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Hyperosmolar Dextrose Injection for Recalcitrant Osgood-Schlatter Disease

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KEY WORDS
Osgood-Schlatter, tendinosis, apophysitis, enthesopathy, dextrose

ABBREVIATIONS
OSD—Osgood-Schlatter disease
NPPS—Nirschl Pain Phase Scale

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WHAT'S KNOWN ON THIS SUBJECT: Osgood-Schlatter disease symptoms may wax and wane until maturity and affect sport confidence and participation periodically. Chronic sequelae may include anterior knee pain, kneeling discomfort, or sports limitation. Symptom reduction parallels resolution of patellar tendinopathy by MRI/ultrasound, although ossicles may persist radiographically.

WHAT THIS STUDY ADDS: Small-needle injection of the patellar tendon enthesis/tibial apophysis with 12.5% dextrose was safe and well tolerated in adolescents with recalcitrant Osgood-Schlatter disease. Dextrose injection resulted in more rapid and frequent achievement of unaltered sport and asymptomatic sport than did usual care.

abstract

OBJECTIVE: To examine the potential of dextrose injection versus lidocaine injection versus supervised usual care to reduce sport alteration and sport-related symptoms in adolescent athletes with Osgood-Schlatter disease.

PATIENTS AND METHODS: Girls aged 9 to 15 and boys aged 10 to 17 were randomly assigned to either therapist-supervised usual care or double-blind injection of 1% lidocaine solution with or without 12.5% dextrose. Injections were administered monthly for 3 months. All subjects were then offered dextrose injections monthly as needed. Unaltered sport (Nirschl Pain Phase Scale < 4) and asymptomatic sport (Nirschl Pain Phase Scale $= 0$) were the threshold goals.

RESULTS: Sixty-five knees in 54 athletes were treated. Compared with usual care at 3 months, unaltered sport was more common in both dextrose-treated (21 of 21 vs 13 of 22; $P = .001$) and lidocaine-treated (20 of 22 vs 13 of 22; $P = .034$) knees, and asymptomatic sport was more frequent in dextrose-treated knees than either lidocaine-treated (14 of 21 vs 5 of 22; $P = .006$) or usual-care–treated (14 of 21 vs 3 of 22; $P < .001$) knees. At 1 year, asymptomatic sport was more common in dextrose-treated knees than knees treated with only lidocaine (32 of 38 vs 6 of 13; $P = .024$) or only usual care (32 of 38 vs 2 of 14; $P < .0001$).

CONCLUSIONS: Our results suggest superior symptom-reduction efficacy of injection therapy over usual care in the treatment of Osgood-Schlatter disease in adolescents. A significant component of the effect seems to be associated with the dextrose component of a dextrose/lidocaine solution. Dextrose injection over the apophysis and patellar tendon origin was safe and well tolerated and resulted in more rapid and frequent achievement of unaltered sport and asymptomatic sport than usual care. *Pediatrics* 2011;128:e000

Osgood-Schlatter disease (OSD) is traditionally described as "a traction apophysitis of the tibial tubercle because of repetitive strain on the secondary ossification center of the tibial tuberosity."[1] Advances in sequential radiographic examination have helped to partially clarify pathology. Sequential knee ultrasound imaging of tennis athletes going through puberty has demonstrated that ossicles (separated cartilage that ossifies) within hypoechoic cartilage are common and usually asymptomatic.[2,3] An ossicle may impinge on the patellar tendon, causing long-term impairment of kneeling or running.[4] However, a sequential MRI study of adolescents with symptomatic OSD revealed 100% with patellar tendon pathology and only 32% with ossicle formation.[5] Improvement in patellar tendinosis was demonstrated in those that became asymptomatic, despite persistence of nonunion ossicles.[5] Hirano et al,[6] in another sequential MRI study, found that a partial tear of the secondary ossification center was in place before patellar tendon swelling but agreed that symptom resolution likely follows the resolution of tendon changes. Thus, although repeated microavulsion fractures may be the first radiographic finding and contribute to OSD pain and pathology,[6] they do not seem to be the primary source of pain and dysfunction.[5,6] Recent MRI and ultrasound reports are also consistent with a description of OSD as "a tendinopathy/apophysosis of the patellar tendon/tibial tubercle."[7–12]

Safety and level A–C evidence of efficacy (per US Preventive Services Task Force criteria) of injection of 10% to 25% dextrose in areas of damaged ligament, tendon, and cartilage in adults has been demonstrated in randomized controlled trials in Achilles tendinosis,[13] finger osteoarthritis,[14] knee osteoarthritis,[15] lateral epicondylosis,[16] sacroiliac joint pain,[17] and in case series collections of patients with Achilles degeneration,[18,19] anterior cruciate ligament laxity,[20] coccygodynia,[21] hip adductor and abdominal tendinosis,[22] and plantar fasciosis.[23] There are no previous reports of application of dextrose injection in a strictly pediatric population, nor are there reports of injection about an apophysis where, as described, the source of pain and pathomechanism are not yet clear.

The common counsel that parents receive is that OSD is "a self-limited process that responds favorably to conservative treatment."[24] The self-limit is closure of the tibial growth plate, and thus the period of potential symptoms can be considerable.[1] A succinct recent description of conservative treatment includes "rest, icing, activity modification, and rehabilitation exercises."[1] Use of a knee strap may protect the tibia from painful contact, but no prospective trials have been reported.[25] Symptoms typically wax and wane for months to years.[26] Gerulis et al,[27] reporting on 178 conservatively treated adolescents, found a mean range of 13 to 16.5 months of pain, depending on whether load restrictions were followed. Mital et al[28] reported that, after a mean of 3.8 years of symptoms and conservative treatment, 12% of subjects merited surgery. Sixteen years later, Hussain and Hagroo[29] reported a 9% surgical rate after a conservative therapy trial. In young adults seen for OSD who received conservative treatment only, telephone interview data a mean of 9 years after diagnosis revealed a 60% incidence of kneeling discomfort and 18% incidence of sport limitation because of pain over the tibial tubercle.[30] Air Force cadets with an OSD history reported more frequent anterior knee pain and significantly diminished Sports Activity Scale scores than a cohort with no OSD history.[31] Alteration of primary sport choice, altered peer group dynamics, self-esteem effects, and occasional withdrawal from all competitive sports are effects of OSD that have not been measured prospectively. Reassuring parents and athletes that OSD is time-limited is appropriate, but dismissing it as benign in effect or brief in duration seems to be at odds with available literature.

In current literature, OSD is depicted as a condition involving degeneration of both tendon and apophyseal tissue, as opposed to an isolated inflammation of the apophysis. Dextrose injection has been found to be safe and potentially effective in treatment of cartilage and tendon degenerative disorders. The purpose of this study was to examine the potential of dextrose injection versus lidocaine injection versus supervised usual care to reduce sport-related symptoms in adolescent athletes with OSD. The hypothesis was that dextrose injection would be superior to either lidocaine injection or supervised usual care.

PATIENTS AND METHODS

Determination of Candidacy

Girls age 9 to 15 and boys aged 10 to 17 in the area of Rosario, Argentina, were screened for anterior knee pain, but only if they were involved in a jumping or kicking sport on an organized team with a coach. Absence of either patellofemoral crepitus or patellar origin tenderness was required, as well as reproduction of the exact pain and localization of pain precisely to the tibial tuberosity during a single leg squat. Once confident of the diagnosis, patients were required to have attempted at least 2 months of formal and gently progressive hamstring stretching, quads strengthening, gradual sport reintroduction, and to have had pain with sport for at least 3 months. At that point, if the patient and guardian demonstrated informed con-

TABLE 1 NPPS Scores Ranging From 0 for Complete Remission to 7 for Continuous Pain That Disturbs Sleep

0	No pain or stiffness before, during, or after sport
1	Stiff/sore after sport for <24 h
2	Stiff/sore before and after sport relieved by warm-up
3	Pain during sport but sport not altered
4	Pain alters sport; nonpainful ADL
5	Pain alters sport and painful ADL
6	Pain prevents sport and alters ADL
7	Pain prevents sport, alters ADL, and alters sleep

ADL indicates activities of daily living.

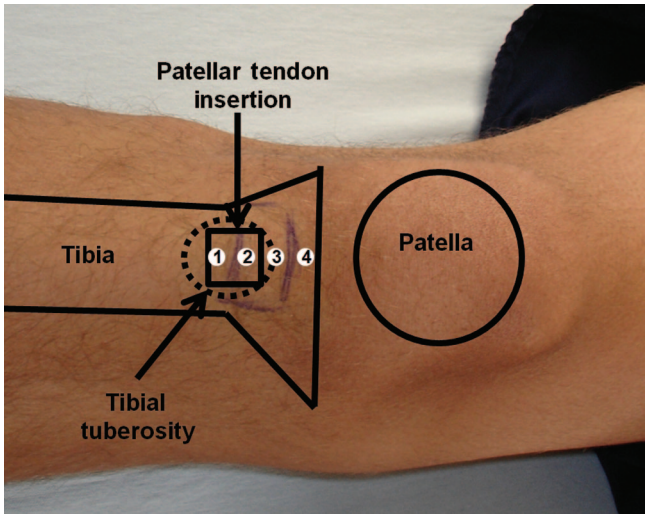

FIGURE 1
Anteroposterior photograph of knee showing injection points starting over the most distal area of pain on the tibial tuberosity and moving proximally in 1-cm increments to the most proximal painful point with pressure. The black square represents the attachment of the patellar tendon to the tuberosity or its fragments.

sent, a random numbers table was used for assignment to supervised usual care or to an injection solution group blinded to the subject, guardian, and the treating/evaluating physician. Subjects with 1 or 2 symptomatic knees were accepted, but both knees were assigned to the same treatment if both knees were treated on a single patient. The solution for each visit was prepared by the physician who assigned the patient, and was prepared in a manner blinded to the patient and the treating/evaluating physician.

Outcome Measures

The Nirschl Pain Phase Scale (NPPS) (Table 1)[32,33] is a 7-level measure of sport inhibition and sport-related symptoms. NPPS scores of 4 to 7 are levels where sport is inhibited by pain. Below 4, symptoms of pain, soreness, or stiffness may be present (NPPS scores 1–3) or may not (NPPS score 0). However the knee in question is uninhibited with sport. The threshold goals we chose, on the basis of NPPS scores, were NPPS scores of <4 and 0.

Treatment

All athletes were given pictorial sheets of gently progressive hamstring stretching and quads strengthening exercises. Those in the usual care group met with a physical therapist who instructed them individually in the stretching and exercise method, and provided a video. Then, those in the usual care groups returned at least once for 1-on-1 confirmation of proper exercise performance and to encourage compliance. Monitoring to this extent meets or exceeds the amount of monitoring that a youth with symptomatic OSD would typically receive, and thus makes a reasonable usual care control group.

The injection groups received solution that always contained lidocaine 1% because, in each session, completeness of injection was determined by complete anesthesia of pain with single-leg squat. Injections in the blinded phases of the study were given at 0, 1, and 2 months. Half of injected subjects received 12.5% dextrose in their injection; half received lidocaine only. For purposes of additional discussion, the dextrose/lidocaine group will be termed the "dextrose" group to distinguish it from the lidocaine-only group.

A single leg squat and palpation were used to mark the most distal and proximal areas of pain/tenderness. Injections were given with a 27-gauge needle beginning at the most distal point of tenderness, with gentle insertion to bony depth, and then injecting ½ mL. Injections were repeated at ~1 cm intervals, moving proximally for a total of 3 to 4 midline injections (Fig 1). The proximal 1 to 2 injections were deep to the patellar tendon and on the tibia above the tuberosity. To avoid injecting the fat pad, the needle was angled toward the tibia, and depth was usually <1.25 cm. Five minutes later, a single leg squat was repeated to detect any additional pain areas, typically medial or lateral to the midline injections. Those areas were injected until painless single leg squat was achieved. Because pain reduction may precede full healing, subjects received treatment on 3 occasions even if they became pain-free.

Acetaminophen was advised if needed for postinjection discomfort. Athletes were advised not to run or kick for 1 week after the first injection, and to run as tolerated after the first week. They were advised not to run or kick for 3 days after both the second and any subsequent injections. Usually, they started playing sports with competition if doing well after the second injection. Note that many athletes with

an NPPS score of 3 were used to playing with pain; these athletes were encouraged to engage in a sporting activity only if the activity was not accompanied or followed by pain during the period of treatment.

As an incentive for study participation, and to potentially avoid sports dropout, all study participants that did not reach an NPPS score of 0 could choose to receive dextrose injection after 3 months (the point at which the actual injectant was revealed to the treating physician and patient). This was offered monthly until 12 months after either elimination of symptoms or plateau of improvement. Athletes were not required to receive dextrose injection if they were satisfied with their status at 3 months. The athletes were seen in clinic at 6 months and 1 year to be sure that those that reported no pain or stiffness were indeed asymptomatic when performing a single leg squat, and to update contact information and minimize potential for data dropout.

Ethics and Analysis

Human subject consent process, method approval, and monitoring were conducted via the Comité de Investigación y Docencia del Hospital Provincial de Rosario. Assent was obtained via guardian or parent. A formal group size calculation was not performed. Our plan for enrollment was to reach a minimum of 20 cases in each group, on the basis of a previous study using a similar injection treatment.[22] Data were analyzed using SPSS 18 (SPSS Inc, Chicago, IL). Analysis of variance was used to compare changes in NPPS scores between groups. Tukey's posthoc procedure was performed to control type I error for multiple (ie, dextrose, lidocaine, and usual care) group comparisons. The α level of the study was set at .05. A Fisher's exact test was used to compare the likelihood of achieving an NPPS score of <4 and 0 between groups.

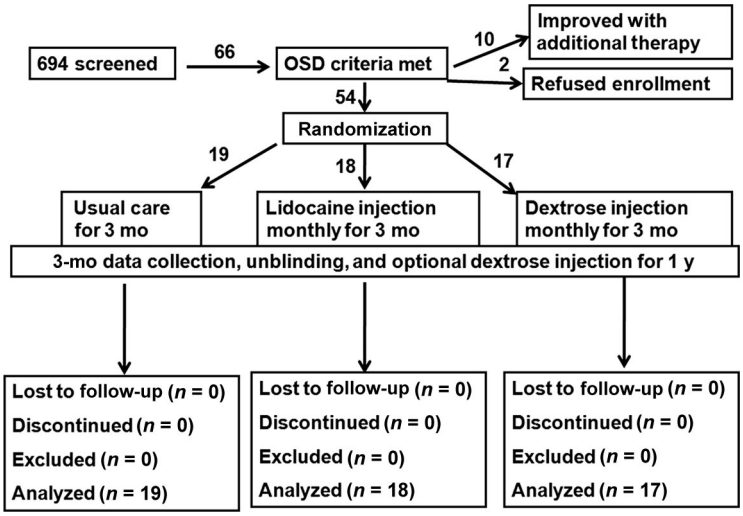

FIGURE 2
Determination of candidacy and study flow. Note the low refusal rate for inclusion and lack of data loss.

RESULTS

Demographics and Group Similarity

Enrollment was from September 1, 2005, through October 2, 2008. The total enrollment was 65 knees in 54 athletes (Fig 2). Data collection was complete to 1 year. The ages of athletes treated ranged from 10 to 17 (mean: 13.3) years. The enrollees, consistent with soccer club composition in the region, consisted predominantly of boys (51 boys of 54 athletes enrolled). An analysis of variance for each variable (age, pain duration, and NPPS score for each of the groups at the time of randomization) revealed that the distribution for each variable was the same for each group.

Blinded Period (0–3 Months)

In the first three columns of Table 2, means and SDs are listed for the NPPS score at 0 and 3 months and NPPS improvement from 0 to 3 months for each group. NPPS scores improved more in dextrose-treated knees than either lidocaine-treated (3.9 vs 2.4; $P = .004$) or exercise-treated knees (3.9 vs 1.2; $P < 0001$). Lidocaine was significantly better than usual care (2.4 vs 1.2; $P =$

TABLE 2 Mean and SD for NPPS Score at 0 and 3 Months, NPPS Mean Difference From 0 to 3 Months, and NPPS Score at 1 Year in OSD-Affected Knees

Group	NPPS Scoreat 0 mo		NPPS Score at 3 mo, Mean (SD)	NPPS Difference at 0–3 mo, Mean (SD)	NPPS Score at 1 y, No Dextrose Received		NPPS Score at 1 y, Dextrose Received	
	Mean (SD)	*n*			Mean (SD)	*n*	Mean (SD)	*n*
Dextrose	4.6 (1.0)	21	0.7 (1.2)	3.9[a] (.3)	—	—	0.2 (0.7)	21
Lidocaine	4.2 (1.0)	22	1.8 (1.4)	2.4[a] (.3)	1.2 (1.5)	13	0.4 (0.7)	9
Usual care	4.3 (1.0)	22	3.1 (1.6)	1.2[a] (.4)	2.5 (1.5)	14	0.1 (0.4)	8

[a] Significant differences between all groups and between pairs: all groups ($P < .0001$); dextrose vs lidocaine ($P = .004$); dextrose versus usual care ($P < .0001$); and lidocaine versus usual care ($P = .024$).

TABLE 3 Three-Month and 1-Year Outcomes for Dextrose-Injected, Lidocaine-Injected, and Usual-Care–Treated Subjects

	3-mo NPPS Score of <4	3-mo NPPS Score of 0	1-y NPPS Score of <4	1-y NPPS Score of 0
Dextrose, *n*/*N*	21/21	14/21	38/38[a]	32/38
Lidocaine, *n*/*N*	20/22	5/22	12/13	6/13
Usual care, *n*/*N*	13/22	3/22	10/14	2/14
Dextrose vs lidocaine, *P*	.488	.006	.518	.024
Dextrose vs usual care, *P*	.001	<.001	.008	<.0001
Lidocaine vs usual care, *P*	.034	.698	.139	.005

Numbers achieving NPPS scores of <4 (unaltered sport) and an NPPS score of 0 (asymptomatic sport [ie, no pain, no soreness, and no stiffness before, during, or after sport]) in each group and Fisher's exact test result for significance of differences between pairs.

[a] After 3 months, 9 lidocaine-treated and 8 usual care–treated knees switched to receiving dextrose, for a total of 38 (21 + 9 + 8) knees that received dextrose injection.

.024). Posthoc analysis (Tukey's procedure) confirmed significant improvement over usual care for both dextrose ($P < .0001$) and lidocaine ($P = .046$).

At the time of enrollment, some knees were already performing at an NPPS score of 3 (pain during sport but unaltered sport). Randomization was successful in achieving a near equal assignment of these knees to each group (ie, 5 of 21 dextrose, 6 of 22 lidocaine, and 6 of 22 exercise-treated). Despite the expected reduction in statistical power to compare intragroup differences in reaching unaltered sport, in comparison to usual care, significantly more dextrose-treated (21 of 21 vs 13 of 22; $P = .001$) and lidocaine-treated knees (20 of 22 vs 13 of 22; $P = .034$) achieved unaltered sport by 3 months (first column of Table 3).

Although unaltered sport was achieved by >90% of both dextrose and lidocaine-treated athletes by 3 months, dextrose-treated knees were significantly more likely than lidocaine-treated knees (14 of 21 vs 5 of 22; $P = .006$) to be asymptomatic with sport (NPPS score of 0) by 3 months (second column of Table 3).

Open Label Period (3–12 Months) Treatment Results

After the blinded period, 13 of 22 lidocaine-treated knees were not injected with dextrose because they did well enough with lidocaine. Of the usual-care–treated knees, 14 of 22 were not injected with dextrose. Seven knees improved enough, 2 were in athletes that quit sport, and 5 were in athletes who were disqualified because of failure to perform usual care exercises.

Columns four and five in Table 2 list mean NPPS scores at 1 year for groups that did not and did receive dextrose injection, and the third and fourth columns in Table 3 list 38 knees that received dextrose (21 original dextrose, 9 lidocaine that switched, and 8 usual-care that switched). Dextrose-treated knees were significantly more likely to be asymptomatic with sport by 1 year than were lidocaine-treated knees not receiving dextrose (32 of 38 vs 6 of 13; $P = .024$), despite the fact that the lidocaine knees not receiving dextrose were those that responded well to lidocaine alone in the first 3 months. Notable is that only 2 of 14 knees treated with usual care for the entire year reached an NPPS score of 0 and that sport drop-out and inability to do exercises only occurred in the usual care group.

In Fig 3 the effect of switching to dextrose injection is depicted by graphing the mean NPPS score to 12 months. Lidocaine and usual-care knees that were treated with dextrose injection beginning at 3 months approximated the same level of improvement by 6 months as those initially treated with dextrose, whereas those lidocaine and usual-care–treated knees not injected with dextrose plateaued.

Of the dextrose-treated knees that reached an NPPS score of 0, 3 knees were later injected after direct contusions to the knee, and again reached an NPPS score of 0. The mean number of dextrose injections received until 12 months was 2.0 for lidocaine-first-then-dextrose-injected knees, and 2.4 for usual-care-first-then-dextrose-injected knees. Knees receiving dextrose injection only were required to receive a minimum of 3 injections, and the mean number of dextrose injections received was 3.8.

DISCUSSION

Synopsis of Key Findings

At the conclusion of 3 months of knee treatment with dextrose injection, 21 of 21 knees functioned unaltered with sport, 14 of 21 were asymptomatic

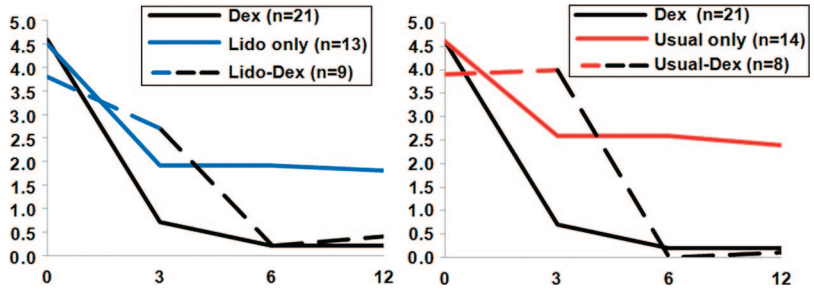

FIGURE 3
Comparison of NPPS scores from 0 to 12 months in the dextrose group compared with the lidocaine group on the left and usual care on the right. The different course for those who chose to receive dextrose after 3 months is shown.

with sport, in contrast with 13 of 22 and 3 of 22 usual-care–treated knees, respectively. At 1-year follow-up, 38 of 38 dextrose-treated knees functioned unaltered with sport, and 32 of 38 were asymptomatic with sport compared with 10 of 14 and 2 of 14 usual-care–treated knees. Those athletes that dropped sport or were unable to perform OSD exercises were only from the usual care group. These results suggest that both the duration of sports limitation and the duration of sports-related symptoms may be reducible by dextrose injection in those with recalcitrant OSD.

Consideration of Possible Mechanisms and Explanations

Traumatic needling (percutaneous needle tenotomy) has been proposed for use in tendinosis.[34,35] Although a needling effect and subtendinous/intratendinous fluid infusion may contribute to the clinical benefit in this study, trauma was minimized via use of a 27-gauge needle, with 3 to 6 gentle entries through a tendon, and only light bone contact. Given identical needling technique in both dextrose and lidocaine groups in this study design, a unique quality of dextrose must account for its superior efficacy.

Alfredson[36] noted increased numbers of small veins (neovessels) in areas of painful tendinosis and demonstrated large numbers of small sympathetic fibers (a potential source of pain) in neovessel regions. A reduction in neovascularity has been demonstrated after 25% dextrose injection in Achilles tendinosis, but staining for a sympathetic nerve fiber count has not been performed.[18,19]

Repair of soft tissue such as ligament and cartilage is accomplished by regenerative polypeptides, called growth factors, which are produced locally.[37] Growth factors require sustained glucose metabolism to promote cell survival, and glucose cannot be transported into the cell without transporter proteins that are stimulated by growth factors.[38,39] Elevation of extracellular glucose promptly elevates levels of transforming growth factor β, connective growth factor, vascular endothelial growth factor, insulin-like growth factor, and fibroblast growth factor.[38–44] Genes for growth factor production are activated within 20 minutes of human cell exposure to 0.45% glucose (normal extracellular level is 0.1%).[45] Studies on glucose effects on neuropeptides are limited thus far, but there are indications that either dextrose elevations or a related reduction in insulin levels downregulate the activity of the transient receptor potential vanilloid type 1 (TRPV1) receptor which reduces production of pain producing (substance P) and degenerative (calcitonin gene-related peptide [CGRP]) neuropeptides.[46–48]

Comparison With Relevant Findings From Other Published Studies

Improved tendon organization after dextrose injection has been shown by interval ultrasound in the Achilles tendon[18,19] and plantar fascia[23] in consecutive case series. The ability of dextrose to tighten loose connective tissue without direct contact was suggested by a pilot study using anterior cruciate ligament machine measurement and simple intra-articular dextrose injection.[20] Another study on sports-altering tendinosis (adductor and abdominal insertions) in elite rugby and soccer athletes resolved career-threatening chronic groin pain in >90% of athletes.[22] The speed and success rate for return to sport in the adductor/abdominal tendinosis study were the same as that reported with far more expensive surgical interventions. In this OSD study, similar efficacy was demonstrated, but it also represents the first study in an exclusively pediatric population, and the first study in which a tendon attachment on an apophysis was injected.

Limitations of the Study

Failure to use a validated measure of symptoms of tendinopathy, such as the Victorian Institute of Sport Assessment-Patella score,[49] with an estimated minimally clinically important difference, was a significant limitation of this study. Although the usual care (supervised exercise) group was a reasonable control, they had already tried exercise. Nevertheless, some in the exercise group did well with the close therapist supervision.

Clinical and Research Implications

Screening at soccer club level identified 5.7% of athletes who failed usual care for OSD. This "early" identification still found quite chronic symptoms with a median of 8 (range: 3–72) months of anterior knee pain.

Tolerance of small needle injection was demonstrated in this age group, and, because of the nonviscous nature of dextrose, 27- to 30-gauge needles should make treatment practical for other conditions in this age group, such as Sever's disease. Less than 10% of athletes required acetaminophen after injection.

Although designing and conducting a similar RCT in this age group would be difficult, we hope that additional consecutive patient studies with follow-up lasting several years will be pursued, given the safety and outcomes demonstrated by this study.

CONCLUSIONS

Dextrose or lidocaine injection over the apophysis and patellar tendon origin was safe, well tolerated, and resulted in more rapid and more frequent achievement of unaltered sport than did usual care in athletes

with intractable OSD symptoms. Dextrose injection resulted in more rapid and frequent achievement of asymptomatic sport than either lidocaine injection or usual care. Those athletes that dropped sport or were unable to perform OSD exercises were only from the usual care group; this finding merits additional prospective study.

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