Wound healing at high altitude: What effect does

hypobaric hypoxia have on physiological response to

tissue damage? A Narrative Review

University of Exeter MSc Extreme Medicine Independent Research Project: HPDM148

Introduction

High altitude environments are popular amongst travellers, and challenging terrains combined with fatigue increases the possibility of injury on expeditions. Tissue healing is a complex process reliant on oxygen (1,2,3) and it is presumed the process may be impaired in hypobaric hypoxic environments, however limited large-scale trials clearly demonstrate this hypothesis in the high-altitude environment. This narrative review looks at:

- The role of oxygen in the wound healing process;
- 2. How this process is impaired in hypobaric hypoxia;
- 3. How known physiological acclimatisation mechanisms may affect wound healing at altitude.
- 4. A study design for future research will be proposed to test the hypothesis that wound healing is impaired in high altitude hypoxic environments compared to sea level



Fig. 1: Four stages of wound healing (1,2,3)

Key Findings

Wound healing is known to be an oxygen dependent process made up of the 4 stages in Fig 1 (1,2,3). A key determinant of wound strength and longevity is quality and quantity of collagen, the production of which is oxygen dependent (4), therefore in hypoxic environments wounds are more prone to breakdown (as seen in critical illness and diseases where perfusion is impaired).

Physiological changes observed at altitude are summarised in Fig 2. These may represent positive adaptations where oxygen delivery is maintained in hypoxia (eg increasing Hb concentration), or illustrate physiological deterioration (eg chronic impairment in stroke volume).

From the literature search, one study was found which looked specifically at wound healing at altitude. This was a study in Saudi Arabia which found more complications from wound healing in their high-altitude clinic compared to clinics at sea level (5).

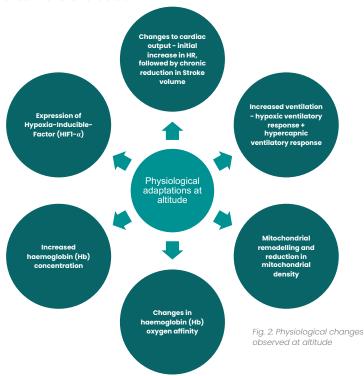
Recent studies on microcirculatory perfusion suggest that following acclimatisation to altitude, perfusion and therefore oxygen delivery to peripheral tissues were significantly improved compared to altitude naïve lowlanders.

- Davies et al (6) studied peripheral perfusion in sherpas (n=61) and native lowlanders (n=83), and found microvascular dilatation as well as oxygen offloading was significantly better in sherpas.
- Carey et al (7) completed a similar study with sherpas (n=46) and lowlanders (n=32). They found heterogenous perfusion associated with local vasocontrol mechanisms to match oxygen supply with
- Hansen et al (8) conclude this may be mediated by adrenergic pathways to restrain blood away from over-perfused areas

Aims & Methods

The aim is to question whether wound healing is impaired at altitude, why this could be, and whether acclimatisation mechanisms could be protective for the process following prolonged exposure to highaltitude.

Widely accessible published literature was used to summarise current understanding of the role of oxygen in wound healing, and physiological changes at altitude. The search engines "PubMed", "Medline", and "Google Scholar" were used to collect relevant articles. Primary search terms were: altitude; hypobaric hypoxia; acclimatisation; wound healing; tissue healing; and tissue perfusion. Animal studies were excluded.



Conclusions

- Wound healing is a complex process that requires oxygen at multiple
- High altitude is a hypobaric hypoxic environment where oxygen delivery to tissues is impaired
- A study by Udeabor (5) demonstrated impairment in normal wound healing in a high-altitude clinic compared to sea-level clinics but more research is needed to demonstrate this on a larger scale study design and key considerations are discussed.
- Physiological mechanisms explaining effect of hypobaric hypoxia on wound healing have been explored.
- Evidence for potential adaptations in acclimatized populations (increased haemoglobin concentration, changes to microcirculatory perfusion, genetic differences in HIF1- α expression) has been evaluated, with discussion on relevance to wound healing.

References

- Guo S, DiPietro LA. Factors Affecting Wound Healing. Journal of Dental Research. 2010 March;
- Schreml S, Szeimies RM, Prantl L, Karrer S, Landthaler M, Babilas P. Oxygen in acute and chronic
- wound healing. British Journal of Dermatology. 2010 March Rodriguez PG, Felix FN, Woodley DT, Shim EK. The Role of Oxygen in Wound Healing: A Review of the Literature. Dermatologic Surgery. 2008 Sep; 34(9). 3.
- Janis JE, Harrison B. Wound Healing: Part I. Basic Science. Plastic and Reconstructive Surgery. 2016 September; 138. Udeabor SE, Halwani MA, Alqahtani SA, Alshaiki SA, Alqahtani AH, Mohamed S. Effects of Altitude
- and Relative Hypoxia on Postextraction Socket Wound Healing: A Clinical Pilot Study.

 International Journal of Tropical Disease & Health. 2017 Aug; 25(3).

 Davies T, Gilbert-Kawai E, Wythe S, Meale P, Mythen M, Levett D, Mitchell K, Grocott M, Clough G, Martin D. Sustained vasomotor control of skin microcirculation in Sherpas versus altitude-naiv
- lowlanders: Experimental evidence from Xtreme Everest 2. Experimental Physiology. 2018 Nov;
- Carey D, Thanaj M, Davies T, Gilbert-Kawai E, Mitchell K, Levett H, Mythen M, Martin D. Enhanced fow-motion complexity of skin microvascular perfusion in Sherpas and lowlanders during ascent to high altitude. Scientific Reports. 2019 Oct; 9(1).
 Hansen AB, Moralez G, Amin SB, Hofstatter, Simpson L, Gasho C, Tymko M, Ainslie PN, Lawley JS,
- Hearon CM. Global REACH 2018: increased adrenergic restraint of blood flow preserves coupli of oxygen delivery and demand during exercise at high-altitude. Journal of Physiology. 2022