Original Article

Bone marrow injection: A novel treatment for tennis elbow

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Abstract

Objective: The objective of this prospective study was assessment of efficacy of bone marrow aspirate (BMA) (containing plasma rich in growth factors and mesenchymal stem cells) injection in treatment of tennis elbow. **Materials and Methods:** A total of 30 adult patients of previously untreated tennis elbow were administered single injection of BMA. This concentrate was made by centrifugation of iliac BMA at 2000 rpm for 20-30 min and only upper layer containing platelet rich plasma and mononuclear cells was injected. Assessment was performed at baseline, 2 weeks, 6 weeks and 12 weeks using Patient-rated Tennis Elbow Evaluation (PRTEE) score. **Results:** Baseline pre-injection mean PRTEE score was 72.8 ± 6.97 which decreased to a mean PRTEE score of 40.93 ± 5.94 after 2 weeks of injection which was highly significant ($P < 0.0001$). The mean PRTEE score at 6 week and 12 week follow-up was 24.46 ± 4.58 and 14.86 ± 3.48 respectively showing a highly significant decrease from baseline scores ($P < 0.0001$). **Conclusion:** Treatment of tennis elbow patients with single injection of BMA showed a significant improvement in short to medium term follow-up. In future, such growth factors and/or stem cells based injection therapy can be developed as an alternative conservative treatment for patients of tennis elbow, especially who have failed non-operative treatment before surgical intervention is taken.

Key words: Bone marrow plasma, lateral epicondylitis, stem cells, tendinopathy

INTRODUCTION

Tennis elbow or lateral epicondylitis is the commonest cause of chronic pain on the lateral side of the elbow and wrist extensor dysfunction.[1] The chief complaints in lateral epicondylitis are decreased grip strength, decreased functional activities and increased pain, which may impart significant disability in activities of daily living.[2]

Historically, the primary lesion in lateral epicondylitis was considered to be inflammatory granulation tissue in the tendinous portion of the common extensor origin. Recent studies of chronic tennis elbow have not found any significant evidence of inflammatory processes and the term epicondylosis or tendinosis has been suggested as a more appropriate term than epicondylitis.[3] Diagnosis of lateral epicondylitis is straightforward but there is no consensus on treatment while efficacy of existing treatments is poor.[4] To reduce the need for surgery, more effective conservative therapies are needed.

Recent studies show a beneficial role of locally delivered biological growth factors in form of platelet rich plasma (PRP) and autologous blood in healing of various tendinopathies.[4] According to a recent report by Pascual-Garrido *et al.*,[5] inoculation of bone marrow mononuclear stem cells (BM-MNCs) aspirated from iliac crest could be considered as a potential therapy for those patients with chronic patellar tendinopathy refractory to non-operative treatments. A combination of BM-MNCs and anabolic growth factors would seem as an ideal approach for managing tendinopathy of tennis elbow. Bone marrow aspirated (BMA) from iliac crest contains both PRP and BM-MNCs. The objective of this study is to evaluate the outcome of single injection of BMA in tennis elbow.

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MATERIALS AND METHODS

Participants

Adult patients, 18-65 years old, were recruited from orthopedic and physiotherapy Out-patient Department of a tertiary medical college. The study was approved by the ethical committee of the medical college and attached hospital. A total of 30, both male (n = 18) and female (n = 12) patients of previously untreated tennis elbow were included in the study. A detailed clinical history and clinical examination along with standard anteroposterior and lateral radiographs of involved elbow were taken in all patients. Only previously untreated patients of tennis elbow and having no other identifiable cause of lateral elbow pain were included in the study. Informed written consent was obtained from all the subjects.

Intervention

Bone marrow plasma was aspirated from anterior-superior iliac spine of pelvis in 10 mL syringe containing 1 mL of heparin. 10 mL of bone marrow was centrifuged for approximately 20-30 min at 2000 rpm. Of the centrifuged plasma, only the clear upper layer (containing plasma) and the buffy coat layer that contained mononuclear cells was used for injection and approximately 4-5 mL was obtained from each patient. BMA was mixed with 1 mL of 2% lignocaine solution. All injections were administered taking aseptic precautions into the point of maximal tenderness at the extensor origin of the lateral epicondyle of the humerus by single author in all the cases. All subjects were advised to rest and moderate their activities to avoid aggravation of their symptoms. There were no adverse events in any patient.

Measurement of outcome

Primary outcome measure was Patient-rated Tennis Elbow Evaluation (PRTEE), (100 points) assessed at baseline, 2, 6 and 12 weeks.[6] It measures three dimensions: Pain, function with the affected arm and usual activities. The PRTEE consists of 15 items. All responses are rated on a visual numeric scale (VNS). This differs from the visual analogue scale in that it is an ordinal scale as opposed to a continuous one. Respondents are asked to circle the number that best describes the situation or condition stated in the question. The numbers on the VNS are placed 1 cm apart from one another. The range of possible values is from 0 to 10, where 0 represents "no pain" or "no difficulty" and 10 represents "worst pain imaginable" or "unable to do," depending on the subscale (pain vs. function/activities). The measurement tool is scored as the mean of all the items. Sub scores for each dimension are scored as the mean of all the items in each particular dimension. Higher scores indicate higher pain and/or higher dysfunction. The PRTEE is a reliable, reproducible and sensitive instrument for assessment of tennis elbow.[6]

Statistical analysis

The data was analyzed using the Open Epi version 3.01 software for windows (www.OpenEpi.com, Copyright (c) 2003, 2008 Andrew G. Dean and Kevin M. Sullivan, Atlanta, GA, USA) and $P < 0.05$ were considered to be significant. Statistical analysis of differences between pre- and post-injection evaluation was performed using the paired t-test. The minimum sample size required for this study was calculated on the basis of PRTEE scores reported by Rompe *et al.*[6] A significance criterion of 0.05 and power of 90% was chosen. Minimum expected difference post-treatment was chosen to be 10 on the PRTEE scale and standard deviation was taken to be 15. The minimum sample size came out to be 22.

RESULTS

A total of 30 patients of previously untreated tennis elbow were recruited for this study out of which four were lost in follow-up. Right elbow (n = 15) was involved more commonly than left elbow (n = 11). Mean age of patients was 35.2 ± 6.84 years and mean duration of symptoms was 7.33 ± 2.49 weeks. Baseline pre-injection mean PRTEE score was 72.8 ± 6.97 which decreased to a mean PRTEE score of 40.93 ± 5.94 after 2 weeks of injection which was highly significant ($P < 0.0001$). The mean PRTEE score at 6 week and 12 week follow-up was 24.46 ± 4.58 and 14.86 ± 3.48 respectively showing a highly significant decrease from baseline scores ($P < 0.0001$).

DISCUSSION

Tennis elbow is a tendinopathy which is a common and often debilitating condition that can be quite difficult to treat. The optimal treatment for tennis elbow has still not been determined. Conservative management consisting of activity restriction, splints and orthotics, non-steroidal anti-inflammatory drugs and physiotherapy are the first line of management. Local corticosteroid injection is the most common treatment given in cases where conservative management fails. A recent Cochrane review has concluded that glucocorticoid injection has only short term effect and it yielded poor results in long-term.[7] Other modalities such as prolotherapy, topical nitroglycerin, iontophoresis, phonophoresis, therapeutic ultrasound, extracorporeal shock wave therapy and low-level laser therapy have less evidence of effectiveness in treatment of tendinopathies.[8] Surgical debridement remains a last option for the treatment of tendinopathy because this has considerable cost and morbidity and modest success in

treating chronic tendinopathy.[4] There is a clear need for effective alternative conservative therapies.

Growth factors have drawn a lot of interest in the field of tendon injury and repair. These humoral growth factors can be given in form of whole blood or PRP injection. A recent review of such studies showed that injections of autologous growth factors (whole blood and PRP) in patients with chronic tendinopathy had a significant improvement with PRP being more effective.[9] Recently stem cell technology is being applied to the treatment of degenerative conditions of the musculoskeletal system such as tendinopathy, creation of tendon and ligament grafts and in enhancing graft incorporation.[4,5,10] According to a recent report by Pascual-Garrido *et al.*, inoculation of BM-MNCs aspirated from iliac crest showed marked improvement in patients with chronic refractory patellar tendinopathy.[5] Once the stem cells are in the desired location, either local signaling or the addition of exogenous factors can drive the pluripotent cells to differentiate into the needed cell line.[4] PRP has been shown to influence the behavior of stem cells. Using tendon stem cells derived from rabbit patellar tendons, Zhang and Wang demonstrated that PRP releasate increased tendon stem cell proliferation, induced tendon stem cell differentiation into tenocytes and increased protein expression and collagen type I and type III production.[11] This explains the results of our study which show a highly significant improvement in terms of pain relief and down staging of the disease following a single injection of BMA. Another advantage of our method is simplicity and ease of application; the time required for centrifugal separation is <1 hour and doesn't requires any special instrument and can be carried out in most clinics without any specialized staff.

The major limitation of this study is the lack of control group, resulting in a low level of evidence study (Level 4). Other major limitation of our study is absence of long follow-up. Long-term follow-up is required to see the sustained effect of bone marrow concentrate (BMC) injection in terms of pain relief and healing of disease. We have chosen a follow-up only up to 12 weeks as improvement in symptoms after this period may be a result of natural healing process and activity modification by patients. Studies with longer follow-up are also required to see any adverse effects like calcification in tendon or tumorogenesis. No hematological analysis was performed to determine the numbers of nucleated cells or platelets in BMC. We didn't perform any pre- or post-injection radiological assessment of tendon healing by magnetic resonance imaging or ultrasonography. Further studies are required to standardize the dose, number and timing of autologous BMC injection for treating refractory tennis elbow.

CONCLUSION

We believe that BMA injection could be considered as an alternative treatment for those patients who have failed non-operative treatment before surgical intervention is considered. In the future, growth factors and/or stem cells based injection can be developed as second line conservative treatment in chronic tendinopathy as they could potentially reverse the degenerative process and encourage the regeneration of healthy tendon.

REFRENCES

1. Allander E. Prevalence, incidence, and remission rates of some common rheumatic diseases or syndromes. Scand J Rheumatol 1974;3:145-53.
2. Dorf ER, Chhabra AB, Golish SR, McGinty JL, Pannunzio ME. Effect of elbow position on grip strength in the evaluation of lateral epicondylitis. J Hand Surg Am 2007;32:882-6.
3. Vicenzino B, Wright A. Lateral epicondylagia: A review of epidemiology, pathophysiology, etiology and natural history. Phys Ther Rev 1996;1:23-34.
4. Andres BM, Murrell GA. Treatment of tendinopathy: What works, what does not, and what is on the horizon. Clin Orthop Relat Res 2008;466:1539-54.
5. Pascual-Garrido C, Rolón A, Makino A. Treatment of chronic patellar tendinopathy with autologous bone marrow stem cells: A 5-year-followup. Stem Cells Int 2012;2012:953510.
6. Rompe JD, Overend TJ, MacDermid JC. Validation of the patient-rated tennis elbow evaluation questionnaire. J Hand Ther 2007; 20:3-10.
7. Pattanittum P, Turner T, Green S, Buchbinder R. Non-steroidal anti-inflammatory drugs (NSAIDs) for treating lateral elbow pain in adults. Cochrane Database Syst Rev 2013;5:CD003686.
8. Childress MA, Beutler A. Management of chronic tendon injuries. Am Fam Physician 2013;87:486-90.
9. de Vos RJ, van Veldhoven PL, Moen MH, Weir A, Tol JL, Maffulli N. Autologous growth factor injections in chronic tendinopathy: A systematic review. Br Med Bull 2010;95:63-77.
10. Hoffmann A, Gross G. Tendon and ligament engineering in the adult organism: Mesenchymal stem cells and gene-therapeutic approaches. Int Orthop 2007;31:791-7.
11. Zhang J, Wang JH. Platelet-rich plasma releasate promotes differentiation of tendon stem cells into active tenocytes. Am J Sports Med 2010;38:2477-86.

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