



## Effect of Hyaluronic Acid Cream in Management of Maxillofacial Wounds

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### Article History:

Received on: 20 Jul 2020  
Revised on: 20 Aug 2020  
Accepted on: 24 Aug 2020

### Keywords:

hyaluronic acid cream,  
wound-healing,  
maxillofacial wounds

### ABSTRACT

The present study aims to determine the efficacy of hyaluronic acid cream in the management of maxillofacial wounds. Total of twenty-five patients who were randomly assigned to study group, was admitted in for trauma management with facial lacerations was administered hyaluronic acid cream 0.5% (BIONECT) for one week twice daily application on the wounds. The wounds were then assessed with PWAT (photographic wound assessment tool) at 3<sup>rd</sup> day, 5<sup>th</sup> day, 7<sup>th</sup> day respectively. The control group (n=25) was administered with povidone-iodine cream. The study group showed a statistically significant difference (p<0.005) in wound healing earlier than the control group at 7<sup>th</sup> day. Patient compliance was higher in the study group than the control group. Hyaluronic acid has been proven to be shown in involvement in various stages of wound healing from promoting initial inflammation, granulation tissue formation tissue, keratinocyte migration and proliferation. The hyaluronic acid cream can be utilised as an alternative to promote ideal healing by protecting the wound from detrimental changes, providing or maintaining a damp environment and remarkably reducing microbial load. Hence from our study, the hyaluronic acid cream benefits in the healing of acute maxillofacial wounds.

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ISSN: 0975-7538

DOI: <https://doi.org/10.26452/ijrps.v11i4.3672>

Production and Hosted by

IJRPS | [www.ijrps.com](http://www.ijrps.com)

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### INTRODUCTION

Wound healing is a complex biological process comprising various roles such as barrier restoration, involving keratinocytes, fibroblasts, and immune cells to restore the balance in lost tissues (Pastar *et al.*, 2014). Wound assessment for appropriate diagnosis, treatment planning and management is

a pivotal step. Hyaluronan or hyaluronic acid (HA) is a biomaterial that can be used as an alternative to enhance wound healing (Brown, 2004; Chen, 1999). It was Karl Meyer from Columbia University, New York in 1934, who first described a substance "Hyaluronic acid" which was isolated from cow's vitreous body. Hyaluronic acid is a Greek word meaning for 'glass' for hyalos and "uronic sugar". The more the HA concentration, that would promote keratinocyte activation and re-epithelialisation during the healing process.

It is found abundant in soft connective tissues, including the synovial fluid in human body fluids of vertebrates. Stimulation of early granulation tissue formation, inhibition of destructive inflammation during the healing phase, and promoting re-epithelialisation and also angiogenesis are the few mechanisms that are significant actions of hyaluronic acid in wound healing (Mendes *et al.*, 2008). Thus, for the prevention or reduction of post-operative inflammation and associated symptoms

during the post-surgical healing period, hyaluronic acid is proven beneficial (Koray et al., 2014). In various fields such as ophthalmology, dermatology, and rheumatology, HA has been used as it is known for its non-immunogenicity and non-toxicity effects. HA can be applied topically in the oral cavity by liquid or gel forms available (Prestwich, 2011; Fatini et al., 1968).

The reason behind the absence of scar tissue and exceptional tissue repair in foetuses is the presence of a considerable amount of hyaluronic acid in their skin (Ferguson and Kane, 1445; Trabucchi et al., 2002). Acceleration and improvement of healing of chronic wounds have been studied extensively; thus, for these objectives, the properties of hyaluronic acid have been examined (Ortonne, 1996).

Various growth factors acting upon cell proliferation and migration are proven to be mediated through the hyaluronic acid pathway (Greco et al., 1998). However, it has not been explained the exogenous benefits application of hyaluronic acid on extracellular matrix remodelling of collagen (Mast et al., 1993).

The present study is, therefore, is undertaken to evaluate the efficacy of Hyaluronic cream for wounds in the maxillofacial region following injuries.

**MATERIALS AND METHODS**

The study group and control were selected by randomisation method. Male and female patients aged ≥18 years appeared with acute skin wounds were included in this study. Patients reporting with traumatic maxillofacial wounds, laceration, were selected for the study. With no previous history of keloid formation and allergic to Hyaluronic acid as well as Patients who were willing to participate for the trial was included.

Patients who were with infectious diseases, medically compromised, uncooperative, as well as those with poor verbal communication were excluded from the study.

The sample size was calculated using G-power software with alpha error as 5% and power of the study at 95%, 25 patients for each group, totally 50 patients.

The wound types included traumatic wounds, dermabrasions for which hyaluronic acid cream (0.5% BIONECT) was applied twice daily.

The cream was administered within the usual wound dressings depending on their size. Each application was evaluated using Photographic

wound assessment tool at 3<sup>rd</sup> day, 5th day, 7th day (Figure 1). Two evaluators carried out wound evaluation for better interrater reliability with the use of high-resolution digital pictures at intermittent intervals.

In the majority of patients, wound sites included associated were facial areas. Alternatively, after two days, wound bandages were changed to evaluate wound for any redness, irritation, pruritus, or pain.

The collected data were analysed with IBM.SPSS statistics software 23.0 Version and mean& S.D were used for continuous variables at 3<sup>rd</sup>, 5th, 7th, post-operative days.

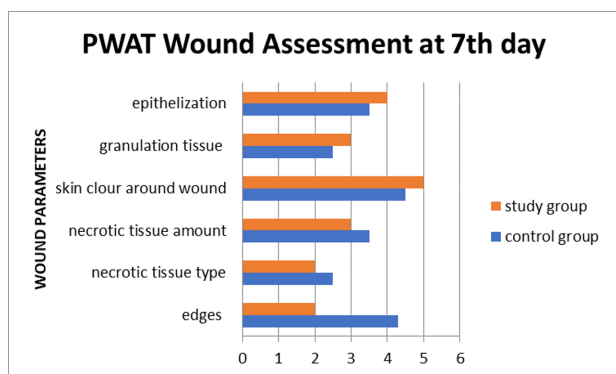
**RESULTS**

Two groups of total 50 patients participated in the study. Out of 25 patients, who received hyaluronic cream had statistically significant (p<0.005) wound healing than that of the control group at 7<sup>th</sup> post-operative day. Patient compliance was towards the study group.

TABLE I PHOTOGRAPHIC WOUND ASSESSMENT TOOL		
Domain	Assessment	Date Score
1. Edges	0 = Indistinct, diffuse, none clearly visible 1 = Distinct, outline clearly visible, attached, even with wound base 2 = Well-defined, not attached to wound base 3 = Well-defined, not attached to base, rolled under, thickened 4 = Well-defined, fibrotic, scarred or hyperkeratonic	
2. Necrotic Tissue Type	0 = None visible 1 = White/gray nonviable tissue and/or nonadherent yellow slough 2 = Loosely adherent yellow slough 3 = Adherent, soft, black eschar 4 = Firmly adherent, hard, black eschar	
3. Necrotic Tissue Amount	0 = None visible 1 = < 25% of wound bed covered 2 = 25% to 50% of wound covered 3 = > 50% and < 75% of wound covered 4 = 75% to 100% of wound covered	
4. Skin Color Surrounding Wound	0 = Pink or normal for ethnic group 1 = Bright red 2 = White or gray pallor or hypopigmented 3 = Dark red or purple 4 = Black or hyperpigmented	
5. Granulation Tissue	0 = Skin intact or partial-thickness wound 1 = Bright, beefy red; 75% to 100% of wound filled and/or tissue overgrowth 2 = Bright, beefy red; < 75% and > 25% of wound filled 3 = Pink, and/or dull, dusky red and/or fills ≤ 25% of wound 4 = No granulation tissue present	
6. Epithelialization	0 = 100% wound covered, surface intact 1 = 75% to < 100% wound covered and/or epithelial tissue extends > 0.5 cm into wound bed 2 = 50% to < 75% wound covered and/or epithelial tissue extends > 0.5 cm into wound bed 3 = 25% to < 50% wound covered 4 = < 25% wound covered	
<b>TOTAL SCORE</b>		
<b>SIGNATURE</b>		

**Figure 1: Photographic wound assessment tool used in the study**

The wound edges were considerably reduced than that of its original size at the end of 7<sup>th</sup> day for the HA group in comparison to control group. The necrotic tissue amount is more than 10% less in the HA group than in the control group on 7<sup>th</sup> day. The skin colour has drastically improved around the study group wounds. The rate of epithelisation was significantly more in the study group on 7<sup>th</sup> day (Graph 1). The



Graph 1: Depicts the results of Photographic Wound Assessment between the control group (series 1), study group (series 2) at 7 th day

rate of epithelisation is seen more in the study group than the control group.

## DISCUSSION

Hyaluronic acid serves different functions in various parts of the body. The increase in cell motility, cell proliferation, cell differentiation, cell interaction and production of cytokines, PGE2 and matrix metalloproteinase is by hyaluronic acid which in turn promotes the wound healing (Liguori *et al.*, 1997; Anderson, 2001).

In the remodelling of an extracellular matrix, Collagendeposition by fibroblasts is the key to factor and its nature of the deposition determines the quality of the scar. The standard of this healing is mostly attributed to hyaluronic acid, and its activation, proliferation of keratinocytes which promotes the dermal collagen and also by inhibiting the late inflammatory phase .all these factors govern the quality of healing and scar (Chen, 2002).

As face has an abundant blood supply and any wound would heal in a much rapid fashion in comparison to other areas, our study has used BIONECT hyaluronic acid (5%), with other standard components such as povidone-iodine which is proven to promote wound healing.

Gold and silver nanoparticles are the various types of Nano-materials tested in wound dressings to promote granulation tissue differentiation (Setyawati *et al.*, 2017; Li *et al.*, 2015). However, these growth factors used during healing can also have adverse effects such as hyperostosis or tumorigenesis (Li *et al.*, 2017). These Nano-materials persist in fibrous tissue during healing for a considerable time more than the required time frame, especially, gold or silver nanoparticles (Chattopadhyay *et al.*, 2016).

Therefore this necessitates the exploration of safer

and more efficacious treatment strategies to promote wound healing. Hyaluronic acid is a proven highly biocompatible, non-immunogenicity and non-toxicity material that can be used to promote wound healing.

Various studies found that cross-linked HA hydrogel films to accelerate the healing of full-thickness wounds, presumably by providing a highly hydrated and nonimmunogenic environment that is conducive to tissue repair.

Oksala *et al.* (1995) found that HA and CD44 were localised in the same region of the mucosal keratinocytes (epithelium) in all stages of wound healing. Wang *et al.* (1992) also noted that both HA and CD44 receptors in the keratinising skin epithelia showed an intense staining and close co-distribution.

Kaya *et al.* (1997) showed that CD44 receptors in response to extracellular stimuli regulate keratinocyte proliferation and the maintenance of hyaluronic acid concentration. For second-degree burns, hyaluronic acid with silver sulfidic-three treatment applications compared with silver sulfadiazine alone. Koller (2004); Costagliola and Agrosi (2005) proven to effective than the latter.

Hyaluronic acid in dermal matrices of chronic wounds assessed for their role. Hollander *et al.* (2001) proved that HYAFF mesh co-cultured with dermal fibroblasts and subsequent- Biopolymers, grafted with Laser skin<sup>®</sup> for traumatic loss, showed that in the chronic wounds, they promote wound healing and less scar contracture.

## CONCLUSIONS

Hyaluronic acid is thus proven to be involved in various stages of wound healing phases, starting from inflammation to granulation tissue formation. The various roles of HA are the promotion of cell migration to wound matrix, epithelisation by keratinocyte proliferation and through free radical scavenging. Furthermore, the hyaluronic acid cream would ensure the favourable healing by providing and maintaining a moist environment, in turn protecting the wound from harmful effects, especially from bacterial colonisation. Thus our study concludes that use of hyaluronic acid cream for maxillofacial injuries is effective and should be further explored in a larger sample for more extended period .the limitation of our study is smaller sample group and a single type of wound evaluation scale for a short time. The use of one or more wound evaluation scales would provide more specific and accurate results.

**Ethical clearance**

Ethical clearance is obtained from the university ethical board before the procedure.

**Conflict of interest**

The authors declare that they have no conflict of interest for this study.

**Funding support**

The authors declare that they have no funding support for this study.

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