Blue M–Healing with Oxygen

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Abstract

Studies reveal that, world's two-third of population suffers from chronic form of oral diseases and wounds. The principle etiological factor behind is a polymicrobial complex, which initiates the increase in the formation of reactive oxygen species e.g. per hydroxyl radicals, peroxyl radicals, aryl peroxyl radicals etc. These ROS may cause damage to protein, lipid and DNA at sub molecular level. To combat these microcosmic reactions, a revolutionary inventiveness for optimum oral health was carried out by a European based company in the form of a product, Blue-M. This acts as a continuous supplier of oxygen and by perfusion of this oxygen, it enhances healing of wound. It further aids in collagen synthesis, angiogenesis and is comprehensively Osseo inductive as well as anti-inflammatory in nature. Thus, this review aims at understanding the obligatory functions of oxygen and the biology behind neutralization of inflammation as well as to recognize the essential benefits of this novel product, which in near future, after numerous studies, may even be used as an effective anti-microbial agent without developing resistance.

Keywords: *Blue-M, Nascent oxygen, Wound healing.*

Introduction

Wound healing is a dynamic nexus of processes, which has inflammation, granulation and maturation phases in it. When it comes to the specialization of oral cavity, occurrence of wounds and inflammation are common. There is accumulation of dental plaque accompanied with enhanced hostinflammatory response as well as inflammation of gingiva.[1] This, in long term, leads to onset of inflammation of bone and other peri-radicular tissues. This can also be associated with other oral problems like mucositis, ulcerations, bad breath etc.

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Apart from maintenance of oral cavity by eradication of microbes,to accelerate the healing of these wounds, ample amount of oxygen is required.

Lately,unconventional mouthwashes and gels, containing oxygenating technology has been introduced (Blue M, Europe), having anti-microbial and anti-inflammatory properties. It prevents formation of plaque biofilm as well as promotes teeth whitening, and improves the rate of wound healing.[2]

Role of Oxygen in Wound Healing: Gingival wounds, as known, involves healing as well as phagocytosis of microbial intruders. "Professional phagocytes of our innate immune system increase their oxygen consumption through the inducible activity of NADPH oxidase (NOX) that generates oxygen and hydrogen peroxide." These oxygen-derived metabolites release Reactive Oxygen Species(ROS), that are potently antimicrobial but which may also cause damage by destroying surrounding tissue and cellsby substantial damage cellular phospholipid, nucleic acid, protein, carbohydrate, and enzymes. These events are

investigated in phagocytes (neutrophilic and eosinophilic granulocytes, monocytes, and macrophages). Exposure of these cells to any of a large number of stimuli activates a ''**respiratory burst**,'' caused by an activation of the plasma membrane-bound NADPH oxidase. Approximately 98% of the oxygen consumed by wound neutrophils, is utilized for respiratory burst.[3]

Topically applied oxygen gas increases the partial pressure of oxygen of the superficial wound tissue. Interestingly, topical oxygen treatment was associated with higher VEGF expression in the wound edge tissue. Pure oxygen is known to induce VEGF. Deliberate hyperoxygenation recruits endothelial progenitor cells to the wound, increases vascular endothelial growth factor (VEGF), and promotes angiogenesis.[4]

Hydrogen peroxide enhances collagen mRNA abundance and other cytokines and growth factors depend on oxygen supply. Another role of oxygen is to support one or more needs of growing vessels such as hydroxylatingprolinerequires oxygen to convert procollagen to collagen.[5] In addition to having this antibacterial property, oxygen is also an antifungal and antihistamine substance.[6]

Therefore, to briefly summarize, oxygen is essential for

- Production of collagen
- Wound tissue epithelialization
- Neovascularization
- Phagocytosis
- Mortification of necrotic wound tissue

Composition of Blue-M and its Basis:

1. **Sodium Perborate:** Key active component and is required for plaque control and facilitate wound healing. Sodium perborate itself doesn't exert any action rather, it reacts with saline and produces nascent oxygen. Since we know that the use of high concentration hydrogen peroxide disinfectant damages the wound tissue, due to production of increased number of free radicals. However lower concentration (<0.15 %) of hydrogen peroxide, when present continuously, is deleterious to pathogenic bacteria only, without causing damage to healthy cells. Hence, acts as a steady source of active oxygen.[7]

2. **Honey[8]:** For plaque control. Basically, honey is phytochemical and has antibacterial characteristics. Its wound healing aspect is attributed to liberation of proinflammatory cytokines i.e. macrophages and monocytes from the neighboring cells.It even exhilarates the production of IL-1β,IL-6 and TNF-α from Matrix metalloproteinase- 6 cells and peripheral blood monocytes. Moreover, Type II arabinogalactan proteins are identified in honey, having immune modulatory characteristics, due to its endotoxin content, which again has stimulatory effect on monocyte family to release TNF-α.

   Honey contains antioxidants that breaks the inflammatory cycle by scavenging the reactive oxygen species. Anti-inflammatory effect of honey is also due to inhibition of COX-2 and inducible NO synthase expression. An in-vitro pilot study has shown that Blue-M mouthwash solution is comparatively effectual than chlorhexidine and is annihilates unicellular as well as multicellular (biofilm) microorganisms.[9]

3. **Xylitol:** Also, for plaque control. Unlike glucose, the classical acid forming bacterial, contained in dental plaque cannot metabolize xylitol as a nutrient. This result due to conversion of xylitol into xylitol 5-phosphate (X5P) once the bacterial cells ingest it and xylitol inhibits acid production. Therefore, xylitol halts the growth of *S*.mutans and S. sobrinus.[10]

   This mechanism credits to retarded cell to cell adhesion of bacteria and polysaccharide production which amounts to less bulk of plaque biofilm and the biofilm is also less sticky.

4. **Methyl Salicylate:** A salicylic acid derivative, this product has been used since long as a constituent of mouth rinses in combination with essential oils (Listerine). It even comes in the group of non-steroidal anti-inflammatory drugs and therefore, also has mild analgesic property. Known to have antisepticand anti-inflammatory effect, methyl salicylate is one of the active ingredients of Blue-M.[11]It acts by disrupting the cell membrane and inhibiting its enzyme activity. Its slight minty characteristic further acts as an add on to the product's flavor.

5. **Lactoferrin:** Acts as bone growth accelerator. From the group of transferrin, there is another iron-binding glycoprotein, Lactoferrin. Apart from being

present in the secondary granules of neutrophils and epithelial secretions, lactoferrin is also readily available in breast milk. This pleiotropic factor has eloquent immunomodulatory and antimicrobial facets. Lactoferrin triggers the differentiation and multiplication of Osteoblast-Like Cells.[12] Therefore, this increased number of osteoblasts has the capacity to orchestrate and mineralize new bone and can also pause cell death. Lactoferrin Inhibits Osteoclastogenesis i.e. even though it directly doesn't affect the osteoclasts' ability to resorb bone but decreases thepotency of precursor cells to produce osteoclasts.[13]

Mechanism of Action of Blue-M: The basic mechanism of Blue-M is controlled delivery of active oxygen i.e. hydrogen peroxide to the site of treatment.

This occurs when Sodium perborate comes in contact with water, it creates a chemical process of hydrolysis, the end products being hydrogen peroxide and boric acid. Hydrogen peroxide further reacts with saline and releases nascent oxygen.

Method of Application

Few elementary steps are followed:

(i) **Preparation and treatment step:** The fundamental procedures like examining the treatment site clinically, taking radiographs and preparation of patient is done. Once the treatment has begun an acute wound is formed. On this wound the gel is applied and left for 2 minutes. The area is then flushed with saline. The previous step is again repeated but now the gel is left as it is in the wound.

(ii) **Patient care:** Patient is instructed to brush twice daily with Blue-M toothpaste. Rinse with blue M mouthwash postoperatively, 4 times a day for 1 minute, for 4 weeks, followed by 2 times a day for 1 minute. In cases of gingival recessions/pockets, use an interdental brush with blue M gel twice daily is recommended.

(iii) **After care:** Follow up period is 2 weeks, 4weeks and 8 weeks. Reevaluation of clinical parameters as well as radiographs are done after 4months and 1 year. This is done to assess the developments in soft/ hard tissue level.

Clinical Indications for Using Blue-M: Gingivitis, periodontitis, periodontal abscess, pericoronitis, periimplantitis, implant treatment and maintenance, halitosis, flap surgeries, endodontic treatments, after tooth extraction, oralmucositis, aphthous ulcer, wound healing, xerostomia.

The products available are Blue M oral gel, mouthwash, fluoridated/non fluoridated toothpaste, mouth spray, oxygen fluid.

Conclusion

Research has shown that nearly all processes in illness can be linked to oxygen deficiency. If we look at the oxygen saturation (pO2 values) of infected or damaged tissue, we find that these values are much lower than they would be in a situation of health. Long-term insufficiency of oxygen saturation will put tissue in what is known as a chronic phase, and no healing is possible thereafter.

The importance of oxygen to the body has long been known, and so oxygen therapy is often practiced nowadays.

Long-term studies on this product can have effective and non-toxic effect on addressing multifactorial infective conditions, without developing resistance to microorganisms unlike antibiotics and can help in accelerating healing process in future practices.

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References

1. Carrico TJ, Mehrhof Jr AI, Cohen IK. Biology of wound healing. Surgical Clinics of North America. 1984;64(4):721-33.
2. Fernandez y Mostajo M, van der Reijden WA, Buijs MJ, Beertsen W, van der Weijden F, Crielaard W, et al. Effect of an oxygenating agent on oral bacteria in vitro and on dental plaque composition in healthy young adults. Frontiers in cellular and infection microbiology. 2014;4:95.
3. Roy S, Khanna S, Nallu K, Hunt TK, Sen CK. Dermal wound healing is subject to redox control. Molecular therapy. 2006;13(1):211-20.
4. Eisenbud DE. Oxygen in wound healing: nutrient, antibiotic, signaling molecule, and therapeutic agent. Clinics in plastic surgery. 2012;39(3):293-310.

5. Cho M, Hunt TK, Hussain MZ. Hydrogen peroxide stimulates macrophage vascular endothelial growth factor release. American Journal of physiology-heart and circulatory physiology. 2001;280(5):H2357-H63.
6. Dalton SJ, Whiting CV, Bailey JR, Mitchell DC, Tarlton JF. Mechanisms of chronic skin ulceration linking lactate, transforming growth factor-β, vascular endothelial growth factor, collagen remodeling, collagen stability, and defective angiogenesis. Journal of investigative dermatology. 2007;127(4):958-68.
7. Hyslop PA, Hinshaw DB, Scraufstatter IU, Cochrane CG, Kunz S, Vosbeck K. Hydrogen peroxide as a potent bacteriostatic antibiotic: implications for host defense. Free Radical Biology and Medicine. 1995;19(1):31-7.
8. Majtan J. Honey: an immunomodulator in wound healing. Wound Repair and Regeneration. 2014; 22(2):187-92.
9. Lévesque DCM. In vitro evaluation of antimicrobial activity of BlueM mouthwash: a pilot study. . Microbiological report. 2018 January 24, 2018. Report No.
10. BROWN JP, DODDS MW. Prevention strategies for dental caries. Prevention in clinical oral health care: Elsevier; 2008. p. 196-212.
11. Osso D, Kanani N. Antiseptic mouth rinses: an update on comparative effectiveness, risks and recommendations. American Dental Hygienists' Association. 2013;87(1):10-8.
12. Naot D, Grey A, Reid IR, Cornish J. Lactoferrin–a novel bone growth factor. Clinical Medicine & Research. 2005;3(2):93-101.
13. Cornish J. Lactoferrin promotes bone growth. Biometals. 2004;17(3):331-5.