

LOCAL IBUPROFEN TREATMENT IN GONARTHROSIS

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SUMMARY: The purpose of this study was to observe the effects of topical forms of Nonsteroidal antiinflammatory drugs (NSAID) which are widely used in the treatment of rheumatological diseases. NSAIDs are presented to the market in the form of tablets, suppositories, injectable and topical forms. The usage of these tablets, suppositories and injectable forms frequently produce some side effects, especially concerning the gastrointestinal system. The aim of topical application of the same drugs is to decrease these complications. From the results of this study we conclude that topical forms of NSAID can safely and effectively be used to reduce the complications of prolonged application of these pharmaceuticals.

Key Words: Ibuprofen, Gonarthrosis.

INTRODUCTION

Nonsteroidal antiinflammatory drugs (NSAID) are widely used in local and systemic rheumatic diseases (1,2). NSAIDs may cause some side effects like gastrointestinal ulceration, hemorrhage and renal diseases. These drugs are especially deleterious for the elderly people (3-5). Transcutaneous application of NSAID is however, safer than oral administration (5,6). This study was performed to investigate the efficacy and tolerability of transcutaneous local ibuprofen administration in patients with gonarthrosis.

MATERIALS AND METHODS

70 patients with osteoarthritis of knee were admitted to Ankara Numune Hospital, Physical Therapy and Rehabilitation outpatient department were included in the study. 35 of them were given placebo and the remaining 35 received treatment with NSAIDs. Both groups were treated for 3 weeks. Ibuprofen topical form was applied to the remaining 35 patients topical form of ibuprofen was applied on 10 cm² areas of the skin over both knees as a layer 3 times a day. The patients were given no other treatment and were controlled on days 7, 14 and 21. They were asked for spontaneous pain, during movement, and upon suppression and 0-4 cm visual analog scale was taken. Joint swelling, limitation of motion and joint circumferences were determined. The results were evaluated using student's t-test and correlation analysis methods.

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RESULTS

70 patients with osteoarthritis of knee were included in the study. 35 patients were given local ibuprofen, the other 35 were given placebo. 39 were female and 31 were male. Their ages were between 42 and 70, with a mean of 49 ± 12.58 years.

In the group treated with ibuprofen spontaneous knee pain was decreased over time and the differences were statistically significant among days 7, 14 and 21 ($p < 0.001$).

In the same group knee pain during movement was decreased slightly over time and this difference was also statistically significant ($p < 0.05$).

Their knee pain on pression was also decreased significantly ($p < 0.001$). Knee swelling and joint circumference were both decreased and these differences were statistically significant ($p < 0.05$) and there was no decrease in the limitation of motion in the knees. On the contrary in the placebo group, spontaneous pain, pain during movement, pain on pression, joint swelling, joint circumference and limitation of motion in the joint revealed no significant alterations ($p > 0.05$) during the period of observation.

DISCUSSION

Oral NSAID administration can cause crucial gastrointestinal side effects. Thus, topical use of these drugs provides safer treatment. The main objective of topical administration of these drugs could be to maintain adequate tissue concentration without producing the systemic complications of these drugs. Two drugs fulfill this criteria: Diclofenac and flurbiprofen. But topical use of some drugs is not available (Glyceril trinitrate etc.) This drug can reach very high concentrations in the circulation (5-7). Many studies were performed to investigate the effects of topical NSAID on the course of rheumatic diseases. Local piroxicam, compared with placebo, produces a remarkable healing in cases of soft tissue injuries.

When administered orally NSAID's gives rise to

serious gastrointestinal side effects. The effective NSAID's dose for local skin application provides a safer treatment. One/main objective in local NSAID is that the drug will reach adequate tissue concentrations without considerable systemic absorption. Two drugs, diclofenac and flurbiprofen fulfill these criteria. However, some NSAID's are not eligible for local skin application e.g. Glycerile trinitrate. This drug attains very high blood levels (5-7).

A great many surveys were performed to investigate the effects of local NSAID's in the treatment of rheumatic diseases. Local piroxicam compared with placebo, yield much superior results in cases of acute soft tissue injuries. The therapeutic response to local diclofenac is quite satisfactory in lateral epicondylitis. In cases of tendinitis, local indo ethacine is notably effective (7-9).

Locally administered ibuprofen is used in a series of conditions listed below: joint rheumatism, painful joint disorders resulting in degenerative arthropathy (osteoarthritis), inflammatory rheumatic diseases of soft tissues adjacent to joint, crunching, sprain and stretch injuries due to sports and crash accidents (1,2,4,9,10).

Shoulder rigidity can likewise be treated by local application. Caution should be exercised not to apply the creme over the mucosal or injured surfaces. Longterm use of the drug during pregnancy is contraindicated. It also should not be applied over wide surfaces of the body. The skin over the affected site should be scrubbed with a 4 to 10 cm tubal creme four times daily. The drug may initiate local erythema and pitting sensation of the skin at the site of scrubbing. The sensation usually lasts for one or two minutes.

The drug should not be used in patients with a past history of ibuprofen allergy or allergy to agents sharing the same biochemical mechanism with ibuprofen. Patients with previous allergic reactions to propilen glycol or PABA should not be treated with ibuprofen (2,7,11,12).

Locally applied ibuprofen may induce a local rash, itching and burning sensation. The drug may rarely cause bronchospastic reactions in few predisposed patients (7,12,18). In our study, only 8 patients of the ibuprofen group developed skin rash, itching and burning sensation. None of the patients developed bronchospastic reaction in the same group. Ibuprofen creme exerts its marked analgesic and antiinflammatory activity through inhibiting prostaglandin synthesis in the inflamed tissues.

Ibuprofen containing creme, directly affects leucocyte migration, lysosomal enzyme release from the inflamed tissue and thrombocyte aggregation. It also affects the pain induced by inflammation.

Locally available ibuprofen creme does not destruct the skin, but causes local temporary skin rash. It also has been demonstrated that the creme does not induce ulcers or mucosal lesions in GIS. Following scrubbing, ibuprofen passes through the stratum corneum of the skin, subdermal tissues and penetrates into the synovial fluid. The drug can then reach therapeutical levels while it still remains in sub-therapeutical concentrations in the blood plasma.

Plasma concentration of ibuprofen is accepted as 0.15 mg/ml according to Peters et al. and 0.64 mg/ml according to Mondene *et al.* (1,3,4,7,13,14).

Percutaneous absorption of the drug is approximately 5% (1-3,13,14).

Creme is a deep acting agent. Ibuprofen, the active component of creme attains concentrations ranging from 12 mg/g to 16 mg/g subcutaneously, which are highly therapeutical. Ibuprofen accumulation in deeper tissues is more prominent. Ibuprofen concentration within muscles and connective tissues is approximately 6.4 mg/g. This level is found to be quite therapeutical. The joint capsule and synovial concentrations are found as 4.4 mg/g and 2.6 mg/g respectively.

In our study 30 patients received local creme application over the skin. In these patients a remarkable reduction in pressure noted. Knee swelling decreased

markedly. A significant improvement compared with placebo was noted compared with the response of patients receiving Vauprofen creme. No other side effect was detected except the skin rash.

In conclusion, patients with gonarthrosis having serious gastrointestinal, renal and liver disease can safely be treated by local NSAID creme therapy.

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