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CASE REPORT

Intra-articular Glucose Injections for Orthoregeneration of Frozen Shoulder. A Clinical Case.

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ABSTRACT

Frozen shoulder or adhesive capsulitis is a difficult to treat disorder characterized by pain and loss of movement. Novel therapies such as hydraulic distension with orthobiologics may improve outcomes among individuals with this debilitating condition. The clinical case in this article describes the treatment of a patient with frozen shoulder using a series of joint injections using high volumes of sugar water. The positive outcome of this novel injection technique is an invitation to design clinical trials using orthobiologics for frozen shoulder.

Keywords: adhesive capsulitis, frozen shoulder, intra-articular injections, orthobiologics, prolotherapy, capsule-preserved hydraulic distension, glucose, dextrose, intra-articular steroids, hydrodilataion

Introduction

Frozen shoulder is a common disorder, affecting 2% to 5% of the general population.^{1,2,3} It is characterized by pain in the shoulder, stiffness, and decreased range of motion. It frequently occurs following periods of immobilization. Diagnosis is based on physical examination and imaging. The pathophysiological process of frozen shoulder involves fibrous inflammation of the joint capsule and intraarticular adhesion of synovial folds leading to capsular thickening and contracture. Adhesive capsulitis is an idiopathic condition and has an increased prevalence in patients with diabetes mellitus and hypothyroidism. Pain is typical worse with certain movements of the arm and may interrupt sleep. Clinical examination reveals global restriction of both active and passive range of movements at least in two planes. Loss of external rotation is one of the early clinical signs.⁴ Ultrasound and magnetic resonance imaging (MRI) studies can rule out other structural lesions. Especially coracohumeral ligament thickening on MRI is specific for adhesive capsulitis.⁵ When left untreated, adhesive capsulitis may evolve over several months to two years. The principal clinical characteristics of the usual three stages are pain, pain and stiffness, and stiffness, respectively.

Treatment of Adhesive Capsulitis

The most effective treatment for adhesive capsulitis is uncertain. Nonsurgical treatments include physiotherapy, nonsteroidal anti-inflammatory drugs, intra-articular steroid injections, injections of orthobiologics, and hydrodilatation. Traditional physical therapy,^{6,7,8,9} trigger point therapy¹⁰ and deep heat

therapy¹¹ can be beneficial adjuvant treatment options. Steroid injections into the joint are applied worldwide since the 1970s.¹² Corticosteroid injections are still considered standard treatment of care today,^{13,14,15} probably because these injections usually produce immediate symptom reduction. The long-term effects of steroids, however, are still unclear. To avoid potential tissue damage caused by steroid injections,^{16,17,18} newer and safer injectates are becoming more popular in the last decade, such as orthobiologics.

Orthobiologics

Orthobiologics, also known as orthopedic biologics, have appeared as a recent technological trend in orthopedics (Table 1). The goal of orthobiologics is to improve regeneration of musculoskeletal tissues by injecting biomaterials.^{19,20,21,22} Orthoregeneration is a solution for orthopedic conditions that harnesses the benefits of biology to reduce pain, improve function and stimulate tissue regeneration. Various orthobiologics have been investigated for tissue healing of rotator cuff tendons, glenohumeral articular cartilage, glenoid labrum and joint capsule.²³ Promising and established treatment modalities include, for example, sugar water (SW), hyaluronic acid (HA), platelet-rich plasma (PRP) and bone marrow concentrate (BMC).²⁴ Both PRP injections²⁵ and HA injections²⁶ have been used for treatment of frozen shoulder. Injections of sugar water are becoming more popular because of their safety and easy application. There have been several studies to confirm the potential of SW injections in knee osteoarthritis^{27,28,29}, but there are no RCTs yet to confirm their clinical efficacy in treatment of shoulder osteoarthritis or adhesive capsulitis.

Sugar Water
Hyaluronic Acid
Platelet-rich Plasma
Bone Marrow Concentrate

Table 1: Examples of Orthobiologics

Hydraulic Distension with Sugar Water

High volumes of injectates can be used to *expand* the shoulder capsule. Hydraulic distension of the shoulder joint capsule can provide pain relief and immediate improvement in range of motion by expanding the capsule. The clinical improvement is greater in capsule-preserved distension than in capsule-ruptured distension.^{30,31} Capsule-preserved hydraulic distension (CPHD) with maximal volume is suggested to be an efficacious treatment option for persistent adhesive capsulitis. To prevent capsule rupture, a volume of up to 20 mL can be used in adults.³² Both saline solution as well as sugar water can be used as injectates for hydraulic distension. Lidocaine or procaine can be added to the injectate but is not mandatory because most patients experience almost no pain during or after the procedure. On top of that, adding local anesthetics is an additional manipulation which may jeopardize sterility of the injectate. As some authors have found that hypertonic saline (3% NaCl) is more effective than normal saline solution (0.9% NaCl) in patients with adhesive capsulitis³³, one can hypothesize that hypertonic sugar water is also more effective than isotonic sugar water when applying CPHD. More clinical studies can confirm this hypothesis.

Intraarticular Sugar Water Injections

Several studies have illustrated that glucose or dextrose can be injected into the joint with

interesting outcome for knee osteoarthritis.^{34,35,36,37,38,39}

The mode of action of these joint injections is probably related to *biological effects* of glucose or dextrose,⁴⁰ such as reduction in urinary C-terminal telopeptide of type II collagen,⁴¹ change in synovial-fluid neurocytokine concentrations,⁴² upregulation of MMP2, EGF, CXCL 9 and IL-22,⁴³ or suppression of MMP1 expression through the FAK, MEK, ERK, and AP1 signaling pathways.⁴⁴ Last year it was found that intra-articular dextrose injection in grade IV knee osteoarthritis leads to prompt and medium-term analgesia, accompanied by potentially favorable changes in synovial fluid neurocytokines SP and NPY.⁴⁵ More research may reveal to what extent clinical outcome is affected by SW volume, SW osmolarity, or both. It is highly likely that similar mechanisms are at work when giving *shoulder* injections with SW. It is hypothesized that the mechanisms as described in Table 2 may also be beneficial for adhesive capsulitis as these five processes may help in supporting tissue damage in the cartilage and joint capsule. More research is required to confirm this. Although there are many studies available about intraarticular SW injections on osteoarthritis, it is obvious that the application of SW into a joint cavity (instead of IV) is off-label use in most countries.

Reduction in urinary C-terminal telopeptide of type II collagen
 Change in synovial-fluid neurocytokine concentrations
 Upregulation of MMP2, EGF, CXCL 9 and IL-22
 Suppression MMP-1 expression through FAK, MEK, ERK, AP-1 signaling pathways
 Favorable changes in synovial-fluid neurocytokines SP and NPY

Table 2: Biological Effects of Glucose or Dextrose Joint Injections

Clinical case

A 62-year-old man had pain in the right arm and shoulder since January 2023. There was no history of trauma or immobilization. There was stiffness and reduced range of motion. He typically woke up each night at 2 am and could not sleep for an hour because of severe shoulder pain. He did not take pain killers nor sleeping tablets. On ultrasound investigation, there was thickening of the joint capsule. When treatment was started, there was restricted external rotation (30°) and restricted lateral elevation (90°).

He first received three weekly intraarticular joint injections with hyaluronic acid (2 mL). As there was no improvement after more than a month, he received a series of hydraulic distensions. He got intraarticular joint injections with 10 mL of glucose 10%, twice a week. This combination of 10 mL of 10% sugar water (Glucose 1g / ampoule) was chosen because these ampoules are registered and available as such in Belgium. It is not clear yet if other volumes or osmolarities of glucose produce better clinical outcome. No steroids were added. The injections were not painful during or after the procedure. The procedure took less than a minute to inject the 10 mL into the joint cavity. The patient was instructed to move his arm in a circle for about half a minute after injection. Immediately after the procedure,

there was an immediate sense of relief and an improved range of motion. This subjective improvement was about 30% for both pain and stiffness, but these effects lasted less than 24 hours. Still, after five sessions, there was an obvious and sustained improvement in range of motion, especially external rotation (45°). Lateral elevation remained at 90°. He was happy to notice that after these five sessions, he no longer woke up each night at 2 am and could sleep again as before. It is, of course, hard to say if these improvements were a direct result of the sugar water injections or due to a natural evolution of his capsulitis. By continuing the above treatment on a regular basis, the pain in his arm went from 7/10 on a visual analog scale (VAS) in the beginning of treatment to VAS 2/10 after 10 sessions. He did not follow the prescribed physiotherapy program and did not take any medication. He mentioned his quality of life had improved, although certain movements were still limited. After these five weeks of treatment, he was now able to take his wallet out of his back pocket without pain. MRI on June 30 showed no rotator cuff tear. There were signs of degenerative chondro-labral changes and some capsular thickening (axillary and anterior), confirming the capsulitis. In a second phase of treatment, he received weekly intraarticular joint injections with 20 mL of glucose 10%. By giving double dose of

glucose (2g instead of 1g) and double volume of injectate (20 mL instead of 10 mL), further improvement of pain, stiffness and range of motion was observed. When injecting large volumes up to 20 mL, there is a potential risk of capsule rupture.⁴⁶ There is no protocol yet

to adapt the volume of injectate to the size or weight of the patient. The procedure with 20 mL is a little painful and gives a sense of pressure in the shoulder for about two minutes.

Mechanical Benefits: Hydraulic Distension

Chemical Benefits: Biological Effects of Sugar Water

Table 3: Benefits of High-Volume Joint Injections with Sugar Water

The goal of this novel approach is to combine the mechanical benefits of hydraulic distension with the biological effects of glucose or dextrose (Table 3). It is hypothesized that a series of these high-volume sugar water injections can speed up the recovery of capsulitis, but more clinical studies are mandatory to confirm if this novel injection method can be a safe and efficient tool in the treatment of frozen shoulder. The combination with other modalities such as physical therapy should be advised at all times.

long-term effect and an excellent safety profile. The downside, however, is that more sessions are required. It would be interesting to design a study on sugar water joint injections for shoulder *osteoarthritis* rather than for *frozen shoulder* because osteoarthritis is easier to treat than adhesive capsulitis. More preclinical and clinical research is needed before this novel injection technique can become part of the current standard treatment protocols.

Conclusion

Frozen shoulder is a common disorder characterized by pain and loss of movement. Hydraulic distension with orthobiologics such as sugar water may improve outcomes among individuals with this chronic condition. The optimal volume and concentration of sugar water is still subject to debate. This clinical case can be regarded as an invitation to design long-term clinical trials using sugar water injections into the shoulder joint. Although sugar water injections are less potent than steroid injections in reducing pain in the short term, they have an interesting

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