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Glucopuncture for Achilles tendinopathy: A descriptive review

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Abstract

As sports related injuries such as Achilles tendinopathy are prevalent, it is important to investigate new treatment modalities which are safe, easy-to-apply and effective. Over the last decade, glucose 5% injections have received more attention among clinicians. Unfortunately, no large randomized clinical trials have confirmed their effectiveness so far. This article invites the medical community for further basic-science and clinical studies to clarify the potential benefits of local glucose 5% injections for Achilles tendinopathy. The goal of introducing the term Glucopuncture is to raise awareness among physicians of the interesting risk-benefit ratio of regional glucose 5% injections and to point out the difference with Prolotherapy.

Keywords: Achilles tendinopathy; Glucopuncture; Pain Modulation; Prolotherapy; Sports Medicine

1. Introduction

Achilles tendinopathy (AT) is a clinical term describing an injury of the Achilles tendon where the patient presents with pain, swelling, reduced performance or a combination of those [1]. Usually, these symptoms exacerbate by physical activities such as walking, jumping, and running [2]. Achilles tendinopathy is commonly observed in runners, tennis players, soccer players, jumpers, basketball players, cyclists, and gymnasts [3-5]. Unfortunately, clinical diagnosis and management of AT are not straightforward [6].

Achilles tendinopathy is often defined as a degenerative, non-inflammatory, condition and is usually described as an overuse injury [7]. It is a painful condition which may be accompanied by alterations in the tendon's structure such as proliferation of tenocytes, degeneration in tendon cells and disruption of collagen fibers [8]. Neo-vascularization may also play an important role [9]. The major histological and molecular features of tendinopathy include disorganization of collagen fibers, increase in sensory nerve innervation, dysregulated extracellular matrix homeostasis, increased inflammatory mediators, increased immune cells, and enhanced cellular apoptosis [10].

Extrinsic causes of Achilles tendinopathy include overuse such as increased intensity or duration of activity, improper shoes, and previous local treatments with corticosteroid injections. Intrinsic causes of Achilles tendinopathy include varus heel or varus forefoot, quinolone antibiotics and oral corticosteroid treatment.

Injections adjacent to the Achilles tendon with corticosteroids can be effective on the short run but are avoided because of poor long-term results and serious side effects [11]. Platelet Rich Plasma and hyaluronic acid injections are sometimes effective but rather expensive [12, 13].

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2. Definition of Glucopuncture

Glucopuncture is an easy-to-learn office procedure which can be performed without ultrasound guidance. Glucopuncture is defined as an injection-based therapy for the management of a variety of musculoskeletal conditions in the inpatient setting [14-17]. It consists of multiple local injections with Glucose 5% in Water (G5W) or Dextrose 5% in Water (D5W). Injections are mainly given in dermis, muscles, fascia, tendons and ligaments. As the injectate is inexpensive, the technique is interesting for low-income countries and for low-income patients in high-income cities.

3. Working Hypothesis

Glucopuncture has two clinical effects, tissue repair (a) and pain modulation (b). Anecdotal evidence suggests that glucopuncture can have favorable effects on the physiological repair mechanisms of damaged or inflamed tissues such as muscles, fascia, tendons, and ligaments (a). In vitro studies suggest that even low concentrations of glucose can induce several growth factors, but it is not clear yet if this is also the case when injecting glucose in the extracellular matrix (ECM). Anyway, growth factor stimulation may explain tissue repair observed after glucose injections. But pain modulation (b) is also an important effect of glucose 5% injections. As multiple injections in soft tissues are given, one also reaches multiple peripheral nerve endings in those muscles, tendons and ligaments. One also reaches the pain receptors in the dermis while giving intradermal injections. When giving intradermal injections, transient receptor potential ankyrin1 (TRPA1), a member of the TRP channels, may act as 'polymodal cellular sensor' on primary sensory neurons where it mediates the peripheral and central processing of pain [18, 19]. It is hypothesized that a major path way in explaining the effects of glucopuncture in pain modulation (analgesia, not anesthesia) is agonism of the transient receptor potential ion channel vanilloid 1 (TRPV1). TRPV1 is commonly referred to as the vanilloid or capsaicin receptor and is critically involved in inflammatory pain [20]. But recent data demonstrate that TRPV1 is also crucial for the needle effect and that it can initiate the excitatory pNR1-pCaMKII pathway, at peripheral DRG and central SC-SSC level [21]. Dry needling might downregulate proinflammatory neuropeptides, proinflammatory cytokines, and neurotrophins, and modulate TRPV1 [22-26]. This means that TRPV1 is probably a *nonspecific* effect of glucopuncture [27]. That is why the ATP hypothesis has been proposed to explain the *specific* effect of glucose injections in the ECM. The energy demands of the nervous system are primarily met by glucose which is oxidized through glycolysis and oxidative phosphorylation to produce ATP [28, 29]. This may explain the importance of glucose abundance for peripheral nerve endings to modulate peripheral (regional) pain [30]. The pathways of ATP production have to respond rapidly to changes in energy demand at the synapse to sustain neuronal activity [31, 32]. However, there is no solid scientific back-up of the ATP hypothesis (yet) to explain the clinical effects of glucopuncture. When giving intramuscular injections, substance P may play an additional role in the antinociceptive effects of glucose injections [33]. And epidermal growth factor (EGF) may play a key role in tissue healing after intradermal glucose injection [34]. Recent findings suggest that glucose can reduce TNF-α-induced NF-κB activation, upregulation of proinflammatory cytokines, and metabolic dysfunction [35].

4. History of Glucopuncture

Glucose and dextrose injections have been used for decades in prolotherapy [36-38]. Prolotherapy is an American injection technique which applies *hypertonic* concentrations of dextrose (10- 20% 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 cells, inducing cell shrinkage. This leads to a series of changes in intracellular kinase cascades [39]. The osmotic shock rapidly leads to cell membrane rupture, cell destruction and cell death. Products such as arachidonic acid from the cell membrane are released in the ECM. This can evoke a strong (local) inflammatory reaction. The latter can lead to deposition of new collagen and tissue proliferation – hence the name *prolo*therapy [40,41]. This process can lead to shrinking of connective tissue, which can be interesting when dealing with elongated ligaments. Prolotherapy can also lead to thickening of tendons [42, 43]. Thickening of connective tissue may be an advantage when dealing with weak tendons or ligaments but it is a disadvantage when treating, for example, Dupuytren's Grade 1. Hypertonic glucose injections may also have negative effects on nerve conduction [43]. In the search for injection solutions without these undesired effects, *isotonic* injectates are recommended, such as glucose 5% or dextrose 5% [44]. Isotonic glucose injections probably stimulate growth factors but they do not evoke inflammatory reaction through osmotic shock (which is typical for prolotherapy). Adding local anesthetics to glucose 5% is not required (see Table 1).

Table 1 Difference between Prolotherapy and Glucopuncture

	Prolotherapy	**Glucopuncture**
What?		
Hypertonic Glucose	x	-
Local Anaesthetics	x	-
Isotonic Glucose	-	x
Where?		
Intradermal	-	x
Intramuscular	-	x
Peritendinous	-	x
Intraligamentous	x	x
Intraarticular	x	-
How?		
Osmotic Shock	x	-
Proliferation	x	-
Growth Factors	x	x
ATP Production	x	x

5. Diverse Application of Isotonic Glucose Injections

The application of glucose 5% injections was first introduced in South Korea by Dr Kim MY in 1997 for treatment of myofascial trigger points [45]. Later on, glucose 5% injections were used to treat Achilles tendinopathy [46], tennis elbow [47], low back pain [48], carpal tunnel syndrome [49], rotator cuff [50, 51], epidural injection [52], sports injuries [53] and nerve hydrodissection [54]. In a recent study, the short term effects of glucose 5% injections were similar to cortisone, and the long term effects were even better than cortisone [55]. It seems that glucose 5% injections might replace steroid injections in the near future, especially in the treatment of non-rheumatic musculoskeletal pain, regional neuropathic pain and sports injuries [56].

6. Clinical Application of Glucopuncture

There are two main injection techniques used in Glucopuncture, superficial injections and deep injections. Superficial injections are given in dermis, deep injections are applied into 'soft tissues' such as myofascial trigger points, tendons and ligamentous pain points. The superficial injections are given for pain modulation, deep injections are given for both local pain modulation and local tissue repair.

As a single session usually gives rise to temporary pain modulation, sessions need to be repeated on a regular basis. Fresh sports-related injuries usually need only one or two sessions which can be given in the same week, chronic tendinopathies require between five and ten weekly (or two-weekly) sessions. In chronic cases, one should also check the calf muscles for muscular trigger points and also check the lower back and hips. The most frequent side effects of GP are bruising, itching and local dermatitis. These usually subside without treatment within a week.

7. 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 of this new term to describe isotonic glucose (or dextrose) injections may increase awareness about this novel technique among both patients as well as professional health care providers.

8. Glucopuncture for Achilles Tendinopathy

Clinical examination is focused on the Achilles tendons, heels and calf muscles. Passive ankle dorsiflexion and active resisted plantar flexion may cause increased pain. Tendon rupture needs to be excluded before injections are started [57]. During clinical examination, the area which is tender to palpation needs to be identified first. This zone may vary depending on the type of tendinopathy. When dealing with mid-portion Achilles tendinopathy, the tender zone is usually from 2,5 to 5 cm (1 to 2 inch) away from the calcaneus. When dealing with insertional Achilles tendinopathy, the tender zone is found near the insertion of the tendon close to the heel bone. Nodules and crepitation may also be present. Myofascial trigger points may be found in the calf muscle.

The treatment itself is remarkably simple and straightforward (Fig 1). Ultrasound guidance is not required as the injections are palpation-guided. This approach makes the procedure less time consuming and less expensive. The injections are given while the patient is lying prone. The procedure typically takes less than a minute to perform. After identifying the tender zone, one gives multiple subcutaneous injections with glucose 5% in that region. The injections are usually given 1 cm apart. About 1 mL is given in each spot with a 30 G or 27 G needle. If both the medial side of the Achilles as well as the lateral side are tender, both sides are injected. If subcutaneous injections are not effective, injections closer to the tendon are advised. The total volume per session is usually between 5 and 10 mL, depending on the size of the tender region. If necessary, injections are also given in muscular trigger points in the calf (Fig. 2).

Figure 1 Subcutaneous Injections of Glucose 5% (Five injections on Each Side)

Figure 2 Intramuscular Injections of Glucose 5%, 1 – 3 cm deep (about 0,4 – 1,2 inch)

Usually, the patient experiences some improvement after the injections. The patient may report that pain has diminished after the procedure, or walking is more comfortable. This is rather surprising, as no local anesthetics are added. Unfortunately, this pain modulating effect of isotonic glucose does not last. To obtain long term and lasting results, repetition is required. More clinical research is required to confirm these anecdotal experiences. It is obvious that glucopuncture can or should be combined with other treatment modalities such as eccentric exercises [58] and functional rehabilitation of the Achilles tendon [59, 60].

9. Conclusion

As Achilles tendon injuries are very prevalent, it is important that patients all over the world 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 technique to modulate pain and to support tendon repair. Glucopuncture can be considered as a low invasive, safe and highly accessible form of treatment for mild forms of musculoskeletal pain, including Achilles tendinopathy. More research in this field may confirm this hypothesis.

Compliance with ethical standards

Disclosure of conflict of interest

Both authors declare there were no conflicts of interests while writing this article.

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