Comparison of the effectivity of oral and intra-articular administration of tenoxicam in patients with knee osteoarthritis


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Received 5 November 2013; accepted 17 December 2013
Available online 6 February 2014

Keywords
Osteoarthritis; Tenoxicam; Knee; Intra-articular administration

Abstract
Background and objectives: Tenoxicam is widely used in osteoarthritis treatment and we aimed to compare the effectivity of oral and intra-articular administration of tenoxicam in osteoarthritis treatment.

Methods: This study was performed between 2011 and 2012 by retrospectively analyzing and comparing the findings of 60 patients who were clinically and radiologically diagnosed with knee degenerative osteoarthritis in Bünyan state hospital pain polyclinic. 60 patients included in the study were divided into two groups. The first group (tenoxicam IA, n = 30) included patient findings of those subjected to intra-articular injection of 20 mg tenoxicam to the knee once a week for three weeks and the second group (oral tenoxicam, n = 30) included patients who were administered 20 mg oral tenoxicam once a day for three weeks. All patients were clinically evaluated pre-treatment and in the 1st week, 1st month and 3rd month post-treatment according to specified criteria.

Results and conclusions: Twenty two of 60 patients included in the study were male and 38 were female. In both groups significant improvements were detected in all of the observed parameters: visual analog scale, Western Ontario McMaster Osteoarthritis Index (pain, physical activity, knee stiffness) and Lequesne index scores and in the evaluations performed in 1st week, 1st month and 3rd month with respect to pre-treatment values. Besides, a better compliance to treatment and gastrointestinal system tolerability in tenoxicam IA group was also observed. Intra-articular tenoxicam administration could be thought as an alternative treatment method in patients with knee osteoarthritis who cannot use oral tenoxicam especially due to systemic gastrointestinal system side effects and those who have difficulties in adapting to treatment.

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Introduction

Osteoarthritis (OA) is the arthritis form most commonly encountered in the world. OA is primarily defined as a repair process developed against joint degeneration and joint destruction that cause a series of biochemical and morphologic changes in joint capsule and synovial membrane and against erosion in joint cartilage, osteophytic hypertrophy of bones in joint edges, subchondral sclerosis.\(^1\) OA is especially one of the leading causes of morbidity that affects life quality of geriatric patients negatively. Pain is the most encountered and the most important symptom. OA pain is complicated and complex. Tissues other than cartilage in the joint have a rich nociceptive net. OA treatment should be conducted with pharmacological and non-pharmacological method. The primary aim in OA treatment is to stop the pain; mainly acetaminophen and NSAI drugs are used for this purpose. But the physicians try to develop new treatment alternatives because the above stated treatment options remain inadequate and side effects develop in the long term.\(^2,3\) Analgesics and NSAI (Nonsteroidal anti-inflammatory) drugs are widely used in OA treatment. But care should be taken in the administration of these drugs in elderly patients due to their serious side effects and the weakness of their effectivity.\(^4\) They must reach a specific concentration in the blood for anti-inflammatory characteristics of NSAI drugs to appear and but their potential side effects cause patients to decrease the dose they use and generally effective dose concentration cannot be reached. Tenoxicam is widely used in OA treatment. Furthermore it is shown that intra-articular injection of tenoxicam is commonly used in OA treatment and has beneficial effects.\(^5\)

With this study we estimated that IA tenoxicam treatment in patients with OA provided a more effective treatment than oral tenoxicam (TXO), with less side effects.

Methods

This study was performed by retrospectively analyzing and comparing findings of 60 patients diagnosed clinically and radiologically with knee degenerative OA in Bünüyan state hospital between 2011 and 2012. Required consents were obtained from the patients by explaining them the disease and the treatment to be performed. Consent of Çanakkale 18 Mart University Clinical Research Ethics Committee was also obtained (15.05.2013/11-08; Aksulu HA). Data of 50–80 years old patients in ASA I–III group were included in the study.

OA diagnosis was established following clinical story, radiographic changes and physical examination. Radiographies of both knees, standing, frontal and posterior and lateral were taken from all patients. The findings of patients with knee arthritis according to American Rheumatism Society, without any laboratory pathology, between 0 and III grade according to Kellgren-Lawrence classification were
Statistical analysis

The SPSS software (SPSS 13, Chicago, IL, USA) was used for analysis. Descriptive parameters are presented as mean ± standard deviation, median (minimum–maximum). Independent simple t test was used for comparing means of continuous variables between two groups. When there were more than two groups, Friedman test was used, Bonferroni correction was used for multiple comparisons (α = 0.05/6 = 0.0083), respectively. A p-value of <0.05 was considered as significant.

Results

22 of 60 patients included in the study were male and 38 were female. Demographic characteristics of patients in both groups were shown in Table 1. Significant recoveries in all the parameters were detected in both groups in VAS, WOMAC (pain, physical activity, knee stiffness) and Lequesne index in 1st week, 1st month and 3rd month when compared with pre-treatment values (Tables 2–4) (p < 0.001).

Significant improvements were detected in all the parameters in VAS, WOMAC (pain, physical activity, knee stiffness) and Lequesne index in the 3rd month evaluations when compared with the post-treatment 1st week values (p < 0.001). But it was observed that these results remained lower than pre-treatment values.

Table 1 Demographic characteristics of patients.

<table>
<thead>
<tr>
<th></th>
<th>Group TXIA</th>
<th>Group TXO</th>
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<tbody>
<tr>
<td>Age (year)</td>
<td>65 ± 5.6</td>
<td>66 ± 4.7</td>
</tr>
<tr>
<td>Body mass index (BMI)</td>
<td>30.9 ± 1.93</td>
<td>30.2 ± 1.31</td>
</tr>
<tr>
<td>Duration of illness (month)</td>
<td>16.2</td>
<td>16.9</td>
</tr>
<tr>
<td>ASA I/II/III</td>
<td>4/14/12</td>
<td>6/13/11</td>
</tr>
</tbody>
</table>

GIS tolerability during the treatment and treatment continuity are shown in Table 5.

Discussion

Significant improvements were detected in all the parameters in scores of VAS, WOMAC (pain, physical activity, knee stiffness) and Lequesne index in 3rd month when compared with pre-treatment values (Tables 2–4) (p < 0.001).
knee stiffness) and Lequesne index in 1st week, 1st month and 3rd month post-treatment in intra-articular tenoxicam administered patients with knee OA, their systemic side effects limit their long-term use. And therefore in the last few years intra-articular procedures became a current issue and for this purpose intra-articular NSAID, corticosteroids, local anesthetics or hyaluronic acid preparations were used. But because hyaluronic acid treatment has a high cost and corticosteroid treatment is not suitable for frequent use, we consider that tenoxicam intra-articular injection with a low cost and few side effects can be used in suitable patients.

All selective COX-2 inhibitors are contraindicated to those with congestive heart failure, ischemic heart disease or stroke history. It should be used with caution in those with cardiovascular risk factor (hypertension, hyperlipidemia, diabetes, cigarette consumption). For this reason minimum effective dose should be used for the shortest period. Selective COX-2 inhibitors are indicated in those with high Gastrointestinal risk and with no cardiovascular risk. FDA demanded black box warning to be put on all NSAID boxes and also a warning stating that it could cause an increase in GI bleeding and Cardiovascular problems to be mentioned. The studies regarding this subject continue. Most of the patients in our study had at least one systemic disease; in other words they were ASA II–III group patients.

Although there are some questions regarding the safety of intra-articular injection of NSAID drugs, it is supposed that tenoxicam is safe in this respect. Especially in patients subjected to arthroscopic surgery it was administered intra-articularly in order to provide post-operative analgesia. Intra-artical tenoxicam appears to be a safe treatment method for knee OA. But although it is encountered rarely, risks such as bleeding and sepsis should be kept in mind. It is stated that tenoxicam does not affect prostaglandin metabolism in cartilage tissue and its effects on hyaluronic synthesis vary depending on the dosage. And it is indicated that it inhibits glycosaminoglycan loss in the cartilage.

In the comparative study between tenoxicam and other NSAID it was shown that proteoglycan and collagen synthesis was suppressed by tenoxicam and tenoxicam could be helpful in decreasing cartilage catabolism in patients with OA. Intra-articular use of tenoxicam in patients with OA becomes increasingly popular due to its ease of use, chondroprotective and pain revealing characteristic. And NSAID drugs should be used with caution in old patients due to their systemic side effects. They increase bleeding risk in patients using anticoagulants. GIS should be thoroughly examined. In the study we conducted, we observed that direct injection of tenoxicam into knee joint provided a good alternative in patients who were required to use NSAID with regards to both gastrointestinal tolerability and treatment continuity. Furthermore, in a study 40 mg single dose tenoxicam was administered to patients with polyarthritis and then concentration of drug in plasma and synovial liquid were measured; half-life was 42 h in the plasma and 45 h in synovial liquid. Thus, half-life of tenoxicam in plasma and synovial liquid was shown to be parallel.

In a study patients with OA were divided into three groups: TXO, TXIA and only exercise group. Patients were followed for 6 months and compared with regards to functional capacity and pain, and no difference was observed between 3 groups. And in another study, single dose intra-articular injection of tenoxicam was performed to patients with knee OA. In the evaluations of patients performed one month later, 40% decrease in pain and 60% increase in the joint movement aperture was observed. Our results show that intra-articular tenoxicam treatment may be preferred to TXO treatment especially for patients that cannot use drug in sufficient doses due to gastrointestinal intolerance. In patients with knee arthritis who cannot use TXO due to systemic, especially GIS side effects or those who have difficulty in adapting to the treatment, intra-articular tenoxicam treatment can be thought as an alternative treatment method.

**Conflicts of interest**

The authors declare no conflicts of interest.

**References**

Intraarticular tenoxicam in patients with knee osteoarthritis