Treatment of Achilles tendinopathy with autologous adipose-derived stromal vascular fraction: results of a randomized prospective clinical trial

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Achilles tendon injuries are involved in 30–50% of all sports-related injuries. About 7–10 ruptures are reported per 100,000, typically men aged 30–50, thus explaining the social impact of Achilles tendinopathy (1). Among conservative treatments the use of platelet-rich plasma (PRP) holds considerable theoretical appeal as a means of combating some of the mechanisms responsible for the development or persistence of the tendon lesions (2). However, very conflicting results about its effectiveness in tendinopathy are reported in literature, probably ascribable to insufficient attention to select patients and to the lack of a clear and uniform formulation of PRP (3). More recently it has been demonstrated that many of the growth factors and molecules contained in the PRP are produced and released by the mesenchymal stem cells (MSCs) in response to tissue injury or trauma. These cells have a perivascular origin and can be described as a subset of pericytes (4). The subcutaneous adipose tissue represents one of the smarter sources to isolate MSCs due to a simple and less invasive method of harvesting. The therapeutic effect of adipose-derived mesenchymal stem cells (ASCs), either expanded or used directly within the stromal vascular fraction (SVF), has demonstrated to possess peculiar anti-inflammatory and immunomodulatory effects, mediated by the release of active factors potentially useful in the treatment of tendinopathy

The aim of this prospective randomised controlled trial was to compare the effectiveness of the injection of a leukocyte-rich PRP formulation with the injection of adipose-derived SVF for the treatment of chronic Achilles tendinopathy. The quality and duration of clinical improvement as well as of radiological findings were assessed at different time points up to 6 months from the treatment.

PATIENTS AND METHODS

The study was approved by an external Ethics Committee (H2454-12MS)

Inclusion criteria:
• Uni- or bi-lateral chronic Achilles tendinopathy to conservative treatments
• Symptoms lasting >3 months and recalcitrant to conventional conservative treatments
• Age between 18 and 55 years/old
• VAS (visual analogue scale) pain at the first visit >5

Exclusion criteria:
• Other musculoskeletal lesions of the target Achilles tendon
• Platelet count in whole blood < 150000/μl
• Inflammatory diseases or other conditions that could affect the joint(s)
• Any previous injective treatment of the target Achilles tendon
• Pregnancy or breast-feeding

RESULTS

Background data: the two patients’ groups were similar at the baseline

<table>
<thead>
<tr>
<th></th>
<th>PRP injection group (GPSIII kit, Zimmer Biomet, USA) (n=28 tendons)</th>
<th>Adipose tissue SVF (FastKiti, Corios, Italy) (n=28 tendons)</th>
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<tbody>
<tr>
<td></td>
<td>V5</td>
<td></td>
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<tr>
<td>Lesion area (MRI) (mm²)</td>
<td>63.2±17.7</td>
<td>63.4±20.1</td>
</tr>
<tr>
<td>VISA-A Score</td>
<td>80±10.1</td>
<td>78.9±10.8</td>
</tr>
<tr>
<td>SF-36 Score</td>
<td>46.6±6.2</td>
<td>47.3±3.8</td>
</tr>
<tr>
<td>VISA-A Score</td>
<td>63.5±17.7</td>
<td>63.8±20.1</td>
</tr>
<tr>
<td>SF-36 Score</td>
<td>46.9±6.2</td>
<td>48.2±3.8</td>
</tr>
<tr>
<td>VISA-A Score</td>
<td>70.3±10.1</td>
<td>70.8±10.1</td>
</tr>
<tr>
<td>SF-36 Score</td>
<td>47.1±6.2</td>
<td>48.5±3.8</td>
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Clinical and functional results: the patients of both groups had a significant improvement with respect to the pre-injection values. These improvements were faster in the SVF patients. Indeed, they showed significantly improvements for VAS, VISA-A, AOFAS scale already after 15 days from the injection, whereas in PRP group the functional scores started to be significantly better than the pre-treatment values only after 30 days. Comparing the two groups, SVF patients scored significantly better results than PRP ones in VISA (15 and 30 days), VISA-A (30 days) and AOFAS (15 days) (p<0.05). **, p<0.01; *** p<0.001 vs SVF

Pre-PRP 15 30 60 120 180
Pre-PRP 15 30 60 120 180

Days

<table>
<thead>
<tr>
<th>SF-36 Score - Physical</th>
<th>SF-36 Score - Mental</th>
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<tbody>
<tr>
<td>40.5±6.7</td>
<td>41.5±6.7</td>
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Patients satisfaction: the patients of both groups showed significant better results in terms of SF-36 Score – Physical in comparison to the pre-injection scores already after 30 days from the treatment, but without any difference between groups. No significant improvement with respect to the pre-injection value was observed for the SF-36 Score – Mental in neither group. ***, p<0.001 vs pre-injection

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CONCLUSIONS

•Both treatments were well tolerated (no AE)
•Patients of both groups had significant clinical improvements within one month from the treatment, with further increase during follow-up
•The clinical results were stable at least until 6 months from the injection
•SVF allowed for a faster recover than PRP and scored better in the first month; at longer follow up no difference between the two groups.
•No improvement from a radiological point of view

SVF could be indicated for patients with higher functional request

Further long-term follow up study will be needed to confirm these findings and better investigate the role of the SVF in the treatment of tendon disorders

DISCUSSION AND INTERPRETATION OF THE RESULTS

Both PRP and SVF were able to significantly ameliorate the clinical and functional scores of the patients. This could be explained by the capacity of both the molecules contained in the PRP and released by the SVF cells to interact with the injury site, promoting the restoration of a more normal tissue homeostasis. The faster results observed in the patients treated with SVF could be ascribed to the ability of the SVF cells to release more abundant, more various and longer lasting growth factors, anti-inflammatory chemokines and other molecules with different functions.

REFERENCES