

Injection treatment for chronic midportion Achilles tendinopathy: do we need that many alternatives?

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An abundant amount of different treatment modalities has been developed for treatment of chronic midportion Achilles tendinopathy. Amongst them are injection treatments with as corticosteroids, Polidocanol, autologous blood, platelet-rich plasma, high-volume injections, hyperosmolar dextrose, brisement, aprotinin and low-dose heparin. The rationale behind these treatments is not always clear. The goal of treatment in general is to relieve symptoms. The main symptom is pain. Up to date, the cause of pain in chronic midportion Achilles tendinopathy has not been elucidated however. So what is the rationale behind these treatments?

Corticosteroid injection has become obsolete in the treatment of midportion Achilles tendinopathy, as tendon rupture has been reported in various cases [1, 2]. The role of chemical inflammation in this pathology is also a matter of debate, and therefore there is no rationale for anti-inflammatory treatment [3, 4]. Ultrasound-guided treatment with Polidocanol (Ethoxysclerol) was first described in 2002 [5] as an effective and promising method to obliterate neovessels in and around the tendon, which were hypothesized to be a possible cause of pain. Studies on patellar tendinopathy, lateral epicondylitis, supraspinatus tendinitis, and the effectiveness of larger doses in Achilles tendons followed [6–9]. However, not all authors have been able to

reproduce a good outcome [10]. The blood vessels are unlikely to be the cause of pain. So what is the rationale behind this treatment?

Platelet-rich plasma (PRP) is possibly the current most controversial in the line-up of minimally invasive treatment options. PRP is defined as ‘any elevated level of platelets’. A PubMed search with ‘platelet-rich plasma’ generates 5,565 results. A search term such as ‘autologous blood’ or typographic changes would add many more references. Medical companies legitimately take business advantage of this hype. It is currently used in tendon, muscle and ligament repair, osteoarthritis, surgical wounds and chronic ulcers. However, application has been confusing as each method leads to a different product with different biological characteristics and possible applications. There are at least four different products: pure PRP, leucocyte- and PRP, pure platelet-rich fibrin, and leucocyte- and platelet-rich fibrin. Some of these products can be activated or non-activated [11]. Many types of platelet collectors have been developed, and platelet concentration varies from 1.6–4.4 fold between suppliers compared to whole blood [12]. One of the goals seems to be to develop a technique that collects the highest concentration of platelets. Autologous whole blood and PRP have been used in midportion Achilles tendinopathy with the aim of providing growth factors to promote healing in areas of *degeneration*. However *if* effective, the questions arise: what concentration would suffice, how long do platelets stay where injected and what is their half-life? Supporting the hypothesis that tendinopathy develops due to a failed chemical healing response would then inducing a new chemical reaction suffice? Or are we trying to induce a chemical response in a neurogenic area? Moreover, in case of chronic midportion Achilles tendinopathy, the exact location of injection is not always clearly described. Is it possible to inject a substance *inside* the opaque but

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degenerative tendon proper? And if so, is this degenerative area really the cause of complaints? Several studies have reported intratendinous changes in up to 34% of cadaver specimens, ultrasound and MRI images of patients without complaints [13–18]. A long-term follow-up study published by Alfredson and co-workers revealed persistent structural abnormalities and thickening of the tendon 13 years after intratendinous surgery for Achilles tendinopathy, whereas all patients were satisfied with the results and went back to Achilles tendon loading activities without restrictions [13]. If the pain does not come from the tendon proper, where *does* it originate? Recently various studies have shown ingrowth of sensory- and sympathetic nerves accompanying neovessels from the paratenon with release of nociceptive substances. Denervating the Achilles tendon by release of the peritendineum would hereby hypothetically suffice to relieve pain. Since pain is the predominant symptom in these patients, and it has never been demonstrated that patients with tendinopathy are more prone to rupture, this approach should be sufficient for obtaining a good clinical outcome.

A minimally invasive technique such as high-volume injection has been successfully performed to produce local mechanical effects in order to release the adhesions formed between peritendineum and tendon proper, thereby obliterating neovascularisation and accompanying neovessels. Brisement, first described in 1997 [19], was initially meant to interrupt the degenerative cycle of the tendon proper by initiating a healing cascade, but in essence seems equivalent to current high-volume injections. Now, could not a combination of these two theories, old and new, be the result of all injections? Meaning that no matter what we introduce, an inflammatory response will be generated? This can be illustrated by a randomized study by De Vos et al., where injection of PRP was compared with saline, producing an equivalent outcome [20]. Corticosteroid injections for lateral epicondylitis did not provide any long-term benefit compared with placebo [21]. Brown et al. performed a double-blind placebo-controlled trial in patients with Achilles tendinopathy, where aprotinin was compared with placebo, showing no statistically significant benefit [22].

Until now, an evidence based algorithm for the (conservative) management of midportion Achilles tendinopathy is unknown. Research on Achilles tendon-related problems is ongoing. Further research should focus on the cause of pain in patients with chronic midportion Achilles tendinopathy. Recognising the cause of pain will help to further define therapeutic strategies.

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