

Unlocking Healing Potentials: Umbilical Cord Mesenchymal Stem Cell-Derived Secretome for Diabetic Foot Ulcer Regeneration

Jefri Unggul Prabowo¹, Ryantino Irdan¹, Cynthia Retna Sartika^{2,3}, Rima Haifa³, Atikah Anwar Hasibuan³, Ditta Kalyani Devi³, Adina Novia Permata Putri³

¹BMC Mayapada Hospital, Jl. Pajajaran Indah V No.97, Bogor, Jawa Barat, 16143, Indonesia
²Universitas Padjadjaran, Jl. Raya Bandung Sumedang KM.21, Hegarmanah, Indonesia
³PT Prodia StemCell Indonesia, Jl. Kramat VII No. 11, Senen, Jakarta, 10430, Indonesia

*Correspondence Author :
Rima Haifa
PT Prodia StemCell Indonesia | rima.haifa@prostem.co.id
(021) 2302629 | (021) 2302642

Abstract

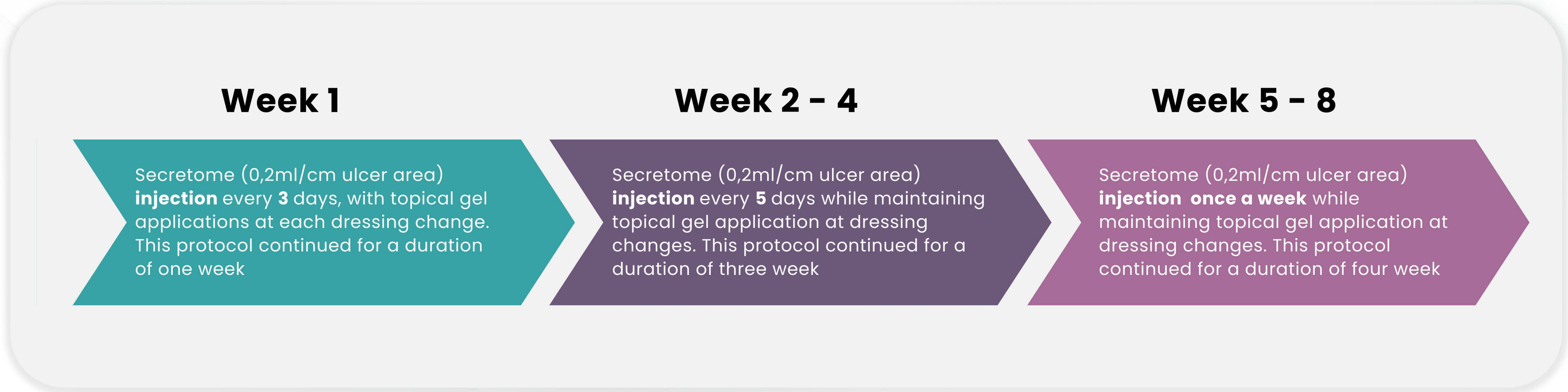
Diabetic foot ulcers (DFU) represent one of the most challenging complications with high prevalences contributing to morbidity and mortality in Indonesia. Emerging within the realm of regenerative medicine are stem cell-based therapies, with a particular focus on mesenchymal stem cells (MSC), offering promising solutions for wound healing management. The therapeutic potential of MSC is extended through secreted bioactive molecules called secretomes. This study delves into the innovative approach of Umbilical Cord MSC-derived secretome for DFU management. The result highlight tissue regenerations in the ulcer area after eight weeks, representing a safe and effective treatment for DFU

Background and Purpose

DFU represents 19–34% of cases in diabetic patients, leading to amputation, quality of life reduction, and social isolation if not treated effectively. Conventional treatments show several obstacles, such as inconsistent efficacy and cost-effectiveness. Emerging to regenerative medicine, Umbilical Cord MSC-derived secretome offers promising solutions for wound healing management. This research offers valuable insights into the development of innovative strategies for managing DFUs and related skin ulcerations

Case Description

A 53-year-old patient presents with three non-healing ulcers on the right foot. The patient has been managing diabetes since the age of 40 and has a history of coronary heart disease, for which the patient underwent coronary artery bypass surgery. Notably, the patient has not been receiving insulin injections since September 2022. Previously, the patient was treated with standard care. The patient was given antibiotic ointment (Nebacetin) for 3 days. However, the wound did not show signs of improvement, leading to the decision to perform debridement. Following that, the patient was given intrasite gel for 3 days. Given the refractory nature of the ulcer and the patient’s limited response to conventional treatments, a novel therapeutic approach was considered. Multiple intralesional injections of Umbilical Cord MSC-derived secretome at 0.2 ml/cm² of the wound area, followed by topical gel application and wound dressing. A total of 41 ml of secretome was administered over 8 weeks. Wound pigmentation, humidity, and depth were recorded at baseline, 2, 3, 4, and 8 weeks after the first injection. Any side effects were monitored and reported.

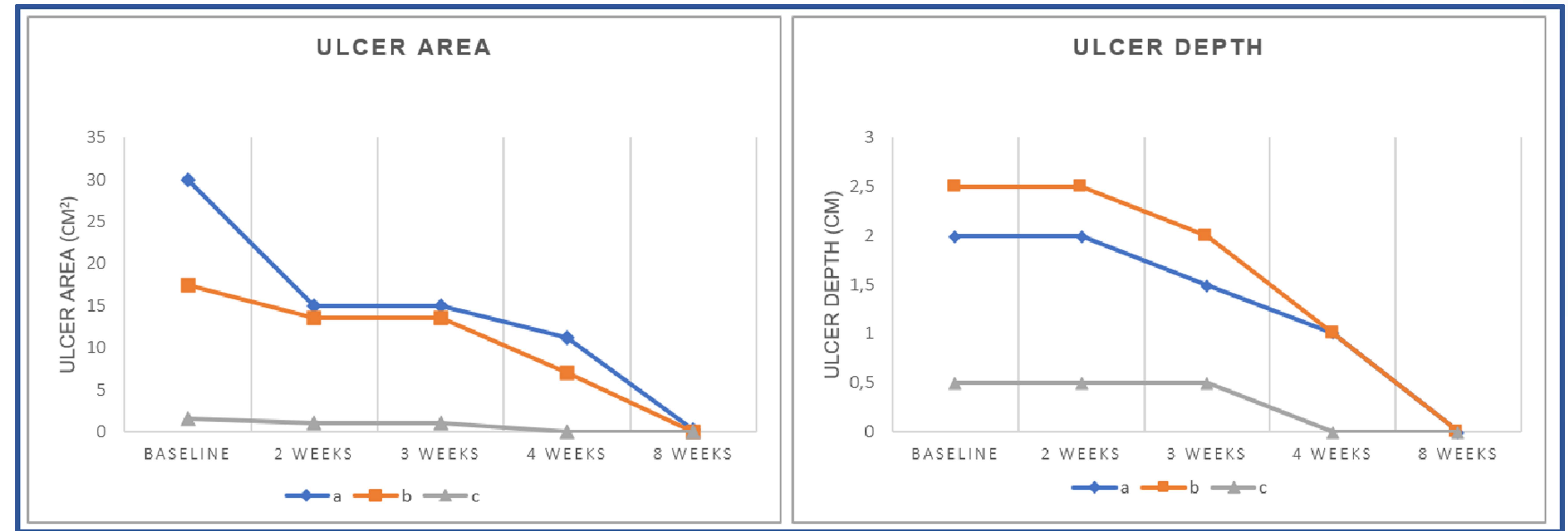


Results and Discussion

The ulcer’s condition improved during follow up on September 17, 2022. Granulation tissue was increased with no infection or adverse reaction. The wound area was moist and superficial, indicated in table 1, 2, and figure 1 below.

Observation	Ulcer	Baseline	2 weeks*	3 weeks*	4 weeks*	8 weeks*
Pigmentation	A	Slough	Slough	Slough	Granulation tissue	Epithelial tissue
	B	Slough	Slough	Slough	Granulation tissue	Epithelial tissue
	C	Slough	Slough	Slough	Granulation tissue	Epithelial tissue
Humidity	A	Wet	Wet	Wet	Wet	Moist
	B	Wet	Wet	Wet	Wet	Moist
	C	Wet	Wet	Wet	Wet	Moist
Wound depth	A	Full thickness	Full thickness	Full thickness	Partial thickness	Superficial
	B	Full thickness	Full thickness	Full thickness	Partial thickness	Superficial
	C	Full thickness	Full thickness	Full thickness	Partial thickness	Superficial

*Observation after 1st injection



The implications of our study for DFU management are profound. The Umbilical Cord Mesenchymal stem cell-derived secretome offers a safe and effective therapeutic for non-healing ulcers by promoting rapid wound closure, enhancing tissue regeneration, and minimizing complications. The pro-angiogenic cytokines in secretome, such as GM-CSF, Ang-1, and Ang-2 promote vascularization and stabilization. In addition, EGF and FGF-2 can stimulate collagen synthesis, re-epithelization, and tissue regeneration. IL-6, IL-8, and MCP-1 contribute to macrophage activation in wound healing.

Conclusion

Umbilical Cord MSC-derived secretome shows tremendous therapeutic potential in accelerating wound healing compared to other therapies. Large sample sizes and route administrations are required to understand the efficacy of Umbilical Cord Mesenchymal stem cell-derived secretome as promising therapy.

References

Akkus, G., & Sert, M. (2022). Diabetic foot ulcers: A devastating complication of diabetes mellitus continues non-stop in spite of new medical treatment modalities. *World Journal of Diabetes*, 13(12), 1106–1121. <https://doi.org/10.4239/wjd.v13.i12.1106>
Balaji, S., Han, N., Moles, C., Shaaban, A. F., Bollyky, P. L., Crombleholme, T. M., & Keswani, S. G. (2015). Angiopoietin-1 improves endothelial progenitor cell-dependent neovascularization in diabetic wounds. *Surgery (United States)*, 158(3), 846–856. <https://doi.org/10.1016/j.surg.2015.06.034>
Chen, L., Cheng, L., Wang, Z., Zhang, J., Mao, X., Liu, Z., Zhang, Y., Cui, W., & Sun, X. (2021). Conditioned medium-electrospun fiber biomaterials for skin regeneration. *Bioactive Materials*, 6(2), 361–374. <https://doi.org/10.1016/j.bioactmat.2020.08.022>
Crocker, R. M., Palmer, K. N. B., Marrero, D. G., & Tan, T. W. (2021). Patient perspectives on the physical, psycho-social, and financial impacts of diabetic foot ulceration and amputation. *Journal of Diabetes and Its Complications*, 35(8). <https://doi.org/10.1016/j.jdiacomp.2021.107960>
Ead, J. K., & Armstrong, D. G. (2023). Granulocyte-macrophage colony-stimulating factor: Conductor of the wound healing orchestra? In *International Wound Journal* (Vol. 20, Issue 4, pp. 1229–1234). John Wiley and Sons Inc. <https://doi.org/10.1111/iwj.13919>
Everett, E., & Mathioudakis, N. (2018). Update on management of diabetic foot ulcers. In *Annals of the New York Academy of Sciences* (Vol. 1411, Issue 1, pp. 153–165). Blackwell Publishing Inc. <https://doi.org/10.1111/nyas.13569>