https://doi.org/10.46344/JBINO.2022.v11i06.08

AUTOLOGOUS MICRO FRAGMENTED ADIPOSE CELLS THERAPY FOR END-STAGE POST TRAUMATIC ANKLE OSTEOARTHRITIS IN YOUNG PATIENTS – CASE SERIES

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ABSTRACT

Introduction: Ankle osteoarthritis (OA) in young patients is predominantly post-traumatic in etiology. Most nonsurgical treatments only provide transient relief of symptoms. Intraarticular injections of adipose tissue have successfully managed hip and knee OA. There is a single case report on using micro-fragmented adipose cell therapy in ankle OA. This pilot study aims to evaluate the efficacy of autologous micro-fragmented adipose cell transplantation in treating patients with end-stage ankle OA. **Materials and Methods:** Patients with post-traumatic, symptomatic Kellgren-Lawrence grade 3 to 4 ankle OA were treated with a single intra-articular injection of autologous micro fragmented fat cells. The cells were obtained through limited abdominal liposuction. Primary outcome measures were the Manchester-Oxford Foot Questionnaire (MOXFQ) score and the Foot and Ankle Ability Measure (FAAM) score. Scores were recorded preoperatively and during clinic follow-ups at 2 weeks, 6 weeks, 6 months, and 12 months. **Results:** Five patients with severe post-traumatic ankle OA were included in the study. The mean age was 43 years. No perioperative complications relating to abdominal liposuction and intraarticular injection were recorded throughout the 12-month follow-up period. The MOXFQ scores showed a statistically significant improvement, from an average score of 63 at baseline to 37.2 at 12 months (p= < 0.0001). Similarly, there was a significant improvement in the mean FAAM scores, from 51.4 at baseline to 57 at 12 months (p= < 0.0001). **Discussion:** This study demonstrates promising early results in managing end-stage ankle OA in young patients using a single-dose autologous micro fragmented fat cells therapy. The improvement in patient-reported symptoms and function is demonstrated to be sustained over 12 months. The findings confirm that this new treatment modality is a safe and effective alternative to other commonly available treatments in carefully selected patients.

Keywords: Ankle osteoarthritis; Intra-articular injections; Post-traumatic arthritis; Lipogems

Introduction

Ankle osteoarthritis (OA) is uncommon in young people, and up to 90 % is post-traumatic in nature [1]. Most nonsurgical treatments for ankle OA give transient relief. This pilot study aims to evaluate the efficacy of autologous micro-fragmented adipose cell transplantation in patients with end-stage ankle OA. We hypothesize that autologous micro-fragmented adipose cell injection can reduce pain and improve the quality of life for patients with ankle arthritis. Literature has shown some evidence of using autologous fat in large joints such as hip and knee OA [2,3]. There is so far only a single case report, which was previously published by our institution, in which micro fragmented adipose cells therapy is used in stage ankle osteoarthritis [4].

Materials and Methods

All patients treated with a single intra-articular injection of autologous micro-fragmented fat cells were prospectively followed up for 12 months. We included adults between the age of 18-55 years, end-stage (symptomatic Kellgren-Lawrence grade 3 to 4) ankle OA and previous failed conservative management. Patients with previous septic and inflammatory arthritis were excluded from the study. Primary outcome measures were the Manchester-Oxford Foot Questionnaire (MOXFQ) score and the Foot and Ankle Ability Measure score (FAAM). Patient demographics and scores were recorded in the clinic preoperatively. All patients had weight-bearing radiographs of the ankle preoperatively. MOXFQ and FAAM scores were compared to the pre-operative baseline at 2 weeks, 6 weeks, 6 months, and 12 months post-procedure.

Surgical Technique

All procedures were performed using a standardized technique by senior orthopaedic and plastic surgeons. Limited abdominal liposuction was performed under general anaesthetic. A stab incision was made over the abdomen (Fig. 1), and about 1000 ml of saline infiltrated the abdominal fat. Using a handheld manual suction technique with a 3mm lipoaspirate cannula connected to a 20mL syringe, lipoaspirate was collected. Lipoaspirate was then transferred to the Lipogems kit for processing, which involved the mechanical breakdown of adipose tissue for around 20 minutes. The final 15 ml of the product was injected into the ankle joint. Procedural steps are illustrated in Fig. 1. Abdominal binder was applied for 7 - 14 days to avoid haematoma or collection. Patients were allowed partial weight bearing in a walking boot for two weeks, with advice to avoid strenuous activities for 6 weeks. Patients were followed up at regular intervals at 2 weeks, 6 weeks, 6 months, and 12 months post-procedure, and MOXFQ and FAAM scores were obtained at each visit.

Results

Five patients with post-traumatic osteoarthritis were included in the study. 3 patients were male, and 2 were female. The mean age was 43 years (31-51). All patients had previous surgery for traumatic fractures. Demographic information and details about the initial injury and its management are presented in Table 1. No perioperative complications were noted relating to abdominal liposuction and intra-articular injection of lipoaspirate. There were no

complications recorded in the 12-month follow-up period.

Microsoft Excel software data analysis tool pack was employed for statistical analysis. P value significance was set at 0.05. MOXFQ scores were analysed using the ANOVA two-factor test. Improvement in scores was shown in all patients after treatment (p=<0.0001). Recorded scores at baseline, 2 weeks, 6 weeks, 6 months, and 12 months are presented in Table 2. Mean MOXFQ scores are illustrated in Fig. 2. There was also a statistically significant improvement in the FAAM ADL scores of all 5 patients, demonstrated using the paired t test (p= <0.0001). Results are shown in Table 3. The mean FAAM score increased from 51.4 to 57 at 12 months (Fig. 3).

Tables:

Table 1: **Patient demographics and details of initial injury**

Patient number	1	2	3	4	5
Gender	M	M	F	F	M
Age	40	51	44	31	51
BMI	31	28.8	23.2	34.8	n/a*
Initial trauma	Bimalleolar fracture	Distal tibia fracture	Trimalleolar fracture	Trimalleolar fracture	Bimalleolar fracture
Initial management	ORIF	IM nail	ORIF	ORIF	ORIF
Year injury sustained	2014	1992	2012	2012	n/a

*information not available

Table 2: MOXFQ scores at baseline, 2 weeks, 6 weeks, 6 months and 12 months post treatment

Patient number	MOXFQ scores				
	Pre-operative	*2 weeks*	*6 weeks*	*6 months*	*12 months*
1	58	45	30	26	31
2	63	50	36	31	36
3	63	51	40	35	44
4	66	47	30	27	30
5	65	50	35	32	45

p= <0.0001

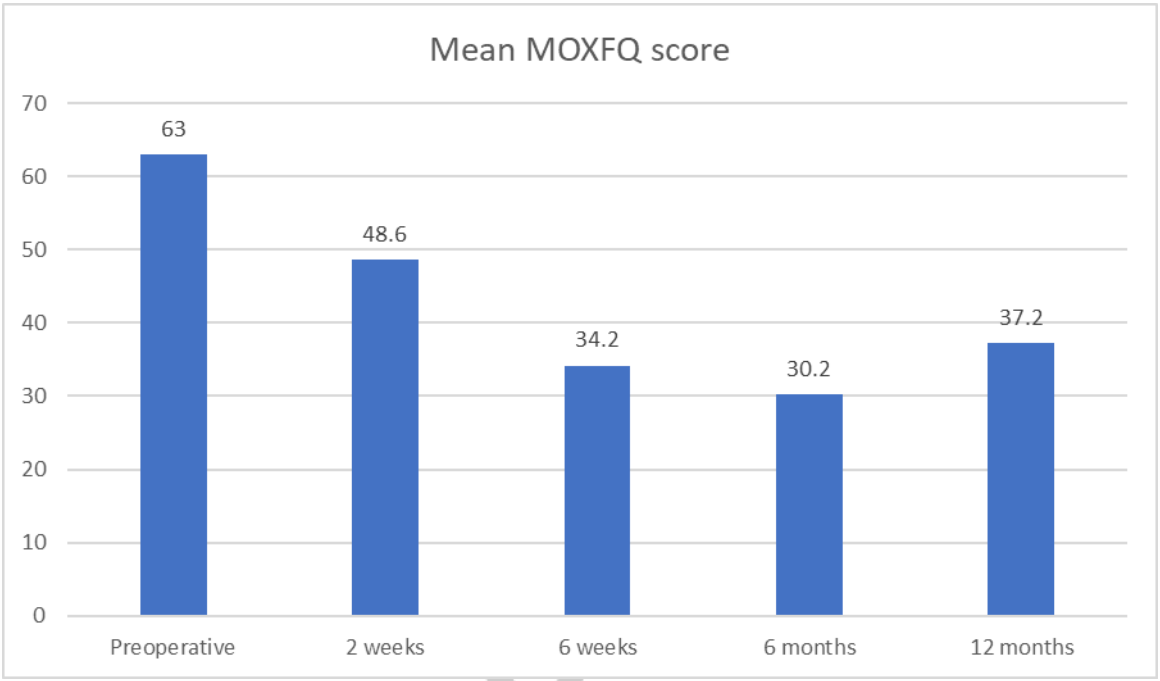


Fig. 2: Mean MOXFQ scores at baseline, 2 weeks, 6 weeks, 6 months and 12 months post treatment

Table 3: FAAM ADL scores at baseline, 6 months, and 12 months post treatment

Patient number	FAAM ADL Score		
	Preoperative	*6 months*	*12 months*
1	59	79	65
2	48	60	52
3	50	71	58
4	45	64	50
5	55	75	60

p= <0.0001

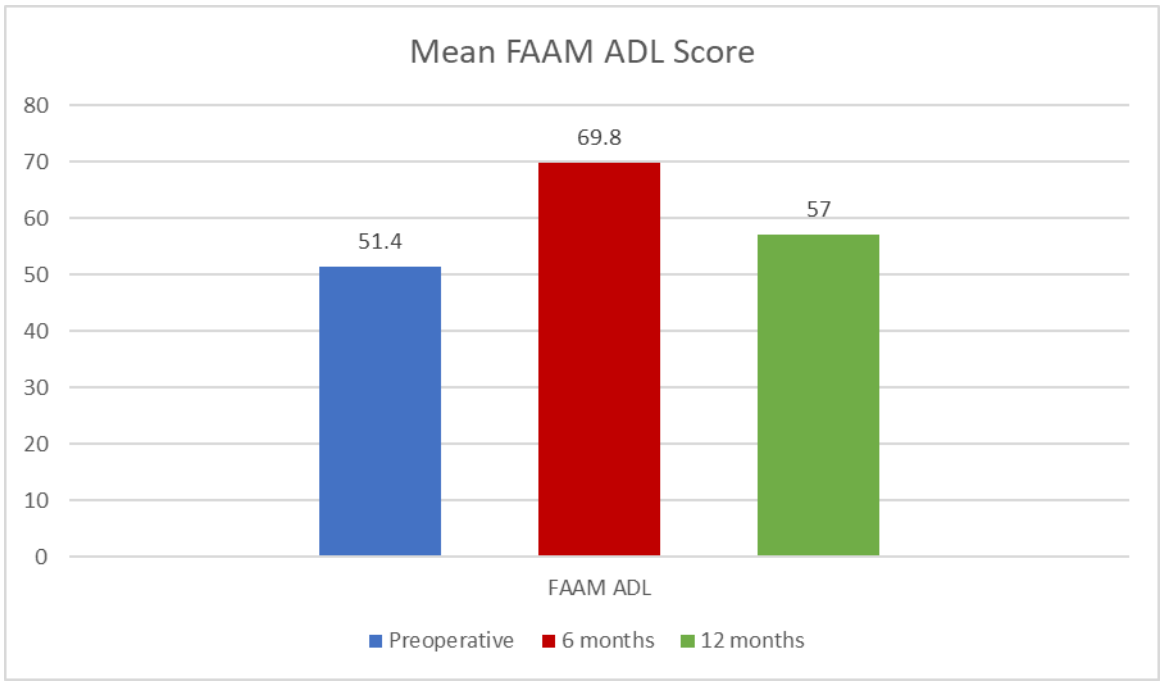
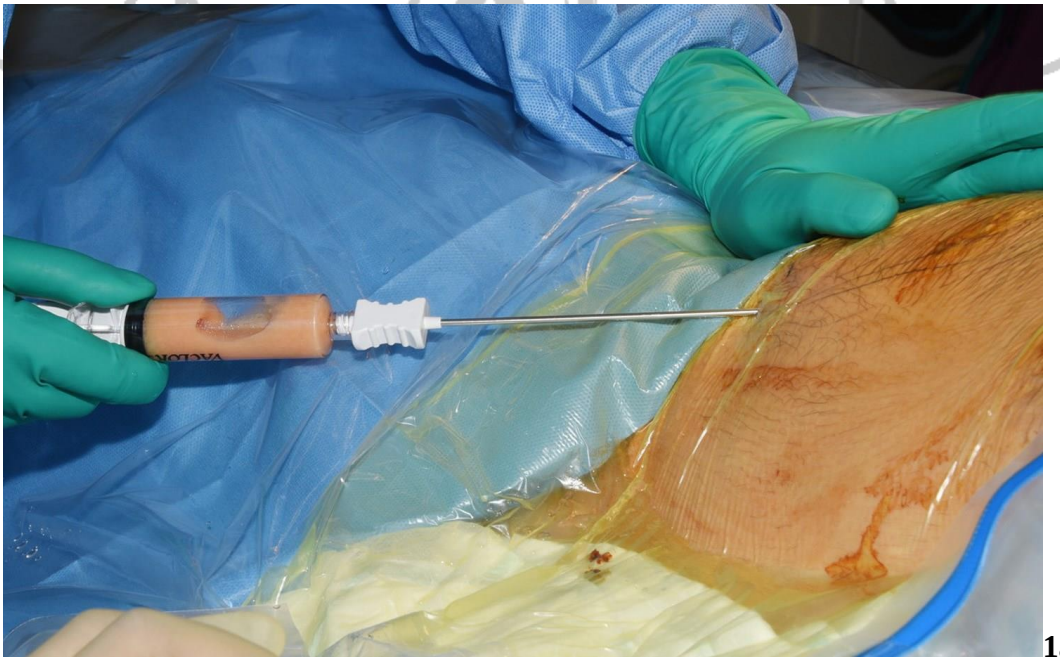


Fig. 3: Mean FAAM ADL score at baseline and 6 months post treatment

Figures:

Fig. 1: Steps involved in aspiration and processing of fat cells using Lipogems procedure and injection of adipose-derived stem cells. a: Aspiration of fat cells from abdomen using wide bore needle. b: Processing of harvested fat. c: Processing and washing of the fat. d: Microfragmented adipose-derived fraction. e: Injection of adipose-derived stem cells into ankle joint.



1a

1b

1c

1d

1e

Discussion

Ankle arthritis is challenging to manage in orthopaedic surgery. Patients with ankle arthritis are usually post-traumatic and younger at the diagnosis; they also progress more rapidly to end-stage disease than patients with hip or knee arthritis [1]. Many non-operative modalities are available to treat ankle osteoarthritis, including weight loss, physiotherapy, braces, nonsteroidal anti-inflammatory drugs (NSAIDs), intraarticular steroids, and hyaluronic acid injections [5]. Currently, no effective therapy can successfully reverse the progression of osteoarthritis [6].

With advances in regenerative medicine, intra-articular injections of mesenchymal cells (MSCs) have emerged as an alternative cellular therapy for the treatment of OA. Most current cell therapies involve MSCs due to their ability to differentiate into adipocytes, chondrocytes, osteoblasts, myocytes, hepatocytes, and endothelial cells, their immunoregulatory function to reduce inflammation in OA, and their ability to provide an adequate environment to regenerate damaged tissues [7]. MSCs were first isolated from bone marrow by Friedenstein and co-workers in 1966 [8] and later used as a significant source of MSCs by different researchers. It is a well-established concept that fat tissue is an optimal source of mesenchymal cells [7]. Fat tissue is available in abundance in the body and can be easily harvested with a minimally invasive surgical approach, thus decreasing morbidity [9].

We used the Lipogems® system to harvest, process, and transfer micro-fragmented adipose tissue, which is well-described in the literature [10]. It involves a simple, self-contained mechanical technique with an enzyme-free technology, able to convert fat aspirate into a micro-fragmented adipose-derived fraction. This technique reduces the size of the adipose tissue clusters using mild mechanical forces and eliminates oil and blood residue. This process provides micro-fragmented fat [3,10] in 15-20 minutes. Lipogems® tissue product represents an autologous implantable product that incorporates the main elements for a perfect natural regenerative response: The Scaffold (adipose tissues), the Cells (Pericytes), and the Growth factors [10]. The resulting product obtained is composed of small intact adipose tissue clusters (250-650 microns) and contains pericytes retained within an intact and biologically primed (by the mechanical trauma) stromal vascular niche [10].

The regenerative potential of fat cells in patients with degenerative and inflammatory joint diseases has been used in the literature [2,3,4,8,11]. The intra-articular injection of Lipogems® for treating osteoarthritis of knees and hips has been successfully used with improvement in short and long-term pain resolution [2,3,8,11]. In a recent randomised clinical trial, autologous adipose-derived stem cell therapy was associated with clinically significant improvement in pain and function in symptomatic knee OA [2]. Another study

has successfully used the micro-fragmented adipose tissue in 32 treated knees showing substantial improvements in terms of pain and cartilage quality for up to 12 months [3]. A recently published multi-centric, international, open-label study showed a clinical improvement after 2 years using micro fragmented fat cells in grade 2 and 3 knee osteoarthritis [12].

There are only a few studies published in the literature in which autologous micro-fragmented fat cells have been used for ankle arthritis [4,13]. Shimozono et al published a retrospective study using arthroscopic debridement and adjuvant autologous adipose tissue injection, showing positive results in the treatment of KT grade 3 ankle arthritis [4]. Niazi et al published a case report in 2020 in which Lipogems therapy was successfully used for advanced arthritis of the ankle. Our series of patients had a mean age of 43 years with advanced ankle arthritis and showed positive results compared to their baseline function. There was no intraoperative or delayed complications observed in all patients included in the study. This therapy uses patients' own fat tissue to provide pericytes and growth factors to promote healing. It benefits young people who do not want to undergo surgery or wish to defer it to a later age.

We compared our results to other well-established, nonsurgical treatments for ankle OA. A Cochrane systematic review by Witeveen et al. [14] evaluated the results of six randomised controlled trials (RCTs) comparing hyaluronic acid (HA) injections to placebo. Evidence of improved functional scores at 6 months was thought to be inconclusive. One of the RCTs comparing different dosing schedules favored 3 courses of HA injections [15]; other studies have used between 3 to 5 courses of injections [5, 16]. This is in contrast to a single intra-articular injection described in our study. Similarly, studies describing platelet-rich plasma (PRP) injections for ankle OA have required 3 to 4 courses of injections [17, 18]. Futawa et al. [18] reported the positive effect of PRP was reduced at only 24 weeks after the last injection. A 2018 systematic review of intra-articular injections for ankle OA treatment [19] found no RCTs available evaluating the use of corticosteroids; the effects of steroid injections were thought to be short-term.

Conclusion

This study shows that a single-dose autologous micro fragmented fat cells therapy improves clinical, functional, and quality of life in post-traumatic ankle OA. All patients involved in the study would otherwise have had to undergo an ankle fusion procedure. The treatment provides sustained, safe, and reproducible results up to and beyond 12 months, with improvement observed in all patients as early as 6 weeks postoperatively. Lipogems treatment can be used when standard treatment options such as physical therapy, NSAIDs or steroid injections have not provided sufficient relief. There were no complications of the therapy observed in this study. The presented findings provide promising early evidence that this treatment modality is a safe and effective alternative in carefully selected patients, with likely superior results compared to other available treatments. Results presented in this study are limited to a

small number of patients; longer follow-up studies with larger patient numbers would be needed to draw more robust conclusions.

Declarations:

Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of Interest:

1. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.
2. The authors received no financial support for the research, authorship, and/or publication of this article.

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