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Exosome-mediated Advancements in Plastic Surgery: Navigating Therapeutic Potential in Skin Rejuvenation and Wound Healing

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Summary: Exosomes, tiny extracellular vesicles derived from various cells such as adipose-derived stem cells, bone marrow-derived mesenchymal stem cells, and human umbilical cord mesenchymal stem cells, exhibit considerable potential in wound healing due to their ability to facilitate cell communication and modulate inflammatory responses. These exosomes contribute positively to collagen synthesis and scar reduction, and have shown efficacy in documented clinical cases of wound improvement. Although research indicates their potential in reducing hypertrophic scars and suppressing keloid fibroblasts, further clinical investigations are warranted. In plastic surgery, exosome application postsurgery can enhance wound healing, particularly in cases prone to swelling or poor healing conditions. This study incorporates five case reports of individuals undergoing exosome treatment (EXOP; Sihler Inc., and Exodew; Hyundaimeditech, Inc.) for wound healing, providing practical insights into the application of this therapeutic approach. The five case reports presented in this study demonstrate the practical applications and efficacy of exosome therapy in promoting wound healing and reducing scarring. Exosomes emerge as a promising avenue within the field of plastic surgery, showcasing their potential to enhance wound healing, reduce scarring, and improve overall outcomes in clinical settings. The findings from this study underscore the importance of further exploration into the therapeutic benefits of exosomes in wound management, paving the way for their widespread adoption in clinical practice. *(Plast Reconstr Surg Glob Open 2024; 12:e6021; doi: 10.1097/GOX.0000000000006021; Published online 1 August 2024.)*

PRESENTATION OF IDEAS AND TECHNIQUES

Exosomes, extracellular vesicles that have become widely known, have attracted considerable research attention owing to their distinct advantages, including an extended half-life, potent penetrative capabilities, and minimal immunogenicity in comparison to stem cell therapy.[1] Their potential therapeutic applications have been extensively investigated, particularly in the context of improving skin aging, promoting skin wound healing, and addressing various inflammatory skin conditions. Although exosomes are commonly used in clinics for skin rejuvenation and pigmentation, plastic surgery practitioners are directing their focus toward understanding the impact of exosomes on angiogenesis and lymphangiogenesis. Plastic surgeons emphasize these aspects due to their significant influence on vascularity, a crucial factor in the wound healing process. Consequently, this discussion aims to explore the potential utilization of exosomes within the field of plastic surgery.

The wound healing process involves dynamic interactions between various types of cells and immune cells.[2] For neocollagenesis to occur, effective cell-to-cell communication is essential, and among the smallest particles involved in this process are exosomes. Exosomes exhibit diverse compositions, including proteins and mRNA, contingent upon their cellular origin. Furthermore, their functional roles are contingent upon their specific destination upon release. The interplay between the type of exosome and

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the recipient cell significantly shapes their functionalities. Notably, exosomes derived from adipose-derived stem cells, bone marrow mesenchymal stem cells, and human umbilical cord mesenchymal stem cells stand out as the most frequently used sources of exosome production in the context of wound healing.[2]

Exosomes are well known for their excellent wound healing properties due to their role in regulating oxidative stress, modulating immune cells, regulating inflammation around wounds, and controlling the secretion of inflammatory factors.[3] Adipose-derived exosomes play a pivotal role in promoting scarless wound healing by initiating the synthesis of collagen I/III during the early stages of wound sites and concurrently inhibiting excessive collagen deposition in the later phases. The study conducted by Yuan et al[4] revealed an accelerated fibrotic response in the initial stages of wound healing, contributing to an increase in dermal thickness. However, during the subsequent phase of extracellular matrix remodeling, a mitigation of this fibrotic process was observed, resulting in a reduction in scar formation. This finding underscores the potential for enhanced treatment outcomes by addressing fibrosis during the remodeling stages after the initial phases of wound healing.[4]

We present five case reports exemplifying the application of exosomes in wound healing, providing valuable insights into their practical effectiveness. Notably, none of the cases exhibited any predisposing factors related to impaired wound healing, such as diabetes (DM), hyperlipidemia (HLD), or smoking. Additionally, no adjuncts were used alongside the exosomes to aid in wound healing, including topical creams/ointments, hyperbarics, or local wound care. In all cases, the treatment area was disinfected and topical anesthetic was applied.

Takeaways

Question: How can exosomes help recover from surgery scars?

Findings: In essence, exosomes have shown promise in various aspects of wound healing and scar management, offering plastic surgeons a valuable tool to enhance post-surgery recovery, minimize scarring, and improve overall outcomes in plastic surgery procedures.

Meaning: Exosomes offer promising potential in plastic surgery by facilitating better wound healing, minimizing scarring, and improving surgical outcomes when applied postsurgery.

Case 1 involved a 43-year-old female patient who experienced ischemic necrosis due to a polycaprolactone filler. Treatment with exosomes notably accelerated the improvement of necrosis, as depicted in Figure 1. She was subjected to applications and treatments everyday over five sessions, employing the topical application of exosomes sourced from the pharynx (EXOP; Sihler, Inc.,

Fig. 1. A 43-year-old woman experienced nasal ischemic necrosis due to a polycaprolactone filler. Upon exosome treatment, a rapid improvement in necrosis was observed. The dates of the recovery sequences are indicated above. A, Initial phase. B, 3 months after.

Seoul, Korea). They were packaged in a set of two vials, one containing only lyophilized exosomes and the other containing 3 mL of normal saline. The half vial of exosomes was utilized for each treatment session.

Case 2 involved a 26-year-old woman with an abrasion wound. Application of exosomes during the initial immature scar stage notably promoted wound regeneration and reduced keloid formation. She received applications and underwent treatment every 2 days for three sessions using the topical administration of exosomes derived from the pharynx (EXOP). The one-third vial of exosomes was utilized for each treatment session.

In case 3, a 25-year-old woman with a tissue wound due to contact burn (third-degree burn) showcased the beneficial effects of exosomes in wound healing. Notably, exosomes proved beneficial even at stages requiring surgical intervention, as illustrated in Figure 2. It was applied and treated at intervals of 2 days for five sessions with the topical application of pharyngeal-derived exosomes (EXOP and Exodew; Hyundaimeditech, Inc., Korea).

In case 4, a 34-year-old woman presented with a keloid scar. The utilization of exosome combined with a microneedling transcutaneous system has demonstrated beneficial effects in treating mature keloids. It was applied and treated at intervals of 3 days for five sessions with the topical application of pharyngeal-derived exosomes (EXOP and Exodew). The one-third vial of exosomes was utilized for each treatment session.

In case 5, a 35-year-old woman underwent a facelift procedure on December 31. Concerns regarding potential partial flap necrosis resulting from compromised circulation around the anterior tragus incision wound led to the application of exosomes with a microneedling transcutaneous system. This intervention prevented complete necrosis and effectively promoted wound healing. It was applied and treated at intervals of 3 days for four sessions with the topical application of pharyngeal-derived (EXOP and Exodew). The half vial of exosomes was utilized for each treatment session.

DISCUSSION

Recently, there has been a growing focus on exosomes derived from the human pharynx (EXOP and Exodew). Stem cells collected through swab-based sampling during examinations such as influenza from early childhood are known for their exceptional differentiation capabilities.

According to a recent article by Li et al,[5] it has been revealed that exosomes can play a positive role in attenuating hypertrophic scars. Additionally, their ability to suppress keloid fibroblasts has been highlighted, further emphasizing the importance of exosomes in future wound management. However, this remains a study at the molecular level, and further clinical research appears to be necessary.[6]

Furthermore, exosomes are becoming a new theoretical basis for promoting vascular regeneration in diabetic patients to enhance wound healing.[7] Utilizing exosomes can accelerate wound healing by increasing the migration and proliferation of fibroblasts and epithelial cells, leading to better therapeutic outcomes.[4]

The suggestion is not to use exosomes solely for patients with existing swelling or poor wound conditions. Similar to the preventive use of antibiotics during surgery, applying exosomes to surgical wounds immediately after surgery can yield much better outcomes. When applied for the purpose of enhancing the overall foundation, it can lead to better results in the wound healing process. It can expedite the healing of surgical sites subjected to considerable tension.

The mechanism behind this lies in the reduced lymphatic circulation, which leads to prolonged swelling, decreased skin quality, delayed wound healing, and potentially poor scar formation. One of the factors involved in lymphatic vessel formation is vascular endothelial growth factor subtype C, which is contained within exosomes. Applying exosomes to surgical wounds results in notably improved outcomes. Additionally, apart from vascular endothelial growth factor, factors such as fibroblast growth factor and platelet-derived growth factor also

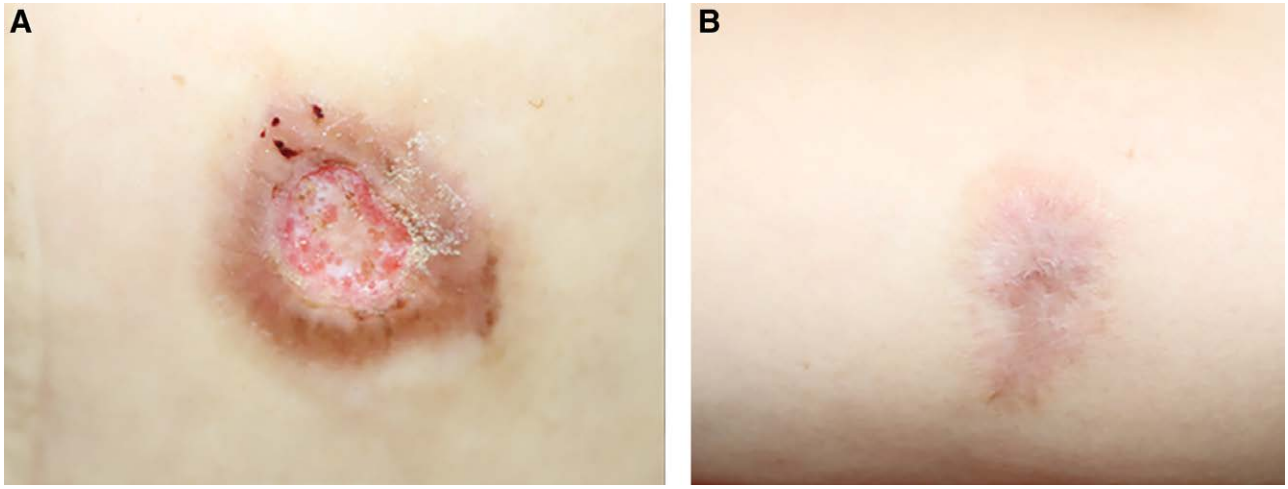

Fig. 2. Exosomes were found to be beneficial in tissue wound healing caused by contact burns in a 25-year-old woman. Even in stages requiring surgical intervention, exosomes can be effectively utilized. A, Initial phase. B, 3 months after.

contribute to lymphatic vessel generation. Therefore, preemptive application of exosomes containing these factors to wounds in patients at risk of poor healing can significantly enhance the healing process. Recent in vivo and in vitro studies have demonstrated a synergistic effect in wound healing when combining exosomes with botulinum toxin.[4,8]

Wound healing involves numerous stages and often leads to scar formation. Therefore, the authors contend that exosomes can be effectively utilized in the field of plastic surgery and surgical practices for scar prevention and minimization.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

PATIENT CONSENT

Patients provided written consent for the use of their images.

DECLARATION OF HELSINKI

This study was conducted in compliance with the principles set forth in the Declaration of Helsinki.

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