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Original Article

Study of Influence of Hemoglobin Levels during Healing of Soft-tissue Wounds of High Energy Trauma to the Extremities

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Abstract

Background: Wound healing requires a higher concentration of oxygen at the local site, which acts against pathogens and helps in wound granulation. The study aimed to observe the relation between hemoglobin levels and its effect on wound healing in orthopedic wound management and also to assess wound-related morbidity associated with it.

Materials and Methods: This is a prospective observational study, conducted at tertiary care hospital from January 2016 to February 2019, for a period of 3 years. 200 patients of orthopedic wounds were included in the study. The sample was divided into two Groups A and B. Group A had patients with hemoglobin more than 12 g%, while Group B had patients with hemoglobin <12 g%. Both the group patients were evaluated and compared for the time taken for wound healing, duration of hospital stay, number of secondary procedures required, and incidence of infection.

Results: Number of wound debridements required in Group A (range 0–2, mean 1) was less compared to Group B (range 2–5, mean 3). Group A patients required less duration of hospital stay (mean −9 days), less secondary procedures, less time for wound healing (mean −12 days), and wound contraction as compared to Group B (mean hospital stay −22 days, mean wound healing time −28 days) and which was statistically significant and the Correlation coefficient was r=0.751.

Conclusion: We recommend to maintain the blood hemoglobin level above 12 g% in the management of orthopedic wounds which helps in early wound healing, less hospital stay, fewer chances of infection, and secondary procedures.

Key words: Hemoglobin, Orthopedic practice, Wound healing

INTRODUCTION

At the emergency room, the common challenge faced by orthopedics surgeons is still managing the larger and deeper wounds of extremities resulting from road accidents. Conditions which require proper wound management include compound fractures, crush injuries, postoperative wounds, and amputation stumps. The proper management of the above conditions is essential to prevent long duration of hospital stay, infections, multiple surgeries and to prevent associated morbidity and mortality in these patients. Hence, proper wound care and early wound healing help in preventing the above complications.

The primary goal of treating compound injuries is the healing of soft tissues first and obtaining wound cover. Before plastic surgeon intervenes, the orthopedic surgeon may have to overcome challenges of preserving soft tissue, avoid soft-tissue sacrifices during repeated debridements, multiple surgical procedures, avoid a prolonged hospital stay, undue expenditure, and financial burden on caregivers, psychological problems such as anxiety, depression amongst patients, and caregivers to delayed results. The burden on the family is the highest due to constant engagement in patients treatment and inability to engage in activities of earnings. The most influential factors delaying or complicating wound healing

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are poor nutrition, unhealthy lifestyle, cardiorespiratory compromise due to bedridden state, lack of aerobic exercises, and breathing exercises. Resultantly decrease local blood flow due to arteriolar/small vessel blockage due to septic thrombi thereby decrease in oxygen to the dying tissues.

Wound healing requires a higher concentration of oxygen at the local site, which acts against pathogens and helps in wound granulation, cell proliferation, vascularization, and synthesis of collagen.[1] Hemoglobin is a very good transporter of oxygen molecules to the tissue.[2] Low hemoglobin before surgery or a decrease in hemoglobin levels while surgery is a potentially modifiable factor. Identification of the above factor in patients who undergoes orthopedic surgery, which helps to create treating protocols to correct the hemoglobin level and assessment of this impact on outcome.[3] Blood and oxygen supply to the traumatic tissue lower than normal levels is associated with wound complications.[2,4,5] According to the current knowledge, tissue hypoxia is the common etiology of wound healing disorders[6] and pathogenesis of chronic wounds.

There are various treatment options available for healing of orthopedic wounds such as repeated debridement, Eusol dressing, hyperbaric oxygen therapy, improving the nutritional status by protein supplementation, vacuum-assisted closure (VAC) application, topical hemoglobin applications,[7] and use of oxygen carrier substitute.[8]

The various treatment options mentioned above do not merely help in wound healing but just support the wound healing if normal blood hemoglobin concentration is maintained. Most of the orthopedic patients are anemic because of blood loss due to compound fractures, crush injuries or during surgery, which hinders the wound healing capacity leads to wound-related morbidity and mortality. Literature suggests adequate hemoglobin levels in blood helps in early wound healing but there is no clarity regarding how much percentage of hemoglobin should be maintained. The objective of this article was to observe the influence of hemoglobin levels during wound healing in orthopedic practice. The hypothesis is that decreased hemoglobin levels are responsible for more tissue death due to low oxygen-carrying capacity and resultant loss of ongoing tissue death increases its dimensions, death cells invite infection, more damage, and constituting further delay. On the contrary, the normal oxygen-carrying capacity is responsible for timely repair of wound thereby reducing complications and delay.

MATERIALS AND METHODS

This was a prospective observational study of 200 patients of orthopedic wounds, conducted at tertiary care hospital from January 2016 to February 2019, over a period of 3 years. The sample was divided into two groups, each group had 100 patients each. Group A had patients with a blood hemoglobin level of more than 12 g% and Group B had patients with a blood hemoglobin level of <12 g%.

Patients who sustained compound fractures (Gustilo Anderson Grade 2 and Grade 3A), amputation wounds and post-operative wounds between 20 and 75 years were included in the study. However, patients having closed fractures, compound fractures with Gustilo Anderson Grade 1 and Grades 3B and C, hematological disorders (hemoglobinopathies and coagulation disorder), cardiovascular problems, patients have comorbidities such as diabetes mellitus, protein-energy malnutrition (criteria as per Constans *et al.*),[9] immunodeficiency (HIV), patients having suspected clostridium welchii (gas gangrene organism), and patients with neurological disease and impaired sensation were excluded from the study.

Patient Evaluation

After the initial evaluation and hemodynamic stabilization of the patients, X-rays of the involved limb AP and Lateral views were taken in cases of fracture by emergency ward orthopedic consultant. Pre-operative investigations such as hemoglobin, complete blood counts, blood sugars, serum proteins, and HIV tests were done.

The baseline wound assessment was done after thorough wound wash using chlorhexidine and copious amount (9L of saline), The parameters included are dimensions of the wound, severity of damage from the skin, subcutaneous tissue, facia, muscles, and loss of periosteum. Wound swab was sent for culture to rule out infection. Gas gangrene clostridium welchii organisms' infection was ruled out in suspected cases. The above-mentioned parameters were assessed by two separate orthopedic consultants at two separate times without knowing the patient details and hemoglobin levels to eliminate the bias.

Secondary wound assessment was done after primary debridement after removal of contaminated dead soft tissues till visibility of punctate bleeding. The parameters included are dimensions of the wound, severity of damage from the skin, subcutaneous tissue, facia muscles, and loss of periosteum. The VAC dressings were applied once wound shows no further necrotic and dead tissues or infection and no further debridements were necessary. The patients were given a high protein diet, and micronutrients to avoid delayed wound healing due to deficiency and avoiding bias in the study. Periodic assessment of wound status was done every 7th day or at the time of removal of dressing in the case where VAC dressing was used as an adjunctive. Periodic every weekly hemoglobin levels

were monitored in both groups. Packed cell volume transfusions were given to maintain hemoglobin in Group B. Perioperative antibiotics cefixime 1 g, gentamicin, and metronidazole were given till 48 h or as per culture sensitivity report in doubtful infected cases. Oral iron supplements were given in both groups.

The parameters include size and dimensions of the wound, color of the granulation tissue, signs of infections, time taken for the shrinkage of the wound, and number of debridement required. The above parameters were used for both Group A and Group B patients and wound assessment was done every alternate day. Hemoglobin percentage in Group B patients was repeated once in every 3 days, we used to transfuse blood for Group B patients to maintain the hemoglobin level above 12.

Every alternate day, we used to assess the wound condition in both Groups A and B by checking the parameters such as the color of the granulation tissue, wound infection, rate of change in wound dimensions, and the number of secondary procedures involved and duration of hospital stay. The above parameters were compared with both the groups.

Statistical Analysis

All statistical analysis was performed using the Statistical Package for the Social Sciences for Windows, version 20.0 (IBM Corp.; Armonk, NY, USA). For categorical variables, the Chi-square test was used to detect differences. Pearson's correlation test was used to determine correlations between Groups A and B patients. Data are presented as mean ± standard deviation. $P < 0.05$ was considered statistically significant.

RESULTS

Group A had 72 male patients and 28 female patients, Group B had 76 males and 24 female patients [Graph 1]. 62 patients were between 20 and 40 years, 36 patients between 41 and 60 years, and 2 patients between 61 and 75 years in Group A as compared to Group B which had 60 patients between 20 and 40 years, 29 patients between 41 and 60 years, and 11 patients between 61 and 75 years and there was no statistical difference between sex and age of Group A and Group B patients [Table 1].

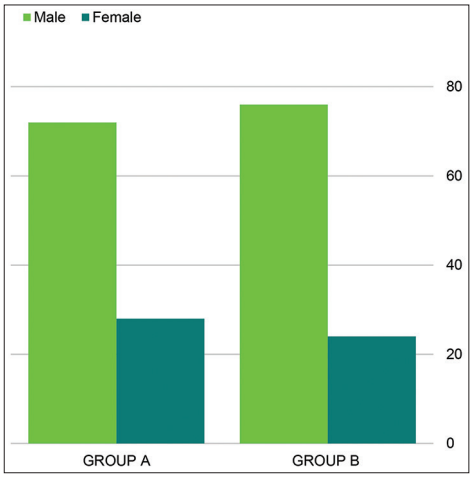
In Group A, 72 patients had road traffic accidents, 23 had railway accidents, and five had fall and in Group B, 68 patients had road traffic accidents, 30 had railway accidents, and two had a fall.

Group A had 18 patients of upper limb trauma and 82 patients of lower limb injuries, in comparison to Group B which had 15 patients with upper limb trauma and 85 patients of lower limb trauma.

About 40% of patients in Group B had associated infections as compared to Group A, which had only 7% of infection which was statistically significant ($P < 0.05$) [Graph 2]. The number of wound debridements required in Group A (range 0–2, mean 1) was less compared to Group B (range 2–5, mean 3) [Table 2] and which was statistically significant ($P < 0.05$).

Group A patients required less duration of hospital stay, less secondary procedures, less time for wound healing, and wound contraction as compared to Group B patients, which was statistically significant ($P < 0.05$). Mean days of hospital stay in Group A patients were, 7 days for compound Grade 2 wounds, 12 days for compound Grade 3B wounds, 8 days for amputation wounds, and 8 days for post-operative wounds. Mean days of hospital stay in Group B patients were, 20 days for compound Grade 2 wounds, 26 days for compound Grade 3B wounds, 21 days for amputation wounds, and 24 days for post-operative wounds [Tables 3 and 4].

Mean days of wound healing in Group A patients were, 9 days for compound Grade 2 wounds, 14 days for compound Grade 3B wounds, 12 days for amputation wounds and 12 days for post-operative wounds. Mean days of wound healing in Group B patients were, 24 days



Graph 1: Bar chart showing the Sex distribution of male and female patients in Groups A and B

Table 1: The age distribution of patients in Groups A and B with range from 20 to 75 years

Groups	20–40 years	41–60 years	61–75 years	Total
A	62	36	2	100
B	60	29	11	100
Total	122	65	13	200

*More patients were between 20 and 40 years age group

for compound Grade 2 wounds, 33 days for compound Grade 3B wounds, 27 days for amputation wounds, and 28 days for post-operative wounds [Graph 3 and Figures 1-3].

Correlation analysis showed a significant positive correlation between the duration of hospital stay, the number of secondary procedures, wound healing time with blood hemoglobin levels (r = 0.751).

DISCUSSION

Default blood supply to the extremities is poorer as compared to face and trunk. Furthermore, there is a watershed area of hypovascularity with proceeding distally.

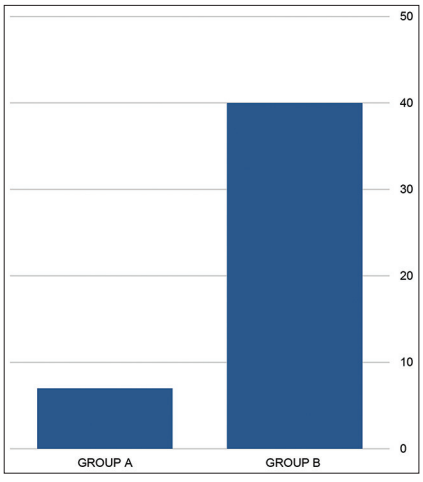
Table 2: The number (mean and range) of debridements required before the wound healing in Groups A and B patients

Groups	Range	Mean
A	0–2	1
B	2–5	3

*More number of debridements were required in Group B patients

Table 3: Comparison of parameters such as wound color, healing time, infection rate, number of debridements required, hospital stay, and secondary procedures between Group A and Group B patients

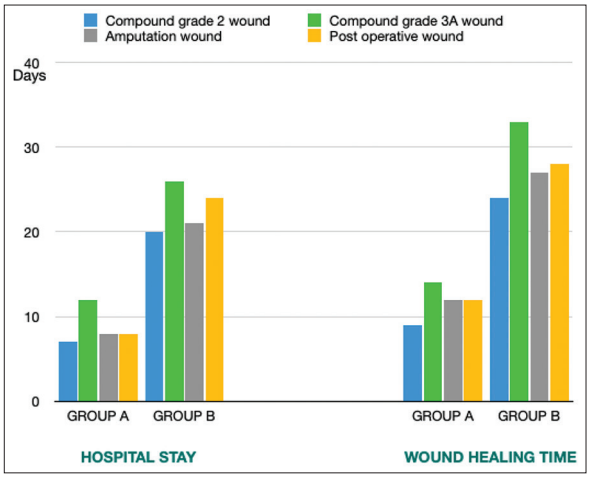
Parameters	Group A (Hb>12g%)	Group B (Hb<12g%)
1. Colour of granulation tissue	Red	Pale
2. Healing time	More	Less
3. Infection rate	More	Less
4. Debridement requirement	More	Less
5. Rate of change in wound dimension	FAST AND EARLY	Slow and late
6. Duration of hospital stay	More	LESS
7. Number of secondary procedures required	More	Less
8. Mental stress to patient and relatives	More	Less



Graph 2: Bar chart showing associated infections in Group A and B

Due to such natural variation and peculiarity of blood supply, wound healing is a naturally complex phenomenon to get a full understanding of the subject. However, concepts and theories postulated have made an understanding of secondary wound healing better. The researcher has taken may efforts to improve wound healing like chemical agents like silver nitrate, dressing materials, hyperbaric oxygen therapy, VAC dressings, local oxygen chambers, Enzymes, and free radicals (nascent oxygen, chloride, hydrogen, etc.) to initiate and progress of granulation tissue which ultimately allow epithelization and complete coverage.

Wound healing is a normal biological process in the human body, which goes through four stages: Hemostasis, inflammation, proliferation, and remodeling. Most of the orthopedics wounds due to substantial soft tissue, that is, skin, subcutaneous tissue, and muscular loss heal with secondary intensions. Potential barriers to the healing are the presence of dead and necrotic tissue, debris, and slough collection. For healing to progress normally, the surgeon has to take the challenge of removing the dead and necrotic materials which is done by debridement of wounds. Chemical debridements achieved using hydrogen peroxide, EUSOL solution helps in removing the little amount of the smaller tissue. They are not effective for the larger one. Hence, surgical debridement of wounds is still the gold standard for removing dead tissues from larger traumatic compound wounds for achieving better secondary healing. However, the procedure itself creates larger soft-tissue defects. Repeated debridements may increase the dimensions of wounds which may further delay healing and granulation tissue, may take longer time to fill the soft-tissue defects, further soft-tissue procedures may get delayed and this hugely contributes to a prolonged hospital stay, and financial burden thereby.



Graph 3: Comparison between Groups A and B in relation to hospital stay and wound healing time in patients with compound Grade 2, 3A wounds, amputation wounds, and post-operative wounds

One of the major steps to reduce healing time and hospital stay is to avoid repeated debridements and the further increase of dimensions of wounds by repeated surgical debridement procedures. A single complete primary debridement, maintaining microscopic debris to be removed by macrophages and achieving healthy progress of granulation tissue till it fills the crater up to the skin so that skin coverage can be easily done.

Oxygen is very essential for cell metabolism, mainly for energy production using ATP, and is very important in wound-healing processes. It prevents wound infection, induces angiogenesis, increases keratinocyte differentiation, migration, and re-epithelialization, enhances fibroblast proliferation and collagen synthesis, and promotes wound contraction.[10]

Low rate of infections observed in patients with hemoglobin more than 12 g% is because of a high level of superoxide production (a key factor for the oxidative killing of microorganisms) by polymorphonuclear leukocytes and is critically dependent on oxygen levels. Faster wound healing and less duration of hospital stay observed in our study with Group A patients, which is because of More hemoglobin in the blood helps in more tissue oxygenation at the local site, which helps in early wound contraction by fibroblast proliferation and collagen synthesis.

During the early stages of wound healing, due to the high oxygen utilization by the metabolically active cells and also due to vascular disruption, the microenvironment becomes hypoxic. Tissue oxygen tension of chronic wounds

Table 4: Comparison of quantitative parameters such as hospital stay, secondary procedures required, and wound healing time between Group A and Group B patients

Parameters	Group A		Group B	
	Range	Mean	Range	Mean
Hospital stay in days				
Compound Grade 2 wound	3–16	7	15–35	20
Compound Grade 3A wound	7–21	12	21–43	26
Amputation wounds	3–20	8	15–30	21
Post-operative wounds	3–15	8	16–36	24
Number of Secondary procedures (Debridements)				
Compound Grade 2 wound	0–1	1	2–3	3
Compound Grade 3A wound	0–2	1	2–5	4
Amputation wounds	0–1	1	2–4	3
Post-operative wounds	0–2	1	2–4	3
Wound healing time in days				
Compound Grade 2 wound	7–18	9	18–40	24
Compound Grade 3A wound	8–26	14	25–51	33
Amputation wounds	7–24	12	20–36	27
Post-operative wounds	8–20	12	17–38	28

*more hospital stay, secondary procedures, and wound healing time were observed in Group B patient

Figure 2: (a) (case 2) Lower limb crush injury when hemoglobin <12 g% (b) (case 2) same patient showing wound healing and contraction after improving the hemoglobin of more than 12 g%

Figure 1: (a) (case 1) - Crush foot wound when hemoglobin was <12 g% (b) (case 1)-same wound after improving of hemoglobin of more than 12 g%

Figure 3: (a) (case 3) Operated wound with necrosis (b) (case 3) same wound after debridement showing pale granulation tissue with hemoglobin level <12 g% (c) (case 3) same wound showing pale granulation tissue, minimal wound healing, and wound contraction with hemoglobin level <12 g%

measured transcutaneously is between 5 and 20 mm Hg as compared to control tissues of 30 and 50 mm Hg and chronic wounds are hypoxic.[11]

In wounds where oxygenation is not maintained adequately, healing is impaired. Temporary hypoxia after injury triggers wound healing, but prolonged or chronic hypoxia delays wound healing.[12] In normally healing wounds, reactive oxygen species such as hydrogen peroxide (H_2O_2) and superoxide (O2) are acts as cellular messengers to stimulate main processes of wound healing, including cell motility, cytokine action, and angiogenesis.

As healing progress from the walls of the debrided subcutaneous tissue walls, the migrating granulation tissue and the cells derive the nutrition from the adjoining capillaries by diffusion. The cell deaths are expected to happen when oxygen is less subtle supply. Hence, the oxygen-carrying capacity of the blood has to be maintained to normal levels and delivery of oxygen's to inured and inflamed tissues are adequate to avoid cell death and subsequently, the progress of granulation tissue goes unhampered. The supply of micronutrients such as zinc, molybdenum which is required for proliferation and phagocytosis function of macrophages needs to be maintained. Essential nutrients for tissue repair such as amino acids, Vitamins c and E are also supplied through the blood only, they are essential to complete wound healing. Their deficiency may delay the healing. Therefore, the supplements of above nutrients are crucial for early and normal progress in the healing of orthopedic wounds.

The cause of most of the orthopedics wounds is higher energy trauma during road traffic accidents causing severe devastating internal injuries to the soft tissues and their internal blood supply. Most micro thrombi cause local hypoxia, low oxygen-carrying capacity due to anemia and low hemoglobin will not stop the further tissue deaths.

In our study, it was noted that the wound healing among female was slightly delayed as compared to the males, this is due to the fact these females have long-standing anemia as nutritional problems. Nutritional deficiency of proteins and micronutrients has been coexisted simultaneously; hence, initial time is taken for the correction of nutritional deficiencies and once hemoglobin levels and nutritional deficiencies have overcome, the wound started healing with a faster rate. Even the initial number of debridements was more. This explained by faster tissue deaths due to preexisting anemic state further increased by blood loss in accidents. However, this problem was very well tackled by faster correction of hemoglobin levels in Group B during the early weeks of post-injury which has reduced delay in the formation of granulation tissue among the female population.

Open wounds have been constantly losing blood products through serous, serosanguinous discharge, blood loss during dressings, and procedures. Even granulation tissue bleeds significantly during dressings. RBCs are often sucked during vacuum-assisted dressings. Damaged RBCs undergo hemolysis. Even transfused red packed cell have a smaller half-life and they undergo early hemolysis. All these factors account for the fall in hemoglobin levels. It often reflected by the quality of wound especially paleness, accumulation of debris and dead tissues and slower granulation tissue formations. Hence, maintaining normal hemoglobin levels throughout the healing phase reduces complications and delay in wound healing.

Delay in wound healing causes a delay in the discharge of the patients from the hospitals, long duration of hospital stay causes psychosocial issues in patients. The long duration of hospital stay make the patients to unnecessary exposure to hospital-acquired infection and also financial issues. The family and caregivers are constantly under stress and burden. The patients themselves may experience psychological problems if things are not moving to heal. Repeated surgical procedures make patients prone to develop anxiety and depressions. The patients may become non-compliant to treatment. There may be a chance of losing faith and trust in treating orthopedicians. Delay in wound healing makes the operating surgeon wait for the definitive management of compound fractures; otherwise, it can lead to infections and if the wound is not healing properly and associated with infections, it gives problem to the plastic surgeons for wound coverage. Overall delay in wound healing complicates the whole scenario of treatment.

Hence, the maintenance of proper oxygen level is crucial for optimum wound healing, which can be done by maintaining adequate hemoglobin level in the blood (more than 12 g%) so that we can prevent wound-related morbidity.

CONCLUSION

Normal hemoglobin levels have a major role in supplying oxygen and nutrients to the healing tissues. Hence, we recommend to maintain the blood hemoglobin level above 12 g% in the management of orthopedic wounds which helps in early wound healing, less hospital stay, and fewer chances of infection. It also decreases the secondary procedures required for the wound management and morbidity associated with it.

HIGHLIGHTS

- Maintaining of blood hemoglobin level of more than 12 g% is essential for early wound healing
- Early wound healing reduces wound-related morbidity
- Blood hemoglobin level of more than 12 g% reduces the chances of infections.

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