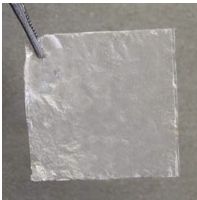


Standard of Care (SOC) vs Amniotic Membrane (AM) Use on Non-Healing Venous Stasis Ulcers and Diabetic Foot Ulcers

Alton R. Johnson Jr, DPM, CWSP; University of Michigan, Shenlone Wu, DO; University of Nevada, Las Vegas, Briana Lay University California -Los Angeles

ABSTRACT

This is a retrospective chart review comparing wound size changes using only standard of care (SOC) versus SOC with amniotic membrane (AM) in patients with non-healing venous stasis ulcers (VLU) and diabetic foot ulcers (DFU). Subjects in the study are chosen when their wound failed to improve significantly after 5 weeks using SOC alone, and thus, application of AM was used as additional treatment for 5 additional weeks. We concluded that amniotic membrane application with standard of care is more efficacious in non-healing VLU and DFU.



METHOD

Demographic data

There were 23 patients identified. Patients' ages range from 33 to 89. 11 ulcers were DFU, and 12 ulcers were VLU patients. 18 were males and 5 were females. All patients met the following selection criteria.

Subject Selection Criteria

Charts were reviewed from 2016-2022 and patients with chronic DFU and VLU were identified. Subjects that underwent 5 weeks of standard of care followed by at least 5 AM applications were selected. Subjects were excluded if any of the following criteria were present:

- Wound healed with less than 5 AM applications
- Noncompliant patients resulting in early termination of the study
- Hemoglobin A1c >10
- Wounds not in proliferation phase (i.e., Infected wounds)
- Any disruption during the study such as acute change in medical status resulting in transfer to an acute facility

SOC TREATMENT

During the first 5 weeks, standard of care treatment is performed based on the guideline suggested by the National Center for Biotechnology Information. (Dreiflik et al., 2014). Treatment of choice includes silver gel, silver or calcium alginate, medical honey, collagenase, antibiotic ointment, negative pressure wound treatment among other treatment modalities. The choice of dressing is determined based on the amount of drainage, with or without odor and location of the wound.

AM TREATMENT

AM treatment was performed once a week. No local or general anesthesia was required. Wound cleanser was first used to prepare the wound bed. Debris was then removed from the wound bed. Gentle wound bed stimulation was performed with a curette creating a refreshed environment. Then AM was placed along with a mesh and secured with steri-strips. Proper secondary dressing was applied, and it was repeated for 5 weeks of treatment.

COLLECTION OF DATA

Patient charts were identified at the start and the wound size was documented under Measurement 1. Afterwards, patients received SOC for 5 weeks and the wound size was recorded under Measurement 2. The subsequent 5 weeks of treatment with amniotic membrane was measured under Measurement 3. See Table 1 & 2.

Table 1.

DFU Patients	Measurement 1	Measurement 2	Measurement 3
1	9 cm ²	8.7 cm ²	5.2 cm ²
2	15 cm ²	29.2 cm ²	27 cm ²
3	12.5 cm ²	14.3 cm ²	5.1 cm ²
4	16 cm ²	16.8 cm ²	14 cm ²
5	37.8 cm ²	39.1 cm ²	15.6 cm ²
6	12.3 cm ²	12.3 cm ²	7.8 cm ²
7	36 cm ²	38.2 cm ²	31.5 cm ²
8	29.9 cm ²	34 cm ²	4 cm ²
9	19.5 cm ²	18.6 cm ²	9 cm ²
10	12.3 cm ²	16 cm ²	3.6 cm ²
11	9.9 cm ²	12 cm ²	8.4 cm ²
Total Average	19.11 cm ²	21.75 cm ²	11.93 cm ²

Table 2.

VLU Patients	Measurement 1	Measurement 2	Measurement 3
1	36 cm ²	36 cm ²	14.4 cm ²
2	12.3 cm ²	12 cm ²	6 cm ²
3	21 cm ²	23.4 cm ²	8.6 cm ²
4	33.1 cm ²	31.3 cm ²	4 cm ²
5	38 cm ²	28.5 cm ²	15 cm ²
6	28 cm ²	15 cm ²	8.4 cm ²
7	28.6 cm ²	27.6 cm ²	16.8 cm ²
8	28 cm ²	18 cm ²	7.6 cm ²
9	26.9 cm ²	30 cm ²	18 cm ²
10	14 cm ²	22.1 cm ²	10.5 cm ²
11	18 cm ²	18 cm ²	1.3 cm ²
12	7.3 cm ²	8.4 cm ²	1.8 cm ²
Total Average	24.27 cm ²	21.53 cm ²	9.37 cm ²

ANALYSIS

Ulcer healing was assessed using the percentage of healed wound area. Wound size difference using standard of care vs. amniotic membrane application were compared. × 100.

FORMULA FOR CHANGE IN WOUND AREA

[Percentage Change in Wound Area] = [Final wound measure] - [Original wound measure] / [Original wound measure] 100% (See table 4 and 5)

Table 4.

DFU Patients	% size change after SOC	% size change after AM treatment
1	-3%	-40%
2	195%	-7%
3	114%	-64%
4	105%	-13%
5	103%	-60%
6	100%	-37%
7	106%	-17%
8	114%	-88%
9	-5%	-52%
10	130%	-77%
11	121%	-30%
Total Average	113%	-45%

Table 5.

VLU Patients	% size change after SOC	% size change after AM treatment
1	100%	-60%
2	-2%	-50%
3	111%	-63%
4	-5%	-88%
5	-25%	-47%
6	-46%	-44%
7	-3%	-39%
8	-36%	-58%
9	112%	-40%
10	158%	-52%
11	100%	-93%
12	115%	79%
Total Average	-11%	-57%

RESULTS

For the DFU patients, the initial size average was 19.1 cm². After 5 weeks of SOC treatment the wound size increased to 21.6 cm², an increase of 113%. After 5 weeks of AM treatment, the wound size decreased to 9.4 cm². There was a reduction of -45% in size.

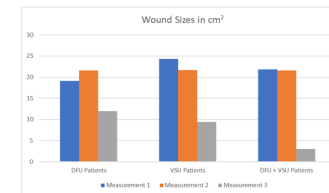
In the VLU group, patients' initial average wound size was 24.3 cm². The wound was slightly smaller after 5 weeks of SOC treatment at 21.7 cm². This is a reduction of -11%. AM treatment was performed for 5 subsequent weeks and the average size was decreased to 9.4 cm². This was a reduction of -57% in size change. (See table 3)

Combining the two subgroups of patients, the initial average size of the wound was 21.8 cm² with a slight decrease in size to 21.6 cm² after 5 weeks of SOC treatment. This was -1% in size change. After 5 weeks of AM treatment, the average size was 11.1 cm², a -51% reduction in size. (See table 6)

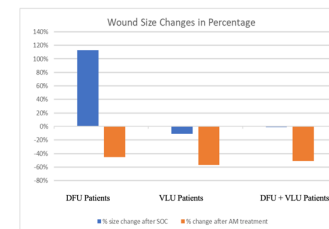
Table 6.

DFU + VLU	% size change after SOC	% size change after AM treatment
Total Average	-1%	-51%

Graph 1.



Graph 2.



CONCLUSION

We purposely selected challenging wounds to evaluate the efficacy of AM treatment. Both DFU and VLU patients were all refractory to SOC treatment after 5 weeks. In fact, VLU patients overall have wound size larger than the initial SOC treatment. DFU patients on average have minimal improvement with SOC treatment. Combining both types of patients, the 5 weeks of AM treatment (-51%) significantly reduces the wound size compared to 5 weeks of SOC treatment (-1%).

DISCUSSION

The study's results indicate that AM treatment appears to be more effective than SOC treatment in promoting wound healing, especially in DFU and VLU patients. However, further research is needed to confirm these findings, explore the underlying mechanisms, and determine the generalizability of these results to a larger patient population. Additionally, it is essential to consider individual patient characteristics and comorbidities that may influence treatment responses. These findings underscore the need for personalized wound care approaches tailored to specific patient profiles and wound types.

REFERENCES

- Dreiflik, M. B., Jayasuriya, A. A., & Jayasuriya, A. C. (2015). Current wound healing procedures and potential care. In *Materials Science and Engineering C* (Vol. 48). <https://doi.org/10.1016/j.mssc.2014.12.068>
- Ehlenhedy, H., Omran, E., Halwagy, A., Al-Inany, H., Al-Ansary, M., & Gad, A. (2016). Amniotic membrane can be a valid source for wound healing. *International Journal of Women's Health*, 8. <https://doi.org/10.2147/IJWH.S26634>
- Kogan, S., Sood, A., & Granick, M. S. (2018). Amniotic Membrane Adjuncts and Clinical Applications in Wound Healing: A Review of the Literature. In *Wounds: a compendium of clinical research and practice* (Vol. 30, Issue 6)
- Hilmy N., Yusuf N., Nather A. *Human Amniotic Membrane*. World Scientific Publishing Co Pte Ltd.; Singapore: 2017. Anatomy and Histology of Amnion; pp. 87-101.
- Irakozie L, et al. Efficacy and time sensitivity of amniotic membrane treatment in patients with diabetic foot ulcers: a systematic review and meta-analysis. *Diabetes Therapy*. 2017;8(5):967-79
- Litwiniuk, M., & Grzela, T. (2014). Amniotic membrane: New concepts for an old dressing. In *Wound Repair and Regeneration* (Vol. 22, Issue 4). <https://doi.org/10.1111/wrr.12188>
- Zelen, C. M., Serena, T. E., Denozier, G., & Feterolf, D. E. (2013). A prospective randomised comparative parallel study of amniotic membrane wound graft in the management of diabetic foot ulcers. *International Wound Journal*, 10(5). <https://doi.org/10.1111/ivi.12097>

ACKNOWLEDGMENTS

Special Thanks to Alyssa Flores and CSQ Bio, LLC for sponsoring this research project. Annabelle Messer for the poster design and printing.

