Low-dose Spironolactone: Treatment for Osteoarthritis-related Knee Effusion. A Prospective Clinical and Sonographic-based Study

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ABSTRACT. ***Objective.*** To evaluate the effectiveness of spironolactone as a treatment for osteoarthritis (OA)-related knee effusion in comparison to ibuprofen, cold compresses, and placebo.

Methods. This study was carried out on 200 patients, aged 40 years or older, attending the outpatient clinic of the Rheumatology Department of Sohag University Hospital with unilateral knee effusion related to OA based on clinical examination, musculoskeletal ultrasonography (US), and synovial fluid analysis. In group 1, 50 patients received spironolactone 25 mg daily for 2 weeks; in group 2, 50 patients took ibuprofen 1200 mg daily for 2 weeks; in group 3, 50 patients used cold compresses 2 times daily for 2 weeks; and in group 4, 50 patients received placebo for the same duration. Fluid > 4 mm was considered as effusion. Decrease in fluid to reach below 4-mm thickness was considered complete improvement, and any decrease that did not reach below 4 mm thickness was considered partial improvement.

Results. The mean age of the participants was 51.2 ± 8.1 years. The mean duration of effusion was 16.5 ± 3.6 days. In group 1, 66% had complete improvement, 20% partial improvement, and 14% no response. In group 2, 24% had complete improvement, 12% partial improvement, and 64% no response. In group 3, 28% had complete improvement, 14% partial improvement, and 58% no response. In group 4, only 6% had complete improvement, 10% partial improvement, and 84% no response.

Conclusion. Low-dose spironolactone is a safe and effective medical treatment for OA-related knee effusion. (First Release April 1 2016; J Rheumatol 2016;43:1114–20; doi:10.3899/jrheum.151200)

Key Indexing Terms:
KNEE EFFUSION
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Osteoarthritis (OA) is a group of mechanical disorders leading to joint degeneration, including articular cartilage and subchondral bone. Associated symptoms can be joint pain, tenderness, stiffness, and effusion. A variety of etiologic causes are known, of which hereditary, developmental, metabolic, and mechanical traits may initiate processes leading to cartilage loss[1]. OA is the most common form of arthritis affecting the elderly population and a main cause of disability. Incidence and prevalence of knee OA is rising by increasing age of the general population and increasing obesity[2]. OA affects about 44% of people older than 80 years of age[3]. The overall prevalence of knee OA worldwide increases to 37.4% in people aged 60 years or older[4].

The 2005 European League Against Rheumatism report on the use of musculoskeletal ultrasound (US) in painful knee OA found that the percentage of effusion among patients with knee pain was around 44%, either alone (29.5%) or associated with synovitis (14.2%)[5]. Moreover, the prevalence of effusion among patients with knee pain during activity was 79%, and it was the most common US finding among these patients[6].

Hill, *et al* found that painful osteoarthritic knee effusion had a prevalence of 55% and painless osteoarthritic knee effusion had a prevalence of 16%[7].

US signs of OA according to frequency are effusion, followed by synovial hypertrophy, cartilage variables, vascularity, Baker's cyst, osteophytes, tendon and ligament abnormalities (hypoechogenicity, tendon thickening), meniscal changes, bursitis, erosions, and panniculitis[8]. US is more sensitive than conventional radiography in the detection of osteophytes and joint space narrowing. Further, it is able to detect effusion and synovitis better than clinical evaluation[9].

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Evaluation of knee effusion by US depends on the examination of 3 recesses: suprapatellar, parapatellar lateral, and parapatellar medial. As fluid is displaceable, care should be taken to avoid pressure with the probe. The knee should be flexed 30° with quadriceps contraction. Fluid can be differentiated from synovial proliferation by compressibility and lack of Power Doppler activity[10]. Treatment of knee effusion includes rest, cold compresses, elevation, nonsteroidal anti-inflammatory drugs (NSAID), and aspiration[11]. Aspiration is an invasive maneuver; therefore, many patients refuse it. However, it provides temporary relief of symptoms and also the possibility of a microscopic evaluation of the synovial fluid (SF) to establish the diagnosis. Knee effusion has a high rate of recurrence. Longstanding benefits of aspiration are not yet confirmed by a randomized controlled study[12].

Spironolactone is a specific pharmacologic antagonist of aldosterone, acting primarily through competitive binding of receptors at the aldosterone-dependent sodium-potassium exchange site in the distal convoluted renal tubule. Spironolactone causes increased amounts of sodium and water to be excreted while potassium is retained; it has a mild antihypertensive effect and can be used in normotensive persons. In a previous study, it was used in a dose of 25 mg per day for 4 weeks without any effect on the blood pressure[13].

Spironolactone is known to have no effect on uric acid metabolism except in some reported cases with chronic renal disease[14].

Spironolactone has been used before in the treatment of ascites in liver cirrhosis and pleural effusion attributable to hepatic cause; nevertheless, there are not enough data about its use in the treatment of knee effusion[15,16].

MATERIALS AND METHODS

Initially, we included 327 participants with knee effusion and OA based on disease history. According to clinical, sonographic, and SF examination, we found that 238 of them fulfilled the inclusion criteria. Twelve of them refused to be included in our study, resulting in a remaining 226 cases. Two hundred of these patients were enrolled in our study. They were subjected to complete history taking (onset, course, and duration of the effusion related to OA, symptoms of infection, or history of trauma, to exclude other causes of knee swelling), clinical examination, SF analysis, and US examination of the knee.

In all of the included patients, the diagnosis of OA was made according to the American College of Rheumatology clinical criteria[17]. Other inclusion criteria were age above 40 years, unilateral knee effusion ≥ 4-mm thickness by US or detected by 1 or more clinical methods, normal creatinine clearance, normal serum sodium and potassium levels, and duration of effusion < 3 weeks. Duration was determined by the subject's report of their history.

Exclusion criteria included patients with causes other than OA of effusion according to synovial and US examination, patients with a recent history of trauma to the examined knee, and inflammatory SF.

Clinical examination was done on the knee to evaluate effusion as follows: inspection, palpation that included the patellar tab, ballottement, and bulge sign[6].

Visual analog scale (VAS) for pain was applied to the study participant at time 0 (baseline), after 2 weeks, and after 4 weeks. The VAS was graded from 0 to 10. Grade 0 expresses no pain and 10 means the worst possible pain[18]. SF analysis was completed for all study participants. All enrolled patients had noninflammatory SF[19] with white blood cell count < 500/mm^3. Only 2 ml was aspirated to avoid changing effusion condition. SF examination was postponed after US examination to avoid altering fluid thickness.

US was applied by the same examiner to avoid interobserver bias. The US machine was a General Electric with an 8–12 MHz linear probe. US examination was completed before knee aspiration. Knee examination was executed in the longitudinal view for the examination of the midline suprapatellar recess, as well as the medial and lateral parapatellar recesses in 30° flexion. The largest of the 3 readings was considered. Fluid was differentiated from synovial hypertrophy by compressibility according to the OMERACT (Outcome Measures in Rheumatology Clinical Trials) guidelines[20]. Fluid ≥ 4-mm thickness (sagittal measurement) in any of the 3 recesses was considered effusion[5]. US examination was completed in all patients before study inclusion, after 2 weeks, and also after 4 weeks for the examination of partial and complete improvement. Any decrease of effusion in comparison with initial measurement, but thickness still at 4 mm or more, was considered partial improvement. If the thickness reached < 4 mm, it was considered complete improvement. If there was no reduction or if there was even an increase in the maximum measurement, it was considered no response. After 4 weeks, recurrence was considered if effusion fluid was ≥ 4 mm in previous completely improved cases or more than the previous measurement in partially improved cases.

For the diagnosis of OA by US, femoral and tibial osteophytes were assessed in the medial and lateral compartments using medial and lateral longitudinal scan positions, respectively. Osteophytes were defined as cortex protrusion identified in 2 views[21].

Knee cartilage was measured by US in the 90° knee flexion position with transverse view in the intercondylar region. A thickness < 2.7 mm for women and 3.5 mm for men was considered OA[22].

Diagnosis of OA and effusion was based on clinical or US examination. The followup examinations of effusion were only done by US.

Patients were divided into 4 groups using a simple randomization method. We numbered the patients from 1 to 200 by asking each patient to select a numbered paper from a box. Then we grouped the patients numbered 1, 5, 9, and 13 and so on as group 1; 2, 6, 10, and 14 as group 2; 3, 7, 11, and 15 as group 3; and 4, 8, 12, and 16 as group 4. Only the pharmacologist was aware of this randomization method. In group 1, 50 patients received spironolactone 25 mg (Pfizer) daily for 2 weeks. Group 2 consisted of 50 patients receiving ibuprofen 400 mg (Abbott) 3 times daily for 2 weeks. In group 3, 50 patients used cold compresses 2 times daily for 10 min each time for 2 weeks. Group 4 consisted of 50 patients who received placebo (starch tablets) once daily for the same duration of time.

Creatinine levels were examined for all study participants and levels between 0.8–1.3 mg/dl for men and 0.6–1.1 mg/dl for women were considered as normal[23]. Potassium levels were examined for all study participants and a level between 3.5–5.1 meq/l was accepted[24]. Sodium levels were also examined and a value between 135–145 meq/l was normal[24]. Both sodium and potassium levels were measured daily for the first 3 days after inclusion in our study, and any disturbances in their levels led to the patients withdrawing from our study.

All patients receiving spironolactone were admitted to the hospital during the first 3 days and their blood pressure was measured every 6 h.

The study data were analyzed using the Statistical Package for Social Sciences, version 22 (IBM). Initially, simple frequencies, means, and SD were done. To compare means, the Student t test and ANOVA were used. Fluid thickness after 2 weeks and after 4 weeks was not normally distributed. The Mann-Whitney U test was therefore used to compare differences in medians between the groups. The chi-square test was used to detect significant changes when comparing categorical data. In all tests performed, a level of significance of $\alpha \leq 0.05$ was accepted.

Ethics committee approval number 13/7.2014 from the Sohag University's ethical committee was obtained before conducting this study. All the patients enrolled in this study were informed about the aim of the study, and a detailed explanation of the study steps was presented to them. A written consent was signed by all of the study participants.

Placebo and spironolactone were both of the same color and of similar size, but ibuprofen was different in color. Each patient did not know the characteristics of the drug given since patients received their treatment in a dark bottle with no name or label. Each group of patients received treatment separately. The rheumatologists were blinded and only the pharmacist was aware of the study groups. Groups 1, 2, and 4 were blinded to the type of treatment, but group 3 patients could not be blinded because of the different design of treatment given.

RESULTS

The mean age of the participants was 52.2 ± 8.1 years (range 40–76 yrs). The ratio of men to women was 3:5. The mean duration of effusion was 16.22 ± 3.1 days (range 10–21 days). There were no significant differences between the 4 groups in regards to age, sex, and duration of effusion (Table 1). None of the study participants had peripheral edema.

We found a statistically significant difference between the 4 groups in regards to the improvement of effusion, especially in the spironolactone group. This was detected by 2 measurements. The first measurement was the mean fluid thickness in the 4 groups before treatment and 2 and 4 weeks after treatment, taking into consideration that US examinations were completed after 4 weeks only for those who presented partial or complete improvement after 2 weeks. The mean fluid thickness in group 1 showed the greatest reduction out of the 4 groups, and this improvement was maintained after 4 weeks posttreatment (Table 2A, Table 2B).

The second measurement considered the number of partially or completely improved cases in each of the 4 groups, and also the number of recurrences in the 4 groups. Using US after 2 weeks, we found that in group 1, 66% showed complete improvement, 20% partial improvement, and 14% no response. In group 2, 24% showed complete improvement, 12% partial improvement, and 64% no response. In group 3, 28% showed complete improvement, 14% partial improvement, and 58% no response. In group 4, only 6% showed complete improvement, 10% partial improvement, and 84% had no improvement at all. The differences between the 4 groups were highly significant (Table 3).

The rate of effusion recurrence was 20.9% in group 1, 55.6% in group 2, 61.9% in group 3, and 87.5% in group 4. The differences were significant among the 4 groups (Table 3).

Age and sex showed no significant relationship with response to treatment in any of the 4 groups.

We found that VAS pain had a strong relation to fluid thickness because it decreased with the improvement of effusion and increased again among those patients who developed recurrence after 4 weeks. The overall VAS in the 4 groups was not significantly different before treatment, but was significantly lower among group 1 patients compared with the other 3 groups, and especially between group 1 and group 4. For the mean VAS in those with complete improvement, it was significantly lower than in those with partial or no improvement, and this was more significant in group 1 patients compared with group 4 patients ($p < 0.001$ and $p = 0.005$, respectively). However, the mean VAS of those with complete improvement among all of the 4 groups was nonsignificant (Table 4).

Further, weight showed significant correlation to fluid thickness at baseline before treatment. After 2 weeks, the mean weight of those who had complete improvement was significantly lower than those who showed partial or no improvement among all of the 200 cases included in our study. However, when we divided our cases into the 4 study groups, we found a nonsignificant relation between weight and improvement (Table 5).

There was a positive relationship between the degree of effusion by US and the association of no improvement, and also for the association of recurrence of effusion in the previously improved cases. The relationship was significant in all of the study groups.

We did 3 US measurements for each joint, including lateral, midline, and medial examinations. The maximum fluid thickness was found to be in the lateral recess in nearly 55%–60% of cases in all the study groups before treatment. This was reversed after 2 weeks of treatment in both groups 1 and 2, where the maximum fluid thickness was in the midline recess in 56% of group 1 and in 48% of group 2. This change was highly significant in group 1 and less significant in group 2. Groups 3 and 4 showed nonsignificant changes, with nearly no change at all in group 4. In the 4 groups, we found that patients with maximum measurements in the lateral aspect of the joint had the highest mean fluid thickness. However, the mean fluid thickness showed no

Table 1. Demographic data of the study groups. Values are n (%) or mean ± SD.

Variable	Group 1, Spironolactone	Group 2, NSAID	Group 3, Cold Compresses	Group 4, Placebo	Total	p
Age, yrs	51.9 ± 8.3	52.6 ± 7.8	51.9 ± 8.3	52.4 ± 8.1	52.2 ± 8.1	0.955
Sex						
Male	19 (38)	18 (36)	18 (36)	20 (40)	75 (37.5)	0.972
Female	31 (62)	32 (64)	32 (64)	30 (60)	125 (62.5)	
Duration of effusion, days	15.64 ± 2.78	16.96 ± 3.27	15.88 ± 3.35	16.40 ± 2.86	16.22 ± 3.1	0.146
Weight, kg	83.64 ± 10.41	85.34 ± 12.85	83.24 ± 10.46	85.78 ± 10.12	84.50 ± 10.98	0.589

NSAID: nonsteroidal antiinflammatory drugs.

Table 2A. Fluid thickness by US before and after treatment. Values are mean ± SD.

Mean Fluid Thickness, mm	Group 1, Spironolactone	Group 2, NSAID	Group 3, Cold Compresses	Group 4, Placebo	Total	p
Before treatment	7.5 ± 2.3	7.5 ± 2.6	7.4 ± 1.9	7.9 ± 1.9	7.6 ± 2.2	0.662
2 weeks after treatment	3.7 ± 3.3	6.3 ± 3.2	5.9 ± 2.7	7.3 ± 2.3	5.8 ± 3.2	< 0.001
4 weeks after treatment	2.4 ± 2.6	5.1 ± 4.1	5.0 ± 2.8	6.9 ± 3.2	4.0 ± 3.4	< 0.001

US: ultrasonography; NSAID: nonsteroidal antiinflammatory drugs.

Table 2B. Mann-Whitney U test between the 4 groups after 2 and 4 weeks.

Comparison	Fluid Thickness after 2 Weeks	Fluid Thickness after 4 Weeks
Spironolactone vs NSAID	< 0.001	0.020
Spironolactone vs cold compresses	< 0.001	0.001
Spironolactone vs placebo	< 0.001	< 0.001
NSAID vs cold compresses	0.647	0.667
NSAID vs placebo	0.130	0.244
Cold compresses vs placebo	0.038	0.111

NSAID: nonsteroidal antiinflammatory drugs.

significant differences in regards to the site of the maximum fluid thickness.

Eight percent of patients in group 1 had a lowering of their blood pressure, but they did not exceed the normal limit. Three patients of the same group were excluded from our study because of disturbances in their sodium and potassium levels. These 3 cases were replaced by other new cases to maintain a total of 50 cases in each group.

Figure 1 presents the corresponding US pictures of the same patient at baseline and after 2 and 4 weeks of spironolactone therapy.

Table 3. Improvement and recurrence of effusion among the study groups. Values are n (%).

US Measurement	Group 1, Spironolactone	Group 2, NSAID	Group 3, Cold Compresses	Group 4, Placebo	Total	p
After 2 weeks						
Complete cure of effusion	33 (66)	12 (24)	14 (28)	3 (6)	62 (31)	< 0.001
Partial improvement of effusion	10 (20)	6 (12)	7 (14)	5 (10)	28 (14)	
No improvement of effusion	7 (14)	32 (64)	29 (58)	42 (84)	110 (55)	
After 4 weeks						
No recurrence of effusion	34 (79.1)	8 (44.4)	8 (38.1)	1 (12.5)	51 (56.7)	< 0.001
Recurrence of effusion	9 (20.9)	10 (55.6)	13 (61.9)	7 (87.5)	39 (43.3)	

US: ultrasonography; NSAID: nonsteroidal antiinflammatory drugs.

Table 4. Relationship between VAS pain and improvement in effusion among the study groups. Values are mean ± SD.

Mean VAS	Group 1, Spironolactone	Group 2, NSAID	Group 3, Cold Compresses	Group 4, Placebo	Total	p*	p**
Before treatment	5.42 ± 2.05	4.64 ± 2.76	5.16 ± 2.21	5.14 ± 2.05	5.09 ± 2.29	0.386	0.496
After 2 weeks							
All cases	2.66 ± 1.94	3.70 ± 2.17	4.00 ± 2.22	4.50 ± 1.61	3.72 ± 2.10	< 0.001	< 0.001
Complete cure of effusion	1.88 ± 1.56	1.50 ± 1.45	1.64 ± 1.55	2.00 ± 1.73	1.76 ± 1.51	0.875	0.902
Partial improvement of effusion	3.80 ± 2.15	3.17 ± 1.70	4.43 ± 1.81	4.80 ± 1.64	4.00 ± 1.81	0.447	0.380
No improvement of effusion	4.71 ± 0.76	4.62 ± 1.91	5.03 ± 1.70	4.64 ± 1.48	4.75 ± 1.63	0.746	0.899
p	< 0.001	< 0.001	< 0.001	0.005	< 0.001	—	—
After 4 weeks							
All cases	1.06 ± 1.67	2.44 ± 2.28	2.53 ± 2.01	4.00 ± 1.85	1.99 ± 2.10	< 0.001	< 0.001
No recurrence of effusion	0.22 ± 0.51	0.17 ± 0.41	0.17 ± 0.41	0	0.20 ± 0.46	0.962	0.670
Recurrence of effusion	3.56 ± 1.42	3.80 ± 1.75	3.62 ± 1.39	4.57 ± 0.98	3.82 ± 1.43	0.489	0.130
p	< 0.001	< 0.001	< 0.001	0.017	< 0.001	—	—

* ANOVA was used to compare means among the 4 groups. ** Student t test was used to compare means between groups 1 and 4 only. VAS: visual analog scale; NSAID: nonsteroidal antiinflammatory drugs.

Table 5. Relationship between body weight and improvement in effusion among the study groups. Values are mean ± SD unless otherwise specified.

Body Weight, kg	Group 1, Spironolactone	Group 2, NSAID	Group 3, Cold Compresses	Group 4, Placebo	Total	p
At baseline						
Mean weight, kg	83.64 ± 10.41	83.34 ± 12.85	83.24 ± 10.46	85.78 ± 10.12	84.50 ± 10.98	0.589
Pearson correlation with fluid thickness	0.309, p = 0.029	0.342, p = 0.015	0.314, p = 0.026	0.364, p = 0.009	0.335, p < 0.001	
After 2 weeks						
No improvement of effusion	86.14 ± 4.95	87.69 ± 11.88	83.03 ± 10.68	85.86 ± 9.94	85.66 ± 10.54	0.394
Partial improvement of effusion	86.40 ± 9.61	86.17 ± 10.80	82.86 ± 10.68	91.80 ± 3.96	86.43 ± 9.42	0.472
Complete cure of effusion	82.27 ± 11.39	78.67 ± 14.81	83.86 ± 10.65	74.67 ± 13.32	81.56 ± 11.96	0.516
p	0.441	0.114	0.967	0.065	0.037	—

NSAID: nonsteroidal antiinflammatory drugs.

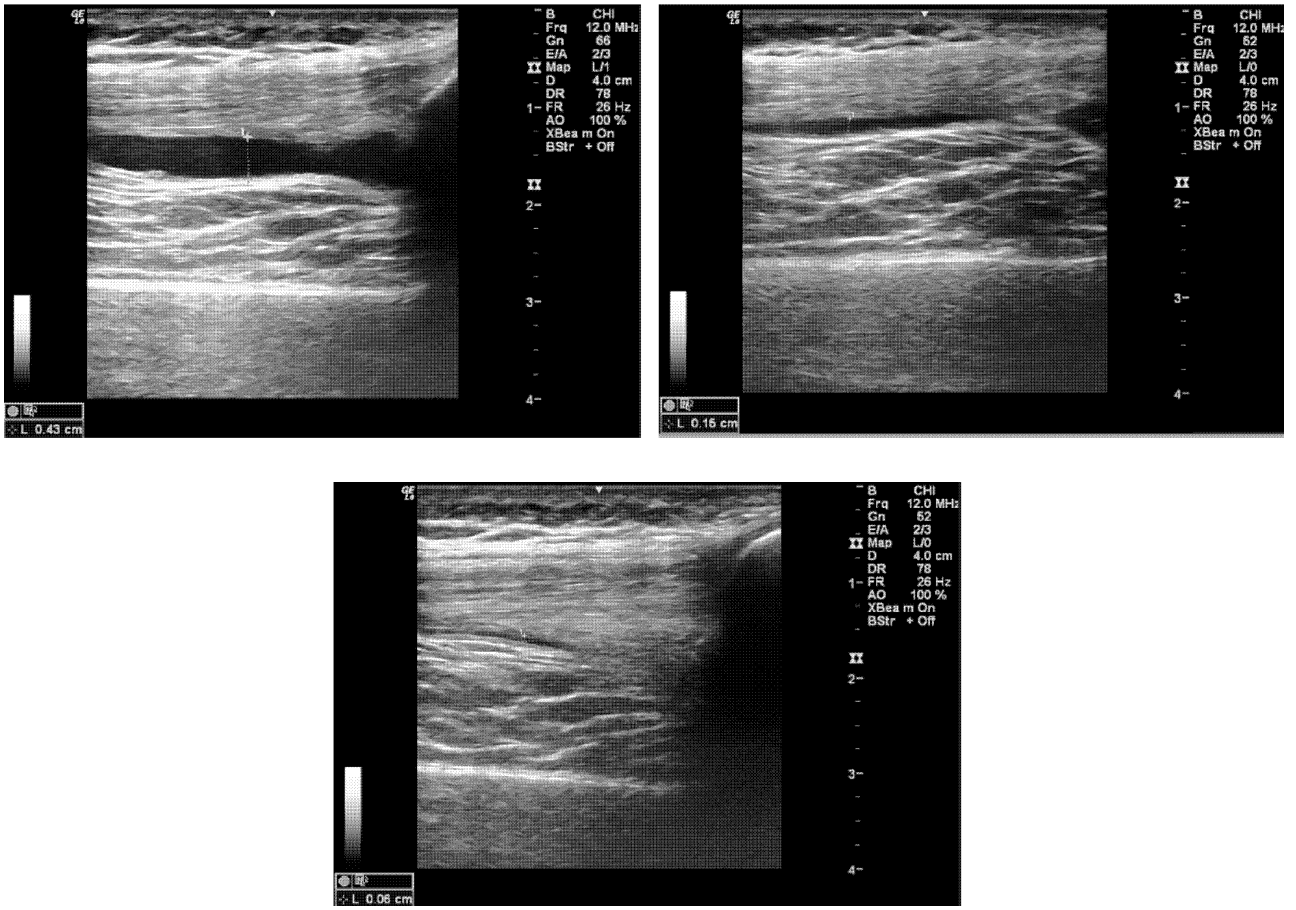

Figure 1. Maximum fluid thickness for the same patient at 0 time, 2 weeks, and 4 weeks. Top left panel: Fluid thickness at 0 time at the knee suprapatellar space, sagittal view, midline. Top right panel: Fluid thickness after 2 weeks of spironolactone treatment at the knee suprapatellar space, sagittal view, midline. Bottom panel: Fluid thickness after 4 weeks of the same patient treated with spironolactone at the knee suprapatellar space, sagittal view, midline.

DISCUSSION

Knee effusion is a common complication of OA and occurs in about 24% of patients with knee OA[2]. Aspiration is a commonly used method for the treatment of knee effusion, but it has the risk of recurrence and many patients refuse this invasive maneuver[12]. Cold compresses and NSAID are also commonly used; however, the results are not satisfactory[11].

US evaluation of knee effusion is more sensitive than clinical examination. US provides quantitative measurements of effusion thickness, and it can detect smaller amounts of effusion that are missed by clinical evaluation[25].

Spironolactone in low doses (50 mg or less) is already used in the treatment of hirsutism, polycystic ovary, acne, and resistant hypertension[26,27,28].

To our knowledge, ours is the first study to evaluate low-dose spironolactone in the treatment of knee effusion caused by OA.

In our present study, the spironolactone group presented the best results — in comparison with the other study groups — regarding reduction of fluid thickness and the rate of recurrence after treatment stop. Also, the spironolactone group showed the best VAS pain score compared with the other 3 groups, especially among those whose effusion shrank. Before treatment, VAS was comparable in the 4 groups with nonsignificant differences, but after 2 weeks of therapy, there was a highly significant difference among the 4 groups, with the lowest VAS seen among the spironolactone group, followed by NSAID, then cold compresses, and last the placebo. This difference in VAS is mostly related to the improvement in effusion, as evidenced by 2 findings: first, when we divided the patients according to fluid thickness, the differences of VAS among the 4 study groups were not significant; and second, when we compared VAS within each of the study groups separately according to fluid thickness, we found that VAS was significantly lower among those with cured effusion, followed by those with partial improvement, and then those with no improvement.

There was no relationship between age and sex and therapeutic effect of spironolactone on knee effusion. This result is comparable with the results from another study that used spironolactone in the treatment of resistant hypertension, where they found no relation between age and sex on the antihypertensive effect of spironolactone[29].

Maximum fluid thickness was found in the lateral measurement before receiving treatment, and then it became highest in the midline view 2 weeks after treatment. Mandl, *et al* found the highest fluid thickness at the midline followed by the medial and finally the lateral recess at 30° knee flexion. However, OA was not the only cause of knee effusion in that study[30]. In another study, fluid thickness was the highest at the lateral followed by the medial and then the midline region. In the study, US measurements were done at the full extension position[31]. It can be said that the examination of the 3 recesses is fundamental to detect maximum fluid thickness, because the position of maximum fluid thickness varies depending on the degree of effusion.

In our present study, it was found that there is a significant relation between severity of pain and fluid thickness, and subsequently between fluid reduction and pain improvement. These results emphasized previous results from Hill, *et al*, who found that painful osteoarthritic knee effusion had a prevalence of 55% and painless osteoarthritic knee effusion had a prevalence of 16%[7].

It is well known that the administration of NSAID can reduce the diuretic, natriuretic, and antihypertensive effect of spironolactone. Combination of NSAID with spironolactone has been associated with severe hyperkalemia. Therefore, with concomitant use of spironolactone and NSAID, close observation should be maintained[32]. In our study, we separated spironolactone from NSAID.

Crystal deposition is a common association with OA. The crystals include calcium pyrophosphate dehydrate, basic calcium phosphate, and monosodium urate crystals. Spironolactone has no effect on uric acid metabolism and there is no known contraindication to use spironolactone with other types of crystal-induced arthritis[14,33].

Spironolactone can be a real alternative treatment for knee effusion related to OA, but its effect has to be proven in larger cohorts. Further, spironolactone is relatively cheap and does not have many side effects when used in small doses and for short-time duration. Its oral administration makes it convenient for many patients who refuse knee aspiration and fear injection. Antiandrogenic and antihypertensive effects of spironolactone appear with doses > 100 mg per day[34]. Spironolactone is being used safely in children to treat congestive heart failure, ascites, edema, and nephrotic syndrome[35].

Under careful monitoring, low-dose spironolactone is a safe and effective treatment for knee effusion related to OA.

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