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CORR Insights®: Platelet-rich Plasma or Autologous Blood Do Not Reduce Pain or Improve Function in Patients with Lateral Epicondylitis: A Randomized Controlled Trial

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Where Are We Now?

Although lateral epicondylitis was described more than 100 years ago and affects 1% to 3% of the population, its causes and the best treatment approaches remain obscure [4]. Earlier, the prevailing thought was that its etiology was inflammatory (thus the "itis" at the end of the condition's name), but more recently, it has been seen as a complex process of degeneration, decreased healing potential, and hypovascularity [4, 8]. Lateral epicondylitis is not a tendinopathy but rather an enthesopathy, associated with myxoid degeneration involving the origin of the extensor carpi radialis brevis muscle. A study comparing cadaveric and surgical specimens found that that the condition evolves through several stages, beginning with degenerative angiogenesis and ending with fibrosis and calcification [1]. Most patients with this diagnosis can be treated effectively without surgery, because in most patients the condition is self-limited and resolves over the course of 12 to 18 months. However, some patients remain symptomatic for years [8].

Nonsurgical treatments range from wait-and-see to a variety of injections, occupational or physical therapy, iontophoresis or phonophoresis, shock wave therapy or laser therapy, and splinting [8]. Corticosteroids are the most-commonly used product in injections for lateral epicondylitis and are usually mixed with a local anesthetic [1, 4, 5, 10]. Retrospective studies showed that corticosteroid injections have short-term effectiveness, but randomized controlled studies suggested that they are not superior to placebo in the long-term [3, 10].

Edwards and Calandruccio [3] described an injection of autologous blood for refractory lateral epicondylitis, with 50% improvement with one injection and 79% with two injections. They suggested that autologous blood may induce angiogenesis and healing in the area of the lateral epicondyle. Platelet-rich plasma (PRP) was also introduced as an injection agent; an increased concentration of platelets may increase the release of growth factors and cytokines from platelets, thus enhancing the healing process [7]. A study showed that botulinum toxin A injections had a beneficial effect, but these injections likely weaken the extensor muscles [8] and there were no long-lasting benefits.

Recent studies add to the confusion. Some studies found a benefit from using corticosteroids [1], autologous blood, or PRP [2, 5], while other studies found no benefit to the use of these approaches when compared with placebo [5, 8, 9].

One systematic review of overlapping meta-analyses found some evidence suggesting that corticosteroid injections provide short-term pain relief and improvement in function [5]. However, in the long-term, there was no evidence that one method was superior to the other or to the wait-and-see approach. Looking at the available

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evidence in aggregate, it appears that nothing outperforms the patient's natural history and placebo effect.

In this issue of *Clinical Orthopaedics and Related Research®*, Linnanmäki et al. [6] compared the effect of injections of PRP, autologous blood, and saline in reducing pain or improving function in patients with lateral epicondylitis. This randomized controlled study did not find any evidence that PRP or autologous blood reduces pain or improves the function of patients with lateral epicondylitis. They recommended against using these injections in patients with lateral epicondylitis. This is an important, well-designed study. I agree with the recommendation not to use PRP or autologous blood, which are somewhat expensive interventions in practice, at least until a more-convincing study finds them to improve symptoms to a clinically important degree.

Where Do We Need To Go?

Although there have been some randomized controlled studies on this topic, we are still searching for strong evidence to support the use of one modality over others (or more-definitive proof that no treatment beats the natural history of this self-limited condition). To compare a certain method of treatment with another may not be the best way. It would be better to compare these treatments with a placebo. Because randomized controlled studies [3, 10] have found that some treatments are better than others, it would be helpful to compare the different types of treatment with a placebo. This should not be in contradiction to the principles of the Declaration of Helsinki [11], because the disease is known to be self-limiting. Furthermore, because the condition is self-limiting, the interpretation of the results of these types of studies may be clouded, especially if the follow-up period extends to several months [9, 10]. Therefore, we need to evaluate the choice of no treatment when comparing different treatment modalities.

Adding surgical treatment as a component of a double-blind study may not be possible because the surgeon and patient know that the operation happened. However, a single-blind study with a surgical option is possible if the outcome assessor is someone other than the surgeon. This may be worth doing because many surgical procedures are still performed for this diagnosis [8, 10].

Educating patients is important given the nature of this condition. However, when patients complain of pain that interferes with their daily living, work activities, and sometimes even with their sleep, physicians may search for any modality that might offer even short-term effectiveness, such as corticosteroid injections, to give their patients some relief [1, 4, 5].

Another issue is the effectiveness of more than one injection. Some previous double-blind studies allowed for one injection of corticosteroids, PRP, or autologous blood [1, 2, 8, 9]. We should study whether a second or even a third injection would improve the efficacy of those treatments. Edwards and Calandurccio [3] suggested that more than one injection of autologous blood resulted was more effective than a single treatment. We still have gaps of information regarding the best alternative line of treatment. We should try to find a more-definitive answer to the question of the best long-term effective treatment of this condition.

How Do We Get There?

To better define the role of a surgical intervention in treating lateral epicondylitis, further studies with long-term follow-up of more than 2 years to elucidate the best lines of treatment are needed. The inefficacy of non-surgical treatment is not itself sufficient as an indication for surgery, as this may result in too many operations being performed in a patient who, given sufficient time, might improve without surgery [8, 10]. It may be difficult to conduct multicenter double-blind studies, and other more-limited studies can still be useful. This current study [6] is a good example of how to compare different lines of treatment for lateral epicondylitis. Similar studies can be very helpful in comparing other lines of treatment. Further long-term studies with multiple treatment arms may answer some of our questions regarding the best long-term treatment of lateral epicondylitis. As I suggested earlier, any such studies should also compare each component of treatment individually and against no treatment [10].

While several studies have compared various treatments in isolation [2, 3, 8, 9], much less is known about how multiple treatments interact in combination [1]. The potential long-term success of combining more than one treatment modality, for instance, therapy and injections, should be investigated [1]. Evaluating and comparing all different types of treatments for lateral epicondylitis would be impractical because of the numerous treatment modalities in use now. However, a study similar to the current one may be very useful in comparing two or three different options of treatment. I believe the most-promising combination might be corticosteroid injections and physical therapy because there has been some evidence that this combination might have a beneficial effect.

Studies that compare the effectiveness of one type of injection with other types of nonsurgical treatment should evaluate multiple injections. There is

some anecdotal information showing potential enhancement of the final results with the use of more than one injection [3]. In clinical practice, it is common for patients to receive more than one injection. Therefore, objective studies should address the benefit—if any—of more than one injection compared with just one.

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