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Literature review

Autologous whole blood or corticosteroid injections for the treatment of epicondylopathy and plantar fasciopathy? A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Objectives: To compare the efficacy of autologous whole blood with that of corticosteroid injections on epicondylopathy and plantar fasciopathy.
Design: Systematic review and meta-analysis.
Methods: The databases of PubMed, Web of Science, CENTRAL, and Scopus were searched up to 6th May 2015. Randomized trials comparing the effects of autologous whole blood and corticosteroid injections on epicondylopathy or plantar fasciopathy were included. Trials exploring the efficacy of platelet-rich plasma were excluded. The primary outcome was pain relief. The secondary outcome included the assessment of composite outcomes. All outcomes were assessed at 2–6 (short-term) weeks, 8–13 (intermediate-term) weeks and 24–26 (medium-term) weeks. Quality assessment was performed with the Cochrane risk of bias tool.
Results: Nine trials were included. For pain relief, there was a statistically significant difference in favour of corticosteroids in the short term (SMD 0.52; 95%CIs 0.18 to 0.86; $I^2 = 53\%$; $p < 0.01$). A statistically significant difference in favour of autologous whole blood was indicated in the medium-term assessment of pain relief on epicondylopathy.
Conclusions: Corticosteroids were marginally superior to autologous whole blood in relieving pain on plantar fasciopathy at 2–6 weeks. Autologous whole blood provided significant clinical relief on epicondylopathy at 8–24 weeks. Conclusions were limited by the risk of bias.

1. Introduction

Epicondylopathy and plantar fasciopathy (PF) are two common musculoskeletal disorders. The former reveals an angiofibroblastic tendinosis (Nirschl, 1992), while the latter represents a spectrum of changes that vary from degeneration of the fibrous tissue to fibroblastic proliferation that may or not exhibit evidence of chronic inflammation (Jarde, Diebold, Havet, Boulu, & Vernois, 2003; Leach, Seavey, & Salter, 1986; Lemont, Ammirati, & Usen, 2003).

Both PF and epicondylopathy are thought to be multifactorial. Reduced ankle dorsiflexion, pes cavus and pes planus feet, increased Body Mass Index (BMI) in non-athletic individuals, weight-bearing activities associated with work, and running are predisposing factors of PF (Bolgla & Malone, 2004; Irving, Cook, & Menz, 2006; Martin et al., 2014). Smoking, being of middle age, partaking in specific activities, and obesity are common characteristics for the development of epicondylopathy (Shiri, Viikari-Juntura, Varonen, & Heliövaara, 2006).

It is strongly recommended that clinicians utilize manual therapy, stretching exercises, taping, foot orthoses (either custom-made or prefabricated), and night splints for the management of PF (Martin et al., 2014). As for the treatment of PF, it is evident that a combination of silicon heel pad, fascia-stretching exercises, intrinsic foot muscle strengthening, and corticosteroid injection relieves pain at 1- and 3-month follow-up assessments (Marabha, Al-Anani, Dahmashe, Rashdan, & Hadid, A, 2008). Moreover, it is postulated that foot and ankle disorders are related. This is because of the overlapping of these disorders in terms of the assessment and therapy. This overlapping is defined as regional

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interdependence. Thus, combination treatments aiming at the ankle dorsiflexion exert a positive clinical impact on PF rehabilitation (Cleland et al., 2009).

On the other hand, the initial treatment of epicondylopathy may include activity modification, counter force bracing (Struijs, Kerkhoffs, Assendelft, & Van Dijk, 2004), nonsteroidal anti-inflammatory drugs (NSAIDs) (Green et al. 2002), corticosteroid injections (Gaujoux-Viala, Dougados, & Gossec, 2009), and physical therapy (including progressive eccentric and isometric strengthening) (Bisset, Beller, Jull, Brooks, Darnell, & Vicenzino, 2006; Croisier, Foidart-Dessalle, Tinant, Crielaard, & Forthomme, 2007; Park et al., 2010; Smidt et al., 2003; Struijs et al., 2004). Secondary management of epicondylopathy may include continued physical therapy and activity modification, corticosteroid injections, and alternative therapies (e.g., autologous blood injections).

Multiple injection therapies recently have become available for both epicondylopathy and PF. One of them is a series of injections with autologous growth factors that are delivered in the form of either platelet-rich plasma (PRP) or autologous whole blood (AWB). Platelet-rich plasma is a volume of autologous plasma with platelet concentration above baseline. It is obtained through the centrifugation of autologous venous blood using various preparation systems. The platelet activation, which occurs during PRP preparation, promotes the release of autologous growth factors through the degranulation of the platelets. These growth factors include platelet-derived epidermal growth factor (PD-EGF), platelet-derived growth factor (PDGF), transforming growth factor beta-1 (TGF-β1), insulin-like growth factor (IGF-I, IGF-II), vascular endothelial growth factor (VEGF), endothelial cell growth factor (ECGF), and basic fibroblast growth factor (bFGF) (Foster, Puskas, Mandelbaum, Gerhardt, & Rodeo, 2009). It is evident that a platelet concentration of 1,000,000 platelets/μl in five ml volume of plasma enhances soft tissue and bone healing (Marx, 2001). In contrast to PRP, AWB intervention is an inexpensive and easy-to-prepare treatment modality. It aims to directly deliver growth factors, which are carried in the blood, to the affected site to stimulate healing mechanism (Iwasaki, Nakahara, Nakata, Nakase, Kimura, & Ono, 1995).

It is noted that the majority of the patients who suffer from epicondylopathy or PF are successfully treated non-operatively (Furey, 1975; Nirschl, 1992). However, persistent cases may be approached surgically.

At present, the evidence on the efficacy of autologous blood injections remains inadequate, according to the National Institute for Health and Clinical Excellence (NICE) (IPG438, 2013). The purpose of the present meta-analysis was to compare the clinical impact of AWB with that of corticosteroid injections on epicondylopathy and PF.

2. Methods

2.1. Protocol registration

The present systematic review was registered with PROSPERO (CRD42014012903). In addition, the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines were followed (Liberati et al., 2009).

2.2. Eligibility criteria

Randomized controlled trials (RCTs) were used to compare the impact of autologous venous blood with that of corticosteroids on either epicondylopathy or PF. Human patients 15 years of age or older were enrolled. Trials investigating the efficacy of PRP were not considered in this systematic review and meta-analysis. Full-thickness tendon and fascia tears were excluded from the present study. In addition, experimental studies in animals were excluded.

2.3. Outcome measure

The primary outcome measure was the change in pain intensity levels reported either by questionnaires that measure pain intensity, or by subscales of composite questionnaires. The secondary outcome included the assessment of composite outcomes, measured by questionnaires that assessed pain intensity and functional disability as a minimum. Side effects were also reported. For all study outcomes, there were three time periods of assessment:

1. 2–6 (short-term) weeks.
2. 8–13 (intermediate-term) weeks.
3. 24–26 (medium-term) weeks.

2.4. Literature search

Two reviewers (KT and AT) independently searched for potentially relevant published and unpublished studies using electronic databases, clinical trial registries, conference abstract books, and reference lists of relevant studies. The databases of PubMed, Web of Science, Cochrane Central Register of Controlled Trials (CENTRAL), and Scopus were comprehensively searched with no language restrictions up to May 6, 2015. In addition, the registries of ClinicalTrials.gov, Australian New Zealand Clinical Trials Registry (ANZCTR), and International Standard Randomised Controlled Trial Number (ISRCTN) were searched up to the same date. Moreover, the corresponding authors of completed unpublished studies were contacted to request their results.

The search strategy for PubMed included the use of the following terms: 'autologous blood', 'autologous plasma', 'growth factors', 'tendinopathy', 'tendinosis', 'tendinitis', 'epicondyl*', 'tennis elbow', 'golfer's elbow', 'plantar fasc*', 'corticosteroids', 'injection', 'controlled trials'. This strategy was adapted for each included electronic database and no specific database filters were applied.

2.5. Study selection

Two reviewers (KT and AT) independently identified potentially relevant records. Then duplicates were removed, and the titles and abstracts of the retrieved studies were screened. The full-text of the remaining articles was assessed for eligibility. Any discrepancies between the two investigators were discussed, and consensus was reached.

2.6. Data extraction

Two review authors (KT and AT) independently abstracted data. This meant cataloguing the data according to the number and demographics of the participants, comparators in the control group, and intervention characteristics. Data extraction also included information about the duration of symptoms, outcome measures, follow-up, and side effects. Furthermore, Centre for Evidence Based Medicine (CEBM) guidelines were followed for the classification of the level of evidence of the included studies (Phillips et al., 2009).

If there were more than two intervention groups in an enrolled trial, only the data from the corticosteroid and AWB groups were used in the quantitative synthesis (Deeks, Higgins, & Altman, 2008). In trials with missing information, the corresponding authors of the studies were contacted twice with a three-week interval to request additional data.

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