Ultrasound guided injection of a painful knee osteoarthritis with medial meniscus extrusion: a case series study

Luca Di Sante[1]
Teresa Venditto[2]
Francesco Ioppolo[2]
Marco Paoloni[1, 2]
Massimiliano Mangone[2]
Federica Alviti[2]

[1] Department of Physical Medicine and Rehabilitation, Azienda Policlinico Umberto I, Rome, Italy
[2] Department of Anatomy, Histology, Forensic Medicine and Orthopedics, Board of Physical Medicine and Rehabilitation, "Sapienza" University, Rome, Italy

Corresponding author:
Teresa Venditto
Department of Anatomy, Histology, Forensic Medicine and Orthopedics
Board of Physical Medicine and Rehabilitation, "Sapienza" University
Piazzale Aldo Moro 5
00185 Rome, Italy
E-mail: teresa.venditto@hotmail.it

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Summary

***Background*: Meniscal subluxation results in the natural history of knee osteoarthritis (OA). Periarticular infiltration should minimize possible complications related to penetration of corticosteroids into the joint space in the treatment of knee OA.**
According to pain relief and improvement of function, the aim of this study is to evaluate the effectiveness of perimeniscal corticosteroid ultrasound guided injection in knee OA.
***Methods*: Thirty-two patients received an injection of 0.5 ml of methylprednisolone-acetate around perimeniscal tissues. Outcome measures were pain relief and knee function, assessed by Visual Analogue Scale (VAS) [24, 29, 30] measured at rest (VAS-R) and during stairs climbing (VAS-C) and by Italian-Western Ontario and McMaster Universities (WOMAC) scale. Clinical evaluation was performed at baseline, at 1 and 4 weeks of follow-up.**
***Results*: Mean baseline values of VAS-R and VAS-C were 6.79 ± 1.17 and 7.6 ± 1.39, respectively. All subjects showed a significant reduction in pain over time ($p<0.001$). Mean baseline values of WOMAC pain, stiffness and physical function were 5.56 ± 1.32, 4.39 ± 1.91 and 4.63 ± 2.31, respectively. According to WOMAC stiffness and physical function was not found a significant improvement over time ($p> 0.05$).**
***Conclusion*: Corticosteroid perimeniscal ultrasound guided injection can be considered as an adjunct to core treatment for the relief of moderate to severe pain in people with knee OA.**
Level of Evidence: IV.

KEY WORDS: corticosteroid injection, knee osteoarthritis, ultrasound guided injection, pain, medial meniscal pain.

Introduction

Knee osteoarthritis (OA) is a progressive joint disorder affecting more than 250 million people worldwide[1]. It has a significant impact on patients' *quality of life*, much of which may be attributed to pain[2, 3].
Radiography is the first imaging modality for the assessment of OA progression and the widely scale used to quantify the severity on radiographs is the Kellgren-Lawrence (K&L) classification[4]. The most frequent abnormalities the narrowing of the joint space due to thinning of articular cartilage that is associated with loss of chondrocytes, sclerosis of the bone, and formation of subchondral cysts and osteophytes. However, typical radiological signs are not correlated with symptoms. Indeed, only about 15% of patients with radiologically demonstrated knee OA complain of knee pain[5, 6].
Ultrasonography is a useful way to demonstrate the soft tissues and fluid-filled spaces. Moreover, this technology[7] offers many advantages, including the acquisition of multiplanar images, the evidence of dynamic structures in real-time, the lack of ionizing radiation, and the support in interventional procedures. Furthermore, it is cost-effective and can be used without contrast enhancement (CE) to visualize various tissues involved in OA[8-10].
Meniscal subluxation is part of the natural history of knee osteoarthritis and it is described as a distance

of 3 mm between the peripheral border of the meniscus and the edge of the tibial plateau[11, 12]. Naredo et al.[13] compared the ultrasonographic findings with clinical and radiographic assessment in fifty patients with bilateral symptomatic knee OA. According to US findings, the Authors showed the presence of effusion, protrusion of the medial meniscus (MMP) with displacement of the medial collateral ligament (MCLD) and Baker's cyst. Moreover, they found that the MMP with MCLD was associated with mechanical pain and pain at rest in knee OA. Moreover, when considering early Kellgren and Lawrence grades, pain intensity was higher in subjects with MMP and MCLD than in knees without these findings.

The main goal of conservative management is to reduce pain thus improving function and quality of life. The therapeutic spectrum ranges from patient education and self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insoles modification, local cooling/heating, acupuncture, and electromagnetic therapy[14, 15]. Pharmacologic therapies are paracetamol, non-steroidal anti-inflammatory drugs, opioids, and glucosamine and chondroitin sulfate.

Intra-articular (IA) injection (corticosteroids, viscosupplements, blood-derived products) is the last non-operative modality that may be considered[16-18].

According to the American College of Rheumatology, IA corticosteroid injections may be recommended in people with OA providing short term reduction in moderate to severe pain[19]. Recently, an increase in vascularity, accompanied by increased sensory nerves, has been noted also in OA menisci, *which may relate the otherwise painless menisci, as a source of pain in knee OA*[20]. Thus, ultrasound-guided injection of periarticular tissues could be useful to avoid adverse events related to intra tendinous or intra ligamentous corticosteroids injection. Therefore, the aim of the present study was to evaluate the effectiveness of perimeniscal corticosteroid ultrasound guided injection in symptomatic patients with knee osteoarthritis in pain relief and improvement of function.

Methods

Study design and Participants

The present case-series study was carried out at the outpatient clinics of Physical and Rehabilitative Medicine from June to September 2015. Patients with diagnosis of knee osteoarthritis associated with medial knee pain and medial meniscus displacement were enrolled in this study.

The study protocol was approved by the hospital's Ethical Review Board and the study was conducted in accordance with the principles of the Declaration of Helsinki and its amendments. Patients were fully informed of the characteristics of the study and gave written informed consent. Demographic characteristics were collected using standard questionnaires.

The radiological criteria of knee joint OA severity were based on the Kellgren-Lawrence classification: grade 0: normal; grade I: small osteophytes without clinical importance; grade II: definite osteophytes but normal joint space; grade III: definite osteophytes with moderate narrowing of joint space; grade IV: definite osteophytes with severe narrowing of joint space[4].

Inclusion criteria were: i) subjects over 18 years of age, ii) history of knee pain for at least 6 months iii) a minimum value of pain required was 4 on visual analogue scale (VAS)[21], iv) stages II and III of Kellgren-Lawrence (K-L)[4], v) medial meniscus involvement assessed by US examination.

- Exclusion criteria: patients with overlying skin infection, other inflammatory arthropathies affecting the knee, diabetes mellitus, coagulation disorders, receiving anticoagulant treatment, non-steroidal anti-inflammatory drugs within five days prior to the treatment, prior injection within 3 months, definite osteophytes with severe narrowing of joint space (K-L grade IV)[4].
- Radiographic and ultrasound evaluations were performed by two independent physicians with more than ten years of experience.

Outcome Measures

Evaluations were carried out in three different times, at the beginning of treatment (T0), 1 week at the end of treatment (T1), and at 4 weeks (T2) of follow-up.

The primary outcome measures were the overall reduction of knee pain assessed byboth VAS [24, 29, 30] measured at rest (VAS-R) and during stairs climbing (VAS-C) and Italian-Western Ontario and McMaster Universities (WOMAC) pain subscale[22].

VAS consists of a 10 cm horizontal line (with 0 cm referring to "no pain" and 10 cm to the "the worst pain ever") and patients were asked to rate their pain intensity by making a mark on this line[21].

As secondary outcome measure, we considered functional improvement measured by WOMAC stiffness and disability subscale. The WOMAC osteoarthritis index is a self-assessment multidimensional instrument that evaluates 17 functional activities, 5 pain-related activities, and two joint stiffness categories in three different subscales[22].

At the end of treatment, patients were interviewed regarding treatment satisfaction, using the 7-point Likert scale. The question which the patient answered was: "How are you today in comparison to your first visit?". The seven response options were: (1) very much worse, (2) much worse, (3) little worse, (4) no change, (5) little improved, (6) much improved, (7) and very much improved[23].

US injection technique

US knee examination (6-15 MHz linear array transducer, Sonosite adge, USA) was performed with patient in supine position, with the knee flexed, and a pillow was placed under the knee for support. US examination of the anterior knee was performed both transversely and longitudinally. To evaluate the medial knee, patient remained in the supine position.

Therefore, the transverse and sagittal views of the medial collateral ligament were taken with the aim of searching for thickening. In the same position but with the knee extended, the anterior part of medial meniscus was also examined to assess the presence of MMP protrusion, associated with medial collateral ligament displacement. If the contour of the meniscus was the same line of the bone, this meniscus was evaluated as normal, and if the contour of meniscus bulged over the bone line, this meniscus was accepted as a protruded meniscus. A long axis ultrasound guided injection of perimeniscal side was performed with patient in the same position. The transducer was aligned with the long axis of the tibio-femoral bone across articular line. By a freehand technique, a 22-gauge (4 cm) needle was then advanced under direct sonographic guidance into the anterior medial meniscus wall (Fig. 1, Video 1). Once the needle touched the medial meniscus wall it was retracted by 1 mm and an injection of 0.5 ml of methylprednisolone acetate around perimeniscal tissues was performed, using strict aseptic administration technique. The drug's administration was confirmed by the visualization of bright echoes filling and visualization of capsule distension. Each patient received only one injection.

Sample Size

A priori power calculation was performed according to the mean change of VAS from baseline to four weeks follow-up, assuming a two tailed α value of 0.05 (sensitivity 95 %), a β value 0.15 (study power: 85%) and an effect size of 0.5. We determined that at least 31 subjects were required for each group (G Power 3 power analysis program).

Statistical Analysis

We used parametric tests if data were normally distributed and homogeneous and/or non-parametric tests if these two conditions were not satisfied. These assumptions were assessed by Kolmogorov-Smirnov's test and Levene's test, respectively. Data are mean ± standard deviation, unless otherwise stated.

Since all parameters were normally distributed, the one way ANOVA for repeated measures was used. Post-hoc multiple comparison procedure was performed according Tukey test.

The Statistical Package for social Sciences (SPSS) version 18 was used for calculations. All data were analyzed by a single researcher. Computed P values were 2-sided, and $p<0.05$ was used to determine statistical significance.

Results

Thirty-two (N=32) patients [20 females and 12 males, mean age ± standard deviation (SD) 69.61 ± 6.2] with pain on the medial aspect of the knee showing anterior horn medial meniscus (MMP) protrusion associated with medial collateral ligament displacement were enrolled in the present study and underwent an ultrasound guided injection of methylprednisolone in perimeniscal space of the medial aspect of the knee. Table I reports the sample baseline characteristics.

According to VAS-R, all subjects showed a significant reduction in pain over time ($F= 14.07$, $p<0.001$). There were significant differences within group between baseline and 1 week ($p<0.001$) and between

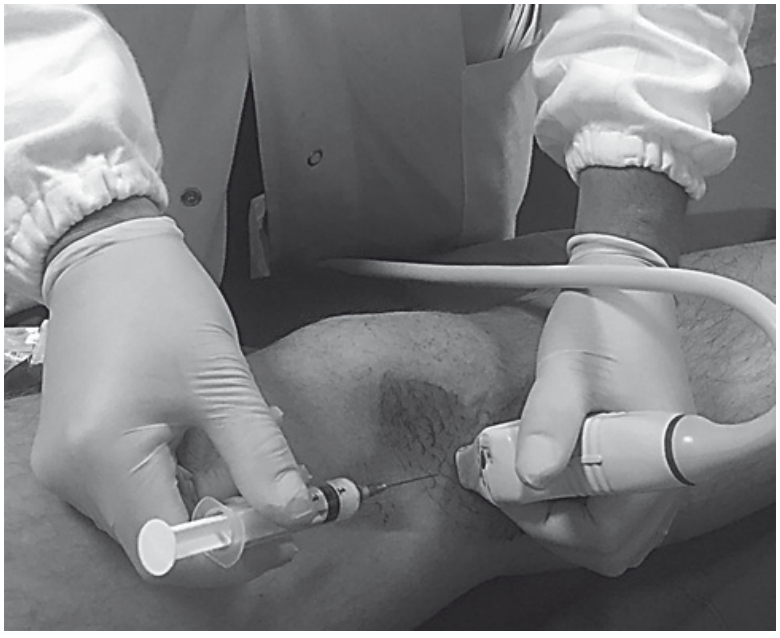

Figure 1, Video 1. Methylprednisolone acetate ultrasound guided injection.
The transducer was aligned with the long axis of the tibio-femoral bone across articular line. By a freehand technique, a 22-gauge (4 cm) needle was then advanced under direct sonographic guidance into the anterior medial meniscus wall. Once the needle touched the medial meniscus wall it was retracted by 1 mm and an injection of 0.5 ml of methylprednisolone acetate around perimeniscal tissues was performed. Length: 32 seconds; Size: 3 MB.

Table I. Baseline characteristic of the sample.

Mean Age sample, years (N=32)	69.61 ± 6.2
BMI	27.45 ± 3.08
- Males (N=12)	28.09 ± 2.91
- Females (N=20)	26.81 ± 3.25
Mean Age, years	
- Males (N=12)	64.33 ± 8.67
- Females (N=20)	63.66 ± 8.35
History of disease (years)	10.14 ± 6.3

Table II. Mean change of VAS score over time.

VAS REST			
	Mean ± SD	CI 95% (Low-Upper)	p-value
Baseline	6.79 ± 1.17	6.16-7.47	Baseline *vs* 1 Week <0.001 Baseline *vs* 4 Weeks= 0.001 1 Week *vs* 4 Weeks= 1.00
1 Week	4.37 ± 1.43	3.55-5.20	
4 Weeks	4.81 ± 1.24	4.10-5.52	
VAS STAIRS CLIMBING			
Baseline	7.6 ± 1.39	6.80-8.41	Baseline *vs* 1 Week <0.001 Baseline *vs* 4 Weeks <0.001 1 Week *vs* 4 Weeks= 1.00
1 Week	3.7 ± 1.23	2.98-4.41	
4 Weeks	3.9 ± 1.32	3.19-4.72	

baseline and 4 weeks (p<0.001) follow-up (Tab. II, Fig. 2).

According to VAS-C, all subjects showed a significant reduction in pain over time (F= 38.38, p<0.001). There were significant differences within group between baseline and 1 week (p<0.001) and between baseline and 4 weeks (p=0.001) follow-up (Tab. II, Fig. 3).

According to WOMAC pain score, all subjects showed a significant reduction in pain over time (F= 8.15, p=0.01). There were significant differences within group between baseline and 1 week (p= 0.002) and between baseline and 4 weeks (p=0.006) follow-up (Tab. III, Fig. 3).

According to WOMAC stiffness subjects did not show a significant improvement over time (F= 1.15, p=0.34). According to WOMAC physical function subjects did not show a significant improvement in physical function over time (F= 0.38, p=0.68).

According to Likert scale, at the end of treatment, 26 (81.25%) patients reported “very much improved” and “much improved”; 2 (6.25 %) patients reported “no change” and 4 (12.5 %) reported “little worse”.

Discussion

The natural history of knee osteoarthritis is variable, with the disease improving in some patients, remaining stable in others, and gradually worsening in others. The management of knee OA is still under debate. Intra-articular injections of HA, corticosteroids or platelet concentrates find their applicability in the treatment of knee OA because they might counterbalance the negative effect of inflammatory mediators on the progression of the disease, thus limiting cartilage destruction, chronic synovitis, joint capsule hypertrophy, subchondral bone remodeling and degenerative

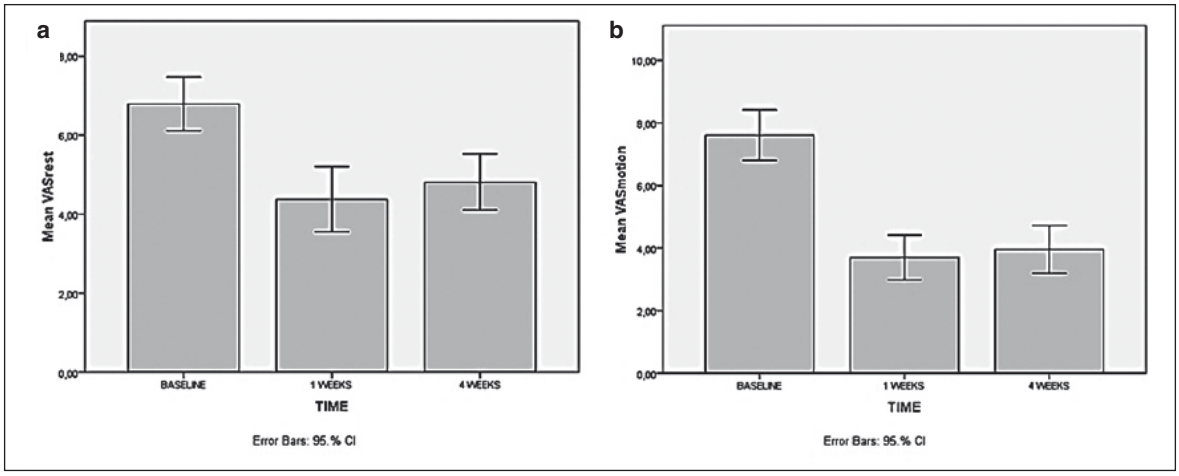

Figure 2 a, b. a) Mean change of VAS score at rest over time. b) Mean change of VAS motion score over time.

Table III. Mean change of WOMAC over time.

WOMAC PAIN			
	Mean ± SD	CI 95% for Mean, Low-Upper	p-value
Baseline	5.56 ± 1.32	4.80-6.33	Baseline *vs* 1 Week= 0.002 Baseline *vs* 4 Weeks= 0.006 1 Week *vs* 4 Weeks= 1.00
1 Week	3.62 ± 1.47	2.76-4.47	
4 Weeks	3.82 ± 1.41	2.99-4.63	
WOMAC STIFFNESS			
Baseline	4.39 ± 1.91	3.28-5.5	Baseline *vs* 1 Week= 0.57 Baseline *vs* 4 Weeks= 0.65 1 Week *vs* 4 Weeks= 1.00
1 Week	3.5 ± 1.99	2.34-4.65	
4 weeks	3.55 ± 1.35	2.77-4.33	
WOMAC PHYSICAL FUNCTION			
Baseline	4.63 ± 2.31	3.23-6.02	Baseline *vs* 1 Week= 1.00 Baseline *vs* 4 Weeks= 1.00 1 Week *vs* 4 Weeks= 1.00
1 Week	4.22 ± 1.97	2.90-5.55	
4 Weeks	3.91 ± 1.41	2.90-4.91	

changes in ligaments and menisci[17].

The present study evaluated the effectiveness of medial perimeniscal corticosteroid ultrasound guided injection in symptomatic patients with knee osteoarthritis in pain relief and improvement of function. As a whole, data analysis of our study revealed that all patients experienced early improvements in pain relief at rest, during stairs climbing compared with baseline values and in WOMAC pain subscale. The reduction of pain was still noted at 4 weeks from baseline.

The main results of our study are in agreement with clinical evidence[20], suggesting that the benefits of corticosteroid injections are short lived, usually one to four weeks. In our study all patients showed a minimally clinically important difference (MCID, the smallest difference in an outcome score which a patient perceives as beneficial) between baseline and 4 weeks follow-up greater than 1.4 points. These val-

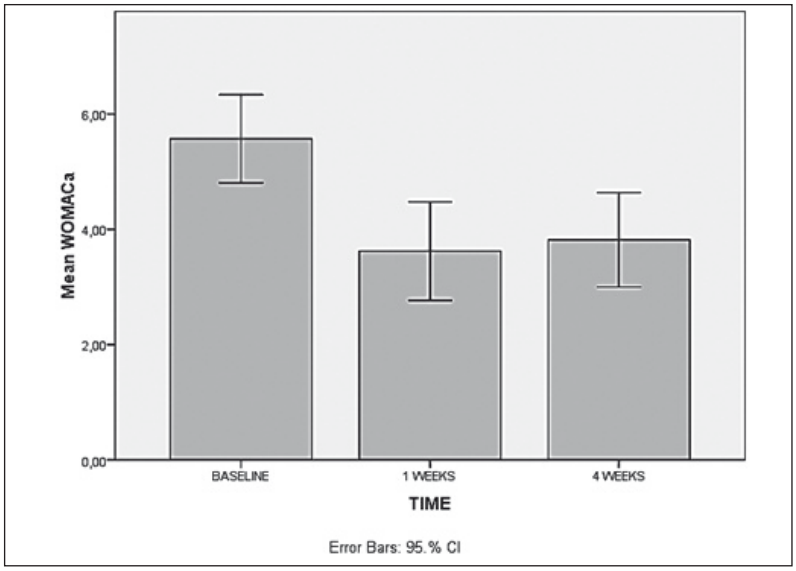

Figure 3. Mean change of WOMAC pain score over time.

ues are in accordance with Tashjian et al.[24] that estimated the MCID values of VAS as satisfactory status of health of patients after treatment.

The present study did not find any significant improvement in stiffness and physical function assessed through WOMAC scale. However, according to Likert scale, the 81.25% of the sample reported at the end of treatment a "very much improved" and "much improved".

Corticosteroids have both anti-inflammatory and immunosuppressive effects, acting directly on nuclear steroid receptors and interrupting the inflammatory and immune cascade at several levels. Moreover, they reduce vascular permeability and inhibit accumulation of inflammatory cells, phagocytosis, production of neutrophil superoxide, metalloprotease, and metalloprotease activator, and prevent the synthesis and secretion of several inflammatory mediators such as prostaglandin and leukotrienes[25, 26]. Therefore, the clinical effects of these actions will be decreasing in erythema, swelling, heat, and tenderness of the inflamed joints[25].

There are many factors that affect the efficacy of intra articular corticosteroid injection in knee OA[27, 28]. Indeed, long term treatment with IA corticosteroid injection could promote joint destruction and tissue atrophy [29], so we aimed to evaluate the relief of pain and the improvement of knee function after only one perimeniscal corticosteroid ultrasound guided injection in patients with stages II-III (K-L scale) knee OA[4].

In accordance with our results, Folman et al.[30], compared the effects of intra-articular and peri-articular injections of methylprednisolone acetate (80 mg) in patients with knee osteoarthritis until three months follow-up, finding an immediate and considerable relief of pain in both groups, even if the greatest relief was reported by the peri-articular group. The Authors hypothesized that peri-articular corticosteroid infiltrations could minimize potential complications related to the penetration of corticosteroid into the joint space and could reduce possible future injury related to the vitality of the cartilage tissue.

Moreover, recently, Ertürk et al.[31], in a prospective single-blinded randomized trial evaluated the clinical effect of intraarticular hyaluronic acid injections alone compared with intraarticular hyaluronic acid injections combined with a single local injection of periarticular corticosteroid-lidocaine in patients with symptomatic knee OA. They found an earlier pain relief in patients treated with the combined injection therapy, suggesting this method as an alternative modality to treat pain in knee OA.

The present study has several important limitations. The main limitation is the small number of patients and a lack of long term follow-up. The absence of a placebo group, which does not allow ruling out the possibility that the improvements detected were due to a placebo effect. Finally, only patients with moderate knee OA were included, and then, results cannot be extended to patients with more severe grade of OA. A larger scale investigation of MME involving the general population is needed.

According to our results ultrasound guided injection of 0.5 cc of methylprednisolone acetate in perimeniscal side of the medial aspect of the knee, is effective in pain relief in patients with anterior horn medial meniscus protrusion associated with medial collateral ligament displacement. Corticosteroid perimeniscal ultrasound guided injection can be considered as an adjunct to core treatment for the relief of moderate to severe pain in people with OA.

Therefore, if the target tissue is not joint cartilage, intra-articular injection of steroid solution is not essential and the periarticular injection could relieve the pain reducing the risk involved by penetration in the joint space.

Ethic

The Authors declare that this research was conducted following basic ethical aspects and international standards as required by the journal and recently update in[32].

Conflict of interests

We are able to declare that there are no financial or other relationships that might lead to a conflict of interests and that no part of this work has been previously published.

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