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Randomized, Prospective, Placebo-Controlled Double-Blind Study of Dextrose Prolotherapy for Osteoarthritic Thumb and Finger (DIP, PIP, and Trapeziometacarpal) Joints: Evidence of Clinical Efficacy

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ABSTRACT

Objectives: To determine the clinical benefit of dextrose prolotherapy (injection of growth factors or growth factor stimulators) in osteoarthritic finger joints.

Design: Prospective randomized double-blind placebo-controlled trial.

Settings/Location: Outpatient physical medicine clinic.

Subjects: Six months of pain history was required in each joint studied as well as one of the following: grade 2 or 3 osteophyte, grade 2 or 3 joint narrowing, or grade 1 osteophyte plus grade 1 joint narrowing. Distal interphalangeal (DIP), proximal interphalangeal (PIP), and trapeziometacarpal (thumb CMC) joints were eligible. Thirteen patients (with seventy-four symptomatic osteoarthitic joints) received active treatment, and fourteen patients (with seventy-six symptomatic osteoarthritic joints) served as controls.

Intervention: One half milliliter (0.5 mL) of either 10% dextrose and 0.075% xylocaine in bacteriostatic water (active solution) or 0.075% xylocaine in bacteriostatic water (control solution) was injected on medial and lateral aspects of each affected joint. This was done at 0, 2, and 4 months with assessment at 6 months after first injection.

Outcome Measures: One-hundred millimeter (100 mm) Visual Analogue Scale (VAS) for pain at rest, pain with joint movement and pain with grip, and goniometrically-measured joint flexion.

Results: Pain at rest and with grip improved more in the dextrose group but not significantly. Improvement in pain with movement of fingers improved significantly more in the dextrose group (42% versus 15% with a p value of .027). Flexion range of motion improved more in the dextrose group ($p = .003$). Side effects were minimal.

Conclusion: Dextrose prolotherapy was clinically effective and safe in the treatment of pain with joint movement and range limitation in osteoarthritic finger joints.

INTRODUCTION

Osteoarthritis is an expensive disorder, with a recent health management organization (HMO) study indicating average cost of $543 per person, per year (Lanes, 1997). Osteoarthritis affects almost 85% of the population by the age of 75 (Sack, 1995). Prevalence of hand osteoarthritis according to a recent study in Iceland is more than 30% in women and nearly

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20% in men, with 6.8% of women symptomatic and 3.3% of men symptomatic at any one time (Aspelund, 1996). Prolotherapy (injection of growth factors or growth factor stimulators) was first described by Hackett in animal studies (Hackett, 1956) and a variety of clinical studies starting in the 1950s (Hackett, 1953, 1954, 1960, 1961; Hackett et al., 1962). Prolotherapy raises growth factor levels or effectiveness to promote tissue repair or growth. Growth factors are complex proteins (polypeptides) that initiate repair processes or replication in cells. The beneficial effects of growth factors on human chondrocytes are under intense investigation (Melching, 1999; Pfander, 1999; Shakibaei, 1999). Human chondrocytes (nasal) have been shown to multiply *in vitro* when exposed to solution containing transforming growth factor-β (TGF-β), insulin-like growth factor-1 (IGF-1), or basic fibroblast growth factor (bFGF) (Bujia, 1996; Dunham, 1998). *In vivo* animal studies have shown chondrogenesis with exposure of animal knee to TGF-β, bone metabolic protein-2 (BMP-2) (Van Beuningen, 1998) or bFGF (Shida, 1996) by injection. Repair of full-thickness cartilage defects by hepatocyte growth factor (HGF) injection has been demonstrated (Wakitani, 1997).

Because human chondrocytes themselves produce most growth factors mentioned above, if they can be stimulated to produce growth factors, the same result could potentially occur. Dextrose (D-glucose form in water) has been utilized in prolotherapy solutions for decades with the stated intent to create cell growth. Studies on human cell cultures in various glucose concentrations have shown that glucose concentrations in culture medium of only .5% (5 times more than the usual cell concentration) causes an increase in IGF-1 and IGF-2 (Pugliese, 1996), TGF-β1 (DiPaolo, 1996; Pugliese, 1996; Reinhold, 1996); platelet derived growth factor B (PDGF-B) (DiPaolo, 1996; Inaba, 1996), bFGF (Ohgi, 1996), and connective tissue growth factor (CTGF) (Murphy, 1999). In 1998, Sharpe demonstrated that as the level of glucose rises, the rate of growth of cells increases (Sharpe, 1998). Growth factor mRNA levels rise within 6 hours of cellular exposure to elevated dextrose (Oh, 1998) with as many as 15 genes induced in the presence of 0.5% glucose (Murphy, 1999).

Dextrose injection as a single-agent proliferant has not been studied in double-blind fashion. Two previous double-blind studies utilized solution containing 1.25% phenol and 12.5% dextrose and 12.5% glycerine in the treatment of chronic low back pain (Klein, 1993; Ongley, 1987). This prevents evaluation of dextrose alone, and because of the inflammatory nature of the solution raises a concern about the effectiveness of the double blind protocol. The purpose of this investigation was to study the clinical effect of injection of noninflammatory levels of dextrose. The decision to use 10% dextrose was based on:

1. Rabbit biopsies (unpublished data) by the late orthopedic surgeon Gale Borden, who did not find any inflammatory response with 10% or less dextrose and
2. Experience with peripheral vein dextrose infusion in hospitals and clinics of up to 10% dextrose without irritating or inflaming peripheral veins.

Although dextrose as a single proliferant has not been studied in a double-blind manner until now, it has been in common use in proliferant solutions for 40 years. Dextrose prolotherapy solutions for maximum safety have typically included bacteriostatic water, a small concentration of lidocaine, and dextrose. Because of the desire to maximize safety and comfort in this study and simulate typical dextrose prolotherapy solutions, the control was the usual bacteriostatic water (0.9% benzyl alcohol) with a very small amount of lidocaine, and the active solution was identical except for the inclusion of 10% dextrose.

METHODS

To qualify for the study patients needed to meet criteria for active osteoarthritis of the hand. Each distal interphalangeal (DIP), proximal interphalangeal (PIP), or trapeziometacarpal (thumb CMC) joint included must have been painful for 6 months or more and meet radiographic criteria. Patients merely had to have had pain sufficient for them to be motivated to receive injection and no pain severity

criteria were applied. Moderate osteophytosis, moderate joint space narrowing, or mild osteophytosis plus mild joint space narrowing are required for diagnosis of radiographic osteoarthritis in most epidemiologic studies (Kallman, 1989; Verbruggen, 1996) and were required in this study. Grading was with a standard atlas of individual radiographic features in osteoarthritis (Altman, 1995), which has been found to have an 85%–95% interreader agreement and an 80%–90% intrareader agreement.

Patients were allowed to continue calcium, multivitamins, nonsteroidal anti-inflammatory drugs (NSAIDs), or occasional narcotics. Only one patient in each group took occasional narcotics. Eight (8) of 13 in the active group and 8 out of 14 in the control group took NSAIDs at study onset. All other oral supplements, such as glucosamine or chondroitin, were discontinued at least 2 weeks before study onset. Patients with a history of rheumatoid arthritis were excluded from the study. Blood was obtained for erythrocyte sedimentation rate, rheumatoid factor, uric acid, and antinuclear antibody. Significant laboratory abnormalities led to referral to a primary physician or rheumatologist for determination of the presence or absence of inflammatory arthritis. No patients required exclusion for inflammatory connective tissue disorders after the initial phone screening and PRN primary physician/rheumatologist evaluation.

Patients came serially in time and, using a random number table, were assigned to group 1 or 2 by one of two data coordinators always in the office. Group assignments were blinded to the chief investigator and research coordinator by using a password-protected access to the assignment database.

The research coordinator asked which arthritis medications were being taken, explained the use of a 100-mm Visual Analogue Scale (VAS), and gave three examples of its use. The patient then self-scored their pain levels at rest, with movement, and with grip in each joint. After this, the research coordinator obtained goniometric readings of joint flexion for PIP and DIP joints by the method described in a standard text (Erickson, 1993).

At each patient visit the assignment database was accessed by a data coordinator who then drew up the appropriate solution blinded to chief investigator and research coordinator. The solution was drawn up in ready-to-use syringes. The solutions were identical in color and viscosity. Dextrose at 10% concentration is slightly sticky if allowed to dry on skin but 4% chlorhexidine gluconate was used for glove and skin preparation that masked any potential for noticing slight solution stickiness. Given the number of joints injected, 25–50 mg intravenous meperidine was used for sedation as needed. Two patients in each group required 50 mg meperidine and the rest 25 mg except for one patient in the control group. The discomfort with finger injection was reduced sufficiently to allow for reliable follow-up. There were no differences noted between active and control patients in amount of meperidine needed, or pain with injection to indicate which solution was being used. Continuous oximetry was utilized with meperidine dosages higher than 25 mg intravenously. All subjective assessments by the patient and objective goniometric measures obtained by the research coordinator were obtained before sedation was given by injection. A 27-gauge needle was inserted at the joint line laterally and medially until firm resistance was felt, at which time 0.25–0.5 mL of solution was injected at each site. All symptomatic DIP, PIP and thumb CMC joints were injected to improve study compliance.

Power analysis showed that a sample size of 14 for each group will give a power of 0.80 at a level of significance of $\alpha = 0.05$. Enrollment totals approximated the power analysis recommendations with enrollment stopped after 27 patients with 150 qualifying joints.

Human subject research approval and monitoring was by the Institutional Review Committee of Bethany Medical Center in Kansas City, Kansas. Procedures followed were in accordance with ethical standards outlined in the Helsinki Declaration revision of 1983. Data were analyzed utilizing software from the Statistical Program for the Social Sciences (SPSS, Version 7.5.3).

Injections of active or control solution were given at 0, 2, and 4 months after VAS pain measures were obtained. Follow-up goniometric measurements were obtained at 6 months. The

double-blind period then ended. In order to encourage long-term compliance with radiographic follow-up, patients in both active and control groups were offered 10% dextrose injection in open-label fashion at 6, 8, 10, and 12 months and then PRN. Although 30-month follow-up radiography is needed to see easily measurable progression of finger osteoarthritis (Kallman, 1989), patients were asked to return at 12 months for repeat x-rays to rule out any unexpected deleterious effect of injection of dextrose or control solution. The research coordinator blinded the x-rays by:

1. Assigning a patient number and blinding patient name.
2. Assigning a random number to 0- and 12-month films and obscuring the date
3. Separating the films so they would not be read in close proximity.

The chief investigator then read the films and data were loaded by the data coordinators. Because interrater and intrarater reliability in rating degree of osteophytic and joint narrowing change are good with the atlas in question (Altman, 1995), the chief investigator prepared for reading by spending 8 hours reading films using the standard atlas until he was comfortable with use of the atlas and felt consistent with grading of marginal findings. All x-rays were read at one sitting to encourage consistency of reading.

RESULTS

Group comparability

Group comparability was evaluated by Hotelling multivariate analysis of independent groups. Descriptive statistics are included in Table 1. These indicate optimum randomization outcome in that the result of blind randomization was two similar groups, suitable for comparison of treatment effects. Female predominance was noted in both groups, reflective of the general population of finger osteoarthritis patients. Noted is that these joints on average had been painful for more than 4 years before study onset. Analgesic consumption at study onset also did not differ between groups with 8 of 13 active treatment patients and 8 of 14 control patients taking NSAIDs or acetaminophen or narcotic regularly. By 1 year, four active treatment patients and two control patients had ceased taking medications for pain for their finger joints. This difference did not reach statistical significance.

Considerations for data analysis

Thirteen patients (13) were assigned to the dextrose group. One dropped out after 2 months because of progressive cardiac failure; one after 4 months because of severe depression; and two after 6 months because of schedule conflicts. Fourteen patients were assigned to the control group with one dropout at 8 months, and two at 10 months. This left 25 of 27 patients available for analysis of double-blind 6-month data and 20 of 27 available for analysis of 1-year data. According to intention-to-treat analysis, the levels of pain and range of motion scores present at the last time of follow-up were included for analysis at 6 months and at 1 year. This ensured that dropout patient outcomes were reflected in data analysis at each period.

Complexity of data analysis was affected by a varying number of qualifying joints in each patient (from 1 to 22, average, > 6). For this rea-

Table 1. Descriptive Statistics for Average Dextrose and Control Joines at Study Entry[a]

	Means and standard deviations (SD) for	
Variable	*Dextrose*[b]	*Control*[c]
Age	64.5 (9.2)	63.9 (9.4)
Pain duration in months	59 (117)	50 (42.2)
Rest pain (VAS)	2.8 (2.0)	2.7 (2.3)
Movement pain (VAS)	4.5 (1.7)	4.3 (1.7)
Grip pain (VAS)	4.9 (1.7)	5.0 (2.2)
Flexion range in degrees	59 (21)	57 (19)
Osteophyte grade	0.9 (.3)	1.1 (.6)
Joint narrowing grade	1.6 (.9)	1.2 (.6)

[a]Average number of joints per patient treated for both groups was 6

[b]Gender distribution 8 females and 5 males

[c]Gender distribution 8 females and 6 males

Number of symptomatic joints per patient averaged 6 for both groups.

VAS, Visual Analogue Scale.

son the VAS pain score for every symptomatic joint in each patient was obtained, added together for a total, and divided by the number of symptomatic joints to provide an average joint pain figure for each patient. The same was done for flexion range to provide an average flexion range. This calculated joint for each patient is termed in this study the "average joint" and values were calculated for 0 months, 6 months, and 1 year.

There was a substantial difference in the number of observations of change in flexion range ($n = 16$) compared to total patients ($n = 27$) because the only symptomatic joints were trapeziometacarpal in nine patients in whom range could not be obtained and two patients did not complete 6 months of the study at which time flexion range was rechecked. Because of the substantial difference in degree of freedom for data analysis, pain and flexion measures were analyzed separately.

Double-blind period (0 to 6 months) pain measures

After three injections, VAS improvements at rest, on movement, and for grip pain averaged 37% in the index dextrose-treated joints compared to 18% in the index placebo-treated joints (Fig. 1). Not unexpectedly, pains with function (movement and grip) improved more than pain at rest, with some of the patients having minimal or no pain at rest, and thus less room for improvement. Hotelling multivariate analysis of paired observations for rest pain, movement pain, and grip pain between 0 and 6 months was conducted on the 27 average joints. The p value for an advantage of dextrose over placebo did not reach clinical significance across all the pain variables ($p = 0.096$). Table 2 lists means, standard deviations, standard errors, confidence interval, and significance of individual paired t tests for the 27 average joints. It demonstrates that improvements in pain at rest and with grip favored the dextrose solution but statistical significance was only seen for pain with movement ($p = 0.027$).

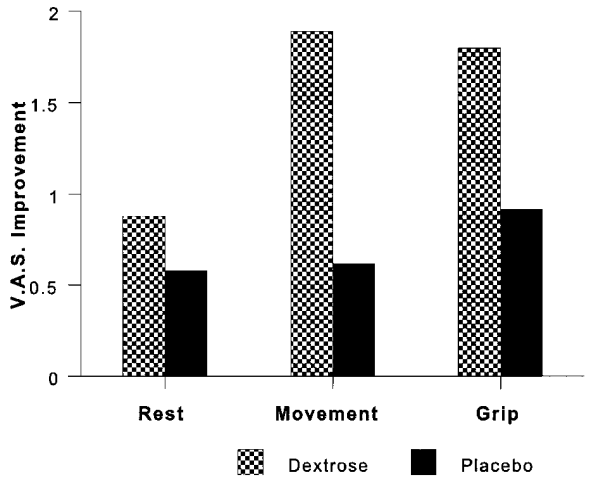

FIG. 1. Improvement of Visual Analogue Scale (VAS) for rest pain, movement pain, and grip pain between 0 and 6 months for an average joint in dextrose- and placebo-treated patients.

Double-blind placebo (0 to 6 months) joint flexion range changes

Flexion range improved significantly more in the dextrose-treated joints (+8 degrees) than the placebo-treated joints (−8.6 degrees) with a p value of .003. Table 2 lists statistical parameters for evaluation of changes in flexion between 0 and 6 months in the active and placebo group.

Pain and flexion range improvements from 6 to 12 months

The group treated with dextrose throughout the year improved further with continued dextrose administration to a 45% average pain improvement level in average joints and 51% in the total joint collection (average 6 joints per patient). The control group, once they began to receive dextrose injections, improved markedly in the second 6-month period of the year. Their pain reduction improved from 18% to 54% in the average joints and from 9.7% to 38% in the total joint collection. Only the two data coordinators had access to information about which group patients were in via password-protected method, and that information was not made available to patient, chief investigator, or research coordinator until 12 months after enrollment of the last patient. Therefore, the rapid improvement in the control patients once they began receiving dextrose is not explained by patient awareness that they were now receiving active solution for the first time. Note also that with dextrose administration the dex-

Table 2. Means, Standard Deviations (SD), and Results of Paired *t*, Tests for Change in Average Pain and Flexion Range of Motion Between 0 to 6 Months in Average Osteoarthritic Finger Joints treated with 1 mL of 10% Dextrose or Control Solution at 0, 2, and 4 Months

	Group	Mean & (SD) 0 months	Mean & (SD) 6 months	Mean difference 0–6 months	Standard error of mean difference	95% CI for the mean difference	Significance between means at 0 & 6 months: within groups	Significance between means at 0 and 6 months: between groups
Rest pain	Active	2.75 (2.02)	1.87 (1.71)	−0.88	0.41	−1.70 to −0.06	0.040	0.597
	Control	2.73 (2.27)	2.15 (1.95)	−0.58	0.39	−1.36 to +0.2	NS	
Movement pain	Active	4.45 (1.69)	2.56 (1.43)	−1.89	0.39	−2.67 to −1.11	0.000052	0.027
	Control	4.25 (1.74)	3.63 (1.82)	−0.62	0.37	−1.36 to −0.12	NS	
Grip pain	Active	4.86 (1.73)	3.06 (1.06)	−1.8	0.42	−2.64 to −0.96	0.00026	0.146
	Control	4.98 (2.21)	4.06 (2.23)	−0.92	0.41	−1.74 to −0.1	0.034	
Flexion motion	Active	59.08 (21.15)	67.09 (23.13)	+8.01	3.56	+0.89 to +15.13	0.043	0.003
	Control	56.82 (16.05)	48.17 (20.66)	−8.65	2.91	−14.47 to −2.83	0.011	

CI, confidence interval.

trose group maintained range improvement in the total joint collection and the control group improved from a minus 8.6 degrees to 0 degrees.

Preliminary (1-year) radiographic findings

In Table 3, the means and standard deviations for blinded radiographic findings at time 0 and 1 year for the dextrose and placebo group are shown. The only statistically significant change was an improvement in joint narrowing score in the dextrose treated patients ($p = 0.006$). Given the early nature of these readings, the only reasonable conclusion is that early progression of radiographic findings was not seen in either group.

Complications and safety issues

A complication of treatment related to the injection itself was that appropriate light sedation precautions were needed due to injection with low-dose (usually 25 mg) meperidine. Discomfort after injection did not appear to vary between groups, typically lasting a few minutes to several days. This discomfort was primarily in the form of a tightness feeling in the joint. Purplish discoloration in the fingertips just after injection implied partial venous return restriction by the volume of fluid injected. This may suggest that 0.25 mL would be a better volume of injection, although no vascular complications have ever been reported with proliferant injection in fingers. Note that patients with rings removed them prior to injection, or the volume in the joints surrounding the ring was reduced to about 0.25 mL each side. This was infrequently necessary and would not be expected to affect results. Prolonged flare-ups of pain related to the injection were not noted. No allergic reactions or infections were noted. One observation at the time

Table 3. Means and Standard Deviations (SD) at Study Entry and at 12-Month Follow-Up for Radiographic Findings for Dextrose and Placebo Groups

Radiographic measure	Group	Study entry	12 Month followup
Joint narrowing grade	dextrose	2.00 (0.86)	1.72 (1.14)
	placebo	1.85 (0.81)	1.98 (0.95)
Osteophyte grade	dextrose	1.17 (0.77)	1.33 (0.89)
	placebo	1.87 (0.86)	1.79 (1.07)
Joint width in millimeters	dextrose	14.03 (3.75)	14.33 (3.99)
	placebo	14.79 (3.40)	14.73 (3.31)

of 12-month follow-up was a flare-up of pain in one patient's thumb with examination suggesting a potential inflammatory source of pain. This responded rapidly to low-dose methylprednisolone.

DISCUSSION

Potential explanations of outcome

Although dextrose elevation *in vitro* in humans and *in vivo* in animals causes growth-factor production and chondrocyte multiplication, is there any other mechanism that could explain the superior outcome of the active treatment group in this study?

The number of patients was small with limited statistical power. However, these 27 patients had a total of 150 symptomatic joints that were treated and observed. The 150 joints as a whole showed an even larger difference between pain improvement (average of rest, movement, and grip pain) in the dextrose-treated joints (48%) and placebo-treated joints (9.7%) than did the 27 average joints. Flexion range of motion changes were similar in magnitude and direction in the 150 joints (dextrose = +6.79 and placebo −6.82 degrees). This reinforces the findings of superior benefit from the dextrose solution, because joints within the same individual do not necessarily react the same. Another consideration is that the above improvements occurred with joints having an average of 4 years of pain. In addition, a concurrent and much larger study on osteoarthritic knees showed statistically and clinically significant improvements in pain and goniometric range in the dextrose group as well (Reeves and Hassanein, 2000).

A second mechanism to explain the apparent benefit of dextrose injection over placebo injection could be a beneficial effect of hypertonicity of the dextrose solution (611.4 mOsm) compared to control solution (105 mOsm). Exposure of human and animal cells to hypertonic solution has been found by several researchers to result in a rise of growth factors. (Berl, 1997; Caruccio, 1997; Krump, 1997; Okuda, 1996; Ruis, 1995; Szaszi, 1997). The number of growth factors produced appears to be more limited than with dextrose elevation and in studies comparing equal osmolar concentrations of glucose and mannitol, glucose caused more growth-factor elevation (Pugliese, 1996).

Third, there may have been a beneficial effect by dextrose on disrepair factors in osteoarthritis, rather than just an effect on growth factors. Among the disrepair factors in osteoarthritis are a variety of interleukins and plasminogen activator (Brandt, 1998). Human cell exposure to dextrose elevation has been found to decrease activity of interleukins 2, 6, and 10 and plasminogen activator (Murphy, 1999; Reinhold, 1996).

Fourth, the dextrose solution may tighten extra-articular ligaments (i.e., collateral ligaments), decreasing soft-tissue sources of pain. This idea is supported by two studies demonstrating improvement in objective electroarthrometric measures of knee laxity with injection of solutions containing dextrose (Ongley, 1988; Reeves and Hassanein, 2000).

Fifth, it may be that the hypotonic (control) solution was harmful in some way, accounting for the apparent benefit of the dextrose solution. Although the control fingers decreased in range of motion during the study, they showed a rather typical placebo effect on pain levels with a reduction in pain levels by 18% on average. During the second 6 months of the study, range of motion returned to baseline. Preliminary 1-year x-rays gave no indication of an adverse effect. Also dropouts did not occur in the control group during the 6-month double-blind period of the study. A concurrent study on knee osteoarthritis showed improvement in range of motion with the same control solution, rather than a decline (Reeves and Hassanein, 2000). In addition, studies on hypotonic solution *in vivo* have indicated that there is a protective response by cells that also causes growth factor–like compounds to be released, but not to the same extent as with exposure to either hypertonic solution or glucose solution (Carruccio, 1997). Mammalian cell osmoregulation can handle osmolar concentrations down to 100 or less without damage to the cell (control in this study was 105 mOsm) (Carruccio, 1997).

Study limitations

Twenty-five percent dropout (25%) by 1 year was noted. However, because 7% dropped out for unrelated medical issues, and 7% dropped out indicating substantial improvement but stating they were too busy to keep lengthy appointments, this leaves only 11% that dropped out because of inefficacy, and their data are included in data analysis. The need to wait until sedation wears off will be a limitation for some patients, although the treatment frequency may be less than the bimonthly follow-up in this study protocol.

An additional limitation includes the potential of leaving an inflammatory joint untreated because some stages or forms of osteoarthritis are more aggressively inflammatory. A flare-up in one patient at 12 months requiring steroid injection is a reminder that pain in finger osteoarthritis may be from nociceptors in bone and connective tissue or may be primarily from inflammation. Protocols for treatment should keep this in mind and consider occasional steroids.

There is a limit in applying the results of this study to other joints in the human because studies on ligaments have shown that different ligaments respond to different growth factors and the same may be true for joints (Lee, 1997; Kang, 1999; Scherping, 1997). That is one reason why we performed concomitant studies on large joints (knees) and small joints (fingers) (Reeves and Hassanein, 2000).

The literature on normal ligament/tendon response to the repair process indicates that loose ligaments tighten as immature collagen matures by dehydration (Banks, 1991). This has been reinforced by two studies with direct measurement of knee laxity response to proliferant injection (Ongley, 1987; Reeves and Hassanein, 2000). This may raise a question about why range of motion of a joint would improve if structures within the joint tighten. In reality, the normal healing mechanism that proliferant injection simulates never overtightens structures that are allowed to mobilize. The limitation in joint range of motion in osteoarthritis is often inhibitory in nature rather than due to a soft tissue restriction. If the underlying cause of inhibition such as pain is addressed the range of motion improves. In the knee osteoarthritis study with anterior cruciate ligament (ACL) ligament substudy the range of knee motion improved despite concurrent tightening of lax ACLs (Reeves and Hassanein, 2000).

Study applications

This is one of two concurrent double-blind studies to demonstrate that dextrose alone is capable of a beneficial effect on introduction into osteoarthritic joints, and that a bimonthly injection appears to be an effective treatment interval. These findings are particularly important because dextrose inclusion in any variety of other solutions introduced into osteoarthritic joints may contribute to therapeutic effect. Because the cost of solution is negligible the cost effectiveness of dextrose injection in finger osteoarthritis may be considerable even given the small amount of sedation required.

Previous prolotherapy studies have suggested that it is necessary to create a brief inflammation during proliferant injection to stimulate repair of tissue. This study provides evidence that other mechanisms such as a direct dextrose effect and hypertonicity contribute to the clinical effects of proliferant solutions.

Future study considerations

Long-term x-ray data. Long-term x-ray follow-up data from the current study patients will be helpful to note net effect on cartilage and osteophytic change and patients are being followed with intention of reporting long-term radiographic findings.

Isotonic saline control. Now that the safety of dextrose in bacteriostatic water has been demonstrated, future studies with dextrose should perhaps have dextrose in sterile water or saline versus an isotonic saline placebo.

Injection frequency and volume of injection. Future studies will also need to focus more on such issues as injection frequency and volume of injection.

Combination with oral agents or primary growth factors. Because of likely differences in mechanism of action and the low cost of dextrose,

studying combinations of dextrose with either oral agents or primary growth factors may be of interest.

CONCLUSION

This study demonstrates that intra-articular 10% dextrose appears to be clinically effective and safe in the treatment of finger osteoarthritis pain and joint stiffness. The clinical efficacy of dextrose is underscored by the ability to obtain clinically significant improvements via use of only 3 mL of dextrose solution over 6 months or 6 mL over 1 year. Because dextrose was deposited along the joint line without an attempt to formally enter the joint, subcapsular infiltration appears to deliver sufficient solution volume for clinical effect. Although *in vivo* clinical improvements occur with prolotherapy and *in vitro* studies clearly indicate rapid elevation of growth factor in chondrocytes, future studies should measure intraarticular growth-factor levels. Whether dextrose proliferant effects can complement the effects of recombinant growth factors is an issue that merits investigation because of the low cost of dextrose solution.

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