Use of collagen in extraoral wounds

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Abstract The basic fundamental elements that collagen bring into the wound activity are its hemostatic effect, its interaction with platelets and interaction with fibronectin, increase in fluid exudates, increase in cellular components (macrophages) and support for fibroblastic proliferation into wound activity. In this way collagen plays a significant parts in almost every function of the body. Previously broad use of collagen was stifled because of cost, recent advances made it possible to develop cost effective collagen. In this study twenty patients of maxillofacial wounds were treated with the use of collagen. The results were satisfactory without any significant complication.

Keywords Collagen dressing · Wound healing

Introduction

Collagen is the most abundant protein in the body. It provides structure and strength to the body's tissue. There are many distinct types of collagen, each of which has its own unique molecular form. This unique molecular form dictates a specific function for each type of human collagen. In order for collagen, to be effective in wound healing it must be in the proper molecular form, specific to skin. It must also have self-assembling capabilities. When there is a wound, body is preprogrammed to respond with a series of complex sequential cellular and vascular activities.

For the body to heal itself it must deliver adequate resources in a timely manner to the wound bed. The body utilizes these resources to 'manufacture' the appropriate materials to close the wound. Various problems such as genetic, vascular, infection, etc., can hinder the body's ability to timely deliver adequate resources to the wound bed. Some of the major causes of interference with the cellular activity of wound healing are: 1) Improper moisture content 2) Inadequate delivery of oxygen 3) pH of wound bed 4) Infection more than 100,000 micro-organisms per gram.

Since collagen is an actual component of the skin, it is used beneficially throughout the wound healing process.

Review of literature

Sumerian cuneiform tables dated prior to 2000 B.C contain lists of different types of wounds and injuries along with passages detailing, how best to treat them. The Edwin Smith surgical papyrus, an Egyptian document dated 1650 B.C believed to be a copy of much older document. Quillen (1993) concluded that Kallogen™ treated wounds healed twice as fast as the wounds that were treated with traditional modalities. Stoop (1970) summarized his experience using collagen sponges in treatment of pressure sore and he observed that wounds were clean and bacterial infection was retarded, wound secretion and drainage were decreased. Burton et al. (1978) showed that collagen sponge reconstituted from bovine tendon provides a porous matrix for permeation of fibroblast and capillaries and a theoretical ground that it should be ideal for stimulating granulation tissue in ulcers. Scar et al. (1983) studied the effect of superficial wound in domestic pigs and suggested that collagen based wound dressing enhance the deposition of oriented, organized fibers by attracting fibroblasts and causing a directed migration of cells. Doillon et al. (1988) Chavapil et al. (1987) compared four wound dressing on epithelisation of partial thickness wounds in pigs and found the encouraging results. Wasserman et al. (1988) evaluated a significant increase in the production of fibroblasts, when collagen sponge dressing were used with

hyaluronic acid and fibronectin (Doillon and Silver, 1986; Doillon et al. 1988). Dunn et al. (1988) observed that rapid fibroblast ingrowths and collagen deposition occurs in reconstituted type I collagen matrix that is implanted on full thickness excised animal dermal wounds.

Mian et al. (1992) stated healthier appearance of artificially produced wounds in collagen treated groups. Palmieri (1992) did an open controlled trial on 72 patients affected by different types of ulcers and found the favorable results. Yoshimitsu et al. (1994) developed a medicated wound dressing. Steven et al. (1995) concluded that a type I bovine collagen matrix provided a safe, readily available alternative to traditional methods of second intention healing. It minimized wound care while reducing the time for complete healing. Griswald et al. (1995) concluded that collagen sheet dressing appears to be less painful and has better healing rate compared with xeroform. Chiro et al. (1998) concluded that collagen matrix is useful not only as a carrier of cytokines such as bFGF but also quick closure of chronic wounds. Rama and Priya et al. (2003) developed a bilayer dressing. Park et al. (2004) evaluated cross linked collagen-hyaauronic acid matrices containing tobramycin or ciprofloxacin as an antibiotic agent. Helary et al. (2006) also showed that a high collagen concentration has a stimulating effect on myofibroblast proliferation and apoptosis, two important events in wounds healing.

Material and methods

This study was conducted on 20 patients with facial injury reported to the Department of Oral and Maxillofacial Surgery, King George's Medical University, Lucknow. Patients with traumatic extraoral wounds were selected randomly, irrespective of age, sex, caste and socio-economic status. Patients with history of diabetes mellitus, immunosuppressive medication, pregnancy and patients on anti-neoplastic therapy were excluded from study. A detailed medical and dental history was taken. Wound was assessed by following protocol:

A. Inspection: 1. Location 2. Size 3. Shape 4. Edges 5. Floor of wound 6. Discharge from wound 7. Colour of wound 8. Surrounding area skin.

B. Palpation: 1. Margins 2. Depth and underlying structure 3. Bleeding.

C. Serial wound culture and sensitivity test was performed at one week interval.

Preparation of wound bed

1) Old dressing was removed and disposed. 2) Wound was gently irrigated with sterile normal saline until it is free of debris (Necrotic tissue, slough etc). Irrigation pressure was enough to enhance wound cleansing without causing trauma to wound bed. It reduces the risk of trauma and wound infection and drives bacteria out of tissue. 3) Gentle bloating was done on wound edges and periwound area.

Method of application of collagen sheet

It was used in surface wound.

1. *Minimally draining or dry wounds:* Collagen sheet was hydrated with sterile saline prior to application.
2. *Moderately draining wounds:* Collagen sheet was used dry on moderately draining wounds. Porous side of collagen sheet was applied on wound. Once collagen sheet had been positioned on wound non-adherent packing was removed. If peri-wound area was risk of maceration collagen sheet was cut to fit the size of wound. Collagen sheet was covered with sterile, non-adherent gauze piece dressing to maintain moist wound environment.

Fig. 1A Patient of gun shot injury on first visit

Fig. 1C After 14 days

Fig. 1B After 7 days

Fig. 1D Healed wound after 21 days

Fig. 2A Patient with firearm injury on first visit

Fig. 2C Appearance after 7 days

Fig. 2B Collagen particles placed

Fig. 2D Healed wound after 14 days

Removal of collagen sheet dressing

1. Secondary dressing and remaining collagen sheet was removed.
2. If collagen sheet was adhered to wound, wound was irrigated with sterile normal saline and dressing was lifted gently.
3. If collagen sheet remained adhered even after irrigation, removal was not attempted. Wound was rehydrated with

sterile saline solution and dressed to maintain moisture.

Method of application of collagen particles

It was used in cavity and deep wounds. Medfill particles were applied to cover wound surface 1/4 to 1/8 inch deep. Particles were loosely packed because it is highly absorbent and space

Fig. 1 Change in mean wound size at different time periods

Fig. 2 The mean pain score

Fig. 3 Correlation of wound healing with wound area at admission

Fig. 4 Improvement in slough from day 1 during the course of follow up

was needed for expansion. It was then covered with moist sterile gauze dressing. Dressing was changed when saturated until excessive drainage was resolved. Once drainage subsided, dressing was changed every 2–3 days until wound healed.

Criteria for follow up- regular follow up was performed at every alternate day till wound healing was achieved. The following parameters were noted:

1. Pain 0 – No pain, pain was measured according to VAS scale (1–10)
2. Swelling 0 – No swelling, present : 1 – mild, 2 – moderate, 3 – severe
3. Slough – Slough absent, + Slough present
4. Haemorrhage – Haemorrhage absent, + Haemorrhage present
5. Discharge 0 – No discharge, 1 – mild, 2 – moderate, 3 – severe
6. Dimension of wound A – first longest dimension (cm), B – second longest perpendicular dimension (cm)

Discussion

Wound healing is a complex process involving a number of chemical and

biological events. The body orchestrates a concerned effort through a series of interlocking and overlapping cellular events to attain wound healing. All wounds follow the same specific steps in the course of healing. The overlapping events include: vasoconstriction, vasodilatation, phagocytosis, granulation, fibroblast formation, angiogenesis, reepithelialization, collagen secretion, removal and remodeling. There is a large body of evidence that suggest collagen is a common denominator in all stages of wound healing. Collagen serves as the key extra cellular component for repair and remodelling of skin tissue. Some of the unique features of collagen include: guiding function, chemotactic properties, nucleation, reutilization, hemostatic properties. As a biomaterial, collagen offers several advantages over traditional dressings, growth hormones and biological coverings. In the present study, the wound area at the time of admission ranged from 1 cm² to 22 cm² with a mean of 7.50±6.27 cm². On day 5, the wound size became 4.823±4.584 cm². Diminution in size of wound was seen on a regular basis. On day 29, the mean wound size

was 0.022±0.031 cm² showing a mean change of 14.142±4.172 cm². On day wise wound healing, the earliest evidence of complete healing was noted in 2 patients on day 11 while the longest period of complete healing was noted in 3 patients on day 31. Mean healing time in the present study was 23.10±6.79 days. This variability in the healing time could be attributed to variation in size of wound, aetiology bacterial pathogenesis and other variables. Our findings correlated with study conducted by Steven et al. (1995), who had shown average healing time of 3 weeks. This reveals that collagen dressing has a significantly faster healing time. In conclusion, only collagen serves as the most important common element in all stages of wound healing. In the present study all the patients complained of some pain up to day 6. On day 7, two patients did not complain of pain. By day 11, as many as 15 (75%) patients did not complain any pain. By day 23, only 2 patients complained of pain. At day 31 all the patients were relieved of pain. Relief of pain was significant achievement in our study as there was no need of daily change of dressing. Decrease in pain in our study

correlate with the findings of Griswold (1995) who observed that skin temp (collagen dressing) is less painful and has better healing than Xeroform dressing. However, in present study no such comparison was made.

Only two patients showed presence of haemorrhage on day 1. By day 3, one of these patients improved. By day 7, both the patients improved. As the number of patients showing haemorrhage was too fewer, it was not possible to deduce any statistically significant correlation in improvement with time. Collagen is a very efficient hemostatic agent because platelets adhere to collagen, swell and release substances that initiate hemostasis (Hovig, 1968; Zucker & Borrelli, 1962). Furthermore, collagen can provide both positive and negative active polar sites. Collagen is also a molecule of sufficient size for platelet aggregation (Wilner et al., 1971). The platelets adhere to collagen more closely than they adhere to the undigested sub endothelial surface (Baumgartner et al., 1980). Various other studies have demonstrated that collagen is an effective hemostatic agent (Abbott, 1974). On day 1, 10 patients showed the presence of slough. There was a persistent improvement in patients showing presence of slough. By day 11, none of the patients showed presence of slough. Thus showing a highly significant improvement ($p<0.001$). This could be attributed to the fact that collagen assists wound debridement. Vasoconstriction and vasodilatation are followed by debridement or cleaning of the wound. During this stage, polymorph nuclear leukocytes and macrophages rapidly accumulate at the site of injury. Neutrophils infiltrate the wound and rid it of bacteria. Monocytes as macrophages, phagocytize the wound and scavenge tissue debris (Clark, 1988). In the present study, at admission 12 patients showed discharge from wound on the first day. Except 1 case with moderate discharge the remaining cases had mild discharge. By day 7 as many as 8 (66.67%) patients improved day 1. Among remaining patients showing discharge by day 23, in no case discharge was seen. Overall a highly significant improvement was seen ($p<0.001$). Collagen can absorb exudate because of its hydrophilic property and provides the moist environment and prevents wound dehydration. All the

patients included in the present study had some degree of swelling on day 1. There were 2 patients with swelling score 3, 4 patients with swelling score 1 and remaining 14 with swelling score 2. A significant improvement ($p=0.001$) in swelling scores was seen on third day. Swelling is often correlated with the presence of bacterial pathogens. In our study, due to better wound management and regular dressing the incidence of bacterial infection was quite low. This has contributed to such lower incidence of swelling. Swelling in some patients may be related to physical causes alone where owing to pressure caused by the dressing some swelling was seen. In our study, we observed that most common bacterial organism was *Staphylococcus aureus*, the other organism was *Klebsiella*. Collagen dressing controls microbes because of its chemotactic properties, PMN cells and macrophages rapidly accumulate at the site of injury and rid it of bacteria (Clark, 1998). Monocytes at macrophages, phagocytize the wound and scavenge tissue debris (Albritton, 1991; Clark, 1988; Mosiello et al., 1994). In the study of Stevens (1999) no wound infection was reported. Although in our study infection was seen in 4 patients which could be attributed to delay in management and different type of etiology of wound. The physical conditions in India could also be attributed as one of the reasons for the higher rate of infection. Collagen dressing can be effectively used in infected wound as observed by Grzybowski. Collagen dressing containing Gentamycin can be used effectively in infected wounds. Kollenberg used Gentamycin impregnated collagen dressing in chronic infected wounds. The results obtained in present study were very encouraging. However, the sample size of the study was small. Although the results are normative, there application in routine clinical use can be used only after a much larger trial with varying demographic and geographic locations.

Conclusion

1. The mean size of wound was 7.503 ± 6.267 cm² and it healed in all the cases by one month. Mean healing time was 23.10 ± 6.79 days.
2. The mean pain score on day 1 was 6.000 ± 1.124 which decreased day by

day. On 31st day all patients were relieved of pain.

3. Significant improvement ($p<0.001$) in presence of slough was seen by day 11.
4. Highly significant improvement ($p<0.001$) was seen in discharge from the wound.
5. Presence of hemorrhage on day 1 was found in 2 (10%) cases only. 1 of them improved by day 3, and another by day 7.
6. All patients had some degree of swelling on day 1, a significant improvement in swelling score was seen in patients. Improvement in swelling continued till day 23, by when no patient showed presence of swelling.

References

1. Burton JL, Etherington DJ, Peachey RD (1978) Collagen Sponge for Leg Ulcers. *Br J Dermatol* 99(6): 681–685
2. Doillon CJ, Silver FH, Olson RM, Kamath CY, Berg RA (1988) Fibroblast and Epidermal Cell-Type-I Collagen Interactions: Cell culture and human studies. *Scanning Microsc* 2(2): 985–992
3. Griswold JA, Cepica T, Rossi L, Wimmer JS et al. (1995) A comparison of xeroform and skin temp dressing in the healing of skin graft donor site. *J Burn Care and Research* 16(2): 136–140
4. Kleinmann HK, Klebe RJ, Martin GR (1981) Role of collagenous matrices in the adhesion and growth of cells. *J Cell Biol* 88(3): 473–485
5. Mian M, Beghe F, Mian E (1992) Collagen as a pharmacological approach in wound healing. *Int J Tissue React* 14(Suppl): 1–9
6. Schlapp M, Friess W (2003) Collagen PLGA Micro particle composite for local controlled delivery of Gentamicin. *J Pharm Sci* 92(11): 2145–2151
7. Palmieri B (1992) Heterologous collagen in wound healing: A clinical study. *Int J Tissue React* 14(Suppl): 21–25
8. Sripriya R, Kumar MS, Sehgal PK (2004) Improved collagen bilayer dressing for the controlled release of drugs. *J Biomed Mater Res B Appl Biomater* 70(2): 389–396

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