

# Efficacy of Decellularized Human Placenta in the Treatment of Infracalcaneal Heel Pain

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## Abstract

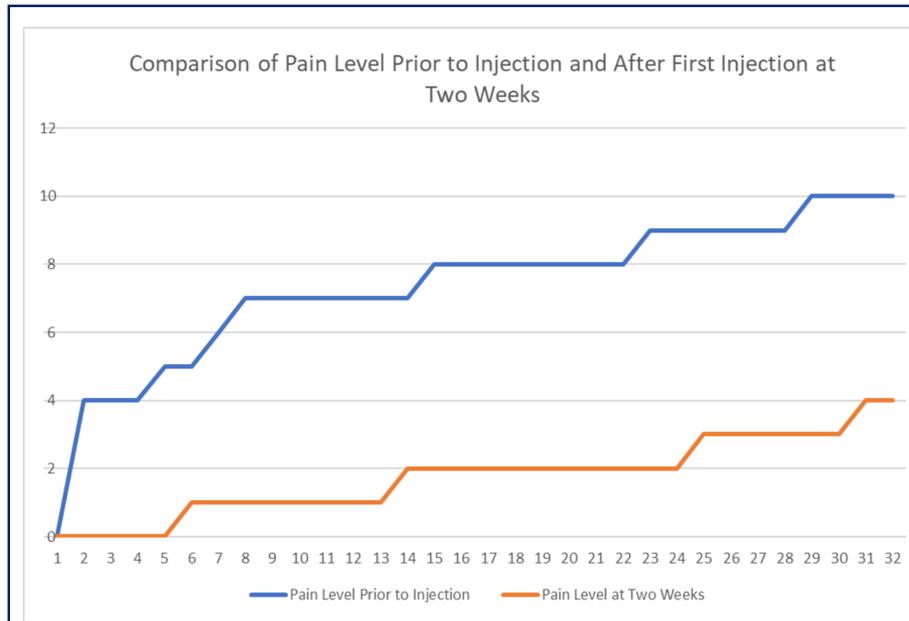
Thirty two feet with chronic plantar fasciitis pain were selected to evaluate decellularized human placenta (Interfyl (TM)) as an agent for pain reduction in the foot and ankle. All patients experienced reduced pain on ambulation two weeks and four weeks post injection of decellularized human placenta, Interfyl (TM), and were able to return to their daily activities with either less pain or no pain. The authors believe that Human decellularized placenta (Interfyl (TM)) achieved these results using growth factors intrinsic to the placenta. Statistically significant differences in pain were found following injection of Interfyl (TM) at 2 weeks and 4 weeks.

## Introduction

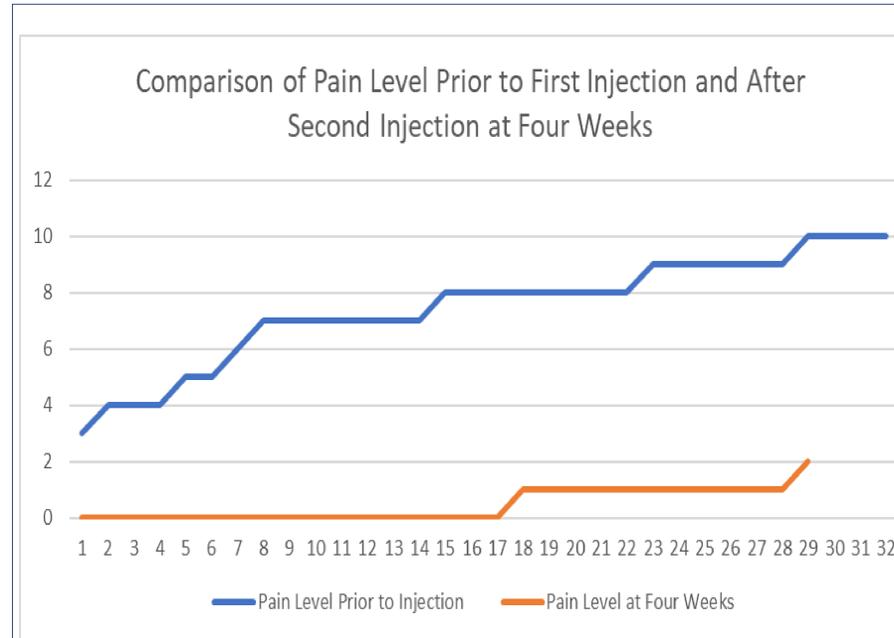
• Infra calcaneal heel pain is a common podiatric condition taking the form of plantar fasciitis, an acute inflammation of the plantar fascial band. The etiology of plantar fasciitis is caused by mechanical overload and excessive strain on the plantar fascia secondary to pronation, a high arched foot, and equinus. Despite the belief that the etiology of the condition is the presence of an infracalcaneal heel spur, the true etiology of the condition is soft tissue inflammation. Conservative treatment for plantar fasciitis includes stretching, corticosteroid injections, and platelet rich plasma (PRP) injections. PRP injections have been shown to provide relief from pain (1). Corticosteroid over use may lead to permanent adverse changes within the joint and surrounding soft tissue structures. Surgical options can include extracorporeal shockwave therapy and plantar fasciotomy(2). Interfyl (TM) is a human connective tissue matrix consisting of allogeneic decellularized human placental connective tissue matrix that possesses both structural and biochemical properties of the extracellular matrix to provide the framework for cellular components to repair the damaged fibrocytes of plantar fascia tissue and promote growth and tissue repair (3). Hence, the ability to inject the healing properties of dehydrated human placenta tissue into the plantar fascia allows for improved treatment and healing of the deeper soft tissue injuries and inflammation. This retrospective chart review of thirty two feet with plantar fasciitis examines the efficacy of decellularized human placenta, Interfyl (TM) for the treatment of infracalcaneal heel pain when conservative therapy failed.

## Materials and Methods

Patients included in the chart review received conservative treatment consisting of rest, ice, compression, corticosteroid injections, stretching exercises, NSAIDs, and orthotics for up to eight months with little to no pain relief as measured on the Wong Visual Pain Analog Scale (4). Patients were excluded if they had prior surgery at the injection or joint site, clinical signs of infection, prior treatment with tissue engineered material, presence of foot and ankle orthopedic comorbidities such as a foot or ankle stress fracture, known nerve entrapment syndrome, and neurological disease of the lower extremity. Thirty two patients were included in the study. Nineteen adult patients with a clinical diagnosis of plantar fasciitis met inclusion criteria for the chart review. The patient population consisted of eight males and eleven females with a mean age of fifty years. The patients age ranged from twenty eight to sixty seven years old. There were seven patients with bilateral plantar fasciitis and twelve with unilateral plantar fasciitis. Six patients received two unilateral injections that were administered two weeks from the initial injection, three were left side, and three were right side because of pain and continued inflammation of the plantar fascia observed on ultrasound. The plantar fascia bands were evaluated using a linear 7.0-MHz ultrasound transducer (Acuson128XT; Acuson Corp, Mountain View, California). During ultrasonography, patients verbalized the absence or presence of pain in the affected area when the plantar fascia bands were palpated. Ultrasonographic examinations were initially performed with patients positioned prone, and feet hanging over the edge of the examination table. The medial, central, and lateral aspects of the heel at the insertion of the plantar fascia were palpated to determine the location of the corresponding bands. A bead of acoustic gel was applied to the cover of the head of the transducer, which was then placed longitudinally on the plantar aspect of the foot. The focus was adjusted to the depth of the plantar fascia at its attachment to the calcaneus. Ultrasonographic scanning was performed during dynamic dorsiflexion of the toes to stretch the plantar fascia, allowing its margins to be delineated to locate the symptomatic plantar fascia bands. After location of the symptomatic plantar fascia 1.5 ml of normal saline was used to reconstitute the 1.5 ml of decellularized human placenta for a total of 3.0 mL then injected at the site of pain. A T-test was used to compare the pre injection pain level of the plantar fascia to the pain level at 2 weeks post injection and pain level at 4 weeks post injection. BMI was also statistically tested for correlation with post injection pain levels.



**Fig 1:** Chart comparing pain level prior to first injection and following first injection at two weeks.



**Fig 2:** Chart comparing pain level prior to first injection and after second injection At four weeks.



Inflamed



Not Inflamed

## Results

Data from 32 patients with refractory plantar fasciitis following injection of Interfyl at 2 weeks and 4 weeks was analyzed. A T test was used to analyze the statistical significance between pain level prior to the first Interfyl injection and pain level at 2 weeks post injection of Interfyl. The P value was  $1.47 \times 10^{-16}$ . A T test was used to analyze the statistical significance between pain level prior to the first Interfyl injection and pain level at 4 weeks post injection of Interfyl. The P value was  $3.39 \times 10^{-21}$ . A T test was used to analyze the statistical significance between pain level at 2 weeks post injection of Interfyl and 4 weeks post injection of Interfyl. The P value was  $7 \times 10^{-7}$ . A positive correlation was also found between patient's with a higher BMI and a greater degree of pain reduction with Interfyl injections at 4 weeks post injection.

## Discussion

Historically, placental extracts have been used for treatment of a variety of pathological conditions most commonly in surgery, neurology, gynecology, and dermatology. Positive effects were realized with treatment of wounds and pain reduction(5). Placental extracts have been shown to enhance the proliferation of fibroblasts and reduce the concentration of free radicals, inflammatory cytokines IL-6, TNF and IL-1 at the same time increasing the formation of progenitor cells and reducing oxidative damage to the cells(6,7,8). In addition, analysis of the bio safety and placental extracts revealed the absence of toxic or mutagenic influence on cultures (9). Decellularized human placenta, is proving to have promising implications in treating patients with recalcitrant plantar fasciitis pain. However, additional work is needed to better assess the use of human decellularized placenta (Interfyl (TM)) within current treatment guidelines for the management of foot and ankle pain. There are many possible treatments for plantar fasciitis pain, however no single treatment can be guaranteed based on quality of life measures that include comorbidities ( arthritis, obesity, diabetes), medication use, and lifestyle factors ( alcohol use, smoking, malnutrition).

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