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Literature review

Autologous blood injection for treatment of lateral epicondylosis: A meta-analysis of randomized controlled trials

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ABSTRACT

Objectives: To appraise existing evidence of autologous blood injection in treating lateral epicondylosis.
Design: Meta-analysis of randomized controlled trials.
Setting: A comprehensive search of the PubMed, Cochrane, SCOPUS, and CINAHL databases was performed to identify randomized controlled trials that reported the efficacy of autologous blood injection in treating lateral epicondylosis. The selected studies were subjected to a meta-analysis and risk of bias assessment.
Participants: Patients with lateral epicondylosis.
Main Outcome Measures: Pain-related measurement in each selected randomized controlled trial was pooled into meta-analysis.
Results: Nine randomized controlled trials were included in the analysis. The results of the meta-analysis including the pain scores indicated that autologous blood injection is more effective compared with corticosteroid injection (standard mean difference: −0.75; 95% confidence interval: −1.14 to −0.37) but not more effective compared with platelet-rich plasma injection (standard mean difference: 0.09; 95% confidence interval: −0.66 to 0.84). The risk of bias assessment indicated that all the included trials exhibited a moderate to high risk of bias.
Conclusion: Autologous blood injection is more effective than corticosteroid injection but not more effective than platelet-rich plasma injection in treating lateral epicondylosis. However, this evidence is limited by the potential risk of bias.

1. Introduction

Lateral epicondylosis (LE), or tennis elbow, is a common syndrome of a degenerative process involving the common tendon of the extensor muscle group of the forearm that originates from the lateral epicondyle of the humerus (Nirschl & Ashman, 2004). Its incidence is approximately 1%–3% in the general population aged between 35 and 54 years, with no sexual predominance (Hamilton, 1986), (Verhaar, 1994). Previous studies have reported that LE is highly prevalent (35%) and severe in competitive tennis players (Carroll, 1981). The clinical characteristics of LE include pain and tenderness over the lateral elbow area, particularly when resisting wrist extension. The syndrome develops progressively and is related to repetitive movements and strenuous tasks (van Rijn, Huisstede, Koes, & Burdorf, 2009). The conservative treatment options for LE include eccentric exercise, shock-wave therapy, splinting, and corticosteroid injection. Reportedly, the long-term outcomes of these management options are similar (Ahmad, Siddiqui, Malik, Abdus-Samee, Tytherleigh-Strong, & Rushton, 2013). However, certain patients are refractory to conservative treatment and experience chronic pain more than 6 weeks.

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Although surgery can be helpful and effective in these patients, the procedure is invasive and destructive (Solheim, Hegna, & Oyen, 2013). Currently, a biological solution injection is being used as an alternative treatment option.

The biological solution, which includes autologous blood and platelet-rich plasma (PRP), was designed based on the underlying pathophysiological mechanism of LE: a degenerative change in the tendon caused by mechanical overload and abnormal microvascular interactions rather than an inflammatory process (Fedorczyk, 2006; Regan, Wold, Coonrad, & Morrey, 1992). The treatments that inhibit inflammatory responses are apparently ineffective in treating LE. Although corticosteroid injections (CSIs) exhibit positive short-term outcomes regarding pain relief, these are associated with a high recurrence rate (Mardani-Kivi et al., 2013).

Autologous blood is collected from peripheral veins and contains several hormonal and cellular mediators that promote the differentiation of tenocytes and substitute degenerated cells to enhance tissue healing (Anitua et al., 2005). Previous studies have used autologous blood for treating chronic tendinopathy and have achieved favorable results regarding pain relief (de Vos, van Veldhoven, Moen, Weir, Tol, & Maffulli, 2010). Edward et al. (Edwards & Calandruccio, 2003) first described the provision of autologous blood injection (ABI) in treating LE and observed reduction of pain and functional improvement during the follow-up period. Although other small-sample randomized control trials (RCTs) have compared the efficacies of CSI and ABI in treating LE, the results have been diverse (Dojode, 2012; Jindal, Gaury, Banshiwal, Lamoria, & Bachhal, 2013; Kazemi, Azma, Tavana, Rezaiee Moghaddam, & Panahi, 2010; Ozturan, Yucel, Cakici, Guven, & Sungur, 2010; Singh, Gangwar, & Shekhar, 2013; Wolf, Ozer, Scott, Gordon, & Williams, 2011).

PRP is the plasma collected from peripheral veins with platelets concentrated after serial processing. The growth factors derived from platelets include platelet-derived growth factor, epidermal growth factor, transforming growth factor-beta 1, vascular endothelial growth factor, basic fibroblast growth factor, hepatocyte growth factor, and insulin-like growth factor, all of which promote tissue healing (Anitua et al., 2005; Middleton, Barro, Muller, Terada, & Fu, 2012). Several studies have used PRP injections for treating sports-related tendinopathies (Ficek, Kaminski, Wach, Cholewinski, & Cieszczyk, 2011; Kaux & Crielaard, 2013). However, the preparation of PRP is more expensive and complex than that of autologous blood. Limited evidence has been documented regarding the relative efficacies of autologous blood and PRP in treating LE (Creaney, Wallace, Curtis, & Connell, 2011; Raeissadat, Sedighipour, Rayegani, Bahrami, Bayat, & Rahimi, 2014; Thanasas, Papadimitriou, Charalambidis, Paraskevopoulos, & Papanikolaou, 2011). In addition, the efficacy of ABI in managing LE in comparison with other treatments remains unknown.

A previous meta-analysis of RCTs compared various injection therapies used to treat LE (Krogh et al., 2013). The results indicated that ABI was significantly more effective than a placebo in treating LE. However, only 2 of the included trials compared ABI with CSI (Kazemi et al., 2010; Ozturan et al., 2010), and only one trial compared ABI with PRP injection (Creaney et al., 2011). Moraes et al. (Moraes, Lenza, Tamaoki, Faloppa, & Belloti, 2013) conducted a meta-analysis and indicated that the effects of PRP injection on LE were uncertain; however, their study did not describe the effects of ABI on LE. Therefore, the present study aimed to perform a comprehensive search of the current literature and to conduct a meta-analysis of RCTs to determine the efficacy of ABI in treating LE.

2. Material and methods

2.1. Eligibility criteria

RCTs reporting the efficacy of ABI in treating LE were included in the metaanalysis. These RCTs compared autologous, whole-blood, intralesional injections with placebos or other types of treatment. Series or duplicate publications in the same or different journals were counted only once. No limitations regarding the language or journal type were considered when including the RCTs.

2.2. Search strategy

Relevant articles were identified using a computer search of the PubMed, Cochrane, SCOPUS, and CINAHL databases. The keywords "blood" and "elbow* or epicond*" were searched within these databases. The relevant RCTs were identified through a set intersection of the keyword "random*" or the limitation function in the databases, if available. In addition, relevant articles were identified using the MeSH function in the databases and by manually searching for the references of the relevant articles. The final search was performed in June 2014.

Two reviewers independently reviewed the full texts of all the relevant articles to identify those fulfilling the selection criteria. The individually recorded decisions of both reviewers were then compared, and any disagreements were resolved by a third reviewer.

2.3. Data items

Information regarding the inclusion criteria, type of control group, age and number of the participants, follow-up period, and type of outcome measurement was extracted from each identified trial.

2.4. Risk of bias assessment

Quality assessment was performed using the Jadad quality score (Jadad et al., 1996) to assess the risk of bias. Trials scoring 4 or 5 points were considered to have a low risk of bias, those scoring 2 or 3 points were considered to have a moderate risk of bias, and those scoring zero or one point were considered to have a high risk of bias. Sensitivity analysis was performed when one or more trial met the criteria of a high risk of bias.

2.5. Outcomes

Because the most typical clinical presentation of LE is lateral elbow pain, we selected pain-related measurement as our outcome. The pain scores in each study were included in our meta-analysis. When pain-related measurements were unavailable, we selected outcomes that were most relevant to pain. Studies with no outcomes relevant to pain were excluded from our meta-analysis. Data representing the longest follow-up duration were pooled in this meta-analysis.

2.6. Statistical analysis

The comparisons that included $\geq$3 studies were pooled in the meta-analysis. The meta-analysis was performed using RevMan (Version 5.0) software. We calculated the standard mean difference (SMD) with its 95% confidence interval (CI) for continues outcome data. Data were pooled using a random effects model considering the possibility of different study methods and follow-up durations in the various trials. The statistical heterogeneity was calculated using I^2 tests.