

THE EFFECTS OF NBF GINGIVAL GEL IN THE TREATMENT OF RECURRENT ORAL ULCERS: CASE REPORT

Popovska Mirjana^{1*}, Fidovski Jasmin², Radojkova- Nikolovska Vera¹, Dimova Cena³,
Popovska Lidija¹, Mijoska Aneta¹, Toseva-Spasovska Natasa¹, Dzipunova Biljana¹

1. Professor, University Cyril and Methodius, Faculty of dentistry, Skopje, Republic of Macedonia.
2. MD, PHI "Fjola Medica", Republic of Macedonia.
3. Assoc. Professor, University Cyril and Methodius, Faculty of dentistry, Skopje, Republic of Macedonia.
4. Professor, University Goce Delcev Stip, Faculty of dentistry, Republic of Macedonia,
1. Professor, University Cyril and Methodius, Faculty of dentistry, Skopje, Republic of Macedonia.
1. Assoc. Professor, University Cyril and Methodius, Faculty of dentistry, Skopje, Republic of Macedonia.
1. Assoc. Prof, University Ss. Cyril and Methodius, Faculty of dentistry, Skopje, Republic of Macedonia.
1. Assoc. Prof, University Ss. Cyril and Methodius, Faculty of dentistry, Skopje, Republic of Macedonia.

Abstract

Patient reported that during the last three years, he had sores appeared on the lips, tongue and cheeks, 2-3 times annually, with severe pain emphasized while taking food, inability to speak normally, and difficulties maintain daily oral hygiene. Clinical examination of oral mucosa showed presence of three lesions, two on buccal mucosa and one on the tongue. The aphthae laid on inflamed and edematous surface, had irregular edges, steep bloody sides and milky white covering. Wide hyperemic ring was presented around ulcerated area. The patient applied topically, NBF gingival gel three times daily after meals, prior rinsing with 12% Chlorhexidine gluconate. Initial improvements were recorded after 7 days of treatment, and after two weeks of gel application significant improvement was noted. There was withdrawal of infiltration and edema, mild epithelization of damaged epithelium with present erythematous base. The pain was moderate, but the problem of maintaining oral hygiene and nutrition was still present. The erythematous area was evidently decreased and epithelization was visibly advanced after the second week. The dimensions of the ulcers was decreased, with depth reduced two times. After the third week ulceration epithelized, but slight redness was still present. Complete withdrew happened after week four.

Case report, Review (J Int Dent Med Res 2016; 9: (1), pp. 81-85)

Keywords: Recurrent aphthae's ulcer, therapy, topical treatment, NBF gingival gel.

Received date: 11 March 2016

Accept date: 28 March 2016

Introduction

Aphthae are ulcerated lesions that look like an erosion, disrupting the epithelial continuity, located in the connective tissue, and appearing on mucosal surfaces⁽¹⁾. Recurrent aphthae lesions are small, round or oval ulcers with erythematous halo and yellow or dirty white

covering⁽²⁻⁴⁾, with the exception of Sutton sores which are large, irregular and infiltrated.

The reasons for their appearance are: allergy, stress, hematologic, gastrointestinal, rheumatic diseases, infectious agents, nutritional deficiencies, genetic predisposition, hormones etc^(5,6).

These factors have direct or indirect impact on the balance of oxidative and antioxidant system. The creation and release of free radicals can be accelerated, and toxic reactions may occur when this balance is disrupted^(7,8). It is possible link between the level of free radicals and recurrent oral lesions⁽⁹⁾, because the role of antioxidants is important in maintaining oral health⁽¹⁰⁾. The treatment of recurrent aphthous ulcers is mainly local (if there

*Corresponding author:

Mirjana Popovska,
Majka Tereza bb 1000 Skopje, Republic of Macedonia.
Tel. +389 2 3299-038

E-mail: popovskam2002@yahoo.com

is not systemic reason), or in terms of systemic factors, local treatment is required in addition to the primary therapy. The choice would be a preparation with anti-inflammatory and antioxidants⁽¹¹⁻¹⁴⁾.

Antioxidants control oxidative stress in wound, healing and accelerate the process of healing⁽¹⁵⁻¹⁹⁾, and products like NBF gingival gel (NanoCureTech, Inc, Korea), based on nanotechnology with antioxidants, may be excellent adjuvant in the healing of oral lesions. NBF gel contains propolis, vitamin C and vitamin E in the form of nano emulsion.

Case Report

Male patient age 18, was admitted at the Department of oral pathology and periodontology at Dental Clinical Centre "Ss. Panteleimon" in Skopje. Patient disease history revealed appearance of sores at the lips, tongue and cheeks, 2-3 times per year, during last three years. The patient complained of severe pain, emphasized by taking food, inability to speak normally and maintain oral hygiene. Anamnesis said there were frequent problems with the stomach, bloating, belching and sour taste. He denied examination at gastroenterohepatologist, endoscopic examination of H. Pylori with CLO-test or serological determination of IgG antibody titer.

Clinical examination of the oral mucosa showed presence of three lesions, two erosions at buccal mucosa and one ulcer on the side of the tongue. Ulcer was localized unilaterally at left lingual region, 1 cm width, 1.5 cm. long and 0.5 cm deep. Aphthae laid on inflamed, edematous and infiltrated surface, edges were irregular, with steep bloody sides, covered with a milky white covering. Around ulcerated area wide hyperemic ring was present (Fig.1).

Clinical diagnosis and history of the disease were in the interest of Sutton's aphthae. Positivity was defined by applying CLO-test in saliva (Gastrex, Poland) (Fig.2).

CLO test or rapid urease test (Campylobacter Like-organism test) was applied, as a quick diagnostic test for *Helicobacter pylori* in saliva. *H. pylori* secretes the enzyme urease, which catalyzes the conversion of urea to ammonia and carbon dioxide. Detection is implemented directly, by changing the color of the sample from yellow to red.



Figure 1. Sutton's aphthae in left lateral area of tongue.



Figure 2. A positive finding of H. Pylori at patient.

The yellow color is a negative finding, a positive assessment are done using four different shades of red color from light pink to red. In all cases, red finding was positive. Assessment of positivity of *H. Pylori* was performed one hour after the procedure for the determination. Controls were conducted three times a week, in first three weeks, once a week, and in fourth week. The patient was suggested to begin with topical application of NBF gingival gel three times daily after meals (after breakfast, lunch, and dinner), prior rinsing with 0.12% Chlorhexidine gluconate. The patient was asked not to take food or drink in the next 20 minutes, and the gel was protected with sterile gauze (Fig.3).

After 7 days of treatment initial improvements were recorded, and after two weeks of NBF gingival gel application significant improvement were noted. Clinical monitoring after the seventh day showed withdrawal of edema and infiltration, with initial signs of mild epithelization of damaged epithelium, but erythematous base was still present.

The patient had moderate pain, but problems with oral hygiene and nutrition remained. After the second week erythematous area was evidently decreased and epithelization was visibly advanced. Painful sensations were present only after meal with significantly reduced intensity. The dimension of the ulcers was decreased, the width of the ulcers was less than 0.5 mm and 0.8 mm length. After the third week ulceration of oral mucosa was healed, but slight redness was still present, and completely withdraw after the fourth week. Ulcer was completely healed without signs of inflammation and infiltration, and the patient had no complaints, speech and nutrition were normalized.



Figure 3. Application of NBF gingival gel.

Discussion

The etiology of recurrent aphthae stomatitis is unknown, so treating aphthous lesions cover modalities with main purpose to relieve the symptoms^(20, 21). Topically applied preparations as fats, pastes, creams or rinses have a regenerative potential, especially desirable in the treatment of ulcers^(22, 23). Current treatment options include topical application of analgesics, antiseptics, corticosteroids, antibiotics, multivitamins, cauterization, various combined techniques⁽²⁴⁾ and even application of low energy lasers⁽²⁵⁻²⁸⁾. In recent years, products based on nanotechnology were presented on the market. They possess bio-adhesive power and contain antioxidants, and can be used as adjuvant in healing of the oral mucosal lesions.

Such a product is NBF gingival gel which contains vitamin C, vitamin E and propolis in the form of nano-emulsion. In this case report we followed a Sutton-aphthae and its healing after topical application of NBF gingival gel. Reduced painful symptoms facilitated chewing and complete epithelization period of four weeks is considered as fairly satisfactory findings. Usually, Sutton's aphthae with presented size is recovering over a period of 6-7 weeks with all known drugs. With application of NBF gingival gel, improvements were observed after the 7th day of treatment. The withdrawal of edema and infiltration, initial signs of mild epithelization, and existing erythematous base were evident. After two weeks of NBF gingival gel application, significant improvement was observed, redness area was evidently decreased and epithelization was visibly advanced. The dimensions of the ulcers were corrected, it was 0.5 cm wide, and length was 0.8 cm and depth about 0.2 cm.

During the third week of treatment there was complete epithelization with slight hyperemic halo, which withdrew after the fourth week. The topical application of NBF gingival gel enabled local clinical effects without the possibility the drug to be vainly distributed or lost throughout the body⁽²⁹⁾. Moghaddamnia et al.⁽³⁰⁾ reported that mucous-adhesive pastes significantly reduce the pain of recurrent aphthous stomatitis. In this regard Martin⁽³¹⁾ recorded a significant decline in the size of the lesion eight days after treatment with mucous-adhesive preparation of herbal origin, and Quinn⁽³²⁾ came to identical clinical findings. Recently, the results of some studies, revealed that the application of certain adhesives reduce pain and shorten the treatment of aphthous stomatitis⁽³³⁻³⁵⁾.

It has been proven that most pathological lesions appear due to the imbalance between the antioxidants and oxidants, caused by multiple heterogeneous causes. The reactive free radicals which are released, are reactive oxygen radicals present in all biological systems. Oxidative stress occurs when the intracellular concentration of free radicals will increase beyond physiological values which lead to cell damage by lipid peroxidation, DNA and many other pro-inflammatory cytokine factors⁽³⁶⁻³⁷⁾.

ROS and anti-oxidative imbalance can play a central role in the emergence and development of recurrent aphthous ulceration⁽³⁸⁻³⁹⁾. Indeed, antioxidant defense systems are very complex

and debatable point is an estimation of the quantity and activity of different antioxidants *in vivo*, in assessment of overall antioxidant status⁽⁴⁰⁾.

NBF gingival gel is a first product containing nano antioxidants, and is manufactured with nano bio-fusion technology. It contains three biocompatible ingredients in nano-emulsion form with antibacterial, anti-inflammatory and antioxidant effects. Vitamin C is very strong antioxidant, vitamin E acts synergistically with vitamin C and participate in healing of the oral mucosa, and propolis whose main ingredient is flavonoids. The clinical findings are based on the composition of the NBF gingival gel - vitamin C, E, and propolis. Vitamin C stimulates phagocyte activation and has a direct role in defending the body⁽⁴¹⁾.

It is a cofactor for at least eight enzyme reactions involved in collagen synthesis and directly participates in the healing of lesions. Nano vitamin C molecule within the gel is twice smaller, 110 times more potent in the synthesis of collagen vs. regular vitamin C, and it is eliminated easily, faster and more efficiently. Propolis has several components essential for the process of healing: antioxidant potential, biocompatibility, antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory properties⁽⁴²⁻⁴⁴⁾.

Conclusions

One of the important components, on which is due the success achieved after topical application of NBF gingival gel is adhesiveness. Propolis provides a very good adhesion, and the nano-emulsion possesses lower surface tension due to the small size of the molecules of the vitamin that cause rapid absorption through the mucosa in the target cells. It can be concluded that the topical application of NBF gingival gel on the recurrent aphthous ulcers demonstrated positive clinical effects on epithelization process and subjective symptoms.

Declaration of Interest

The authors report no conflict of interest and the article is not funded or supported by any research grant.

References

1. Riera Matute G, Riera Alonso E. Recurrent aphthous stomatitis in Rheumatology. *Reumatol Clin*. 2011 Sep-Oct;7(5):323-8.
2. Caglayan F, Miloglu O, Altun O, Erel O, Yilmaz AB. Oxidative stress and myeloperoxidase levels in saliva of patients with recurrent aphthous stomatitis. *Oral Dis* 2008; 14: 700-704.
3. Momen-Beitollahi J, Mansourian A, Momen-Heravi F, Amanlou M, Obradov S, Sahebamee M. Assessment of salivary and serum antioxidant status in patients with recurrent aphthous stomatitis. *Med Oral Patol Oral Cir Bucal* 2010; 15: e557-e561, doi: 10.4317/medoral.15.e557.
4. Akoglu G, Metin A, Kilinc F, Pektas SD, Isikoglu S, Akbas A, et al. Total serum oxidant/antioxidant status and arylester-ase activity in recurrent aphthous stomatitis. *Ann Dermatol* 2013; 25: 273-277.
5. Scully C. Clinical practice. Aphthous ulceration. *N Engl J Med*. 2006 Jul 13;355(2):165-72.
6. Al-Omiri MK, Karasneh J, Alhijawi MM, Zwiri AM, Scully C, Lynch E. Recurrent aphthous stomatitis (RAS): a preliminary within-subject study of quality of life, oral health impacts and personality profiles. *J Oral Pathol Med*. 2015 Apr;44(4):278-83.
7. Boras VV, Lukac J, Brailo V, Picek P, Kordic D, Zilic IA. Salivary interleukin-6 and tumor necrosis factor-alpha in patients with recurrent aphthous ulceration. *J Oral Pathol Med* 2006; 35: 241-243. 5.
8. Eguia-del Valle A, Martinez-Conde-Llamosas R, Lopez- Vicente J, Uribarri-Etxebarria A, Aguirre-Urizar JM. Salivary levels of tumour necrosis factor-alpha in patients with recurrent aphthous stomatitis. *Med Oral Patol Oral Cir Bucal* 2011; 16: e33-e36.
9. Avci E, Akarslan ZZ, Erten H, Coskun-Cevher S. Oxidative stress and cellular immunity in patients with recurrent aphthous ulcers. *Braz J Med Biol Res*. 2014 May; 47(5):355-60.
10. Niki E. Antioxidant capacity: Which capacity and how to assess it? *J Berry Res* 2012; 1: 169-176.
11. Mossalayi MD, Rambert J, Renouf E, Micoulet M, Mérillon JM. Grape polyphenols and propolis mixture inhibits inflammatory mediator release from human leukocytes and reduces clinical scores in experimental arthritis. *Phytomedicine*. 2014; 21:290-7.
12. Miguel MG, Antunes MD. Is propolis safe as an alternative medicine? *J Pharm Bioallied Sci*. 2011; 3:479-95.
13. Dodwad V, Kukreja BJ. Propolis mouthwash: A new beginning. *J Indian Soc Periodontol*. 2011; 15:121-5.
14. Miguel MG, Antunes MD. Is propolis safe as an alternative medicine? *J Pharm Bioallied Sci*. 2011; 3:479-95.
15. Gómez-Caravaca AM, Gómez-Romero M, Arráez-Román D, Segura-Carretero A, Fernández-Gutiérrez A. Advances in the analysis of phenolic compounds in products derived from bees. *J Pharm Biomed Anal*. 2006; 41: 1220-34.
16. Almas K, Mahmoud A, Dahlan A. A comparative study of propolis and saline application on human dentin. A SEM study. *Indian J Dent Res*. 2001; 12: 21-7.
17. Parolia A, Thomas M, Kundabala M, Mohan M. Propolis and its potential uses in oral health. *Int J Med Sci*. 2010; 2:210-5.
18. Abdulrhman M, El Barbary NS, Ahmed Amin D, Saeid Ebrahim R. Honey and a mixture of honey, beeswax and oliveoil-propolis extract in treatment of chemotherapy induced oral mucositis: A randomized controlled pilot study. *Pediatr Hematol Oncol*. 2012; 29:285-92.
19. Kuo YY, Lin HP, Huo C, Su LC, Yang J, Hsiao PH, et al. Caffeic acid phenethyl ester suppresses proliferation and survival of TW2.6 human oral cancer cells via inhibition of akt signaling. *Int J Mol Sci*. 2013; 14:8801-17.
20. Convissar R. A., Massoumi-Sourey M. Recurrent aphthous ulcers: etiology and laser ablation. *General dentistry*. 1992; 40(6):512-515. [PubMed]
21. Haghpanah P, Moghadamnia AA, Zarghami A, Motallebnejad M. Muco-bioadhesive containing *ginger officinale* extract in the management of recurrent aphthous stomatitis: A randomized clinical study. *Caspian J Intern Med*. 2015 winter; 6(1): 3-8.
22. Burgess JA, Johnson BD, Sommers E. Pharmacological management of recurrent oral mucosal ulceration. *Drugs*. 1990; 39:54-65. [PubMed]

23. Natah SS, Konttinen YT, Enattah NS, et al. Recurrent aphthous ulcers today: a review of the growing knowledge. *Int J Oral Maxillofac Surg.* 2004; 33:221–34. [PubMed]
24. Aggarwal H, Pal Singh M, Nahar P, Mathur H, Sowmya G. V. Efficacy of low-level laser therapy in treatment of recurrent aphthous ulcers—a sham controlled, split mouth follow up study. *Journal of Clinical and Diagnostic Research.* 2014; 8(2):218–221.
25. Vale FA, Moreira MS, Souza de Almeida FC, Ramalho KM. Low-Level Laser Therapy in the Treatment of Recurrent Aphthous Ulcers: A Systematic Review. *Scientific World Journal.* 2015; 2015: 150412.
26. von Ahlften U. Erfahrungen bei der Behandlung aphthoser und herpetiformer Mund-schleimhautrekrankungen mit einem neuen Infrarotlaser. *Quintessenz.* 1987; 38(5):927–932.
27. Salamat-Miller N, Chittchang M, Johnston TP. The use of mucoadhesive polymers in buccal drug delivery. *Adv Drug Deliv Rev.* 2005; 57:1666–91. [PubMed]
28. Sudhakar Y, Kuotsu K, Bandyopadhyay AK. Buccal bioadhesive drug delivery—a promising option for orally less efficient drugs. *J Control Release.* 2006; 114:15–40. [PubMed]
29. Mishra SS, Maheshwari T. NU. Local drug delivery in the treatment of oral lichen planus: A systematic review. *Int J Pharm Bio Sci.* 2014; 5:716–21.
30. Moghadamnia AA, Motalebnejad M, Khanian M. The efficacy of the bioadhesive patches containing licorice extract in the management of recurrent aphthous stomatitis. *Phytother Res.* 2009; 23:246–50.
31. Martin MD, Sherman J, van der Ven P, Burgess J. A controlled trial of a dissolving oral patch concerning glycyrrhiza (licorice) herbal extract for the treatment of aphthous ulcers. *Gen Dent.* 2008; 56:206–10.
32. Quinn J, Wells G, Sutcliffe T, et al. A randomized trial comparing octylcyanoacrylate tissue adhesive and sutures in the management of lacerations. *JAMA.* 1997; 277:1527–30
33. Jasmin JR, Muller-Giamarchi M, Jonesco-Benaiche N. Local treatment of minor aphthous ulceration in children. *ASDC J Dent child.* 1999; 60:26–8. [PubMed]
34. Kutcher MJ, Ludlow JB, Samuelson AD, Campbell T, Pusek SN. Evaluation of a bioadhesive device for the management of aphthous ulcers. *J Am Dent Assoc.* 2001; 132:368–76. [PubMed]
35. Ludlow JB, Kutcher MJ, Samuelson A. Intraoral digital imaging documenting recurrent aphthous ulcer healing in 2-octyl cyanoacrylate versus sham-treated lesions. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2000; 89:425–31. [PubMed]
36. Momen-Beitollahi J, Mansourian A, Momen-Heravi F, Amanlou M, Obradov S, Sahebamee M. Assessment of salivary and serum antioxidant status in patients with recurrent aphthous stomatitis. *Med Oral Patol Oral Cir Bucal.* 2010; 15:e557–e561.
37. Chapple IL, Brock G, Eftimiadi C, Matthews JB. Glutathione in gingival crevicular fluid and its relation to local antioxidant capacity in periodontal health and disease. *Mol Pathol.* 2002; 55:367–373.
38. Sezer E, Ozugurlu F, Ozyurt H, Sahin S, Etikan I. Lipid peroxidation and antioxidant status in lichen planus. *Clin Exp Dermatol.* 2007; 32:430–434.
39. Aly DG, Shahin RS. Oxidative stress in lichen planus. *Acta Dermatovenerol Alp Pannonica Adriat.* 2010; 19:3–11.
40. Alfadda AA, Sallam RM. Reactive oxygen species in health and disease. *J Biomed Biotechnol.* 2012; 2012:936486.
41. Akhilender NK. Vitamin C in human health and disease is still a mystery? An overview. *Nutrition Journal* 2003; 2:7.
42. Krol W, Czuba Z, Scheller S, Gabrys J, Grabiec S, Shani J. Anti-oxidant property of ethanolic extract of propolis (EEP) as evaluated by inhibiting the chemiluminescence oxidation of luminol. *Biochem Int.* 1990; 21(4):593-7.
43. Bankova V, Christov R, Kujumgiev A, Marcucci MC, Popov S. Chemical composition and antibacterial activity of Brazilian propolis. *Z Naturforsch C.* 1995 Mar-Apr; 50(3-4):167-72.
44. Sforcin JM, Orsi RO, Bankova V. Effect of propolis, some isolated compounds and its source plant on antibody production. *J Ethnopharmacol.* 2005 Apr 26; 98(3):301-5.