

## Prolotherapy

### Dextrose Prolotherapy Injections for Chronic Ankle Pain

In this retrospective observational study of chronic unresolved ankle pain, Hackett-Hemwall dextrose prolotherapy helped promote a measurable decrease in the pain and stiffness of the treated joints and improvement in clinically-relevant parameters.



*In this continuing series, Dr. Hauser reports on patients treated for unresolved ankle pain at a volunteer charity clinic having limited resources and personnel between 2000 to 2005. Treatment consisted of injecting a dextrose solution at specific ankle sites to stimulate healing of ligaments, tendons and joints. Patients—including those who were told by prior doctors that 'nothing more could be done' or that 'surgery was the only option'—responded favorably to treatment as demonstrated by reports of reduced pain levels, increased range of motion, extended ability to exercise, reduced depression, reduced anxiety, and a reduction in medications needed.*

—Donna Alderman, DO

By Ross A. Hauser, MD; Marion A. Hauser, MS, RD; and Joe Cukla, BA, LPN

Ankle sprains, especially of the lateral ligaments, are extremely common injuries in the general and athletic populations. Approximately 25,000 people sprain their ankles daily.<sup>1</sup> Sprains constitute 85% of all ankle injuries and, of these, 85% are inversion sprains.<sup>2</sup> Sprains of the lateral ankle complex make up 38-45% of all injuries in sports.<sup>3,4</sup> The recurrence rate for lateral ankle sprains has been reported to be as high as 80%.<sup>5</sup> Up to 40% of individuals have residual ankle symptoms due to chronic instability.<sup>6</sup> A 2005 study from the University of Basel in Switzerland found that 70% to 80% of patients with chronic

ankle instability end up with arthritic ankles.<sup>7</sup> Long term residual symptoms from ankle sprains that do not heal can result in ongoing problems including pain, stiffness, limited range of motion and the inability to exercise or walk long distances.

Options such as medications, physical therapy, steroid shots, bracing and surgery typically leave the patient with residual symptoms.<sup>8</sup> While the response to acute ankle sprains is usually quick; treatment for chronic ankle pain has had limited success. According to a 1999 review, there are more than 20 different delayed surgical procedures available for chronic ankle pain and instability. While most of these procedures are reconstructive in nature, none really restore true anatomy.<sup>9,10</sup> Because of this, many patients with chronic pain, including ankle pain, are open to alternative treatments. One of the treatments they are receiving is prolotherapy since more physicians are getting trained to perform it.<sup>11</sup> Prolotherapy for ankle ligament injuries has even been mentioned in the *Mayo Clinic Health Newsletter*.<sup>12</sup>

While prolotherapy has been used for decades to treat ankle injuries and chronic ankle pain, no specific studies on the results of prolotherapy on patients with chronic ankle pain have been done.<sup>13</sup> Because of this, we decided to measure the response of patients who received dextrose prolotherapy. Not only did we look

at pain levels, but we also reported on a host of quality of life measures that are important to those with chronic ankle problems.

#### PATIENTS AND METHODS Framework and setting

In October 1994, the primary authors (R.H., M.H.) started a Christian charity medical clinic called Beulah Land Natural Medicine Clinic in an impoverished area in southern Illinois at which the primary treatment modality offered was



**FIGURE 1.** Typical prolotherapy injection sites for Hackett-Hemwall prolotherapy of the ankle

**TABLE 1. Patient Characteristics Prior to Prolotherapy**

Ankle patients n=19	
Percentage of female patients	63%
Percentage of male patients	37%
Average age of ankle patients	52
Average years of pain	3.3
Average number of MD's seen	3.3
Average number of pharmaceutical drugs	1.0
No other treatment options available	63%
Surgery only treatment option available	11%

Hackett-Hemwall dextrose prolotherapy for pain control. Dextrose was selected as the main ingredient in the prolotherapy solution because it is the most common proliferant used in prolotherapy, is readily available, inexpensive (compared to other proliferants), and has a high degree of safety.<sup>14</sup> The clinic met every three months until July 2005. All treatments were provided at no cost to the patients.

**Patients**

Patients who received prolotherapy for their unresolved ankle pain in the years 2004 to 2005 at the charity clinic were called by telephone and interviewed by a data collector (D.P.) who had no prior knowledge of prolotherapy. General inclusion criteria were an age of at least 18 years, possessing unresolved ankle pain that typically responds to prolotherapy, and an ability to undergo at least four prolotherapy sessions, unless the pain remitted with fewer prolotherapy sessions. Typical ankle conditions that respond to prolotherapy include ankle instability, ankle ligament sprain, and ankle degenerative arthritis.

**Interventions**

The Hackett-Hemwall technique of prolotherapy was used to treat each ankle. Each patient received 20 to 30 injections of a 15% dextrose, 0.2% lidocaine solution with a total of 15 to 30 cc of solution used per ankle. Injections were given into and around the areas on the ankle that were painful and/or tender to touch. The typical areas injected, each with 0.5 to 1 cc of solution, can be seen in Figure 1. Tender areas injected were on the lateral and medial malleolus, talus, calcaneus, and into and around the tibiotalar joint. The tender areas of the attachments of the deltoid, anterior and posterior talofibular, and calcaneofibular ligaments were also injected. As much as their pain would allow, the patients were asked to cut down or stop the pain medications they were taking.

**Outcomes**

D.P. was the sole person obtaining the patient follow-up assessment information during the telephone interviews approximately 21 months after they were treated. They were asked a series of questions about their pain and various symptoms before starting prolotherapy. Their response to prolotherapy was also de-

tailed with an emphasis on the effect prolotherapy had on their ankle pain, stiffness, and quality of life. Specifically, patients were asked questions concerning years of pain, pain intensity, stiffness, number of physicians seen and medications taken, quality of life concerns, psychological factors, and whether the response to prolotherapy continued after the treatment sessions stopped.

**Analysis**

The patients' responses to the telephone questionnaire were gathered and analyzed before prolotherapy and then compared with the responses to the same questions after prolotherapy. The responses were also analyzed in a subset of patients who answered "yes" to the following statement: "Before starting prolotherapy it was the consensus of my MD(s) that there were no other treatment options that he or she knew of to get rid of my chronic ankle pain."

**Patient characteristics**

Complete data was obtained on a total of 19 ankle patients who met the inclusion criteria. Of these, 63% (12) were female and 37% (7) were male. The average age of the patients was 52 years old. Patients reported an average of 3.3 years (40 months) of pain and on average saw 3.3 MDs before receiving prolotherapy. The average patient was taking 1.0 pain medication. Sixty-three percent (12) stated that the consensus of their medical doctor(s) was that there were no other treatment options for their chronic pain. Eleven percent (2) stated that the only other treatment option for their chronic ankle pain was surgery (see Table 1).

**Treatment outcomes**

Patients received an average of 4.4 prolotherapy treatments per ankle. The average time of follow-up after their last prolotherapy session was twenty-one months.

Patients were asked to rate their pain and stiffness levels on a scale of 1 to 10 on a visual analog scale (VAS) with 1 being no pain/stiffness and 10 being severe crippling pain/stiffness. The 19 ankles had an average starting pain level of 7.9 and stiffness of 5.4. Ending pain and stiffness levels were 1.6 and 1.5 respectively (see Figures 2a and 2b). Ninety-five percent reported a starting pain level of 6 or greater, while none had a starting pain

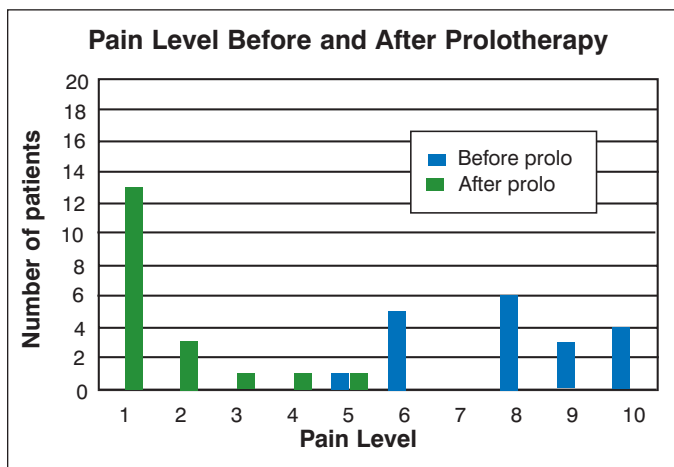


FIGURE 2a. Pain levels before and after receiving Hackett-Hemwall prolotherapy in 19 patients with unresolved ankle pain.

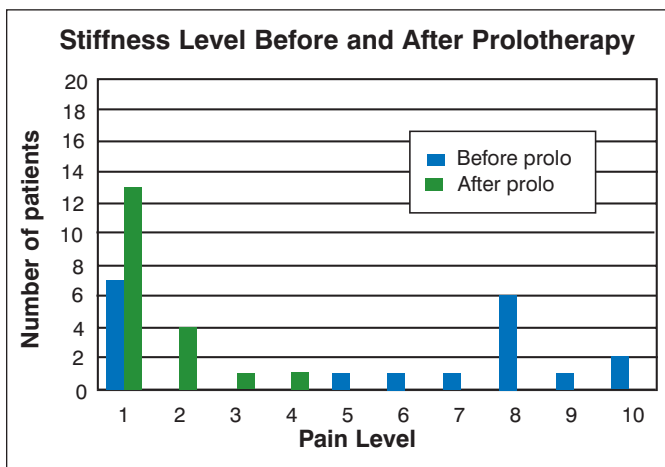
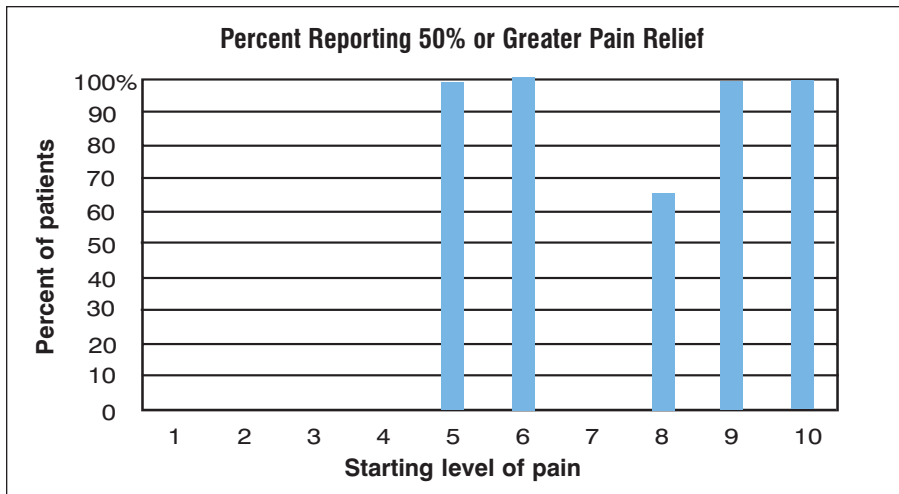


FIGURE 2b. Stiffness levels before and after receiving Hackett-Hemwall prolotherapy in 19 patients with unresolved ankle pain.



**FIGURE 3.** Percent of patients who reported 50% or greater pain relief after receiving Hackett-Hemwall dextrose prolotherapy.

level of four or less. After prolotherapy none had a pain level of 6 or greater, while 90% had a pain level of two or less.

One hundred percent of patients stated their pain and stiffness was better after prolotherapy. Over 78% reported that pain and stiffness since their last prolotherapy session had not returned. Ninety percent of patients stated prolotherapy relieved them of at least 50% of their pain (see Figure 3). One hundred percent of patients experienced at least 25% pain relief with prolotherapy. In regard to pain medication usage, before prolotherapy the average patient was taking 1.0 pain medications but this decreased to only one patient needing one pain medication after prolotherapy. No one not on medications when their prolotherapy sessions ended had to subsequently return to tak-

ing medications because of increased ankle pain.

Patients ranked their crepitation (crunching) on a scale of 1 to 10 with 1 being no crepitation and 10 being severe crepitation. Before prolotherapy, the average crepitation was rated as a 3.2, but after prolotherapy 1.3. Forty-seven percent reported at least 75% of normal motion before prolotherapy, but this increased to 95% percent of normal motion after prolotherapy (see Figure 4).

In regard to quality of life issues prior to receiving prolotherapy, 74% noted problems with walking, but after prolotherapy only 37% experienced compromised walking. In regard to exercise ability before prolotherapy, only 47% could exercise longer than 30 minutes, but after prolotherapy this increased to 90% (see

Figure 5).

Prior to prolotherapy, 47% of patients expressed feelings of depression and anxiety. After prolotherapy, only 5% expressed depressed feelings and 16% anxiety (see Figure 6 and Figure 7). In regard to sleep, 79% of patients felt pain interrupted their sleep. After prolotherapy, 74% experienced improvements in their sleeping ability.

To a simple yes or no question, “Has prolotherapy changed your life for the better,” all of the patients treated answered “yes.” One hundred percent of patients knew someone who had received prolotherapy. Sixty-seven percent came to receive their first prolotherapy session because of the recommendation of a friend. One hundred percent of patients have recommended prolotherapy to someone.

**Results for those whose MDs said no other treatment option available**

As previously noted, 63% of patients (12) prior to prolotherapy were told that there were no other treatment options for their pain. As a group they suffered with pain on average 53 months. In analyzing these patients, their starting average pain level was 8.0 and after prolotherapy 4.3. Prior to prolotherapy, they rated their ankle stiffness and crunching as 5.9 and 3.5 respectively. After prolotherapy stiffness and crunching were 1.4 and 1.3, respectively. Ten of twelve (83%) experienced 50% or greater pain relief. Before prolotherapy all twelve felt that their exercise ability was compromised. After prolotherapy, 75% felt their exercise ability was completely back to normal.

**Statistical analysis**

A matched sample paired t-test was used to calculate the difference in responses between the before and after measures for pain and stiffness for the 19 patients and the subgroup of 12 patients who were told by their medical doctor(s) that there were no other treatment options available. Using the paired t-test, all p values for pain and stiffness for the two groups reached statistical significance at the  $p < 0.0007$  level or less (see Table 2).

**DISCUSSION**

**Principle Findings**

The results of this retrospective, uncontrolled, observational study show that prolotherapy helped to decrease pain and stiffness in the patients’ treated joints and

Demographics	All Ankle Patients	No Other Treatment Options
Total number of patients	19	12
Average months of pain	40	53
Average pain level before Prolotherapy	7.9	8.0
Average pain level after Prolotherapy	1.6	4.3
Paired t ratio	22.855	4.851
P value	$p < .000000$	$P < .000128$
Average stiffness level before Prolotherapy	5.4	5.9
Average stiffness level after Prolotherapy	1.5	1.4
Paired t ratio	22.429	4.624
P value	$p < .000000$	$P < .000736$
Greater than 50% pain relief	90%	83%

**TABLE 2.** Summary of results of Hackett-Hemwall dextrose prolotherapy ankle study.

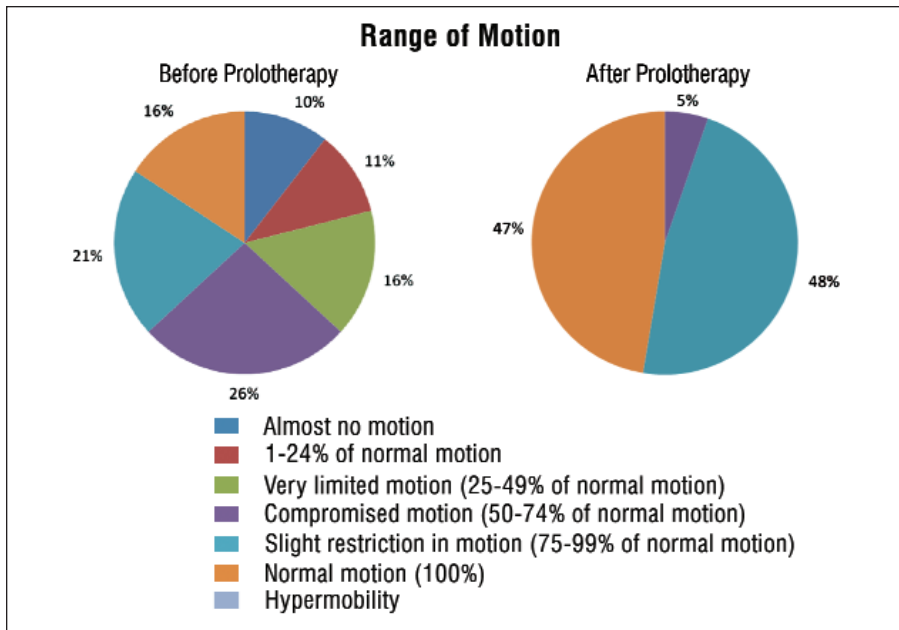


FIGURE 4. Starting and ending range of motion before and after receiving Hackett-Hemwall dextrose prolotherapy in 19 patients with ankle pain.

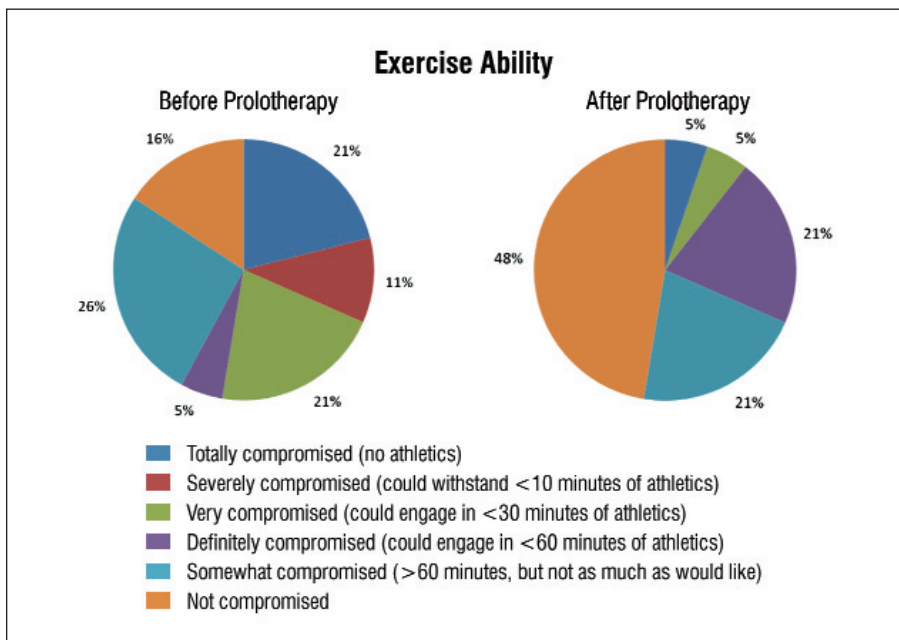


FIGURE 5. Starting and ending ability to exercise before and after receiving Hackett-Hemwall dextrose prolotherapy in 19 patients with ankle pain.

improved their quality of life that had been compromised due to unresolved ankle pain. The Hackett-Hemwall dextrose prolotherapy gave 90% of them at least 50% pain relief. All (100%) experienced at least 25% or more pain relief. One hundred percent of patients stated their pain was less and their life improved with prolotherapy. Notable improvements in quality of life issues including

stiffness, crepitation, range of motion, walking ability, depression, anxiety, sleep, exercise ability, and medication usage was also observed with prolotherapy.

When the data was analyzed for just the 63% (12) of patients who stated their doctors said there were no other treatment options available, significant improvements in pain, stiffness, and exercise ability with Hackett-Hemwall dextrose pro-

lotherapy was also observed.

### Strengths and Weaknesses

Our study cannot be compared to a clinical trial in which an intervention is investigated under controlled conditions. Instead, its aim was to document the response of patients with unresolved ankle pain to the Hackett-Hemwall technique of dextrose prolotherapy at a charity medical clinic. Clear strengths of the study are the numerous quality of life parameters that were examined. Quality of life issues such as range of motion, stiffness, athletic (exercise) ability, sleep, anxiety and depression, in addition to their pain levels, are important factors affecting the person with unresolved ankle pain. Decreases in medication usage were also documented. The improvement in such a large number of variables treated solely by prolotherapy is likely to have resulted from prolotherapy. So while there is no medical test to document pain improvement or the progress with prolotherapy, the patients' increased abilities to exercise and sleep, and their ability to become less dependent on pain medications are measurable changes.

The quality of the cases treated in this study is also a strength. The average person in this study had unresolved ankle pain for three years and four months and had seen over three physicians. Twelve (63%) patients were told by their MDs that there was no other treatment option for their pain. So clearly this patient population represented chronic unresponsive ankle pain. Follow-up time on average of twenty-one months since their last prolotherapy session and having the improvements from the prolotherapy endure, also represented clear strengths and an indication that the positive changes were due to prolotherapy.

Because this was a charity medical clinic with limited resources and personnel, the only therapy initiated was prolotherapy. The prolotherapy treatments could only be given every three months whereas in private practice, the Hackett-Hemwall technique of dextrose prolotherapy is typically given every four to six weeks. If a patient is not improving or has poor healing ability, the prolotherapy solutions may be changed and strengthened and the client is advised on additional measures to improve their overall health. This can include advice on diet, supplements, exercise, weight loss, change in

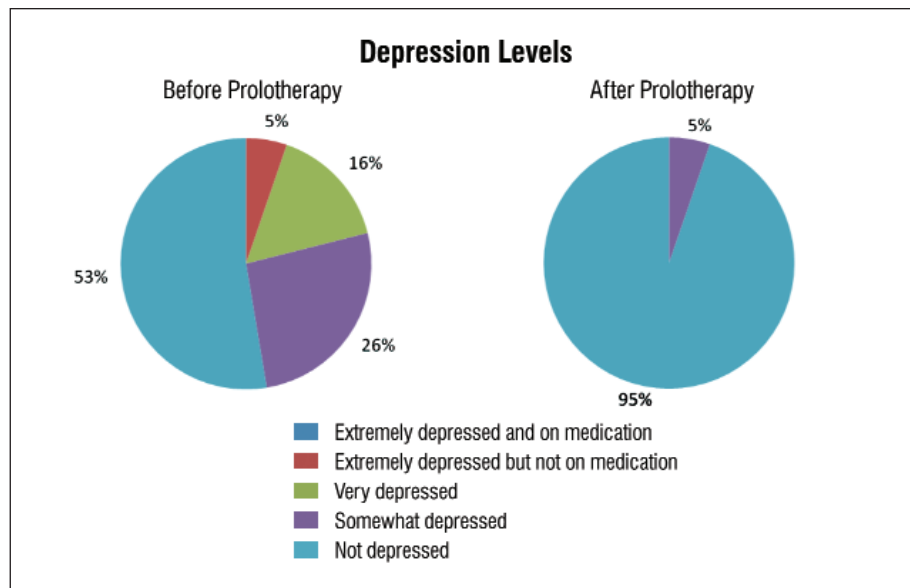
medication, additional blood tests and/or other medical care. Patients are typically weaned immediately off anti-inflammatory and opioid medications that inhibit the inflammatory response that is needed to produce a healing effect from prolotherapy. Since this was not done in this study, the results at this charity clinic are an indication of the minimum level of success with Hackett-Hemwall dextrose prolotherapy. This makes the results even that much more impressive.

A shortcoming of our study is the subjective nature of some of the evaluated parameters. Subjective parameters of this sort included pain, stiffness, anxiety, and depression levels. The results relied on the answers to questions by the patients whose respective changes in their answers were documented pre- and post-prolotherapy. A lack of X-ray and MRI correlation for diagnosis and response to treatment also represents a potential weakness. Lack of physical examination of documentation in the patients' charts made categorization of the patients into various diagnostic categories impossible.

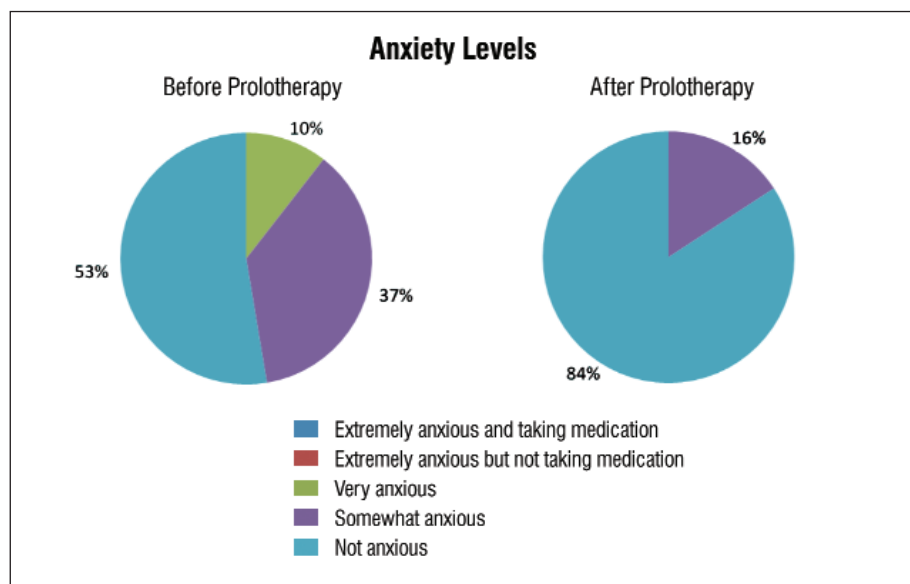
**Interpretation of Findings**

Hackett-Hemwall dextrose prolotherapy was shown to be very effective in eliminating pain and stiffness and improving the range of motion and quality of life in this group of patients with unresolved ankle pain. This included the subgroup of patients told by their MDs that there were no other treatment options for their pain or that surgery was their only option. Current conventional therapies for unresolved ankle pain include medical treatment with analgesics, non-steroidal anti-inflammatory drugs, anti-depressant medications, steroid shots, trigger point injections, muscle strengthening exercises, bracing, physiotherapy, weight loss, rest, massage therapy, manipulation, acupuncture, surgery, education and counseling. The results of such therapies are typically short term and often leave the patients with residual pain.

While the exact cause of chronic ankle pain is still debated, this study did show that the Hackett-Hemwall technique of dextrose prolotherapy improves not only the pain level of those with chronic ankle pain, but also a host of other quality of life measures. This treatment to the ankle involves injections into all of the various ligaments that stabilize the part of the ankle where the person is experiencing symp-



**FIGURE 6.** Starting and ending depression levels before and after receiving Hackett-Hemwall dextrose prolotherapy in 19 patients with ankle pain.



**FIGURE 7.** Starting and ending anxiety levels before and after receiving Hackett-Hemwall dextrose prolotherapy in 19 patients with ankle pain.

oms. For lateral ankle pain this involves the ligaments of the lateral ankle complex, including the anterior talofibular, calcaneofibular, and posterior talofibular. For anterior ankle pain that is higher, the syndesmotic ligament complex is injected. The ligaments involved include the anterior tibiofibular, posterior tibiofibular, and the distal interosseus membrane between the tibia and fibula. For medial ankle pain, the deltoid ligament with its complex of very strong thick ligaments is injected. Prolotherapy gets at both the superficial and deep deltoid ligaments in-

cluding the posterior tibiotalar and anterior tibiotalar ligaments (see Figure 8).

Prolotherapy is the injection of a solution for the purpose of tightening and strengthening weak tendons, ligaments, or joint capsules. Prolotherapy works by stimulating the body to repair these soft tissue structures. It starts and accelerates the inflammatory healing cascade by which fibroblasts proliferate. Fibroblasts are the cells through which collagen is made and by which ligaments and tendons repair. Prolotherapy has been shown in one double-blinded animal study in a

six-week period to increase ligament mass by 44%, ligament thickness by 27%, and the ligament-bone junction strength by 28%.<sup>15</sup> In human studies on prolotherapy, biopsies performed after the completion of prolotherapy showed statistically significant increases in tendon and ligament collagen fibers and diameters by 60%.<sup>16,17</sup> Its primary use is in pain management associated with tendinopathies and ligament sprains in peripheral joints.<sup>18,19</sup> It is also being used in the treatment of spine and joint degenerative arthritis.<sup>20,21</sup> Some before and after prolotherapy X-ray studies document the reversal of osteoarthritis.<sup>22,23</sup>

One explanation for the lack of response of chronic ankle pain sufferers to traditional conservative therapies is that their underlying problem, ligament laxity, is not being addressed. Ligament injury has been implicated as the cause of degenerative osteoarthritis not just the ankle but in joints in general.<sup>24-26</sup> Since prolotherapy is given at the ligament/bone interface, it presumably stimulated ankle ligament repair in this patient population, causing a marked decrease in pain and improvement in patients' quality of life. The question of whether or not ankle degenerative changes are reversed with prolotherapy is left for further research.

### Conclusions

The Hackett-Hemwall technique of dextrose prolotherapy used on patients who had an average duration of three years four months of unresolved ankle pain and who were twenty-one months out from their last prolotherapy session was shown in this observational study to improve their quality of life. They reported less pain, stiffness, crepitation, depressed and anxious thoughts, medication usage, as well as improved range of motion, walking ability, sleep and exercise ability. Overall average pain levels dropped from 7.9 on a 10-point VAS scale before treatment to a 1.6 level after treatment. This included patients who were told by their medical doctor(s) there were no other treatment options for their unresolved ankle pain or that they needed surgery. Ninety percent of the participants experienced 50% or more pain relief. Since this retrospective observational study found such significant improvements in chronic unresolved ankle pain, further studies under more a more controlled environment and

with a larger patient population should be done. Hackett-Hemwall dextrose prolotherapy is a treatment that should be strongly considered for people suffering with unresolved ankle pain.

Hackett-Hemwall dextrose prolotherapy helped the patients make significant improvement in stiffness, range of motion, exercise ability, activities of daily living and walking ability, as well as decreasing their levels of anxiety and depression. Prolotherapy helped all patients on pain medications reduce the amount of medications taken. All 19 patients have recommended prolotherapy to another person. ■

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