

## Isotonic glucose injections for anterior knee pain: A clinical case study

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### Abstract

A case study is presented which gives insight into a new treatment modality for mild anterior knee pain of unidentified origin. This report describes a case of a 58-year-old patient who complained about non-traumatic knee pain for several months. She received local intradermal glucose 5% injections in the pain region every two weeks and was almost completely pain free after four sessions. Glucopuncture is a new term to describe regional glucose 5% (or dextrose 5%) injections into soft tissues such as dermis, muscles, tendons and ligaments. The goal of this technique is to replace steroid injections with glucose 5% injections in cases of mild non-rheumatic musculoskeletal pain.

**Keywords:** Anterior Knee Pain; Glucose; Dextrose; Intradermal Injection; Glucopuncture; Prolotherapy

### 1. Introduction

In this article, a patient is presented who complained about pain in the medial-anterior part of the right knee for several months. She received a series of local treatments with subcutaneous glucose 5% injections in the pain region. The goal of this clinical case is to share clinical experience with this palpation-guided technique and to invite colleagues to initiate more research to investigate the safety, working mechanisms and efficacy of this new injection technique in the treatment of mild musculoskeletal pain. Until large randomized clinical trials have been performed, no definitive claims about glucopuncture can be made. In other words, glucopuncture does not rely on sound scientific basis (yet).

### 2. Anterior Knee Pain

Anterior knee pain (AKP) is one of the most common knee problems in physically active patients [1-4]. The reason for anterior knee pain has been suggested to be multifactorial with patella abnormalities or extensor mechanism disorder leading to patellar malalignment. As patients present with a variety of symptoms and clinical findings, clinical examination is crucial for optimal treatment. Weakness of the quadriceps muscle is often present. One may also find active trigger points in the quadriceps muscle, frequently a few centimeter (one inch) superior to the patella. However, some patients have no other symptoms but localized pain in the anterior part of the knee without any other clinical or radiological findings. In many cases, MRI findings are negative. The goal of the treatment described here is to reduce pain by local glucose 5% injections and to get the patient back to normal activities without injecting corticosteroids. If necessary, one can afterwards apply physiotherapeutic measures to improve the balance between vastus medialis and vastus lateralis, restore normal gait, and improve postural control.

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### **3. Differential Diagnosis**

In the diagnosis of AKP, it is important to rule out serious and morbid causes of knee pain, including infection and tumor [5]. Although these causes are very uncommon, X-rays, lab tests, ultrasound and MRI can be used in case of doubt. When a serious patellar malalignment is suspected, referral to an orthopedic surgeon who is specialized in this field may be required.

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### **4. Management of Anterior Knee Pain without Medical Imaging**

The weakness of this article is its lack of a specific diagnosis, as no ultrasound or MRI has been executed. However, this weakness is also its strength. This case may illustrate that in many cases ultrasound and MRI are normal despite the patient complaining about anterior knee pain. On top of that, physicians who work in remote areas or deal with patients with low income and no insurance coverage, can apply the described technique as a test-and-treatment approach. If the clinical outcome is positive after a few sessions, no extra radiological investigations are required. However, when a series of local isotonic glucose injections does not produce any clinical improvement, it is worth considering ultrasound or MRI, and ask a second opinion from an orthopedic surgeon.

#### **4.1. Treatment Options for Anterior Knee Pain**

Most family physicians, orthopedic surgeons and sports doctors prescribe NSAIDs in combination with physical therapy to manage chronic knee pain, including anterior knee pain. If these do not prove effective, local corticosteroid injections are the next step. Corticosteroid injections are effective for short-term pain relief in patients with osteoarthritis but are no longer advised because of the side effects and poor long-term benefits of injectable steroids in the treatment of musculoskeletal pain [6-9]. Although corticosteroid injections are still one of the most commonly used treatment modalities for musculoskeletal disorders, there is an obvious lack of good trials defining the indications for and efficacy of such injections. In other words, many of the recommendations for the use of local corticosteroid injections do not rely on sound scientific basis [10, 11]. Regional subcutaneous Glucose 5% injections, also known as Glucopuncture, is a new treatment modality which is still understudied [12, 13].

#### **4.2. Glucose 5% injections for Anterior Knee Pain**

In the search for efficient yet safe treatment modalities, local subcutaneous glucose 5% (G5W) or dextrose 5% (D5W) injections have become more popular in recent years. It has been used for myofascial pain [14] and other forms of musculoskeletal pain [15-18]. It has been applied for carpal tunnel syndrome [19], epidural injection [20] and nerve hydrodissection [21]. In a recent study, the short term effects of perineural glucose 5% injections were similar to steroids, and the long term effects were even better than steroid injections [22].

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### **5. Mode of Action**

The exact mechanisms of glucopuncture are probably multifactorial. It is hypothesized that neurogenic inflammation and TRPV1 receptors play a role when it comes to pain modulation by glucose 5% injections. Although research into glucose 5% injections is still at an early stage, the available clinical evidence indicates that in the near future, glucose 5% injections can replace corticosteroid injections in the treatment of mild non-rheumatic musculoskeletal pain. Unfortunately, the exact mechanism of action of glucose 5% injections is largely unknown. One of the hypotheses is the ATP theory, which suggests that glucose molecules injected in the extracellular matrix (ECM) might be transported into the cell and stimulate ATP production in the mitochondria. Glucose is transported across the cell membrane by a specific transport system [23]. ATP is considered to be a crucial indicator for cellular energy status and viability, thus a vital variable for tissue regeneration and in vitro tissue engineering [24]. It is hypothesized that injecting glucose in the ECM may lead to “charging” of the cells via ATP production. Recent findings suggest that glucose can mitigate TNF- $\alpha$ -induced NF- $\kappa$ B activation and upregulation of proinflammatory cytokines [25].

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### **6. Difference between Prolotherapy and Glucopuncture**

Glucose (and dextrose) injections have been used for several decades in prolotherapy [26-29]. However, prolotherapy typically uses high concentrations of dextrose (10% to 15% net concentration) and requires adding local anesthetics to reduce injection discomfort. Such hyperosmolar solutions lead to cell shrinking, osmotic rupture, and subsequent cell destruction. This phenomenon creates a local inflammatory reaction [30]. This may lead to tissue proliferation – hence the description “prolo”. Because isotonic solutions such as glucose 5% do not evoke osmotic cell rupture, the term

“prolotherapy” does not apply to injecting isotonic solutions such as G5W (or D5W). Hence the new term “Glucopuncture”.

### 6.1. Clinical Case

The patient, a 58-year-old language teacher presented with pain in the right knee for several months (Fig 1). She mentioned her knee pain was worse after biking for more than half an hour. Walking up or down the stairs did not evoke or worsen the pain. There was no obvious redness or swelling. There was no limited range of motion of the knee or hip. There was no history of a traumatic event such as an accident or fall on her knee. There was no family history of rheumatoid arthritis.



**Figure 1** Pain in the right knee



**Figure 2** Patient indicated the pain region



**Figure 3** One particular point, 1, 5 cm medial to the patella tendon



**Figure 4** An intradermal injection (SC: subcutaneous) with 5mL of G5W into the pain point

On the first visit, the patient indicated the pain region, which she pointed out with one finger (Fig 2). The pain region was located at a distance of 1, 5 cm (0,4 inches) to the medial side of the patella tendon. The sore region was an area of 1 cm by 1 cm (the size of her fingertip). On clinical examination, all knee tests were normal. When palpating the pain region, the pain could be reproduced by exerting light pressure on that one particular point, 1, 5 cm medial to the patella tendon (Fig 3). This particular point was described as the “pain point”. As the pain was evoked while putting the fingertip only a few mm deep, it was hypothesized that the lesion must also be very superficial. As a result, the needle should be inserted only a few mm deep. The patella tendon itself was not tender. There was no patellar malalignment. No ultrasound examination nor x-rays were ordered yet. After performing hand hygiene and applying gloves, the treatment

zone was sterilized with an antiseptic swab. After allowing the site to dry, she received an intradermal injection (SC: subcutaneous) with 5mL of G5W into the pain point (Fig 4). No local anesthetics or corticosteroids were added. Syringe, needle and injectate were all sterile and single use. The syringe used was a 5 mL syringe with screw lock. The needle used was a 27G x 3/4" needle (2, 5 cm). The procedure only took a few seconds and was not painful.

On the second visit, two weeks later, she mentioned that the knee pain improved for about 50% after the first session and that the improvement lasted for almost a week. Then the pain reappeared while biking during the weekend. She received again an intradermal injection with G5W into that particular pain point (1 x 5 mL).

On the third visit, again two weeks later, she mentioned that the knee pain improved almost completely for almost two weeks. The pain reappeared slightly while biking but did not reappear for the rest of the two weeks. She received again an intradermal injection with G5W into the pain region (1 x 5 mL).

On the fourth visit, again two weeks later, she mentioned that the knee pain improved almost completely. The pain did not reappear while biking. She mentioned a temporary discomfort during squatting for a few seconds. She received a final intradermal injection with G5W and was instructed to get in touch with the clinic as soon as the complaints would reappear. During treatment she did not take any other medication such as pain killers or nonsteroidal anti-inflammatory drugs.

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## 7. Conclusion

As anterior knee pain is prevalent, it is important that family physicians, sports doctors and orthopedic surgeons can offer their patients treatment modalities which are easy to apply, safe and effective. Several clinicians worldwide have experienced that glucose 5% injections are an interesting treatment modality for non-rheumatic musculoskeletal conditions, including anterior knee pain. The term glucopuncture was introduced to inform both physicians as well as patients about the potential benefits of this easy-to-apply treatment modality and to point out the difference with prolotherapy. This article is an invitation to do more research in the field of glucose 5% injections for musculoskeletal pain.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

The authors declare that there are no conflicts of interest or source of funding. The corresponding author declares that he is the practitioner who has given the regional injections, exactly as described above.

### *Statement of informed consent*

Informed consent was obtained from the patient. She has provided a permission by email (June 7, 2022) to use her medical file for this case report.

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