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Case Series

A Novel Approach to The Use of Flowable Human Amniotic Fluid for Diabetic Foot Ulcers in High-Risk Veterans Affairs Patients

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Abstract

As of 2017, there are 425 million people worldwide who suffer and are affected by Diabetes Mellitus. Among those 425 million people, approximately 34% of people go on to develop diabetic foot ulcers with more than 50% becoming infected. There are many causes of ulcers, including metabolic, biomechanical, traumatic, or post-operative complications. The use of human amniotic fluid has the potential to be an additional treatment for pedal wounds in patients with diabetes mellitus. Indications may include wounds which have prolonged or delayed healing as a result of biomechanical complications, co-morbidities, or failed conservative treatment. This case series explores the effectiveness at topical application of flowable human amniotic fluid in 3 different high risk diabetic patients who all suffered from a pedal ulcer. Each patient had a different location and circumstance for their wound allowing for some variety in surgical planning and wound care decision making. Two of the three patients were able to heal completely within 3 months of initial consult with the remaining patient healing within 4 months of initial consult. Per chart reviewing, all three patients have remained healed at the 1 year follow-up with no evidence of reoccurrence. This series hopes to open a discussion regarding the novel use of topical application of human amniotic tissue as an advanced wound care option for those who may have failed conservative therapy or may be looking for alternative methods to help heal pedal ulcers.

***Keywords:** Amniotic fluid; Diabetic foot ulcer; Wound healing*

Introduction

Diabetes mellitus is a vicious metabolic disease which affects the body in some of the worst ways. Some of the consequences of diabetes includes peripheral neuropathy, ischemia, callus formation, deformities, edema, and peripheral artery disease (1). Unfortunately, as a result of these comorbidities in various combinations, patients living with diabetes are at increased risk for developing diabetic foot ulcers (DFUs). The global prevalence of DFUs is 6.3%, with males being affected more often than females, in addition to Type 2 being more prevalent than Type 1 (2). An additional aspect of DFUs is the financial burden is places on the health care system. As of 2013, the cost of diabetes related foot ulcers and amputations was up to 17 billion dollars in the United States health care system (3). On a global scale, it was predicated that the expenditure of diabetes would reach 850 billion dollars (4). Currently, the standard of care (SOC) involves four established principles: pressure relief, debridement, infection management, and revascularization when indicated (2). When treating DFU patients with the standard of care, which may appear to become ineffective, it is worth considering advanced care such as biologics, surgical intervention, or a combination of the two.

The concept of using amniotic tissue is not a novel idea, but dates back as far as 1910 when human amniotic membranes were being used in multiple surgical applications, including temporary wound dressings, burn care, and leg ulcer treatment (5). The use of amniotic fluid also has shown great potential for healing of DFUs due to their antimicrobial properties and promotion of re-epithelization of wounds (6). In this case study, we look at three separate high-risk patients who were treated for DFUs. Each patient had a different anatomical location, clinical presentation, and past medical history. While standard of care was utilized for each patient, the timeline for application of flowable amniotic tissue was approached individually. The aim of this study is to examine 3 individual cases of a novel approach to treating DFUs with topical advanced biologic care in hopes of finding successful alternative ways to treat pedal wounds should standard of care fail.

Methods

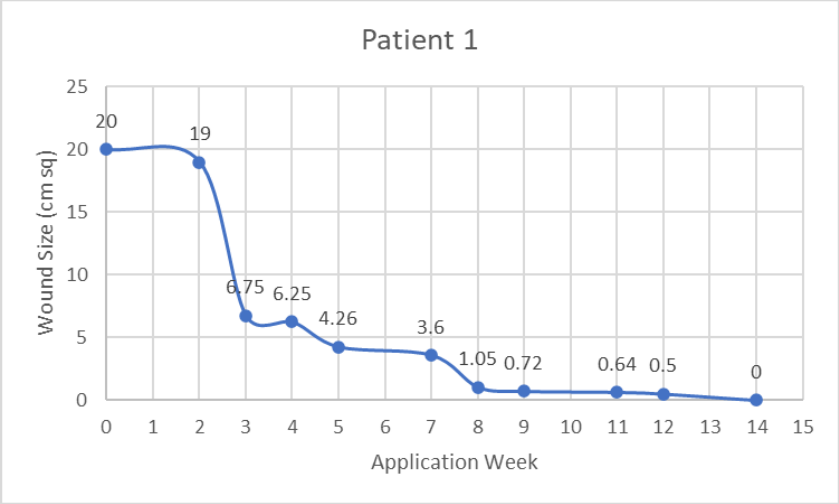
Each patient was examined and evaluated in a clinical setting either in the outpatient clinic or on the hospital ward floors. All wounds were undressed with care, followed by cleansing via available wound cleansers. All wounds were evaluated for maceration and/or hyperkeratotic formation. Debridement was carried out via sterile scalpel blades and sterile dermal curettes. Final wound measurements were taken prior to application of amniotic tissue. Amniotic tissue consisted of either PalinGen ® SportFlow (Flow) or PalinGen ® Hydromembrane (Membrane). In order assist in maintaining contact with the wound surface area, Promogran Prisma ™ (Prisma) was utilized as a vehicle for the topical amniotic fluid. Once in contact with the wound bed, the wound was secured with a non-adherent layer followed by a sterile dressing. Appropriate offloading was gained via offloading post-operative shoe, walking boot with offloading modifications, or offloading Prevalon boots while patients were non-weight bearing.

DFUs were treated via topical application of Flow, a product of Amnio Technology. Flow is a human allograft tissue matrix which is chorion free and derived from human amnion and amniotic fluid. Tissue is obtained from healthy donors who voluntarily offer their placentas following elective Caesarian delivery. Flow is indicated for any sized wound; however, a common range includes 1cm to 3cm per the manufacture guidelines. Flow offers properties such as anti-microbial, anti-adhesion, anti-inflammatory, and regeneration to help aid in the healing process of these DFUs.

Case History/Report

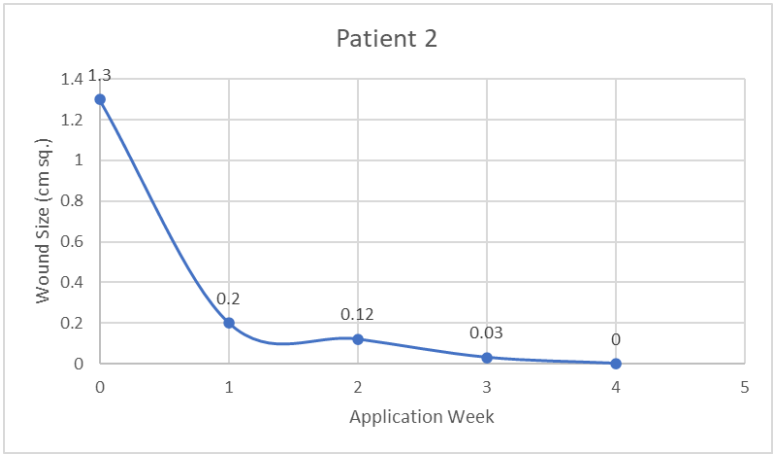
Patient 1

Patient 1 was seen as an ED consult for a right second digit infection. Past medial history includes hypertension, mixed hyperlipemia, diabetes mellitus type 2, hypothyroidism, and iron deficiency anemia. Upon examination, there was a large blister filled with purulence on the plantar aspect with additional erythema coursing proximally to the midfoot. A bedside incision & drainage was performed with saline flushing, followed by a betadine dressing and admission with IV antibiotics. Following antibiotic therapy, it was decided to proceed with a second digit amputation and debridement to the level of the metatarsal phalangeal joint in the operating room. 4 days post-operatively, negative pressure wound therapy was initiated via a KCI Wound VAC. VAC changes were conducted every 3-4 days either by the on-call resident or the wound care nursing team. 10 days post-operatively, the first topical application of Flow was initiated while maintaining therapy via the Wound VAC. The patient underwent topical amniotic tissue therapy for 1 month in conjunction with KCI VAC therapy while inpatient. Of note, wound measurement documentation changed from 1 continuous surgical incision to separate dorsal and plantar wound measurements. With the plantar wound healing with more progression, amniotic therapy was focused primarily on the dorsal aspect of the wound. Following 1 month of amniotic therapy, a 1-week trial of Membrane only therapy was applied to the dorsal wound. KCI VAC therapy was maintained as well. After the 1-week of Membrane therapy, it was decided that Flow therapy would be restarted for 1 additional week. Due to skin maceration from the KCI VAC, therapy was paused 6 weeks following initiation. Based on clinical presentation of purulence during a dressing change, a further work-up of osteomyelitis was conducted despite no evidence of constitutional symptoms. Radiographs demonstrated boney erosion to the second metatarsal head which leads to the decision to return to the operating room for a partial 2nd metatarsal amputation with the implantation of antibiotic impregnated beads & iodoform packing for delayed closure. Once the infection had been removed based on pathology results and lab results had stabilized, a new therapy of Flow with Prisma was initiated 5 days post-operatively along with reinitiating KCI VAC therapy 6 days post-operatively. This therapy was carried out for 1 week before officially discontinuing KCI VAC therapy. Prisma and Flow therapy was conducted for another week before transitioning to 3 applications of singular membrane therapy over the span of 5 weeks. At the conclusion of the final membrane therapy, the patient presented clinically with fully epithelialized skin and no further open wounds. In total, the wound was treated over the span of 20 and a half weeks with 6 applications of Flow, 8 applications of Membrane, and 2 applications of Prisma. The patient has remained healed to date with no evidence of re-ulceration per chart reviewing.



Patient 2

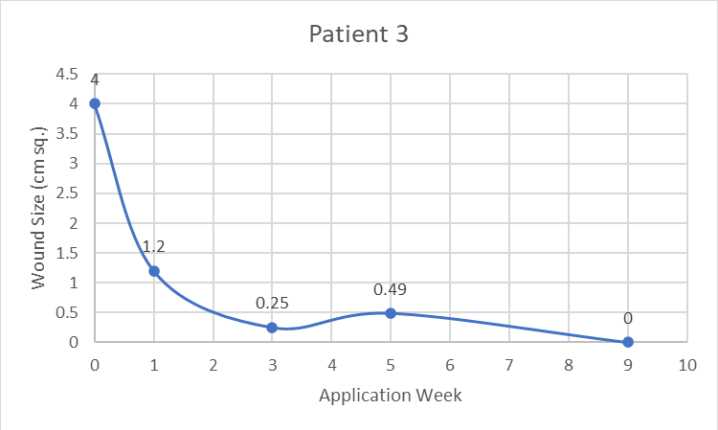
Patient 2 was seen in the ED as a consult for concerns of cellulitis to the left foot. Past medical history included hypertension, diabetes mellitus type 2, left hallux amputation, peripheral neuropathy, history of MRSA, hypokalemia, and tinea pedis. This patient was seen in the ED 16 days status post left hallux amputation from a community hospital and was lost to follow-up with the community surgeon. The patient presented to the ED to have the surgical site evaluated and possible suture removal. The surgical site demonstrated erythema coursing proximally to the midfoot with probing to both the first and second ray. There was a mild amount of purulence expressed along with a small of necrosis dorsally. There were also various social circumstances at home (i.e. lack of electricity, lack of wound care support at home) which made post-operative care difficult and unrealistic for this patient. The patient was admitted with IV antibiotics with recommendations for a vascular consult as well as ordering ABIs. Following 10 days of local wound care & antibiotic tailoring with the help of Infectious Disease, it was decided to proceed with an incision & drainage with debridement of all non-viable tissue and bone. An intraoperative decision was made to place a Penrose drain for secondary closure. Two days post-operatively, the Penrose drain was removed, and the first topical application of Flow was initiated in conjunction with negative pressure wound therapy via KCI Wound VAC. Following 1 week of treatment, we decided to discontinue the VAC therapy due the healing progression that was noted clinically. We elected to proceed with a second round of Flow, but this time it was applied in combination with Prisma. This therapy was maintained for 1 week; with the following 2 weeks of treatment consisting primarily of Membrane therapy. Upon physical examination prior to discharge, the patient was found to be completely healed. In total, the wound was treated over the span of 6 weeks with 2 applications of Flow, 2 applications of Membrane, and 1 application of Prisma. The patient has remained healed to date with no evidence of re-ulceration per chart reviewing.



Patient 3

Patient 3 was an in-patient consult for a chronic lower extremity wound. Past medical history includes diabetes mellitus type 2, peripheral neuropathy, venous insufficiency, cellulitis, chronic kidney disease stage 3, essential hypertension, heart transplant recipient, and gout. Of note, this patient was known to the podiatry clinic dating back to October of 2019.

The patient had a history of previous wounds, which had been healed and re-ulcerated. Prior to the beginning of this case series, podiatry had been consulted twice in the span of 1 month. At the time of the case series, the patient was still suffering from a chronic ulcer to the plantar surface of the 1st metatarsal phalangeal joint on the left foot. The patient was treated previously with conservative wound care, but the wound was yet to fully heal. Based on the chronicity of the wound in addition to conservative measures being ineffective despite appropriate offloading, it was decided to pursue an advanced conservative care plan. 1 day following initial consult, therapy was initiated via Flow soaked in Prisma with the addition of Membrane. Following 1 week of therapy, the wound had decreased by 50%, so it was decided to commence a second round of Flow soaked in Prisma. 2 weeks later, the wound continued to decrease in size and a final round (3rd) of Flow soaked in Prisma was applied. Following discharge from the hospital, the patient was seen in clinic for routine wound monitoring. Based on the nature of the wound depth decreasing, but the wound edges slightly increasing, it was decided to focus on reapproximating the wound edges and therefore proceed with a final application of a membrane. Upon physical exam 2 weeks late, the wound had healed with fragile epithelium and was treated with a simple non-adherent bandage for added protection. The patient was referred out to the out-patient wound clinic due to additional wounds not cared for by podiatry. However, based on chart review, the patient's pedal wound was absent upon first presentation to the wound clinic within 2 weeks from being referred out of the clinic. In total, the wound was treated over the span of 9 weeks with 3 applications of Flow, 2 applications of Membrane, and 3 applications of Prisma. The patient has remained healed to date with no evidence of re-ulceration per chart reviewing.



Discussion

At the conclusion of the series, it was determined that all three patients were able to fully heal their diabetic foot ulcers with the assistance of advanced wound care via amniotic fluid. While each patient had their own respective past medical history, wound etiology, and treatment course, this study aids in the consideration of using amniotic tissue for treating DFUs. The literature demonstrates various justifications on the effectiveness of amniotic tissue when treating wounds. Biologic dressings, such as human amniotic membranes, have the capability to reduce bacterial contamination & prevent further contamination, reduce pain, reduce the loss of fluid, protein, heat & energy, promote healing, and protect underlying structures (7). When assessing amniotic fluid, it has been said that trophic factors act in order to stimulate cell differentiation, as well as cell movement and proliferation which may ultimately lead to the re-epithelialization of a wound (6). Additionally, amniotic fluid was found to activate mitosis, angiogenesis, and increase the rate of wound closure in diabetics (6). Further consideration should also be given regarding the complexity and high-risk nature of having a DFU. DFUs were found to double mortality and heart attack risks while simultaneously increasing the risk of stroke by 40% (8). When assessing mortality, patients are at risk for death at 10 years with a DFU twice as much as a patient with diabetes and no DFU (9). As of 2007, the relative 5-year mortality rate following limb amputation was 68%, second only to lung cancer at 86% (10). The cost of treating is not something to be ignored either. Patients who suffer from DFUs are twice as costly to US Medicare as opposed to those with Diabetes Mellitus alone (11). In 2013, the cost of a DFU was greater than that of the five most costly forms of cancer (3). To add to the heavy financial impact, 1 million dollars is spent on diabetic foot complications every 30 seconds in the USA alone (3).

Conclusion

The use of amniotic tissue when treating wounds has dated back to 1910 and to this day in this new century, there is still justifications and new avenues where this type of treatment may be utilized. This case series was able to examine three different patients, all with diabetic foot ulcers, and demonstrated that topical flowable amniotic tissue may be useful for healing high-risk patients with diabetic foot ulcers. This is likely due to the use of amniotic fluid and its ability to reduce & prevent contamination, reduce pain, promote cellular movement & proliferation, and most importantly, promote healing.

The use of amniotic tissue as an advanced method for wound care in patient who suffer from DFUs continue to show clinical promise and should be given full consideration for utilization in the future.

Conflict of Interest

The authors declare they have no conflict of interest.

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References

1. Niami F, Molavynejad S, Hemmati AA, et al. Evaluation of the effect of a gel made with amniotic fluid formulation on the healing of diabetic foot ulcers: A triple-blind clinical trial. Frontiers in Public Health. 2022; 10. doi:10.3389/fpubh.2022.1025391
2. Mohammed, Y.A., Farouk, H.K., Gbreel, M.I. et al. Human amniotic membrane products for patients with diabetic foot ulcers. do they help? a systematic review and meta-analysis. J Foot Ankle Res 15, 71 (2022). doi.org/10.1186/s13047-022-00575-y
3. Barshes NR, Sigireddi M, Wrobel JS, et al. The system of care for the diabetic foot: objectives, outcomes, and opportunities. Diabet Foot Ankle. 2013;4:10.3402/dfa.v4i0.21847. Published 2013 Oct 10. doi:10.3402/dfa.v4i0.21847
4. Els. (2017). IDF Diabetes Atlas - 8th Edition. Retrieved April 18, 2023, from https://d-net.idf.org/en/library/487-idf-diabetes-atlas-8th-edition.html
5. Talmi YP, Sigler L, Inge E, Finkelstein Y, Zohar Y. Antibacterial properties of human amniotic membranes. Placenta. 1991;12(3):285-288. doi:10.1016/0143-4004(91)90010-d
6. Wollmuth C, Foti D, Taylor R, Pergolizzi JV, Tribuiani A. (2019). Human Amniotic Fluid Injection as a Treatment for Diabetic Foot Ulceration: A Case Report. Int J Case Rep Clin Image 1(3): 111
7. Gruss JS, Jirsch DW. Human amniotic membrane: a versatile wound dressing. Can Med Assoc J. 1978;118(10):1237-1246.
8. Brownrigg JR, Davey J, Holt PJ, et al. The association of ulceration of the foot with cardiovascular and all-cause mortality in patients with diabetes: a meta-analysis. Diabetologia. 2012;55(11):2906-2912. doi:10.1007/s00125-012-2673-3
9. Iversen MM, Tell GS, Riise T, et al. History of foot ulcer increases mortality among individuals with diabetes: ten-year follow-up of the Nord-Trøndelag Health Study, Norway. Diabetes Care. 2009;32(12):2193-2199. doi:10.2337/dc09-0651
10. Armstrong DG, Wrobel J, Robbins JM. Guest Editorial: are diabetes-related wounds and amputations worse than cancer?. Int Wound J. 2007;4(4):286-287. doi:10.1111/j.1742-481X.2007.00392.x
11. Rice JB, Desai U, Cummings AK, Birnbaum HG, Skornicki M, Parsons NB. Burden of diabetic foot ulcers for medicare and private insurers [published correction appears in Diabetes Care. 2014 Sep;37(9):2660]. Diabetes Care. 2014;37(3):651-658. doi:10.2337/dc13-2176

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