

## Role of Prolotherapy in Wound Bed Preparation

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### Abstract

Wound is a common problem following burn, trauma or infection. There are various methods to limit the infection and to cover the raw area. But there is no well-established method that accelerates the wound healing rate. Prolotherapy is a technique that involves injecting some irritant locally in the wound that is claimed to hasten the healing. This article highlights the role of prolotherapy in wound bed preparation.

**Keywords:** Prolotherapy; Wound; Management.

### Introduction

Wound is a common problem encountered by plastic surgeon. Many methods are there with varying success.<sup>1</sup> Large wounds often require graft or flap for wound coverage, but for this wound bed should be prepared first. Various modalities exist that helps in enhancing the wound bed preparation.

Prolotherapy is one of the recent therapeutic strategies for wound healing. Prolotherapy is a procedure in which an irritant is injected into wound that instigating an inflammatory reaction, thought to promote healing of wound.<sup>2</sup> The most common prolotherapy agent used in clinical practice is dextrose, with concentrations ranging from 12.5% to 25%. Dextrose is considered to be an ideal proliferant because it is water soluble, a normal constituent of blood chemistry, and can be injected safely into multiple areas and in large quantity. Hypertonic dextrose solutions act by dehydrating

cells at the injection site, leading to local tissue trauma, which in turn attracts granulocytes and macrophages and promotes healing. In review of literature we have seen very few Indian studies on prolotherapy in wound management. We share our experience on prolotherapy using Dextrose 25%, in wound management.

### Methodology

This is case report of use of prolotherapy in post burn raw area. This study was conducted in a tertiary care hospital in 2019. The patient was 20 year female with post thermal burn raw area on thigh. Patient was thoroughly investigated. Wound tissue culture was sent and appropriate antibiotic therapy was given. Regular cleaning and dressing was done, but wound was not showing any good sign of healing. To hasten the wound bed preparation decision was made to give trial of prolotherapy.

Dextrose 25% solution was used as agent for prolotherapy. It was spread evenly on to the wound followed by gauze dressing. Repeated session of prolotherapy was given every three days. After 4 session of prolotherapy wound bed was prepared and skin grafting was done. There was almost complete uptake of graft and in follow-up after 6 weeks, the scar was well settled and of good quality.

## Result

After 4 session of prolotherapy over two weeks period, the wound bed was prepared and grafting was done. Graft uptake was satisfactory. No adverse local or systemic effect was noted with the use of prolotherapy.

## Discussion

The spectrum of modalities available to manage a wound is very wide. Conveniently it can be grouped into four categories – conventional therapy, novel therapy, reconstructive therapy and cell based. Conventional therapies include – conventional dressings with or without topical

application of anti-microbial agents, growth factors; various biological dressings such as silver and alginate; hyperbaric oxygen etc. Novel therapies include the use of platelet-rich plasma, negative pressure wound therapy (NPWT), and skin substitutes. These are minimally invasive with much better healing efficacy than conventional therapies. Reconstructive therapy, such as skin and flap grafting, are invasive and damage the normal tissue also. Cell based therapy is rapidly emerging as a part of wound management, but is seldom used alone. These cell can be harvested from bone marrow or adipose tissue.

The term prolotherapy was coined by Dr. George Hackett in 1956. This word is derived from the Latin word *proles* meaning offspring or progeny and the English word–therapy. It involves injecting an irritant substance (such as dextrose) into aligament or tendon to promote the growth of new tissue. Multiple agents are used in prolotherapy, some classified as irritants (such as phenol), some as chemo attractants (commonly sodium morrhuate), and others as osmotic agents (commonly dextrose).

Although the exact mechanism of prolotherapy is not clear, proponents of the technique believe



Fig. 1: Raw area on thigh



Fig. 3: Skin grafting after the wound bed preparation



Fig. 2: Dextrose 25% used for prolotherapy



Fig. 4: 6<sup>th</sup> week Post-operative

that the injection of hypertonic dextrose causes cell dehydration and osmotic rupture at the injection site that leads to local tissue injury that subsequently induces granulocyte and macrophage migration to the site, with release of the growth factors and collagen deposition.<sup>3</sup> In vitro studies have shown that even concentrations as low as 5% dextrose have resulted in production of a number of growth factors critical for tissue repair. Some of these growth factors include PDGF, TGF- $\beta$ , EGF, b-FGF, IGF-1, and CTGF.<sup>4</sup>

In vitro studies have shown that cultivation of cells in high glucose culture medium can increase PDGF expression. PDGF has multiple pro-reparative effects in skin wounds, including promotion of angiogenesis, fibroblast proliferation, extracellular production. TGF- $\beta$  expression is also upregulated by high glucose.<sup>5,6</sup> TGF- $\beta$  is involved in all steps of wound healing including inflammation, angiogenesis, fibroblast proliferation, collagen synthesis, matrix deposition, and remodeling, and wound reepithelialization. Other growth factors upregulated by high glucose include EGF, b-FGF, IGF and CTGF, all having multiple proreparative functions and improves healing in some animal wound models of impaired healing.

Some studies on prolotherapy suggest that there are direct effects on collagen synthesis.<sup>7</sup> A few studies demonstrate up-regulation of matrix in response to dextrose prolotherapy or in vitro cultivation with high concentrations of glucose. Collagen expression is increased after exposure of patellar tendon fibroblasts to the prolotherapy agents dextrose and thus may contribute to tissue regeneration within a cutaneous wound. Collagen type I synthesis is also increased in high-glucose cultivation of renal fibroblasts, in a TGF- $\beta$ -mediated pathway.<sup>8</sup> Changes in the cartilage matrix protein aggrecan is reported in chondrocytes cultured in high glucose, and in patients who have received intra articular injections of 12.5% dextrose.<sup>4,8</sup>

## Conclusion

In this study we found that prolotherapy has role in healing of the wound and the wound heals at faster rate. The resultant scar was also of better quality. But since it is a single case study, definite

conclusion cannot be made. Large randomized control trials are required to confirm the efficacy of prolotherapy in wound healing.

*Conflicts of Interest:* None.

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## References

1. Frykberg RG, Banks J Challenges in the treatment of chronic wounds. *Adv Wound Care (New Rochelle)* 2015;4:560–582.
2. Farpour HR, Fereydooni F Comparative effectiveness of intra-articular prolotherapy versus periarticular prolotherapy on pain reduction and improving function in patients with knee osteoarthritis: a randomized clinical trial. *Electron Physician* 2017;9:5663–5669.
3. Barrientos S, Stojadinovic O, Golinko MS, Brem H, Tomic-Canic M. Growth factors and cytokines in wound healing. *Wound Repair Regen* 2008; 16:585–601.
4. Oh JY, Choi GE, Lee HJ, et al. High glucose induced reactive oxygen species stimulates human mesenchymal stem cell migration through snail and EHZ2-dependent E-cadherin repression. *Cell Physiol Biochem* 2018;46:1749–1767.
5. Penn JW, Grobbelaar AO, Rolfe KJ. The role of the TGF-beta family in wound healing, burns and scarring: a review. *Int J Burns Trauma* 2012;2:18–28.
6. Freeman JW, Empson YM, Ekwueme EC, Paynter DM, Brolinson PG. Effect of prolotherapy on cellular proliferation and collagen deposition in MC3T3-E1 and patellar tendon fibroblast populations. *Transl Res* 2011;158:132–139.
7. Wu TJ, Fong YC, Lin CY, Huang YL, Tang CH Glucose enhances aggrecan expression in chondrocytes via the PKC $\alpha$ /p38-miR141-3p signaling pathway. *J Cell Physiol* 2018;233:6878–6887.
8. Topol GA, Podesta LA, Reeves KD, et al. Chondrogenic effect of intra-articular hypertonic dextrose (prolotherapy) in severe knee osteoarthritis. *PM R* 2016;8:1072–1082.