ALTERNATIVE MEDICINE

AN EVIDENCE-BASED APPROACH

Prolotherapy for Chronic Back Pain

History and Rationale for Use

Prolotherapy, or proliferative injection therapy, involves the injection of irritant substances into regions of ligaments and tendons with the intention of strengthening the ligaments through local proliferation of granulocytes, fibroblasts, macrophages, and growth factors.

Similar techniques were used in the late 19th century for hernia repair and in the 1930s for subluxation of the temporomandibular joint. Prolotherapy gained popularity after Dr. George S. Hackett gave a presentation on it at the American Medical Association's annual meeting in 1955.

A variety of substances from three classes of proliferants have been used with this technique, with osmotic proliferants being the most common. This class includes solutions of glucose, glycerin, and zinc sulfate that act by provoking cellular osmotic shock, causing the release of proinflammatory cytokines. A second category, referred to as irritants, includes phenol, tannic acid, and guaiaco, and can damage cell surfaces, rendering them antigenic. The third type, chemotactics, also cause a local influx of inflammatory cells. Sodium morrhuate belongs to this class.

Clinical Studies

A recent Cochrane review identified five high-quality studies that included 366 patients aged 18 years and older with chronic low back pain. The protocols were notably heterogeneous, which the authors acknowledged made intertrial comparisons difficult and meta-analysis and levels of evidence summaries impossible (Cochrane Database Syst. Rev. 2007;doi:10.1002/14651858CD004059.pub3).

One study compared injections of a solution containing glucose, glycerin, phenol, and lidocaine with injections of a control solution of normal saline, and two studies compared a glucose, glycerin, phenol, and lidocaine solution with a lidocaine control solution. A fourth compared a glucose plus lidocaine solution with saline solution, and the fifth compared a solution of phenol, dextrose, glycerin, and procaine with a procaine control solution.

In two of the studies, only three injection treatments were given, using only 10 mL of solution. In the other studies, at least six treatments were given, using at least 20 mL of solution. Other protocol differences were related to prior administration of triamcinolone and lidocaine into muscle tender points and lumbosacral ligaments.

The authors of the review reported that three studies that compared prolotherapy alone with control injections alone found no evidence for efficacy, whereas benefits were seen in the two studies that compared prolotherapy plus other modalities such as spinal manipulation and exercise.

Of the two positive studies, one that included 79 patients found a greater proportion of patients in the active prolotherapy group had achieved a decrease of 50% or more in pain or disability 6 months after a series of six weekly injections, compared with patients in the control group, who received injections of xylocaine/saline solution (J. Spinal Disord. 1993;6:23-33).

► Prolotherapy involves the injection of irritant solutions into ligamentous regions with the goal of alleviating chronic back pain.

► Two studies that combined prolotherapy with spinal manipulation and exercise have demonstrated benefits for chronic low back pain, and more studies are planned.

Another study that included 81 patients found a regimen of spinal manipulation plus proliferant injections of a dextrose, glycerin, and phenol solution was more effective in reducing pain than was a program of sham manipulation plus saline injections. Significant differences favoring the prolotherapy treatment also were seen between the groups in the proportion of patients who had an improvement in disability scores of more than 50% at 6 months. This proportion was 88% in the group receiving prolotherapy, manipulation, and exercise, compared with 55% in the control group (Lancet 1987;2:143-6).

This last study "has some of the most impressive results for low back pain I've ever seen," the lead author of the Cochrane review, Simon Dagenais, D.C., Ph.D., said in an interview. He and his colleagues have sought permission from the Food and Drug Administration to conduct further studies, but the agency has been reluctant to accept any of the older data. He has completed two animal toxicity studies, and once the data analysis is complete, he plans to file an investigational new drug application for a phase I study of the mixture of dextrose, glycerin, phenol, and lidocaine.

Safety Concerns

With the burgeoning of prolotherapy in the 1950s came clinical experimentation with a variety of irritant solutions, sometimes by inexperienced practitioners, and several serious adverse events occurred. A 50-year-old woman who received injections of a solution of zinc sulfate and phenol solution developed adhesive arachnoiditis and hematoma and died. A 53-year-old woman was injected with vegetable oil and anesthetic and developed spastic paraplegia that was unrelieved by laminectomy. A 56-year-old man was injected in the lower back with an unknown substance and developed pain and nausea, urinary urgency, and incontinence and later died (Spine 2005;5:310-28).

Adverse events other than spinal puncture headache have not been reported with injection of solutions containing dextrose, glycerin, and phenol. The safety of prolotherapy is likely comparable to that of other commonly used injections for chronic low back pain, such as epidural steroid injections, said Dr. Dagenais, of the division of orthopedic surgery, University of Ottawa, and CAM Research Institute, a nonprofit organization based in Irvine, Calif., that is sponsoring this research.

—Nancy Walsh

Crystal Shape, Size Distinguish Types of Gout

BY DIANA MAHONEY

New England Bureau

BOSTON — To differentiate definitively between acute gout and pseudogout, look at the crystals.

On UV light microscopy, fluid aspirated from the inflamed joint of a patient with pseudogout will be teeming with rhomboid-shaped calcium pyrophosphate dihydrate (CPPD) crystals, which are morphologically different from the needle-shaped monosodium urate (MSU) crystals implicated in the pain and swelling of acute gout, Dr. Dwight R. Robinson said at a meeting on rheumatology sponsored by Harvard Medical School. "[CPPD] crystals are less well formed and show more variation in size and shape than [MSU] crystals."

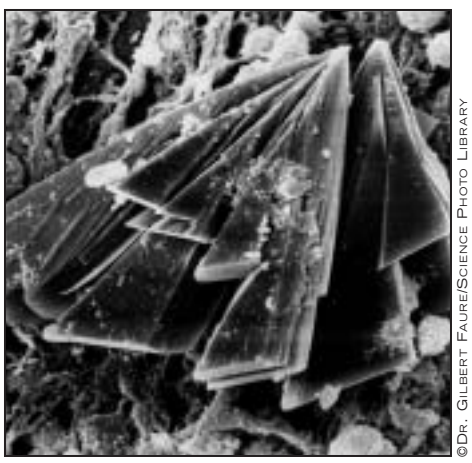
Like MSU crystals in gout patients, the deposition of CPPD crystals in pseudogout causes acute pain and swelling the joints. The acute attacks can last from 1 day to 4 weeks and may be accompanied by fever, leukocytosis, and elevated acute-phase reactants, said Dr. Robinson, a rheumatologist and professor of medicine at Harvard Medical School, Boston. The latter signs also may be indicative of septic arthritis, so sepsis first must be excluded by Gram stain and culture of synovial fluid.

CPPD crystals have a predilection for depositing in articular and fibrocartilage, said Dr. Robinson. In pseudogout, this process commonly involves the knee or wrist joint but also may involve the first metatarsophalangeal joint, as occurs in gout, or almost any other joint. Radiographically, the diagnosis of pseudogout often can be confirmed by evidence of chondrocalcinosis in the affected joint.

In addition to mimicking the clinical patterns of gout, CPPD joint disease symptoms may overlap with other inflammatory conditions. It may be asymptomatic in many patients.

CPPD disease develops in patients older than age 50. In younger patients, "it's more likely to be a complication of osteoarthritis, a late consequence of joint trauma or knee meniscectomy, or related to an underlying metabolic disease." There also may be a familial component.

The exact mechanism for the development of CPPD deposition disease is uncertain, but an overactivity of enzymes that break down nucleoside triphosphates has been implicated, as have genetic defects.



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Rhomboid-shaped calcium phosphate crystals are typical of pseudogout.

Acute attacks can be treated effectively with nonsteroidal anti-inflammatory drugs, said Dr. Robinson. Given the risks of gastrointestinal and renal toxicities associated with NSAIDs, particularly in elderly patients, intra-articular corticosteroid injection into the affected joint is a reasonable treatment option, he said. ■