Autologous Bone Marrow Aspirate Therapy in Wound Healing

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Objective: To study the role of autologous bone marrow aspirate therapy (ABMAT) in wound healing.

Approach: This is a retrospective analysis of 9 patients (11 chronic nonhealing wounds) in whom ABMAT was used. Patients (wounds) were grouped into two groups. Group 1 included 4 patients (5 wounds) refusing/unfit for reconstruction and managed only with ABMAT. Group 2 included 5 patients (6 wounds) who agreed/fit for reconstruction after wound bed preparation with ABMAT. End point of the study was complete wound healing.

Results: ABMAT helped in complete healing of chronic nonhealing wounds by secondary intention in group 1 patients and enhanced process of wound bed preparation for reconstruction in group 2 patients.

Innovation: This study highlights the importance of ABMAT in the management of chronic nonhealing wounds.

Conclusion: ABMAT helps in wound bed preparation to allow the wound to heal completely or cover by skin graft/flap.

INTRODUCTION

WOUND HEALING CAN BE considered as a coordinated process involving complex mechanisms that proceeds in various stages from blood clotting to inflammation, cellular proliferation, angiogenesis, and reconstruction of extracellular matrix. Failure of any of these processes due to ischemia, reperfusion injury, bacterial infection, or aging can result in chronic inflammation and a non-healing wound.¹

Chronic wounds are a cause of significant morbidity and mortality and pose a large financial burden on the healthcare system. Therapies to expedite the wound healing process are one of the most active areas of research. But due to the multitude of causes, a single modality to therapy as a solution for chronic

wounds is not possible. One of the reasons for the chronic nonhealing wound is the increased senescence and the decreased response of the resident cells to growth factors.² To overcome this block, the suggested therapy involves introduction of stem cells into the wound. The bone marrow is an important source of hematopoietic stem cells that regularly regenerate components of the blood, and nonhematopoietic stem cells, including mesenchymal stem cells (MSCs). There have been reports proving the plasticity of the stem cells harvested from the bone marrow and its ability to convert into many cell lines.³ The present study highlights the role of autologous bone marrow aspirate therapy (ABMAT) in healing of chronic wounds.

CLINICAL PROBLEM ADDRESSED

Healing of chronic nonhealing wounds.

MATERIALS AND METHODS

This study is a retrospective analysis of the patients with chronic nonhealing wounds treated in a tertiary care hospital in India during July 2012 to July 2014 who underwent ABMAT. Patients of all age groups and gender with chronic nonhealing wounds of different etiologies were included in the study. Written informed consent was obtained from the subjects. Nine patients (11 wounds) matched the inclusion criteria. Patients were grouped into two groups. Group 1 (4 patients, 5 wounds) included patients unfit for anesthesia or refusing for surgery. Group 2 (5 patients, 6 wounds) included patients fit for anesthesia and agreed for surgery. In group 1, only ABMAT was used. In group 2, once the wound bed preparation was completed with ABMAT, the wound was covered with Skin Graft or Flap. Details, including age, gender, etiology, duration, site, size, comorbid factors, total duration of wound healing, etc. were recorded in the study proforma. Wound Score was documented using the Bates Jansen Wound Assessment Tool. Wound measurements were recorded by the Digital Planimetry using the ImageJ Software. Wound Score and measurements were recorded weekly. Investigations required for fitness for anesthesia were done. Wound tissue culture was sent and antibiotic was started according to the sensitivity. Debridement of necrotic tissue was done before the application of autologous bone marrow aspirate. The bone marrow was aspirated from the iliac crest (Figs. 1 and 2) and applied

Figure 2. Bone marrow aspiration. To see this illustration in color, the reader is referred to the web version of this article at www.liebertpub.com/wound

(Fig. 3) as described by Falanga and colleagues⁴ Complete wound healing was considered as end point of the study.

RESULTS

In our study cohort ($n=9$ patients, 11 wounds), age of the patients ranged from 24 years to 72 years (mean age 49 years). Males were more than females (with ratio 2:1). The most common etiology was diabetic foot ulcer (3 patients, 4 wounds) followed by posttraumatic raw area (2 patients, 3 wounds), pressure ulcer (2 patients, 2 wounds), trophic ulcer (1 patient, 1 wound), and varicose venous ulcer (1 patient, 1 wound). The most common site was lower extremity (9 wounds) followed by sacrum (1 wound) and ischium (1 wound). In group 1 (4 patients, 5 wounds) all wounds healed by ABMA alone (Figs. 4 and 5). In group 2 (5 patients, 6 wounds), 3 wounds were covered by skin graft and other 3 wounds by flap after wound bed was prepared by ABMAT. In group 1 (treated by ABMA only) the mean size of the wounds was 18.4 square

Figure 1. Bone marrow aspiration needle.

Figure 3. Application of bone marrow aspirate. To see this illustration in color, the reader is referred to the web version of this article at www.liebertpub.com/wound

Figure 4. Chronic nonhealing wound leg. To see this illustration in color, the reader is referred to the web version of this article at www.liebertpub.com/wound

cm (range 9–42 square cm). In group 2 (treated by ABMA + Skin Graft/Flap) the mean size of the wounds was 41 square cm (range 4–105 square cm). The mean duration of healing in group 1 was 4.8 weeks (range 4–8 weeks) and in group 2 the mean duration of healing was 4.5 weeks (range 4–6 weeks).

DISCUSSION

With the increasing prevalence of nonhealing wounds, the therapies to tackle such problems

Figure 5. Complete healing with autologous bone marrow aspirate therapy only. To see this illustration in color, the reader is referred to the web version of this article at www.liebertpub.com/wound

have also increased. But there is substantial evidence to indicate our lacunae in the treatment of chronic wounds particularly of more than 1 year duration.⁵ Stem cell therapy has been extensively studied to fill in this void. With the inherent difficulties involved in using embryonic stem cells, both from the technical and regulatory standpoints, adult autologous bone marrow-derived stem cells become an attractive alternative. When bone marrow-derived MSCs were linked to the origin of epidermal cells, their role in cutaneous wound healing was investigated. It is postulated that MSCs mobilize from the bone marrow niche and traffic to ischemic tissue through the peripheral circulation in response to cytokine signalling.⁶ After reaching the site of injury, they differentiate into various cells of the epidermis and dermis. New vessel formation, or neovascularization, is a critical component of wound healing as it is necessary to supply oxygen and nutrients to and carry waste away from the damaged tissue. *In vitro* experiments have demonstrated that MSCs are capable of differentiating into vessel-forming endothelial cells suggesting that they may contribute to postnatal vasculogenesis during the wound healing process. Another important mode of action of these MSCs is by the paracrine signaling pathways.⁷

With the increasing evidence to prove the usefulness of stem cell therapy in wound healing, the focus of research is shifting toward modalities to optimize cell delivery as studies have shown that the clinical effectiveness of MSC therapy is dependent on the number of cells delivered. Newer modes of delivery have now been introduced with the aim of increasing the number of cells delivered and increase engraftment and reduce the impeding factors. Ichioka *et al.*, showed that bone marrow-impregnated collagen matrix can promote the wound repair process through augmentation of angiogenesis.⁸ Hydrogels, because of their hygroscopic nature of extracellular matrix, has been a preferred choice for MSC delivery.⁹

INNOVATION

This study highlights the importance of ABMAT in the management of chronic nonhealing wounds.

SUMMARY

To conclude, we can summarize that MSC-based therapy like ABMAT is useful for expediting wound healing and in the preparation of wound bed for reconstruction.

AUTHOR DISCLOSURE AND GHOST WRITING

No competing financial interests exist. The content of this article was expressly written by the authors listed. No ghostwriters were used to write this article

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KEY FINDINGS

- MSCs (bone marrow) have been shown to augment each step of wound healing process.
- More importantly, these effects have been observed in clinically relevant conditions of impaired healing such as diabetes, pressure sore, etc.
- We recommend further large-scale randomized human studies to substantiate ABMAT.

(Plastic Surgery), and Dinesh Kumar Sivakumar, MCh (Plastic Surgery) are Clinical Associate Professors in the Department of Plastic Surgery, JIPMER, Pondicherry, India, and actively involved in clinical practice and research related to wound healing. **Arjun Asokan and Vijayaraghavan Nandhagopal** are pursuing their postgraduation (M.Ch.) in plastic surgery in the Department of Plastic Surgery, JIPMER, Pondicherry, with their thesis research work on wound healing.

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Abbreviations and Acronyms

ABMAT = autologous bone marrow aspirate therapy
MSC = mesenchymal stem cells