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Visually-guided irrigation in patients with early knee osteoarthritis: a multicenter randomized, controlled trial

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Summary

Objective: To determine if visually-guided arthroscopic irrigation is an effective therapeutic intervention in patients with early knee osteoarthritis.

Design: Ninety patients with knee osteoarthritis were randomized in a double-blind fashion to receive either arthroscopic irrigation with 3000 ml of saline (treatment group) or the minimal amount of irrigation (250 ml) required to perform arthroscopy (placebo group). The primary outcome variable was aggregate WOMAC score.

Results: The study did not demonstrate an effect of irrigation on arthritis severity as measured by aggregate WOMAC scores, the primary outcome variable; the mean change in aggregate WOMAC score at 12 months was 15.5 (95% CI 7.7, 23.4) for the full irrigation group compared to 8.9 (95% CI 4.9, 13.0) for the minimal irrigation group (P=0.10). Full irrigation did have a statistically significant effect on patients' self-reported pain as measured by the WOMAC pain subscale and by a visual analog scale (VAS) (the secondary outcome variables). Mean change in WOMAC pain scores decreased by 4.2 (95% CI −0.9, 9.4) for the full irrigation group compared with a mean decrease of 2.3 (95% CI −0.1, 4.7) in the minimal irrigation group (P=0.04). Mean VAS pain scores decreased by 1.47 (95% CI −1.2, 4.1) in the full irrigation group compared to a mean decrease of 0.12 (95% CI 0.0, 0.3) in the minimal irrigation group (P=0.02). A hypothesis-generating post-hoc analysis of the effect of positively birefrigent intraarticular crystals showed that patients with and without intraarticular crystals had statistically significant improvements in pain assessments and aggregate WOMAC scores at 12 months; patients with crystals had statistically greater improvements in pain.

Conclusions: Visually-guided arthroscopic irrigation may be a useful therapeutic option for relief of pain in a subset of patients with knee OA, particularly in those who have occult intraarticular crystals. © 2000 OsteoArthritis Research Society International

Key words: Arthroscopy, Irrigation, Knee osteoarthritis.

Introduction

Joint irrigation with saline has been used therapeutically for patients with knee osteoarthritis (OA), with anecdotal reports of pain relief attributed to the removal of debris from the joint space.[1] Joint irrigation with saline is an integral part of all arthroscopies; it is necessary to distend the joint for adequate exploration and to remove blood and debris that cloud the inspection of intraarticular structures.[2] Indirect evidence supports the concept that irrigation relieves pain in knee OA by removing cartilaginous particles. Cartilage fragments have been demonstrated in synovial fluid[3,4] and the synovium[5] of osteoarthritic knees. Further supporting data derive from *in vivo* experimental osteoarthritis in dogs[6] and rabbits[7] injected intraarticularly with autologous cartilage, and from *in vitro* demonstration of protease release from cultured monocytes and synovial cells challenged with cartilage fragments.[8] No studies, however, have adequately addressed the hypothesis that irrigation is an effective treatment modality in OA.

Our study prospectively compares large volume saline (3000 ml) irrigation and minimal saline (250 ml) irrigation in terms of clinical and functional outcome in patients with early knee OA. The study was conducted in early disease (defined by symptom duration of 5 years or less and normal or minimally abnormal radiographs) because medical or surgical intervention may be most effective in modifying disease severity and progression of articular damage in early disease.[9,10] In order to ensure that both treatment groups had similar cartilage damage and synovial inflammation at entry and to ensure that all compartments of the joint were irrigated, arthroscopy was utilized rather than percutaneous irrigation. Arthroscopic evaluation was felt to be ethically justified and important in order to ensure adequate irrigation of all compartments of the joint and to identify morphological characteristics that might be predictive of outcome.

Methods

This study was a multicenter, randomized, double-blind controlled trial. After obtaining written informed consent,

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patients were randomized at the baseline visit to receive either large (3000 ml) or minimal (250 ml) volume irrigation prior to undergoing arthroscopy. Data were collected at baseline (prior to arthroscopy), and at 1-, 3-, and 12-month follow-up visits. Patients were assigned to treatment groups by simple randomization using a random number generator. Articular aspirates were attempted in patients before performing arthroscopy and polarizing microscopy was performed when synovial fluid was obtained.

PATIENT SELECTION

Patients were enrolled at the University of Alabama at Birmingham (UAB) (N=39), the University of California at Los Angeles (UCLA) (N=35), Indiana University (IU) (N=12) and the University of Michigan (UM) (N=4). Inclusion criteria were age greater than 40 years, knee pain for 10 years or less, unsatisfactory pain relief as assessed by both the patient and their primary physician despite at least 6 weeks of supervised physical therapy (isometric exercises and joint protection techniques) and two or more different non-steroidal antiinflammatory drugs (NSAIDs) and/or analgesics given for 3 or more weeks each. If the patient was unable to tolerate NSAIDs and/or analgesics, then the criterion for failure to respond to these agents was waived. If the patient was unable to undergo supervised physical therapy because of third-party payor limitations, then the criterion for failure to respond to these modalities was waived. Patients had to demonstrate a willingness to attend follow-up visits and were required to give written informed consent; the protocol was approved by the institutional review boards at each of the participating centers. Subjects were given the option of conventional therapy including percutaneous irrigation as an alternative to participation in this study. All patients were required to have normal or minimally abnormal radiographs (Kellgren/Lawrence grades 0–2).[11] All patients were required to fulfill American College of Rheumatology (ACR) criteria for the classification of knee OA using either clinical and radiographic, traditional clinical or clinical and laboratory methods or classification tree clinical or clinical and laboratory methods.[12] Eighty-five patients fulfilled traditional clinical and radiographic criteria, 77 fulfilled traditional clinical criteria and 72 fulfilled traditional clinical and laboratory criteria. Sixty-seven patients fulfilled tree clinical classification criteria and 48 fulfilled the tree clinical and laboratory criteria. There were nine patients with normal radiographs; eight of these patients fulfilled traditional clinical criteria, seven fulfilled traditional clinical and laboratory criteria, seven fulfilled tree clinical criteria and five fulfilled tree clinical and laboratory criteria.

Exclusion criteria included: back/hip or ankle/foot disease of significant severity to confuse the clinical assessment of the patient's knee pain; intraarticular corticosteroid injection into the affected knee within 1 month prior to enrollment; significantly abnormal radiographs (Kellgren/Lawrence grades 3–4); body mass index greater than 35 kg/m^2; sensitivity to amide anesthetic agents; any serious medical illness that would, in the opinion of the investigators, place the patient at increased risk should the patient participate in the study; and a recent history of substance abuse.

TREATMENT

Patients were randomized either to irrigation with 3000 ml of normal saline (treatment group) or to the minimum (250 ml) amount of irrigation (control group) that is necessary to perform a routine diagnostic arthroscopy. The use of a minimal irrigation group rather than a sham arthroscopy group was felt to be a more prudent choice as a control group as there are significant ethical limitations involved in the utilization of a sham arthroscopy control group in which subjects undergo incisions and anesthesia without a diagnostic or therapeutic procedure; this design also allowed for control of pathological disease between the two groups.

All patients underwent small-caliber knee arthroscopy using local anesthesia. Patients at UCLA and IU underwent arthroscopy with a Dyonics (Andover, MA, U.S.A.) 2.7 mm arthroscope with glass optics and a 30 degree field of view; procedures at UAB and UM utilized Medical Dynamics (Englewood, CO, U.S.A.) 1.7 mm arthroscopes with fiberoptics and a zero degree field of view. Patients were blinded to their treatment group and were evaluated by blinded assessors before arthroscopy and at follow-up visits. The blinded assessors were rheumatologists who did not participate in the arthroscopic irrigation procedures.

STUDY MEASUREMENTS

Baseline measurements included: demographics (age, gender, race), clinical signs (swelling and tenderness on four-point ordinate scales determined by the blinded rheumatologist-assessors; range of motion), radiographic score (using assessments determined by a radiologist blinded to treatment group using a scale that characterized the patellofemoral, lateral and medial tibiofemoral compartments each on a five-point ordinate scale with a maximum score of 15), patient assessment of pain using a 10 cm visual analog scale), intraarticular cartilage damage and inflammation scores by direct arthroscopic inspection using the validated ACR/Knee Arthroscopy Osteoarthritis Scale (ACR/KAOS) (13) with scores determined by a blinded rheumatologist trained in arthroscopy who was not involved in the arthroscopic irrigation procedures using blind-coded videotapes of procedures (maximum cartilage damage score=280 and maximum inflammation score=60), and assessment of pain, stiffness and functional activity using the Likert 3.0 scale version of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), a validated self-administered health status instrument for patients with OA of the hip or knee.[14] Aggregate WOMAC and individual WOMAC subscale scores of pain, stiffness, and disability were assessed. The aggregate WOMAC score used was the summation of the pain, stiffness and function WOMAC subscores.

The primary outcome variable was the aggregate WOMAC score at 12 months. Secondary outcome measurements were patient assessment of pain by visual analog scale (patient VAS), and assessment of knee pain, stiffness and functional activity using subscales of the WOMAC instrument.

STATISTICAL ANALYSIS

Summary statistics describing the baseline characteristics of the two treatment groups were examined to determine whether randomization resulted in comparable groups. Summary statistics on the primary and secondary outcomes were computed for 1-, 3- and 12-month follow-up visits.

Table I
Baseline patient characteristics

Characteristic	Minimal irrigation	Full irrigation	*P*-value
No. of patients	49	41	
Mean age (years)	58.3 (range 40–85)	60.9 (range 41–88)	0.39
Gender:			
Female	26	22	
Male	23	19	
Race:			
Caucasian	40	32	0.59
Non-Caucasian	9	9	
Symptom duration (months)	34.4 (range 2–120)	30.0 (range 2–120)	0.99
Knee swelling*	0.45 (range 0–2)	0.78 (range 0–2)	0.01
Knee tenderness*	0.60 (range 0–2)	0.85 (range 0–2)	0.07
Radiographic score (total)†	4.44 (rang 0–12)	4.00 (range 0–10)	0.66
Cartilage damage score	37.8 (range 3–91.3)	44.8 (range 5–118.4)	0.25
Inflammation score	10.8 (range 0–25.8)	10.7 (range 0–36.8)	0.94
Patient assessment (VAS)	3.63 (range 0–9.2)	3.67 (range 0–7.9)	0.75
Aggregate WOMAC	40.67 (range 8–86)	41.09 (range 1–75)	0.64

*Physician ratings on a 4-point ordinal scale.
†Physician ratings on a 5-point ordinal scale for each compartment; the total score represents a summation of the scores for the three compartments.

Table II
Change (reduction) in aggregate WOMAC, subscores, and pain VAS from baseline to 12 months, by treatment group

	Minimal irrigation Mean (95% CI)	Full irrigation Mean (95% CI)	*P**
Aggregate WOMAC	8.9 (4.9, 13.0)	15.5 (7.7, 23.4)	0.10
WOMAC pain	2.3 (−0.1, 4.7)	4.2 (−0.9, 9.4)	0.04
WOMAC stiffness	0.7 (−0.5, 1.9)	1.2 (−1.6, 4.0)	0.22
WOMAC function	6.1 (2.8, 9.4)	9.9 (4.9, 13.0)	0.15
Patient pain (VAS)	0.12 (0, 0.3)	1.47 (−1.2, 4.1)	0.02

*Analysis of covariance with irrigation group as independent variable, baseline score and swelling as covariates.

The mean changes of aggregate WOMAC scores (the primary outcome variable) in the two groups were compared at 12 months. Hypothesis testing was conducted by analysis of covariance, controlling for significant covariates. Potential covariates tested were baseline aggregate WOMAC score, age, tenderness, symptom duration, radiographic score, intraarticular damage and inflammation. Only those covariates that significantly ($P<0.05$) affected change in aggregate WOMAC score were retained in the model. The secondary outcome variables, changes in the WOMAC subscales (pain, stiffness, function) and change in patient pain VAS at 12 months were similarly tested.

The significance criterion (α) was set at 0.05. With the planned sample size of 50 subjects in each group, there was 80% power to detect a treatment effect explaining 30% of the residual variance after controlling for baseline score and any other significant covariates.

Results

BASELINE PATIENT CHARACTERISTICS

Ninety patients were enrolled in the study. The simple randomization program resulted in 41 patients randomized to full volume irrigation and 49 patients to minimal irrigation.

Characteristics of the patients are shown in Table I. There were no significant baseline differences in mean age, gender, race, symptom duration, knee tenderness, radiographic score, total cartilage damage and inflammation scores, patient VAS, aggregate WOMAC scores or subscale scores for pain, stiffness and function. Patients in the full irrigation group had significantly more knee swelling at baseline than patients randomized in the minimal irrigation group. No crystals were detected in any patients in whom fluid was obtained from percutaneous aspiration prior to arthroscopy.

Primary endpoint: change in aggregate WOMAC scores

Outcomes in the two treatment groups are shown in Table II. Details on outcomes at intermediate observational points are illustrated in Fig. 1(a-e).

Both treatment groups showed significant improvement over time in aggregate WOMAC scores. Mean improvement in the full irrigation group was 15.5 (95% CI 7.7, 23.4) and 9.0 (95% CI 4.9, 13.0) in the minimal irrigation group. The effect of full irrigation was not statistically significant either alone ($P=0.13$) or when controlling for the significant covariates, baseline aggregate WOMAC scores and baseline swelling ($P=0.10$).

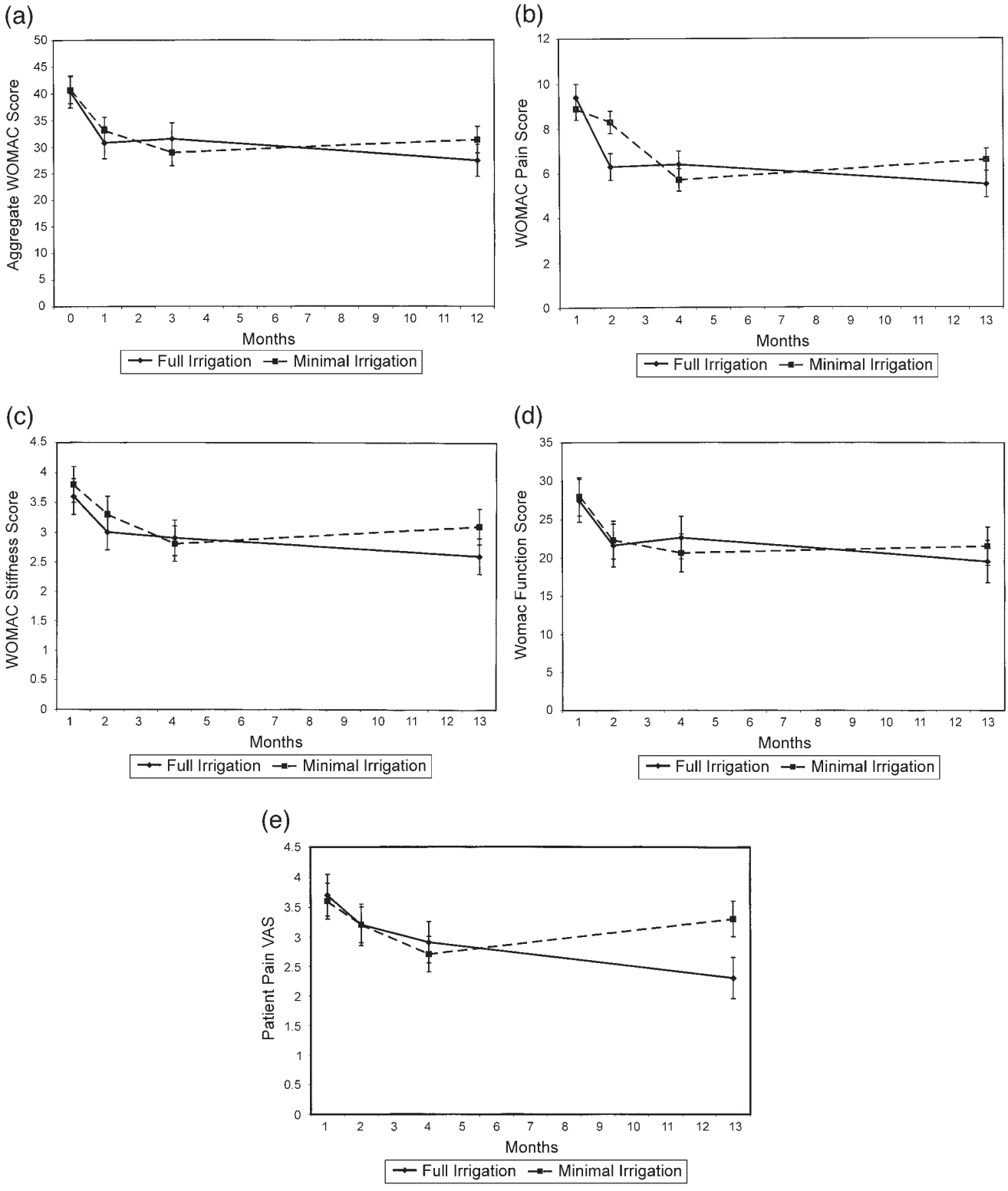

Fig. 1. (a) Aggregate WOMAC scores vs time in the treatment groups. Minimal irrigation utilizes 250 ml or less of saline. This is the minimal amount of fluid necessary for arthroscopic visualization. The treatment group received 3000 ml of saline irrigation. (b) WOMAC pain subscale scores vs time for each treatment group. Minimal irrigation utilizes 250 ml or less of saline whereas the treatment group received 3000 ml of saline irrigation. (c) WOMAC stiffness subscale scores vs time for each treatment group. Minimal irrigation utilizes 250 ml or less of saline whereas the treatment group received 3000 ml of saline irrigation. (d) WOMAC function subscale scores vs time for each treatment group. Minimal irrigation utilizes 250 ml or less of saline whereas the treatment group received 3000 ml of saline irrigation. (e) Patient pain visual analogue scale (VAS) vs time for each treatment group. Pain was rated by the subject on a 10-cm VAS.

Table III
Crystal substudy: outcomes by presence of crystals

	Patients without crystals Mean (95% CI) *N*=14	Patients with crystals Mean (95% CI) *N*=18
Baseline patient pain assessment by VAS	3.99 (3.03, 4.95)	4.11 (3.24, 4.98)
12-month patient pain assessment by VAS	2.68 (1.46, 3.87)	2.09 (1.13, 3.05)†
Baseline WOMAC pain	8.73 (6.62, 10.84)	9.56 (7.95, 11.17)
12-month WOMAC pain	6.00 (4.02, 7.98)	5.50 (3.88, 7.12)†
Baseline WOMAC stiffness	4.00 (2.95, 5.05)	3.25 (2.14, 4.36)
12-month WOMAC stiffness	3.90 (3.08, 4.72)	2.45 (1.57, 3.33)‡
Baseline WOMAC function	24.50 (15.34, 33.66)	28.63 (21.46, 35.80)
12-month WOMAC function	23.56 (15.13, 31.99)	15.72 (10.67, 20.80)‡
Baseline aggregate WOMAC	39.31 (28.12, 50.50)	41.44 (32.40, 50.47)
12-month aggregate WOMAC	32.67 (22.30, 43.04)	22.91 (15.57, 30.25)†

*Statistical improvement (P<0.05) in both groups without statistical differences in improvement between the two groups.
†Statistically significant (P<0.05) in both treatment groups and statistically significant (P<0.05) improvement in full irrigation group compared to minimal irrigation group.
‡Statistically significant (P<0.05) only in crystal group.

Secondary endpoints: change in WOMAC subscores and in pain VAS

Mean improvement in the WOMAC pain subscore was 4.2 (95% CI −0.9−9.4) in the full irrigation group and 2.3 (95% CI −0.1, 4.7) in the minimal irrigation group. The effect of full irrigation was of borderline statistical significance alone (P=0.05) and was statistically significant when controlling for the significant covariates, baseline WOMAC pain subscore and baseline swelling (P=0.04).

Mean improvement in the WOMAC stiffness subscore was 1.2 (95% CI −1.6, 4.0) in the full irrigation group and 0.7 (95% CI −0.5, 1.9) in the minimal irrigation group. The effect of full irrigation was not statistically significant alone (P=0.32) or when controlling for the significant covariates, baseline WOMAC pain subscore and baseline swelling (P=0.22).

Mean improvement in the WOMAC disability subscore was 9.9 (95% CI 3.9, 15.9) in the full irrigation group and 6.1 (95% CI 2.8, 9.4) in the minimal irrigation group. The effect of full irrigation was not statistically significant alone (P=0.23) or when controlling for the significant covariates, baseline WOMAC pain subscore and baseline swelling (P=0.15).

Mean improvement in the patient pain VAS score was 1.5 (95% CI −1.2, 4.1) in the full irrigation group and 0.1 (95% CI 0.0, 0.3) in the minimal irrigation group. The effect of full irrigation was statistically significant alone (P=0.04) and when controlling for the significant covariates, baseline VAS and baseline swelling (P=0.02).

CRYSTALS SUBSTUDY

There appeared to be a center effect at 12 months in that the UCLA cohort had statistically significant differences between treatment groups in aggregate WOMAC scores. There did not appear to be any baseline differences in this group of subjects to explain this center effect except for the notation on the ACR/KAOS of intraarticular crystals present in the suprapatellar bursa in 15 of the 35 subjects enrolled at that center. Consequently, we conducted a hypothesis-generating post-hoc analysis of the effect of crystals on outcome. This analysis was limited to patients at centers with equipment adequate to visualize macroscopic crystals, including glass optics with 30 degree field of view (UCLA, IU) and in whom adequate visualization was achieved. In the 47 arthroscopies performed at these two centers, there was adequate visualization in 32 of the procedures; in 18 of the 32 procedures, there was macroscopic calcified deposits in synovium and/or cartilage representing crystals as determined by a blinded assessor (RS) who viewed video recordings of the procedures. Polarized microscopy had been performed on the synovial fluid from 10 of these patients at the time of the arthroscopic procedures; all had evidence of positively birefrigent crystals. There were no significant differences between patients with and without crystals in baseline age, swelling, or patient VAS; the patients with crystals had significantly higher baseline inflammation scores.

Table III summarizes outcome for the patients in the crystal substudy. Both patients with and without crystals had statistically significant improvements in aggregate WOMAC scores, WOMAC pain subscale, and patient VAS over 12 months. However, patients with crystals had statistically significant greater improvement compared with patients without crystals for each of these outcome measurements. Interestingly, statistically significant improvements in WOMAC stiffness and function subscales were observed only for patients with crystals.

Discussion

EFFICACY OF FULL IRRIGATION

Attempts to study the effect of irrigation associated with arthroscopy dates to the 1940s with Watanabe's efforts at 'articular pumping',[15] in which saline was repeatedly injected, removed and reinstilled; 58 of 64 patients with knee OA undergoing this procedure had favorable results. The significance of the studies by Watanabe and subsequent investigators have been hampered by flaws in study design, including blinding of subjects and/or physician observers, insufficient control of baseline patient characteristics or the use of inadequate or non-validated outcome measurements.

Reports by Livesley *et al*.[16] and Ike *et al*.[2] support the concept that joint irrigation may be beneficial to patients with knee OA. Livesley[16] compared 45 knee OA patients who underwent arthroscopic irrigation using 2 l of saline without tissue resection with 42 knee OA patients assigned to physical therapy. Compared with patients receiving physical therapy, those in the arthroscopic irrigation group experienced modest but significant improvement in three different pain scores that were sustained over 12 months. Ike *et al*.[2] evaluated the efficacy of tidal knee irrigation (joint irrigation without direct visualization) in a multicenter single-blind, randomized prospective trial comparing irrigation and comprehensive medical management isometric exercises, joint protection, individually adjusted anti-inflammatory or analgesic medications) to comprehensive medical management alone in 77 patients with definite knee OA. In a 14-week trial, significant improvements were noted in several pain and stiffness assessments, physician assessment of knee tenderness and overall assessments of therapeutic effectiveness by both patient and physician. Neither of these studies employed validated outcome measurements or assessed baseline intraarticular pathology.

Chang *et al*.[17] compared arthroscopic surgery and tidal knee irrigation in 32 patients with non-end-stage knee OA in a randomized, controlled study. Patients randomized to the arthroscopy group received continuous saline irrigation during the arthroscopic procedure and had other interventional procedures as indicated by findings noted at arthroscopy, including debridement of torn menisci, removal of proliferative synovium and excision of loose articular cartilage fragments. As the arthroscopy treatment group had outcomes similar to the closed-needle irrigation group at 12 months, the authors concluded that most patients with non-end-stage knee OA can be treated with non-surgical modalities. However, there were significant differences in the amount and extent of irrigation that the two treatment groups received and there was no control for baseline intraarticular cartilage damage or inflammation. In addition, irrigation associated with arthroscopy is visually guided to ensure that all three compartments of the knee are irrigated, whereas irrigation associated with tidal knee irrigation (non-visualized irrigation) ensures irrigation only of the patellofemoral compartment; this may be important if debris and/or crystals are concentrated in areas distant to the patellofemoral compartment and intraarticular adhesions restrict flow of irrigant fluid to these areas.

The purpose of our study was to determine if visually-guided irrigation is effective in early knee OA that is refractory to medical management including non-steroidal antiinflammatory drugs and/or analgesics and physical therapy. The study design was developed to include assessments of baseline radiographic change as well as intraarticular cartilage damage and inflammation. In addition, the two treatment groups were chosen to focus on irrigation alone rather than debridement.

We chose a control group that received minimal irrigation for several reasons. First, arthroscopic inspection of the control population was necessary to verify that randomization resulted in equivalent degrees of cartilage damage and inflammation in both treatment groups. Second, there are significant ethical limitations involved in the utilization of a sham arthroscopy control group in which subjects undergo incisions and anesthesia without a diagnostic or therapeutic procedure. Third, a control group in which subjects did not undergo a procedure that simulated the treatment procedure would have resulted in an unblinded trial, which would have introduced bias to the subjective patient-oriented outcome measurements.

In this study, we failed to confirm our research hypothesis as aggregate WOMAC scores, the primary endpoint, improved to a similar degree in both treatment groups at 12 months. Although there were no significant differences in stiffness or function between the two groups as measured by WOMAC subscales, we did demonstrate significantly greater improvements in pain in the full irrigation group. This was a consistent finding as it was noted by both patient VAS and the WOMAC pain subscale. Unlike previous studies, both groups received arthroscopy, implying that the differences in results cannot be attributed to placebo effects related to arthroscopy or confounding aspects of arthroscopy other than the irrigation itself.

Our results suggest that there may be determinants other than pain that predict functional outcome. A clinical component that could conceivably affect function is stiffness; we did not observe differences in stiffness between the treatment groups. It is possible that stiffness could have a greater impact than pain on function in this patient population. There may be other unmeasured effects that have important roles in defining functional change. Differences in the sensitivities to change in the WOMAC subscales have been noted (18); these differences may also have affected our ability to detect meaningful differences in improvement. Radiographic changes were recorded by compartment (patellofemoral, medial tibiofemoral, lateral tibiofemoral) in an attempt to stratify outcome effects by compartmental radiographic scores; differences in response by compartmental involvement were not noted.

EFFECT OF CRYSTALS

The presence of macroscopic intraarticular crystals at baseline arthroscopic examination correlated with a greater degree of improvements in aggregate WOMAC and patient VAS scores regardless of the amount of irrigation performed. Clinical improvement in the presence of crystals may be related to the removal of the crystals and perhaps only minimal irrigation is needed to achieve this outcome. Stiffness and function appeared to improve only in patients with crystals, which suggests that the removal of crystals may affect pain, stiffness and function. Patients without intraarticular crystals at baseline arthroscopic examination appear to have less improvement than patients with crystals, and only in pain measurements; this effect may be related to removal of degenerated cartilage debris, which may have a lesser impact on pain, stiffness and function than the removal of crystals. It is difficult to explain the discrepancy between arthroscopically visualized crystals and the lack of crystals by percutaneous arthrocentesis; possibilities include avid deposition of crystals on synovial viallae or capsular wall deposition or large crystalline size relative to the needle used for the percutaneous aspiration.

LIMITATIONS

There are several limitations to the study including differences in camera optic clarity among the individual participating centers; because of these differences in equipment, it is difficult to ensure that patients in the two groups were controlled for the presence of intraarticular crystals. The seemingly high prevalence of intraarticular crystals among the UCLA patients may represent the

effects of a patient selection bias at that center or greater arthroscopic visualization. If a selection bias did exist, then perhaps more restrictive inclusion criteria would have led to different results.

We performed multiple hypothesis testing in the crystals substudy without correcting α (e.g. Bonferroni correction). As this was a post-hoc hypothesis-generating study, we determined that adequate power required maintaining α at 0.05. Statistically significant results of the substudy form a basis for further research rather than confirming an *a priori* hypothesis.

Without a second arthroscopic inspection at the end of the follow-up period, it is difficult to assess the effect of the treatments on morphologic change in the randomized patients, including effects on cartilage damage, synovial inflammation and deposited crystals. Therefore, the results of this study cannot be used to assess whether irrigation yields any chondroprotective effects.

RECOMMENDATIONS

Although there was no statistical differences in aggregate WOMAC scores between the full and minimal irrigation groups, full irrigation had a more significant effect on pain as measured by the WOMAC pain subscale and the patient VAS. In order to determine whether the modality of irrigation delivery affects outcome, percutaneous tidal irrigation should be compared to arthroscopic irrigation in a randomized, controlled trial.

In a small hypothesis-generating substudy, it appeared that patients with knee OA and concomitant crystals improved to a greater extent than patients without crystals, as assessed by improvements in pain, stiffness and function. Three liters of irrigation appeared to be adequate to reduce pain for patients with refractory knee OA; patients with crystals respond to even minimal amounts of irrigation. One hypothesis for these effects may be that only minimal irrigation is needed to removal crystals but that greater volumes may be necessary to remove non-crystalline materials such as cartilage debris; the effects of removing crystals may be more immediate than the removal of other materials.

Irrigation may be appropriate for the treatment of pain in patients with early knee OA that is refractory to conventional therapy including analgesics and NSAIDs. These data suggest that functional improvements may also be expected in patients with crystalline-associated knee OA; however, another randomized controlled trial is necessary to focus on the effects of irrigation in patients with crystalline-disease before definitive recommendations can be made. A set of clinical indicators that are predictive of occult crystalline disease is needed to identify candidate patients who may be appropriate for this intervention.

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