two months at ambient conditions. Aceclofenac, a non-steroidal anti-inflammatory drug, has been used in the treatment of rheumatoid arthritis and osteoarthritis. In order to decrease the gastric ulcerogenic effects, aceclofenac gels have been developed. This study was conducted to develop a gel formulation of aceclofenac using four types of gelling agents: carbopol, hydroxypropylmethylcellulose (HPMC), carboxymethylcellulose sodium (Na CMC) and sodium alginate. Effect of penetration enhancer (propylene glycol) on the release has been studied. The gels were evaluated for physical appearance, rheological behavior, drug release and stability. The drug release from all gelling agents through a standard cellophane membrane was evaluated using Keshary-Chien diffusion cell. All gels showed acceptable physical properties concerning color, homogeneity, consistency, spreadability and pH value. Among all the gel formulations, carbopol showed superior drug release than followed by Na CMC, HPMC and sodium alginate. Drug release decreased with increase in polymer concentration. Drug release was not linearly proportional with the concentration of penetration enhancer or co-solvents. Stability studies showed that the physical appearance, rheological properties, and drug release remained unchanged upon storage for two months at ambient conditions. [4,5,6]

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most commonly prescribed drugs for the treatment of OA. NSAIDs are definitely better than placebo and are enjoying the status of popular "over the counter" medicines amongst the health professionals and the patients.[5] Aceclofenac, a US-FDA approved drug in 1988, is the most commonly prescribed NSAID for the treatment of OA-related pain. The efficacy of Aceclofenac is still believed to be unmatchable as it is as effective as the newer approved pain relief medications for OA and continues to be a benchmark pharmacological treatment option for OA to the physician. Despite several advantages, Aceclofenac is also associated with the NSAID-category side effects like gastrointestinal (GI) adverse effects including bleeding, ulceration, and perforation of the stomach, small intestine, or large intestine, which can be fatal too. These drawbacks of a timely tested drug always motivated the medicinal chemists to develop a new/modified NSAID with enhanced safety and comparable efficacy. This driving force resulted in the development of ACE, that is, a derivatized Aceclofenac developed by Grau *et al* in 1991 to improve its gastrointestinal tolerability ACE offered a relatively better gastric tolerance vis-à-vis the other NSAIDs including Aceclofenac. The incidence of gastric ulcerogenicity of ACE

has been reported to be significantly lower than that of the other frequently prescribed NSAIDs, for instance, 2-folds lesser than naproxen, 4-folds lesser than Aceclofenac, and 7-folds lesser than indomethacin. ACE is also expected to provide economic benefits owing to its better tolerability and marked efficacy On pharmacokinetic fronts, ACE is well absorbed from gastrointestinal tract and circulates mainly as unchanged drug, while the food presence rarely alters its pharmacokinetic properties Model independent pharmacokinetic parameters like, and half-life as well as the absorption of ACE are not affected by escalating age and, therefore, dose manipulations are not generally advocated in the elderly patients. Though reported to be well-tolerated, a few incidences of rare hypersensitivity reactions after oral intake of ACE are reported including hypersensitivity vasculitis photoallergic contact dermatitis, exudative erythema multiforme anaphylactic reaction and acute tubulointerstitial nephritis Also, two NSAIDs with similar chemical structure with ACE, namely, alclofenac and fenclofenac, have been associated with higher incidences of rashes and, subsequently, withdrawn in late 1970s and 1980s, respectively.[7]

Mechanism of Action of Aceclofenac

The mode of action of ACE is mainly based on the inhibition of synthesis of prostaglandins (PG). ACE inhibits the cyclooxygenase (Cox) enzyme, which is involved in the synthesis of PG [*In vitro* data in unstimulated bovine aortic coronary endothelial cells indicated the selectivity for Cox-2 by ACE more than Cox-1. ACE also inhibits the synthesis of the inflammatory cytokines, interleukins, and tumor necrosis factors. Also, effect of ACE on the cell adhesion molecules from the neutrophils has also been proposed.

Its interleukin-1 (IL-1) inhibition activity may be linked to its stimulatory effects on cartilage matrix by release of glycosaminoglycan and a chondroprotective agent, 42-hydroxyacelofenac. The decreased production of nitrous oxide in human articular chondrocytes is also linked to its anti-inflammatory activity. As 42-hydroxy aceclofenac participates in chondroprotection by interfering with IL-1-mediated production of promatrix metalloproteinase-1 and metalloproteinase-3 and the release of proteoglycans from chondrocytes, ACE is classified as a novel NSAID. It simultaneously down regulates the production of promatrix metalloproteinases as well as prostaglandin E2 in osteoarthritis and/or rheumatoid arthritis. Surprisingly, ACE is not involved in the tendon cell proliferation unlike indomethacin and naproxen and can be safely prescribed for the treatment of pain after tendon injury and surgery. In patients with OA of the knee, ACE decreases pain resulting in reduction of disease severity and improves the functional capacity of the knee. It reduces joint inflammation, pain intensity, and the duration of morning stiffness in patients with rheumatoid arthritis.[7]

Tender point is defined as the places on muscles that when touched with enough pressure, elicits a feeling of sensitivity in the location of point. Pain does not refer anywhere else in the body; pain is confined to tender point itself. They are usually no bigger than 1 cm.[1]

The presence of tender points in patients is closely associated with their current anxiety, and patients with a history of psychological trauma associated with anxiety (for example, childhood trauma or sexual abuse) have an increased number of tender points.[4] US is a modality which involves the generation of high frequency sound waves, and their transmission through the skin to the structures desired to be affected. US generators used clinically are limited by government regulation to approximately 1,000,000 Hertz (1 megahertz).[8]

Phonophoresis was first used to treat polyarthritis of the hand by delivery of hydrocortisone ointment into inflamed areas in 1954. Since then it has been reported to be used in the treatment of various dermatological and musculoskeletal disorders.[9]

The mechanism by which ultrasound

enhances the transdermal penetration of substances is not entirely clear. One could think of the vasodilation observed on macroscopic examination, but this would certainly not be enough on its own, since it does not imply any change of the waterproof keratin layer of the skin, which should necessarily be altered.[8]

The purpose of this study is to study the effectiveness of acelofenac gel as the coupling medium in the immediate pain relive of tender point.

Methodology

Number and Source

30 subjects were taken from young population.

Inclusion Criteria

1. Male or Female with age of 20-30 years.
2. Subjects with upper trapezius muscle spasm.

Exclusion Criteria

1. Subjects with trigger point of trapezius muscle.
2. Subjects with musculoskeletal disorder that would limit performance in these subjects.
3. Skin disorders which would irritate by either increase in warmth of the part or by the lubricants which might be used, e.g. eczema.
4. In presence of malignant tumours.
5. In case of any previous fracture or surgery at neck.
6. All contraindications of ultrasonic therapy.

Method of selecting & assigning subjects to groups

40 subjects having an upper trapezius muscle spasm were considered for this study. They were then screened to remove the subjects who did not fulfil the criteria for the study. After screening, the subjects they were randomly divided into two groups.

Instruments and Tool used

1. Ultrasound machine Meditek Ultrasonic digital, Meditek cooperation
2. Tropical ointment consisting of Aceclofenac 10gm Chlorzoxazone 500 mg Paracetamol 500 mg Aceclofenac 10 gm Chlorzoxazone 500 mg Paracetamol 500mg.
3. Ultrasound gel.

Research Design

Experimental design.

Variables

Independent variables - Ultrasonic Therapy

Dependent variables - Visual Analogue Scale, ROM

Procedure

Subjects fulfilling the inclusion criteria were taken into consideration. The procedure was explained to the subjects and a written consent was taken after explaining the benefits and clearing the doubts of the subject regarding study. After pain level assessment by help of visual analogue scale (VAS) and Range of Motion using the universal goniometer they were randomly divided into two groups namely, A and B.

Group A were given phonophoresis ultrasound with Aceclofenac along with aquasonic gel as coupling medium and Group B were given ultrasound with aquasonic gel as coupling medium. The ultrasound was given for 5 minutes at 0.8 w/cm2 16. After the treatment pain level and Range of Motion is taken again.

Result

A paired sample t test reveal a statistically reliable difference between the mean number of VAS pre and post in Aceclofenac /Group A(M= 6.6, s =1.03280) and (M= 3.8, s =1.48645) that the t(14)=12.582, P(á)= .000 at two tail test A paired sample t test reveal a statistically reliable difference between the mean number of ROM pre and ROM post in Aceclofenac/Group A (M=27.0000, s= 5.29150) and (M= 36.07, s = 4.20) that the t (14) = -11.093, P(á)= .000 at two tail test.

A paired samples t test reveal a statistically reliable difference between the mean number of VAS pre and VAS post in Group B (M=-6.8000, s = 1.22017) and (M 4.5, s=1.50238) that the, t (14) =8.9, P(á) = .000 at two tail test.

A paired samples t test reveal a statistically reliable difference between the mean number of ROM pre and ROM post in Group B (M=-24.01, s=10.73357) and (M=34.111, s=9.51290) that the, t (14) = -10.569, P(á) = .000 at two tail test.

An independent-samples t-test was conducted to compare VAS post treatment in Group B and Group A. There was a significant difference in the scores for pulsed (M=4.5, SD=1.5) and Group A (M=3.96, SD=1.48) conditions; t (28)=0.855, p = 0.400. the result suggest that VAS decreases more in Group A mode than in Group B. An independent-samples t-test was conducted to compare ROM post treatment in Group B and Group A. There was a significant difference in the scores for Group B (M=33.73, SD=9.51) and Group A (M=37.06, SD=4.19) conditions; t (28)=-1.24, p=0.225. The result suggest that ROM increases more in Group A.

Discussion

According to the unpaired t test done between post values of VAS in case of pulsed mode and continous mode the p value is <0.005. The post value of ROM in Group A and Group B the p value is <0.005.

From the experimental work finding it can be concluded that Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic activities and used for the treatment of rheumatoid arthritis. Aceclofenac by oral administration can produces stomach indigestion, so it is not suitable for the treatment of rheumatoid arthritis patient with gastric ulcer, so, to avoid gastric irritation to G.I.T, minimizing systemic toxicity. To overcome the side effects associated with oral aceclofenac therapy and to have the benefits associated with topical therapy; Aceclofenac topical gels are prepared in this study. Studies showed that drug release was decrease with increase in gelling agent concentration because polymer concentration increases; viscosity increasesFrom the experimental work finding it can be concluded that Aceclofenac is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic activities and used for the treatment of rheumatoid arthritis. Aceclofenac by oral administration can produces stomach indigestion, so it is not suitable for the treatment of rheumatoid arthritis patient with gastric ulcer, so, to avoid gastric irritation to G.I.T, minimizing systemic toxicity. To overcome the side effects associated with oral aceclofenac therapy and to have the benefits associated with topical therapy; Aceclofenac topical gels are prepared in this study. Studies showed that drug release was decrease with increase in gelling agent concentration because polymer concentration increases; viscosity increases[5] gel formulations provide a suitable delivery system for drugs because they are less greasy and can be easily removed from the skin. Percutaneous absorption of drugs from topical formulations involves the release of the drug from the formulation and permeation through skin to reach the target tissue. The release of the drug from topical preparations depends on the physicochemical properties of the vehicle and the drug employed. In order to enhance drug release and skin permeation, methods such as the selection of a suitable

vehicle[5], co-administration of a chemical enhancer[3] have been studied. Gel base formulation makes the drug molecules more easily removable from the system then cream and ointment.[4,5]. Gels for dermatological use have several favorable properties such as being thixotropic, greaseless, easily spreadable, easily removable, emollient, nonstaing, compatible with several excipients and water-solubleor miscible.[10]

Aceclofenac is chemically [[[2-[(2,6,Dichlorophenyl) amino] phenyl] acetyl] oxy] acetic acid[7], is a new orally effective NSAID of the phenyl acetic acid group. It posses a remarkable antiinflammatory, analgesic and antipyretic properties. The continue use of aceclofenac through oral route causes ulcerogenic effect, flatulence, indigestion (dyspepsia), vertigo, dizziness, dyspnoea, stomatitis, itching (pruritis).[8,9] When a drug system is applied topically, drug diffuses passively out of its carrier or vehicle. A unique feature of aceclofenac.s pharmacology is that it stimulates glycosaminoglycans (GAG) synthesis, which in turns enhances skin permeation of NSAIDs. [4,5,10]

Aceclofenac when presented in the form of topical gel can reduce local inflammations. Hence for local inflammation or pain in the body, the topical application of aceclofenac may be useful which also avoids the side effects associated with the oral therapy. Hence, a topical ointment containing aceclofeac was prepared It is established that gel formulations are superior topical formulation over any other topical formulations, because these system have better application property in comparison to creams and ointments.[12] The objective of present study was conducted to develop a gel formulation of aceclofenac using four types of gelling agents: carbopol, hydroxypropylmethylcellulose (HPMC), carboxymethylcellulose sodium (Na CMC) and sodium alginate. Effectof penetration enhancer (propylene glycol) on the release has been studied.

The gels were evaluated for physical appearance, rheological behavior, drug release and stability. The drug release from all gelling agents through a standard cellophane membrane was evaluated using Keshary-Chien diffusion cell.[6] The mechanism by which ultrasound enhances the transdermal penetration of substances is not entirely clear. One could think of the vasodilation observed on macroscopic examination, but this would certainly not be enough on its own, since it does not imply any change of the waterproof keratin layer of the skin, which should necessarily be altered. No volunteers presented any complication of any kind nor did they report any discomfort with the treatment at any time, all of them resuming normal life immediately after the end of treatment Apart from slight redness and a temperature increase on touch, no sign of local irritation was detected by macroscopic inspection of the irradiated areas.[4,10]

Conclusion

The study concludes that ultrasound with acelofenac gel is better for immediate pain relive as compared to ultrasound with aquasonic gel only for immediate pain relive in tender point in muscles all over the body.

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