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SHORT COMMUNICATION

The outcomes and cost-effectiveness of intraarticular injection of the rheumatoid knee

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Abstract Although intraarticular injections are important to the management of rheumatoid arthritis, there are few studies regarding the cost-effectiveness of alternative injection techniques. This randomized controlled study addressed the cost-effectiveness of two different low-cost, anatomic landmark palpation-directed intraarticular injection techniques. Ninety-six symptomatic rheumatoid knees were randomized to two different low-cost, palpation-guided intraarticular injection techniques utilizing (1) a conventional syringe or (2) a mechanical syringe, the RPD (the reciprocating procedure device). Three milliliters of 1% lidocaine were used to anesthetize the synovial membrane, followed by arthrocentesis and hydrodissection, and injection of 80 mg of triamcinolone acetonide utilizing the one-needle two-syringe technique. Baseline pain, procedural pain, aspirated fluid volume, pain at outcome (2 weeks and 6 months), responders, reinjection rates, cost/patient/year, and cost/responder/year were determined. Pain was measured with the 10 cm Visual Analogue Pain Scale (VAS). Both techniques significantly reduced pain scores at outcome from baseline ($P < 0.001$). The mechanical syringe technique resulted in a greater volume of aspirated fluid ($P < 0.01$), a 38% reduction in procedural pain ($P < 0.001$), a 24% reduction in pain scores at outcome ($P < 0.03$), an increase in the responder rate ($P < 0.025$), 33% increase in the time to next injection ($P < 0.001$), 23% ($35 US) reduction in cost/patient/year for a patient treated in a physician office ($P < 0.001$), 24% reduction ($26 US) in cost/patient/year for a hospital outpatient ($P < 0.001$), and 51% ($151 US) reduction in cost/responder/year ($P < 0.001$). The outcomes and cost-effectiveness of intraarticular injection of the rheumatoid knee can be improved significantly with low-cost alternations in technique.

Keywords Injection · Corticosteroid · Intraarticular · Outcome · Cost-effectiveness

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Introduction

Intraarticular corticosteroid injection is effective for the symptomatic knee in rheumatoid arthritis; however, therapeutic response can be highly variable [1–11]. There is growing evidence that use of image guidance improves injection accuracy; however, there are concerns that image guidance is expensive (150–200% increase in costs) and thus not cost-effective [5, 11–14]. Therefore, the role of

safe low-cost methods to improve intraarticular injection outcomes is assuming greater importance [2, 4–11, 14–16].

We hypothesized that low-cost alternations in intraarticular injection technique could improve outcomes. The present randomized controlled study determined whether two different low-cost, non-imaging techniques affected the clinical outcomes and cost-effectiveness of intraarticular injection of the rheumatoid knee.

Method

Subjects

This project complied with the Helsinki Declaration was approved by the institutional review board (IRB) and was registered at C*linicalTrials.gov* (Clinical Trial Identifier NCT00651625). Rheumatoid arthritis was classified using the American College of Rheumatology 1987 revised criteria [17]. All patients received chronic disease-modifying medications with stable doses of prednisone (<10 mg per day). Inclusion criteria included the following: (1) rheumatoid arthritis, (2) persistent pain and synovial thickening and/or effusion in an involved knee unresponsive to low-dose oral prednisone (10 mg or less), (3) significant joint pain by 10 cm Visual Analogue Pain Sale (VAS) where VAS $\geq$ 5 cm, (4) failure of exercise, rest, and oral analgesics, and (5) the desire of the patient to have an intraarticular injection [7]. Exclusion criteria included the following: (1) end-stage rheumatoid joint (bone on bone), (2) osteoarthritis without synovial thickening, (3) hemorrhagic diathesis, (4) the use of warfarin or antiplatelet therapy, (5) the presence of infection, or (6) allergy or intolerance to lidocaine. One hundred and fifteen subjects were assessed for eligibility, and 19 excluded based on the above inclusion and exclusion criteria. A total of 96 painful rheumatoid knees were randomized between a conventional syringe (49 knees) and a mechanical procedure syringe (47 knees) (% difference: −4.1; 95% CI: −7.6% to +7.3%, $P = 0.50$). Palpable effusions were present in 16% (8/49) of the conventional group and 15% (7/47) of the mechanical syringe group ($P = 0.4$).

Outcome measures

Patient pain was measured with the validated 10 cm Visual Analogue Pain Scale (VAS) [5, 18]. Significant pain was defined as a VAS $\geq$ 5 cm [5, 12]. Pain was determined (1) prior to the procedure (baseline pain), (2) during the insertion of the needle (procedural pain), (3) during injection (injection pain), (4) 2 weeks post-procedure (pain at primary outcome), and (5) 6 months post-procedure (secondary outcome) [3, 5, 12]. Responders were defined as an asymptomatic joint (VAS < 2 cm) at 2 weeks [5, 12]. Duration of therapeutic response was the time interval in months when the joint became symptomatic (VAS $\geq$ 2 cm). Time to next injection or referral for surgery was determined 12 months after the initial injection and expressed in months.

Injection technique

The one-needle two-syringe technique was used where (1) one needle is used for the entire procedure, (2) a first syringe is used to anesthetize, aspirate effusion, and dilate the joint space, and (3) a second syringe is used to inject the intraarticular therapy [5, 12]. A 21-gauge, 2-inch (5.1-cm) needle (305783- 21 g BD Needle, BD, 1 Becton Drive, Franklin Lakes, NJ 07417, website: http://www.bd.com) was mounted on an RPD mechanical procedure syringe (Reciprocating Procedure Device procedure syringe, AVANCA Medical Devices, Inc, Albuquerque, New Mexico, USA. website: http://www.AVANCAMedical.com). A 3-ml mechanical syringe was used with no palpable effusion and larger sizes (10 or 25 ml) if an effusion was present.

Fig. 1 Mechanical syringe in aspiration. The mechanical syringe is held in one hand and the smaller plunger is depressed to aspirate. A pulley is attached from the smaller plunger to the larger plunger; thus, depression of the smaller plunger forces the larger plunger to retract causing vacuum and aspiration. To inject, the fingers remain on the flanges, and the thumb moves to the injection plunger and injection is completed conventionally

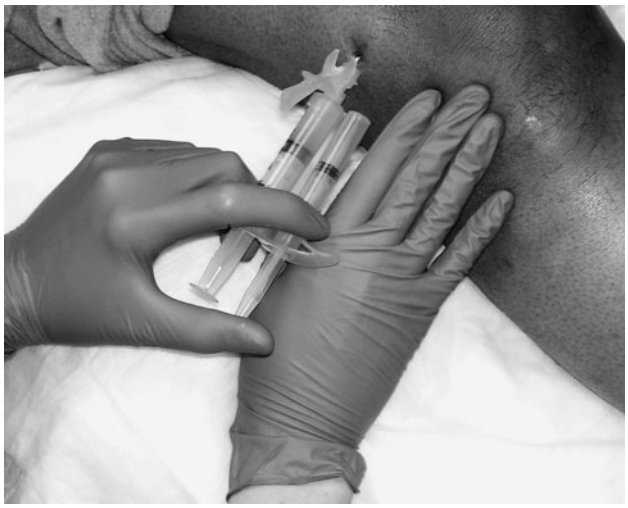

Fig. 2 One-handed arthrocentesis with the mechanical syringe. The needle is advanced while aspirating until synovial fluid is obtained or the needle tip has pierced the synovial membrane. Once the needle has encountered synovial fluid, the aspiration plunger is depressed to perform arthrocentesis, decompress the joint, anesthetize and dilate the joint space if necessary, and optimize intraarticular positioning. If synovial fluid is not encountered, then 1% lidocaine is injected to anesthetize the structures and dilate the synovial space, pushing the synovial membrane over the needle bevel. The mechanical syringe is then rotated off of the intraarticular needle and the treatment syringe attached and treatment injected

The mechanical syringe formed around the core of a conventional syringe barrel and plunger, but has a parallel aspiration plunger and an accessory barrel (Figs. 1, 2). This device permits detection of small amounts of synovial fluid that flash back into the barrel confirming true intraarticular positioning and provides enhanced control [5, 15, 16, 19].

Prior to the procedure, the mechanical syringe was filled with 3 ml of 1% lidocaine (Xylocaine® 1%, AstraZeneca Pharmaceuticals LP, Wilmington, DE, USA). As the needle was advanced if synovial fluid was obtained by flash back into the syringe, the needle position was maintained until the joint was fully aspirated (Fig. 2). If synovial fluid was not obtained, the needle was advanced until intraarticular, and then lidocaine was injected intraarticularly to expand the intraarticular space [5, 12]. After lidocaine was completely injected intraarticularly and/or complete arthrocentesis was achieved, the mechanical syringe was rotated off the intraarticular needle, and a 3-ml syringe prefilled with 80 mg triamcinolone acetonide (Kenalog® 40, Westwood-Squibb Pharmaceuticals, Inc (Bristol-Myers Squibb), New York, NY, USA) was attached and the treatment was injected.

The palpation-guided conventional injection procedure was also performed in a standardized manner as above with a conventional syringe (Ref 309604, Becton–Dickinson & Co., Franklin Lakes, NJ 07417).

Economic calculations

Costs of the procedure in US dollars ($) were defined by 2010 Medicare (United States) national rates for HCPC/CPT 20610 code for a large joint arthrocentesis for a physician office ($73.01/procedure) and hospital outpatient ($48.67/procedure), 2 ml triamcinolone acetonide ($14.94/procedure), and $2.00/procedure for each mechanical syringe or $0.30 for each conventional syringe [12, 13]. Yearly costs were calculated by multiplying the costs/procedure × 12 months divided by the months to reinjection or referral to surgery. Yearly cost per responder was calculated by dividing the yearly cost by the proportion of responders [12, 13].

Statistical analysis

Data were entered into Excel (Version 5, Microsoft, Seattle, WA) and analyzed in SAS (SAS/STAT Software, Release 6.11, Cary, NC). Differences between parametric two group data were determined with the *t*-test with significance reported at $P < 0.05$. Differences in categorical data were determined with Fisher's Exact Test.

Results

Subject age (Syringe: 50.5 ± 15.6 year; Mechanical Syringe: 51.0 ± 12.2; % difference: +1.0%; 95% CI: −10% to +12%; $P = 0.86$), female gender (Syringe: 96% (47/49); Mechanical Syringe: 94% (44/47); % difference: −4%; 95% CI: −17% to +6%; $P = 0.61$), subjects who completed study (100% for both, $P = 0.5$), and pre-procedure baseline pain (10 cm VAS Pain Scale) (Syringe VAS: 7.6 ± 1.9 cm; Mechanical Syringe VAS: 8.4 ± 2.1 cm; % difference: +11%; 95% CI: −0.1% to +21%; $P = 0.06$) were similar between the two treatment groups.

Table 1 shows that intraarticular corticosteroid injections using a conventional syringe was effective in relieving pain, resulting in a 71% reduction in absolute pain scores at 2 weeks (Baseline VAS: 7.6 ± 1.9 cm; 2 week VAS: 2.2 ± 1.8 cm, $P < 0.001$) with a complete responder rate of 35% (17/49) as defined by an asymptomatic knee (10 cm VAS < 2 cm) at the 2-week outcome. The duration of therapeutic effect was 4.0 ± 2.0 months; and time to reinjection was 7.0 ± 2.6 months with the conventional methods.

Direct comparisons between conventional and mechanical syringe palpation-guided methods are shown in Tables 1 and 2. Relative to a conventional syringe, the mechanical syringe reduced needle introduction pain by 38% ($P = 0.001$), reduced significant needle introduction pain (VAS ≥ 5 cm) by 44.5% ($P = 0.03$), increased mean

Table 1 Outcomes of injection of the rheumatoid knee

Number of subjects	Conventional syringe	Mechanical syringe			
	49	47	Percent difference (%)	95% Confidence interval	*P* value
Pre-procedure baseline pain (10 cm VAS pain scale)	7.6 ± 1.9 cm	8.4 ± 2.1 cm	+11	−16% to +12%	0.06
Needle introduction pain (10 cm VAS pain score)	5.0 ± 3.2 cm	3.1 ± 2.4 cm	−38	−61% to −15%	0.001
Significant needle introduction pain (10 cm VAS ≥ 5 cm)	49% (24/49)	28% (13/47)	−45	−87% to −18%	0.03
Mean aspirated synovial fluid (ml)	1.0 ± 3.9 ml	8.2 ± 17.8 ml	+720	+203% to +1237%	0.009
Injection pain (10 cm VAS pain score)	2.8 ± 3.4 cm	1.3 ± 2.0 cm	−54	−94% to −19%	0.01
Pain at outcome (2 weeks) (10 cm VAS)	2.2 ± 1.8 cm	1.6 ± 2.1 cm	−27	−63% to +9%	0.14
Reduction in pain from baseline (10 cm VAS)	5.4 ± 3.1 cm (71 ± 41% reduction from baseline VAS, $P < 0.001$)	6.7 ± 2.8 cm 76 ± 33% reduction from baseline VAS, $P < 0.001$)	+24	+2% to +46%	0.03
Responders (VAS < 2 cm)	35% (17/49)	57% (27/47)	+65	+3% to +42%	0.025
Non-responders (VAS ≥ 2 cm)	65% (32/49)	43% (20/47)	−35	−119% to −10%	0.025
Pain at outcome (6 months) (10 cm VAS)	5.3 ± 2.9 cm	4.2 ± 2.8 cm	−21	−43% to +2%	0.06
Reduction in pain from baseline (10 cm VAS)	2.3 ± 3.0 cm	4.2 ± 2.9 cm	−83	−135% to −30%	0.002
Duration of therapeutic effect (months)	4.0 ± 2.0 months	4.7 ± 2.0 months	+18	−3% to +38%	0.09
Time to next procedure (months)(reinjection or referral to surgery)	7.0 ± 2.6 months	9.3 ± 3.0 months	+33	+17% to +49%	0.0001

Table 2 Costs and cost-effectiveness associated with injection of the rheumatoid knee

Number of subjects	Conventional syringe	Mechanical syringe			
	49	47	Percent difference	95% Confidence interval	*P* value
Cost per year–physician office	$151 ± 57/year	$116 ± 37/year	−23% (−$35/year)	−36% to −10%	0.0005
Cost per year–hospital outpatient	$110 ± 41/year	$84 ± 27/year	−24% (−$26/year)	−37% to −11.6%	0.0002
Cost per responder per year–physician office	$434 ± 153/year	$202 ± 64/year	−53% (−$232/year)	−64% to −43%	0.0001
Cost per responder per year–hospital outpatient	$297 ± 111/year	$146 ± 47/year	−51% (−$151/year)	−63% to −40%	0.0001

aspirated synovial fluid by 7.2 ml/procedure (+720%) ($P = 0.009$), and reduced injection pain by 54% ($P = 0.01$). The mechanical syringe resulted in improvements in outcome: VAS pain scores at 2 weeks were 27% less, reduction in pain scores from baseline were 24% greater ($P = 0.03$), responder rates were increased by 65% ($P < 0.025$), and non-responder rates were reduced by 35% ($P < 0.025$). At 6 months, absolute pain scores were 21% less with the mechanical syringe, and reduction in pain from baseline was 83% greater ($P = 0.002$). The time to the next procedure was significantly prolonged by 33% (2.3 months) in the mechanical syringe group ($P < 0.001$).

Due to a longer time to next procedure, the mechanical syringe was associated with a 23% ($35) reduction in total cost/patient/year for a patient treated in a physician office ($P < 0.001$), and a 24% reduction ($26) in total costs/patient/year for a hospital outpatient ($P < 0.001$) (Table 2). Use of the mechanical procedure syringe was associated with a reduction of $232/responder/year in a physician office, and a reduction of $151/responder/year for a hospital outpatient.

Discussion

A number of studies have demonstrated that alterations in injection technique can improve the outcomes of intraarticular injections [2, 4–16, 19, 20]. Selection of an optimal anatomic portal is critical for accuracy, adds no additional cost to an intraarticular procedure, and is certainly to be recommended [4–12]. There is also compelling evidence that formal arthrocentesis should be performed prior to injection [2, 6]. A demonstration of a "flash-back" of synovial fluid aspirated into the syringe confirms true intraarticular positioning of the needle tip and thus optimizes injection accuracy and outcome [2, 5, 6, 20]. Second, removing synovial fluid from the joint prior to injecting a medication reduces intraarticular volume and increases effective intraarticular concentrations of the medication, resulting in improved outcomes [2, 6]. Finally, a flare of rheumatoid arthritis in a joint is indistinguishable from an infected joint; thus, as a matter of patient safety, all rheumatoid joints should be aspirated prior to injecting [21, 22]. Thus, performing arthrocentesis prior to injecting the rheumatoid joint is a no-cost intervention that improves outcomes, contributing to substantial cost-effectiveness [2, 5, 6, 20–22].

Other methods improve intraarticular injection accuracy, but it is unclear whether these methods improve outcome and cost-effectiveness [2, 5–12]. Certain of these methods, including pre-injection of air, saline or lidocaine to dilate the intraarticular space, aspiration of droplets of synovial fluid or moisture into the barrel of the syringe, minimal retraction of the needle tip after palpation of an articular cartilage or bone surface, use of highly controlled mechanical syringes, the one-needle two-syringe technique, and the use of the longer-acting triamcinolone esters, do not substantially increase the overall cost of intraarticular injections and are either cost-effective or cost-neutral [2, 5–12, 22–25].

Although mechanical syringes have been shown previously to improve immediate procedural outcomes and aspirated fluid volumes, the present study is the first report of improvements in intermediate and long-term outcomes with a mechanical syringe without image guidance [15, 16, 19, 22–24]. The mechanism for improved outcomes of intraarticular procedures performed with mechanical syringes may be a direct result of more successful arthrocentesis, reduced intraarticular fluid volume, greater intraarticular accuracy, higher intraarticular concentrations of corticosteroids, and less intraarticular trauma and hemorrhage, all of which have been demonstrated to improve outcome [2, 4–6, 12, 20, 23].

There is growing evidence that use of fluoroscopic or sonographic needle guidance results in a clinically significant improvement in intraarticular accuracy relative to traditional palpation-guided methods [11, 12]. However, recent data suggest that the use of image guidance may not improve cost-effectiveness due to a potential 150–200% increase in costs (US $180 to $210/procedure) [12–14]. In contrast, compared to the overall costs of arthrocentesis and intraarticular injection, the relative cost of the conventional and mechanical syringes are trivial, amounting to 0.4% and 3% the total costs, respectively. Thus, although the use of the mechanical syringe was associated with a modest 23% reduction ($26 to $35) in total cost/patient/year these cost

savings far exceeded the cost of the technology at $2.00/syringe. Thus, low-cost technologies or alterations in technique that even modestly enhance outcomes of injection of the knee are quite cost-effective.

The present study is one of the first studies examining outcome, costs, and cost-effectiveness of different low-cost, non-imaging techniques for intraarticular injection of rheumatoid arthritis of the knee. The present study demonstrates that intraarticular injections of the rheumatoid knee utilizing low-cost techniques, in this case a mechanical syringe, can significantly and meaningfully reduce procedural pain, reduce pain scores at outcome, and increase responder rates while enhancing cost-effectiveness. Future research is required to address the global cost-effectiveness of low-cost interventions in intraarticular injections in various joints, other musculoskeletal diseases, and individual practice venues.

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