Treatment of chronic patellar tendinosis with buffered platelet rich plasma: a preliminary study

Trattamento delle tendinopatie croniche del tendine rotuleo con fattori di crescita (plasma ricco di piastrine): studio preliminare

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SUMMARY

Eight athletes considering surgical intervention for chronic patellar tendinosis that was recalcitrant to conservative physical therapy and a variety of non-operative treatments were recruited into the study. Following pre-injection MRI imaging and VISA score assessment, patients received a single injection of PRP (Platelet-Rich Plasma). Patients were given individualized rehabilitation protocols and followed until a final assessment at 120 days post-injection. Seven of the eight patients were assessed at the final follow-up, with all of them demonstrating an improvement on the VISA score. One patient elected to have surgical intervention prior to the final follow-up and was not included in the analysis. The average VISA score at the final assessment was 75.0 compared to a pre-injection average of 39.25. This represented a 91% of average improvement in the VISA score (p<0.001). MRI images at the final follow-up demonstrated a noticeable reduction in irregularity of the affected tendon compared to pre-injection images for 80% of the treated tendons.

Treatment of chronic patellar tendinosis in a series of athletes resulted in a statistically significant improvement in VISA score for seven of the eight patients treated. Pre and post-injection MRI demonstrated reduced irregularity in eighty percent of the injected tendons. Further evaluation of this treatment is warranted.

KEY WORDS: Platelet-rich plasma - Patellar tendon - Tendinosis - Tendonitis.

RIASSUNTO

Nel presente studio sono stati inclusi otto atleti con indicazione all’intervento chirurgico per tendinopatia cronica del tendine rotuleo, recalcitranti alla terapia fisica conservativa e ad altri trattamenti non chirurgici. Dopo aver eseguito una MRI e aver raccolto i dati relativi ai valori di VISA pre-infiltrazione, i pazienti sono stati trattati con un singolo infiltrazione di PRP (Plasma Ricco di Piastrine). I pazienti, a cui è stato indicato un programma riaffermativo individuale, sono stati seguiti periodicamente fino ad una valutazione finale a 120 giorni post-intervento. Sette degli otto pazienti valutati al follow up finale hanno mostrato un miglioramento del valori di VISA. Per un paziente si è reso necessario l’intervento chirurgico prima del raggiungimento del follow up finale e dunque non è stato incluso nell’analisi.

Il valore medio finale dei punteggi della VISA è di 75.0, contro un valore medio iniziale di 39.25, che rappresenta un miglioramento medio del 91% (p<0.001).

Nell’80% dei casi, la MRI al follow up finale mostra un’apprezzabile riduzione dell’irregularità tendinea se comparata alle immagini pre-infiltrazione.

In conclusione, il trattamento delle tendinopatie croniche in una serie di atleti risulta in un miglioramento statisticamente significativo dei valori di VISA per sette pazienti degli otto inclusi nello studio e le immagini MRI pre e post-infiltrazione mostrano una netta diminuzione dell’irregularità nell’80% dei tendini trattati.

Tuttavia, gli Autori ritengono che, nonostante i buoni risultati mostrati, siano necessari ulteriori studi per validare la metodica e confermare i dati ottenuti.

PAROLE CHIAVE: Plasma ricco di piastrine - Tendine rotuleo - Tendinosi - Tendiniti.
Tendinopathy of the patellar tendon, in particular at the proximal origin, has been demonstrated to cause significant morbidity in elite and recreational athletes. Repetitive stress has been identified as the primary cause of this condition, which affects athletes involved in sports such as basketball, volleyball, tennis, skiing, and soccer. Patellar tendon overuse is also common in military recruits, representing approximately 15% of all soft-tissue injuries in a study on US Marine recruits. The underlying cause is theorized to be an aborted healing response to microtears caused by poor vascularity of the tendon origins.

Methods of treatment for this condition include active rest, eccentric muscular training, non-steroidal anti-inflammatory drugs (NSAIDs), local steroid injection, shock-wave therapy, and surgery. Frequently, the condition will become chronic and be resistant to conservative management (rest, exercise, NSAIDs, injections) with Cook et al. reporting that 33% of the subjects presenting with a patellar tendinopathy unable to return to full sport activity for more than 6 months. Results on surgical tenotomy of the patellar tendon are various, with limited reliable outcome studies available. Retrospective analysis has reported suboptimal functional outcome results with patients never returning to preinjury levels of sporting activity.

Histopathology of chronic tendinopathies has demonstrated an absence of inflammatory cells normally present in acute conditions. Affected tissue will be distinct from normal tendon by appearing gray, dull and often edematous. At the microscopic level, the normal order seen in healthy tendon tissue is disrupted by the invasion of immature fibroblast and non-nucleated vascular cells. This angiofibrotic tissue is a self-perpetuating tissue because of the insinuation of the immature cellular elements into healthy tendon fibers, avoiding the normal repairing process.

The goal of treatment of angiofibrotic tendinosis should cease and ultimately reverse the degenerative tissue disruption that is at the root of the condition. Therapies to heal the affected tissue should work with and enhance the biologic healing response necessary for full repair. This response acts through the proliferation of fibroblasts into the affected area, the promotion of angiogenesis and the collagen deposition, thereby allowing the tissue to work with and enhance the biologic healing response necessary for full repair.

An abnormally slow tissue repair process is observed in chronic tendinopathy. A lack of mature collagen fibers is observed in chronic tendinopathy, which is demonstrated by a lower density of collagen fibers and a decrease in the tensile strength of the tendon. The lack of mature collagen fibers is believed to be the result of an impaired tissue repair process. This impaired tissue repair process is characterized by a decrease in the proliferation of fibroblasts, a decrease in the collagen deposition, and an impaired tissue repair process.
resulting in the organization of fully mature tendon tissue.

Cytokines present in platelet -granules are known to be key facilitators in the three healing stages necessary to reverse a chronic tendinosis condition,27 above all transforming growth factor beta (TGF-ß), vascular endothelial growth factor (VEGF), and platelet derived growth factor (PDGF). Moreover the thrombin-activated platelets release further cytokines in addition to the mentioned ones, which has been demonstrated to promote proliferation of human tendon cells in culture.2

Autologous platelet rich plasma (PRP) contains concentrated platelets and white blood cells that are suspended in plasma. Typically, PRP is produced from a small sample of the patients blood by centrifugation.

The use of PRP has been advocated for numerous indications.3, 15, 23, 39 It is hypothesized that elevated cytokine levels released during platelet degranulation induce an accelerated healing response at the site of application. The concept of PRP as a potential therapy for tendinopathy is well described in the work by Edwards et al.10 Mishra et al.26 reported data on 15 patients who received a single PRP injection into chronic epicondylar tendinosis, after failing more traditional non-surgical therapies.26

This early but relevant evidences merit further investigation in the use of autologous PRP injections for the treatment of chronic tendinopathies.

The following case studies provides preliminary proof about the efficacy of PRP injections for the treatment of chronic patellar tendinosis. This series represents the first known report of the application of this therapy for patellar tendinopathies. Follow-up reports include assessment of pain and function using the VISA score (Victorian Institute of Sport Assessment) and MRI imaging of the affected tendon pre and post-injection.

Materials and methods

Patients

Table I provides the information collected for each patient. From November 2005 to May 2006, 11 PRP injections were carried out in 7 male and one female patients, with an average age of 26.6 years (range of 21–41). Six of the patients played sports at a high level, whereas the other two practiced sports at amateur level. All the patients presented chronic tendinopathies localized at the
third proximal of the patellar tendon since at least one year, recalcitrant to various treatments including NSAIDs, traditional physiotherapy treatments, shock-wave, TECAR therapy. All the procedures were performed under the control of a haematologist of the Immuno-haematology Service and Transfusional Medicine (SIMT) of the Niguarda Hospital of Milan, in agreement with Italian decree (DL) 19-08-2005 no. 191 and under patient’s informed consensus. The patients underwent MRI for visualization of the existing tendinopathies and were assessed by means of the patellar tendinosis VISA score. The VISA scoring tests the function and ability to play sport and assigns a score between 0 and 100 with 100 representing a fully performing individual. After treatment, patients were clinically evaluated at 7, 30, and 60 days with follow-up MRI imaging and VISA scoring occurring at 120 days.

Preparation of PRP

An Anticoagulant Citrate Dextrose Solution A was mixed with total blood in 1:10 proportion, for a final volume of 30 ml and then processed in GPSTM II Platelet Concentration System (Biomet Biologics, Warsaw, IN). After separation for centrifugation, it was possible to obtain a concentration of around 10 times, resulting approximately in 3ml of PRP. A small amount (50-150µL) of 8.4% sodium bicarbonate solution was added to the PRP solution prior to injection to re-establish the physiologic pH, facilitating a direct injection of the PRP into the affected tendon. This technique allows the degranulation of the platelets by the surrounding collagen at the injection site, thereby eliminating the necessity of an exogenous platelet activator such as bovine thrombin. 

TABLE I.—patients demographics for case series receiving PRP injection for chronic patellar tendinosis.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sport</th>
<th>Side</th>
<th>Follow up (d)</th>
<th>Pre-injection</th>
<th>Post-injection</th>
<th>Improvement after injection</th>
<th>Improvement after injection (%)</th>
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</thead>
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<tr>
<td>24</td>
<td>Rugby</td>
<td>Left</td>
<td>N/A</td>
<td>42</td>
<td>Surgical treatment</td>
<td>—</td>
<td>—</td>
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<tr>
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<td>Football</td>
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<td>28</td>
<td>73</td>
<td>45</td>
<td>161</td>
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<td>Sailing</td>
<td>Left</td>
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<td>64</td>
<td>58</td>
<td>15</td>
<td>23</td>
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<tr>
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<td>109</td>
<td>51</td>
<td>82</td>
<td>51</td>
<td>165</td>
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<tr>
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<td>Right</td>
<td>125</td>
<td>42</td>
<td>68</td>
<td>26</td>
<td>62</td>
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</tbody>
</table>

Table 1. — Informazioni raccolte per ogni singolo paziente sottoposto ad infiltrazione di PRP per tendinopatia cronica del tendine rotuleo.
**Injection technique**

After disinfection of the injection site with a betadine solution, the sterile field was set up. The cutaneous and the subcutaneous layers were infiltrated with 0.5 ml of local anaesthetic (lidocaine). Under ultrasound guidance, a 22-gauge needle was inserted into the affected tissue with a perpendicular approach. PRP was then injected in small aliquots with the needle being repositioned 5-8 times within the affected tissue. After the entire volume of buffered PRP had been injected, the needle was removed and the skin was disinfected again. A compressive bandage was then applied and the patient was asked to remain in a supine position for 20-30 minutes without moving the treated limb.

**Post injection protocol**

The patients were discharged approximately one hour after the PRP injection with an individualized rehabilitation protocol. In general, the patients were asked to rest for the first seven days, walking with a normal gait and applying cryotherapy for 15 minutes twice a day. From 7 to 21 days after treatment, walking in the water, light swims and controlled exercises was suggested. Stretching exercises and two 20-minute sessions on an exercise bike with no resistance were also carried out during this rehabilitation period. At 5 weeks post-injection the patients began eccentric quadriceps training with resistance as well as concentric strengthening of the flexor muscles under the supervision of a therapist. At 7 weeks post-injection there was an increase of muscular strengthening and the patients could begin jogging. At 9 weeks post-injection sports specific exercises under trainer supervision were commenced with patients returning to full sporting activities at 12 weeks post-injection.

**Statistical assessment**

Mean and SD are calculated for single data. A two-tailed t-test ($\alpha=0.05$) was performed on the pre and post-injection VISA scores by GraphPad Prism.

**Results**

Seven patients, for a total of 10 treated tendons, were assessed at the final follow-up, 120
days post-injection (range of 109-127 days). The patient not included in follow-up did not comply with the suggested rehabilitation protocol and returned to full sporting activity too early (about 40 days post-injection). Due to reoccurrence of pain, this patient were selected to undergo surgical treatment. All patients making the final assessment demonstrated an improvement of the VISA score if compared to the pre-injection score (Table I). The average improvement of the final VISA score for the ten treated tendons was 36.1 points (range 6-68) points, ranging from an initial mean of 39.25 (range 24-64) to a final mean of 75.0 (range 58-92) at the last follow-up visit. A two-tailed t-test (α=0.05) performed on the pre and post-injection VISA scores demonstrated a statistically significant difference (p<0.001) (Figures 1, 2).

In 8 of the 10 tendons examined at the final follow-up, MRI imaging showed signs of reduced irregularity at the level of tendon insertion and the perinsertional oedema. Figure 3 shows an example of MRI imaging of the patellar tendon before and after treatment, demonstrating a reduction in irregularity from pre-injection to final follow-up.

**Figure 1.**—Pre- and post-injection Visa Score of each patients followed until final assessment at 120 days. 

**Figure 2.**—Comparison of average pre- and post-injection Visa Score at 120 days of follow up (p<0.001).

**Figure 3.**—MRI imaging of patellar tendon showing reduction in irregularity from pre-injection (A) to final follow-up (B).

*GIOVANNONE BOND STRENGTH TO DEEP CORONAL DENTIN: EFFECT OF BONDING STRATEGIES*
Discussion

Patellar tendinopathy is one of the most frequent diagnoses in sports medicine and especially in chronic forms is difficult to resolve therapeutically. Different physiotherapeutic treatments and injection of corticosteroids do not seem to demonstrate any long-term efficacy. Currently, the most reliable and safest treatment continues to be a conservative rehabilitation program involving specific and gradual eccentric work of the surrounding muscles, though positive results in the most chronic tendinopathies is only around 50%.9, 24

In recent years, the use of autologous growth factors has been suggested for a variety of indications. The actions of individual growth factors on in vitro models of tendon repair have been reported in the literature.2, 17, 29 Recent work from Sanchez et al.36 demonstrated improved outcome in a group receiving PRP application during achilles tendon repair compared to a control group. The safe autologous nature of this therapy, a mechanism of action based on basic biologic principles, and promising pilot data in lateral epicondylitis by Mishra et al.24 prompted the current investigation of PRP for chronic tendinosis of the patellar tendon.

In athletes, patellar tendinopathy can be very difficult to solve using conventional therapies. In the present study a series of affected athletes who failed these therapies and were considering surgical intervention was recruited. This challenging patient population was considered a good model for a preliminary investigation of the use of a PRP injection for chronic patellar tendinosis. The single PRP injection was complemented by a rehabilitation program and patient progress was assessed using VISA scoring and evaluation of pre and post-injection MRI imaging. The current study has a small number of patients and lacks a control group due to concerns of the ethics committee and the inherent difficulty in treating and controlling the long-term follow-up of severe tendinopathies in athletes. Prospective

Non abbiamo osservato alcuna complicanza legata al trattamento: nessuna infezione, infiammazione, edema o complicanza vascolo-nervosa è stata rilevata in alcun paziente.

Discussione

La tendinopatia rotulea rappresenta una delle diagnosi più frequenti in medicina dello sport, e specialmente nelle forme croniche è di difficile risoluzione terapeutica. I diversi trattamenti fisioterapici e le infiltrazioni di corticosteroidi non sembrano dimostrare efficacia a lungo termine. Attualmente il trattamento più affidabile e sicuro continua ad essere il programma riabilitativo conservativo, che comprende lavoro eccentrico specifico e graduale dei muscoli circostanti, benché i risultati positivi nelle tendinopatie maggiormente cronicate si trovino solo attorno al 50%9, 24

In studi recenti, l’uso di fattori di crescita autologhi è stato proposto per una varietà di indicazioni. L’azione di fattori di crescita individuali in modelli di riparazione tendinea in vitro è stata descritta in letteratura.2, 17, 29 Un recente studio di Sanchez et al. 36 ha dimostrato un miglioramento di risultati in un gruppo trattato con applicazione di PRP per la riparazione del tendine d’Achille, rispetto a un gruppo di controllo. La natura autologa sicura di questa terapia, il meccanismo d’azione basato su principi biologici di base, e i promettenti dati iniziali riportati da Mishra et al.24 nell’epicondiliti laterale, hanno suggerito questo studio sul PRP nel trattamento delle tendinosi croniche del tendine rotuleo.

Negli atleti può essere molto difficile trattare la tendinopatia rotulea con le terapie convenzionali. Nel presente studio è stata arruolata una serie di atleti che non sono stati beneficiati da queste terapie e stavano considerando il trattamento chirurgico.

Questa impegnativa popolazione di pazienti è stata considerata un buon modello per un’indagine preliminare sull’uso delle infiltrazioni di PRP nelle tendinosi rotulee croniche. La singola infiltrazione di PRP è stata integrata con un programma di riabilitazione e i progressi del paziente sono stati valutati utilizzando il punteggi VISA e la valutazione delle immagini RM pre- e post-infiltrazione. L’attuale studio ha un ridotto numero di pazienti e manca di un gruppo di controllo a causa dei dubbi del comitato etico e le inerenti difficoltà nel trattamento e controllo del follow-up a lungo termine delle tendinosi gravi negli atleti. Per valutare la reale efficacia delle infiltrazioni di PRP nel tratta-
double-blind randomized trials should be performed to measure the true value of PRP injection for the treatment of tendinosis conditions. Longer follow-up periods should be studied as well, to determine the longevity of a treatment effect. The current study was not intended to be confirmatory in nature, with the study intent being to provide a preliminary investigation on the use of PRP injection for chronic patellar tendinosis.

In a series of eight athletes with recalcitrant patellar tendinosis, having failed conventional treatments and facing the prospect of surgical intervention, a single PRP injection was well tolerated with no therapy related adverse events.

One patient did go onto surgery, however this patient did not comply with the post-injection rehabilitation protocol. The other patients all demonstrated improved VISA scores at a 3–4 month follow-up with the average improvement being 36.1 points on a 100-point scale, a difference that was shown to be statistically significant. 80% of the injected tendons had visually evident reduction in tissue irregularity on follow-up MRI imaging. In conclusion, this study provides evidence to suggest PRP injections may be a valid therapeutic option in patient with chronic patellar tendinosis who have failed non-operative treatments. Further investigation and analysis of this therapy are warranted to verify the real effectiveness of PRP in promoting tendon regeneration.

References/Bibliografia

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