Glucopuncture for Rotator Cuff Related Shoulder Pain: an Alternative for Cortisone?

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ABSTRACT
As rotator cuff related shoulder pain is quite prevalent, it is important that doctors continue to look for new treatment modalities, which are safe and effective. Over the last decade, isotonic glucose (or dextrose) injections have received more attention among clinicians. Unfortunately, no large randomized clinical trials have confirmed their effectiveness so far. However, their safety profile is very likely to be much better than subacromial corticosteroid injections. This article invites the medical community for further basic-science and clinical studies to investigate the potential benefits of local isotonic glucose injections for rotator cuff related shoulder pain. The goal of introducing the term Glucopuncture is to explain the difference with prolotherapy, to inform doctors about the interesting risk-benefits ratio of these regional isotonic glucose injections and to invite them to use these sugar water injections instead of cortisone injections.

Introduction
Shoulder injuries come in many forms. There is rotator cuff tear, joint capsule pain, and biceps tendon overuse, pain originating from the acromioclavicular (AC) joint, shoulder instability, supraspinatus tendinopathy, calcific tendinopathy, and adhesive capsulitis. Rotator cuff related shoulder pain (RCRSP) is a clinical term describing an injury of the rotator cuff tendons where the patient presents with pain, limited range of motion, stiffness, reduced muscle strength or a combination of those. Usually, these symptoms exacerbate by specific movements of the neck, arm and shoulder blade. Age above 50 years, diabetes and overhead activities are associated with increased risk of rotator cuff tendinopathy [1]. Unfortunately, clinical diagnosis and management of RCRSP are not straightforward.

Management of Rotator Cuff Related Shoulder Pain
Rotator cuff related shoulder pain (RCRSP) is a term which encompasses a wide spectrum of shoulder conditions including sub acromial pain (impingement) syndrome, rotator cuff tendinopathy, and symptomatic partial and full thickness rotator cuff tears [2]. MRI of the shoulder can lead to a precise classification system for tear thickness, size, and degree of retraction [3]. The goal of treatment is to achieve symptom free shoulder movement and function.

Recent investigations suggest that an exercise approach confers at least equivalent benefit as that derived from surgery for impingement syndrome, rotator cuff tendinopathy, partial thickness rotator cuff tears and atraumatic full thickness rotator cuff tears [4]. Rehabilitation protocols for RCRSP should be tailored based on the different phases of tendon healing [5]. Despite growing evidence of the importance of physiotherapy, in particular active exercise therapy, little data is available to guide treatment [6-8]. Platelet Rich Plasma (PRP) and hyaluronic acid (HA) injections are safe and sometimes effective for tendinopathies [9,10]. Subacromial corticosteroid injection for rotator cuff disease and intra-articular injection for adhesive capsulitis may be beneficial although their effect may be small and not well maintained [11]. Despite many RCTs of corticosteroid injections for shoulder pain, their small sample sizes, variable methodological quality and heterogeneity means that there is little overall evidence to guide treatment [11]. Although cortisone is still popular among family physicians and orthopedic surgeons, most investigators conclude
that injections with corticosteroids can be effective on the short run but should be avoided because of poor long-term results and serious side effects [12].

**Calcific Tendinopathy**

Calcific tendinopathy of the shoulder involves calcification and degeneration of the rotator cuff tendon near its insertion point on the greater tuberosity. Extracorporeal shockwave therapy (ESWT), ultrasound-guided percutaneous irrigation of calcific tendinopathy (US-PICIT), and surgery are all options in today’s medicine [13]. The question remains whether the calcification noticed on imaging is the actual cause of the pain. Many patients with calcifications are pain-free, and many patients have pain without calcifications. In other words, it is important to treat the patient and not the X-rays or MRI.

**Definition of Glucopuncture**

Glucopuncture (GP) is an easy-to-learn outpatient procedure, which focusses on the patient’s clinical symptoms rather than on X-rays and MRI. Glucopuncture is defined as an injection-based therapy for the management of a variety of musculoskeletal conditions and mild regional pain [14]. It consists of multiple local injections with Glucose 5% in water (G5W) or Dextrose 5% in water (D5W) into musculoskeletal soft tissues. Adding local anesthetics is not required. Injections are mainly given in dermis, muscles, fascia, tendons and ligaments. GP requires only a short treatment time. The mode of action of G5W or D5W is still subject to debate. ATP may play an important role [15-18]. The mechanism of action is probably complex and multifactorial. In vitro studies have shown that glucose resulted in production of a number of growth factors such as PDGF, TGF-β, EGF, b-FGF, IGF-1, and CTGF. This may be important for tissue repair [19]. It remains to be illustrated in vivo if this mechanism is also playing an important role when injecting isotonic glucose in the extracellular matrix. One could also argue that the needlestick trauma alone may be sufficient to induce an inflammatory response [19]. TRPV1 upregulation in sensory neurons may also play a role [20,21] but it is still unclear if this phenomenon is specifically related to the glucose itself or rather to the needle effect [22,23]. Recent findings suggest that glucose can reduce TNF-α-induced NF-κB activation, upregulation of proinflammatory cytokines, and metabolic dysfunction [24].

**History of Glucopuncture**

**Hypertonic Solutions**

Glucose and dextrose injections have been used for decades in prolotherapy [25-27]. Prolotherapy is an American injection technique, which uses hypertonic concentrations of dextrose (more than 10% net concentration) into the entheses of tendons and ligaments. Such hyperosmolar injections into the extracellular matrix (ECM) cause an immediate osmotic shock. This hyperosmotic stress extracts water from the cells, inducing cell shrinkage. This leads to a series of changes in intracellular kinase cascades [28]. The osmotic shock rapidly leads to cell membrane rupture, cell destruction and cell death. Products such as arachidonic acid are released from the cell membrane into the ECM, which can evoke a local inflammatory reaction. The latter can lead to a tissue repair cascade resulting in deposition of new collagen and tissue proliferation – hence the name prolotherapy [29,30]. However, as cell damage and cell death are not the goal of glucopuncture because it may create small tissue scars, hypertonic solutions such as glucose 10-15% net concentration are avoided. In the search for injection solutions without this side effect, isotonic injectates are recommended, such as G5W or D5W. Adding local anesthetics is avoided as these might be neurotoxic [31].

**Isotonic Solutions**

The subcutaneous approach of isotonic glucose was first introduced in the literature by Dr Lyfgott in a tendinosis pilot study with three month follow up [32]. Later on, glucose 5% (or dextrose 5%) injections were used to treat other forms of musculoskeletal pain [33-35]. Some physicians also used glucose 5% injections for tennis elbow [36], Dupuytren’s stage 1, carpal tunnel syndrome [37], perineural injections [38], epidual injections [39] and nerve hydridissection [40]. In a recent study, the short term effects of perineural glucose 5% injections were similar to cortisone, and the long term effects were even better than cortisone [41]. It seems that glucose 5% injections might replace corticosteroid injections soon, especially in the treatment of mild forms of non-rheumatic musculoskeletal pain and regional neuropathic pain.

**Clinical Application of Glucopuncture for RCRSP**

**Intradermal and Intralesional Injections**

To decide how deep to inject and which points to inject, the doctor does not rely on ultrasound or MRI but on questioning and clinical examination. Questioning is required to identify the pain region. This pain region is treated with multiple intradermal injections. Clinical examination is required to localize sore points in soft tissues such as pectoral muscle, deltoid muscle, biceps tendon, joint capsule, infraspinatus muscle, trapezius muscle, AC ligament. These palpation-guided injections in soft tissues are given for tissue repair. It is obvious that X-rays, ultrasound and MRI can still be important to rule out serious lesions, which cannot be treated with Glucopuncture, such as fracture or tumor.

**Questioning and Clinical Examination**

One should ask the patient to point out the region of pain referral (the pain region), and in what position the pain is evoked (evoked pain region). Tenderness is often localized to the greater tuberosity, the biceps tendon, the acromium and the deltoid muscle while the arm is at 90 degrees elevation. Sometimes the major tender region on palpation is the anterior side of the joint capsule, or even a specific area in the forearm muscles. If only light pressure is needed to evoke the patient’s pain, one should give only shallow injections in the tender region, otherwise deeper injections are necessary. When the patient experiences pain when lying on the affected shoulder, one should pay extra attention to pain points in the lateral part of the deltoid muscle, subacromial bursa and lateral border of the acromium. Multiple injections of about 1 ml are given in the region. The total amount of volume usually ranges from 5 to 25 ml each session. Improvement is expected after two or three weekly sessions. Fresh injuries require only one or two sessions, chronic shoulder problems between five and ten sessions.
However, if no clinical improvement is noticed after five sessions, one should look for another treatment modality.

A Call for More Research
It is obvious that large randomized controlled trials are required to make specific recommendations regarding ideal protocols and indications of Glucopuncture. In the meantime, no strong claims about glucopuncture can be made. The introduction in 2021 of a new term to describe these isotonic injections may make it better known among patients and professional health care providers (www.glucopuncture.com). Doctors, who have experienced the benefits of Glucopuncture, can afterwards improve their skills by following a training in prolotherapy, neuroprolotherapy, PIT, ultrasound guided perineural injections, ultrasound guided hydrodissection, joint cavity injections or epidural injections.

Conclusion
As rotator cuff related shoulder pain is very prevalent, it is important that patients have access to treatment modalities which are safe, affordable and effective. Several clinicians have experienced that glucose 5% injections are an inexpensive and easy to learn treatment to modulate pain and to support periarticular tissue repair. More research in this field may confirm their clinical findings.

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Table 1: Difference between PT (Prolotherapy) and GP (Glucopuncture).

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ID: Intradermal (IC or SC); IM: Intramuscular; PT: Peritendinous; IL: Intraligamentous; IA: Intraarticular.

References


