Topical Sesame Oil for Severe Corneal Alkali Burn in Rabbits

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Abstract

***Purpose*:** To evaluate the effects of topical sesame oil in the treatment of severe corneal alkali injury in rabbits

***Methods*:** In a double-blind experiment, 30 healthy white rabbits were randomized into a sesame oil treatment group (n=15) and a control group (n=15). Under general anesthesia, severe corneal alkali injuries were induced by application of 1 N sodium hydroxide for 40 seconds to the right eye of each rabbit. The sesame oil group was treated with sesame oil drops 4 times daily for 1 month. Both groups received chloramphenicol eye drops, 4 times daily. Daily examination with fluorescein staining and photography were performed, and details of corneal erosion and ulceration were recorded. The main outcome measure was descemetocele and perforation of the cornea. The animals were euthanized at the end of the study or earlier if corneal perforation had occurred, and the corneas were excised and fixed in 10% neutral-buffered formalin for histologic examination.

***Results*:** Mean time to perforation in sesame oil group was longer than control group (29.6 versus 25.5 days, respectively; P=0.01). Four eyes in sesame oil group and 8 eyes in control group developed descemetocele and perforation (P=0.13). Extent of corneal vascularization was 66.6% in sesame oil group and 49.3% in control group (P= 0.065).

***Conclusion*:** Topical sesame oil seems to have beneficial effects on alkali-injured corneas. It delays corneal perforation in rabbits compared to control group.

***Keywords*:** Sesame Oil, Corneal Alkali Burn, Corneal Perforation

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Introduction

Chemical burns are one of the true ophthalmic emergencies which can lead to permanent and complete visual disability. Alkaline agents in particular produce the most severe burns by penetrating deep into the corneal tissue and even the whole anterior segment of the eye. Immediate, prolonged irrigation, as the first step of management is used to decrease the extent of damage.[1-3]

Several studies have evaluated the efficacy of different medical and surgical interventions in severe ocular burns. Topical antibiotics and steroids,[4] topical and systemic ascorbate,[5] citrate,[6] tetracycline,[7] amniotic membrane transplantation,[8] and oxygen therapy[9,10] have been used and described in the literature.

Sesame seeds contain compounds collectively known as lignans. Sesamin and sesamolin are fat-soluble lignans present in sesame seeds and their oil.[11]

Sesamin has been reported to have antihypertensive and antioxidative properties[12-14] and anti-inflammatory effects.[15]

Sesame oil derivatives have been successfully used as a topical disinfectant in several serious skin diseases.[16] Daily sesame oil attenuates oxidative stress-associated renal injury by reducing oxygen free radicals in gentamicin-treated rats.[17] Sesame oil has also shown beneficial effects on oxidative stress-induced biochemical changes in arthritis.[18] When given topically, it might attenuate oxidative stress by inhibiting the production of xanthine oxidase and nitric oxide in rats.[19] It may also increase collagen synthesis.[18]

Considering the antioxidant and anti-inflammatory effects of sesame oil and the increase in collagen synthesis which it may cause, we conducted a study to evaluate the effects of topical sesame oil in the treatment of severe corneal alkali burn in rabbits.

Methods

This study was performed at animal research center and in accordance with the guidelines for the care and use of laboratory animals.

Since no ocular preparation is available for sesame oil, we performed a pilot study to investigate any potential side effects and ocular toxicity of topical preparation of sesame oil. Four rabbits (2 from each group) received 100% pure sesame oil drops (Barij Essence, Kashan, Iran) in their left eye four times a day for 1 month and no toxicity or reaction was seen.

To induce severe corneal alkali burn we used a Plexiglas cylinder covering the entire cornea and adjacent limbus filled with sodium hydroxide. (Figure 1) Previously, it was shown that this method is superior to placing 12-mm filter paper discs soaked in sodium hydroxide on the cornea in that it produces a uniform total corneal injury also including 1 mm of the adjacent limbus.[9] Twelve-mm filter paper discs do not cover the entire corneal surface and they produce a less uniform injury because of placing a flat disc on the curved surface of the cornea. The internal diameter of the Plexiglas cylinder was 15 mm. The palpebral fissure of the rabbit did not allow a larger cylinder to produce more extensive ischemia.

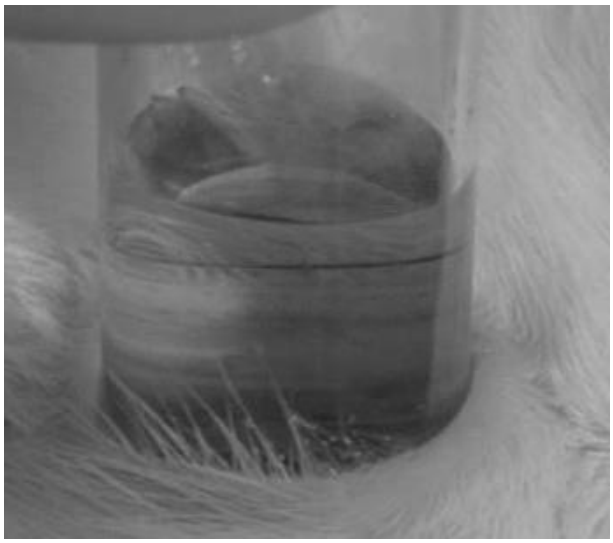

Figure 1. Inducing corneal alkali burn using a Plexiglas cylinder covering the entire cornea and adjacent limbus filled with sodium hydroxide

In this double-blind experimental study, 30 healthy New Zealand albino rabbits underwent general anesthesia using ketamine 35 mg/kg and xylazine 5 mg/kg. Severe corneal alkali injuries were then induced by application of 1 N sodium hydroxide for 40 seconds to the right eye of each rabbit with a Plexiglas cylinder covering the entire cornea and adjacent limbus. After exposure, the alkali was removed in one step with a syringe, and immediate irrigation was done with 500 ml of Lactated Ringer solution.

The rabbits were randomly divided into a control group (n=15) and a sesame oil treatment group (n=15). Both groups received chloramphenicol eye drops 4 times a day. The sesame oil group was additionally treated with sesame oil drops, 4 times a day for 1 month.

Daily corneal examination with use of fluorescein staining and photography from the rabbits' eyes were performed, and details of corneal epithelial defect and ulceration, beginning of ulceration and perforation, beginning of corneal vascularization and extent of vascularization in degrees were recorded.

Corneal opacity was graded based on Herretes et al study[20] according to visibility of iris and pupil.

All the images were processed and analyzed by two independent blinded observers to the treatment. The areas of corneal epithelial defect and corneal vascularization were outlined with digital imaging software and the corneal epithelial defect and corneal vascularization were calculated as a percentage of the total corneal area by Matlab software version 7.12 (R2011a, New Mexico).

The principal endpoint was descemetocele and perforation of the cornea. The animals were euthanized at the end of the study or earlier if corneal perforation had occurred, and the corneas were excised and fixed in 10% neutral-buffered formalin for histologic examination.

Data were analyzed using SPSS version 16 (SPSS, Chicago, IL) with independent t-test and χ^2 test. P<0.05 was considered as significant.

Results

Experimentally induced severe eye burns gave similar opacity (Grade C) of the cornea in both groups (Figure 2). Table 1 compares corneal changes between the two groups. Sesame oil group showed better results compared to control group in terms of total number of perforation and ulceration, mean time to beginning of perforation and ulceration, extent of vascularization and epithelial defect of the cornea. However, the difference was statistically significant only for mean time to perforation (P=0.01).

Additionally, 6 eyes in sesame oil group and 8 eyes in control group developed deep stromal ulcer (P=0.46). Histological evaluation confirmed clinical ulceration and perforation.

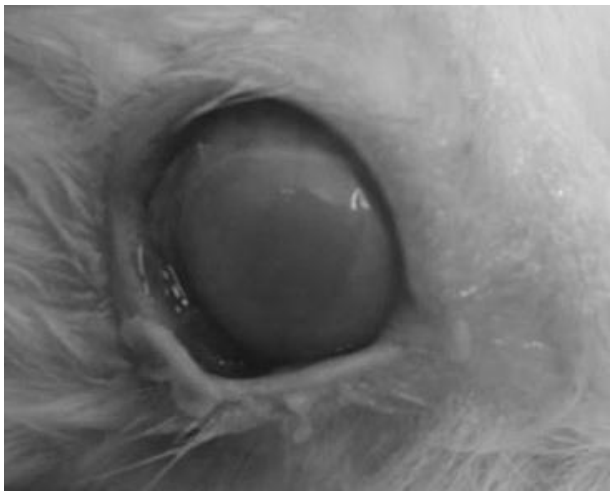

Figure 2. Total corneal clouding immediately after experimentally induced severe alkali injury

Table 1. Comparison of corneal changes between sesame oil and control groups after severe corneal alkali injury

Group	Perforation time*	Beginning of ulceration*	Beginning of Vascularization*	Extent of Vascularization†	Degrees of Vascularization	Epithelial defect†	Perforation	Ulcer
Sesame oil	29.6±1.5	24.2±6.8	6.3±2	66.6±18.4	272.6±59.3	12.6±11.4	4	6
control	25.5±5.5	22.3±8.8	8.6±6.4	49.3±29.3	224±106.2	16.7±8.6	8	8
95% CI of the difference	1 – 7	-4 – 7.9	-5.9 – 1.2	-1 – 35.6	-15.7 – 113	-11.7 – 3.5	-0.6 – 0.06	-0.48 – 0.21
P	0.01	0.51	0.19	0.065	0.13	0.27	0.13	0.48

*: Days after injury
†: Measured as percent of corneal surface at the end of study

Discussion

This study showed that sesame oil may have some beneficial effects in treating corneal alkali burns especially in delaying corneal perforation.

In alkali-injured cornea, inflammatory mediators are released which are chemotactic to neutrophils. These in turn release leukotrienes which exacerbate inflammation. Additionally, alkali injury of collagen releases inflammatory mediators that stimulate neutrophils to undergo respiratory burst. This results in production of oxygen free radicals that are highly destructive of tissues finally leading to corneal ulceration and perforation.[21]

Sesamin, a lignan present in sesame oil, has shown antihypertensive and antioxidative properties in several studies,[12-14] and also an inhibitory effect on secretion of interleukin 8 (IL8) and Endothelin-1 (proinflammatory factors).[15] Additionally, it may increase collagen synthesis.[18]

Other reported effects of sesame seed lignans include inter alias modulation of fatty acid metabolism, inhibition of cholesterol absorption and biosynthesis, antioxidant and vitamin E-sparing effects, hypotensive effects, improvement of liver functions in connection with alcohol metabolism, and anti-aging effects.[22] It has also been used as a topical disinfectant in several serious skin diseases.[16]

Hsu et al showed that daily sesame oil supplement attenuates oxidative stress-associated renal injury by reducing oxygen free radicals and lipid peroxidation in gentamicin-treated rats.[17] In another study by Sotnikova et al sesame oil showed beneficial effects on oxidative stress-induced biochemical changes in arthritis.[18] Kapadia et al showed that sesame oil has anti-cancer potentials and profound free radical scavenging activity and anti-oxidant capability that acts as chemopreventive agent in reducing skin cancer.[23] In a study by Yamada et al sesamin enhanced tocotrienol effects in reducing UVB-induced skin damage in mice.[24] Additionally, sesame oil consumption beneficially affects blood glucose, glycosylated hemoglobin, lipid peroxidation, and antioxidant levels in diabetic rats.[25] Chiang et al showed that topical sesame oil might attenuate oxidative stress in rats.[19] In another study by Valacchi et al, they reported the efficacy of ozonated sesame oil in cutaneous wound healing in mice.[26]

To the best of our knowledge this is the first study evaluating the effects of topical sesame oil on severe alkali burn of cornea in an animal model. Our study showed that topical sesame oil can delay perforation of cornea (29.6 days in sesame oil group versus 25.5 days in control group; P=0.01). Although in this study sesame oil group showed better results in terms of other study variables as well, e.g. perforation occurred twice as frequent in control group as in sesame oil group (8 versus 4 eyes, respectively; P=0.13), the difference failed to reach the significance level. We assumed that it may be due to small sample size.

A major shortcoming of our study is that there is no ocular preparation for sesame oil and we used topical preparation instead. However, the pilot study on uninjured rabbit eyes showed no ocular toxicity.

The beneficial effects of sesame oil for severe corneal alkali burns in rabbits and the absence of side effects warrant more studies with larger sample size and ocular preparations.

Conclusion

In this study on alkali-injured corneas, we observed better results with topical sesame oil compared to control group, specially in terms of delaying corneal perforation.

References

1. Merle H, Gérard M, Schrage N. [Ocular burns]. J Fr Ophtalmol 2008;31(7):723-34.
2. Hodge C, Lawless M. Ocular emergencies. Aust Fam Physician 2008;37(7):506-9.
3. Spector J, Fernandez WG. Chemical, thermal, and biological ocular exposures. Emerg Med Clin North Am 2008;26(1):126-36.
4. Scuta GL, Cantor LB, Weiss JS, eds. Basic and Clinical Science Course: external diseases and cornea. Singapore: American Academy of Ophthalmology; 2010-2011:355-8.

5. Pfister RR, Paterson CA. Additional clinical and morphological observations on the favorable effect of ascorbate in experimental ocular alkali burns. Invest Ophthalmol Vis Sci 1977;16(6):478-87.
6. Pfister RR, Haddox J, Paterson CA. The efficacy of sodium citrate in the treatment of severe alkali burns of the eye is influenced by the route of administration. Cornea 1982;1:205-11.
7. Seedor JA, Perry HD, McNamara TF, et al. Systemic tetracycline treatment of alkali-induced corneal ulceration in rabbits. Arch Ophthalmol 1987;105(2):268-71.
8. Meller D, Pires RT, Mack RJ, et al. Amniotic membrane transplantation for acute chemical or thermal burns. Ophthalmology 2000;107(5):980-9.
9. Sharifipour F, Zamani M, Idani E, Hemmati AA. Oxygen therapy for severe corneal alkali burn in rabbits. Cornea 2007;26(9):1107-10.
10. Sharifipour F, Baradaran-Rafii A, Idani E, et al. Oxygen therapy for acute ocular chemical or thermal burns: a pilot study. Am J Ophthalmol 2011;151(5):823-8.
11. Ide T, Lim JS, Odbayar TO, Nakashima Y. Comparative study of sesame lignans (sesamin, episesamin and sesamolin) affecting gene expression profile and fatty acid oxidation in rat liver. J Nutr Sci Vitaminol (Tokyo) 2009;55(1):31-43.
12. Guillén MD, Ruiz A. Formation of hydroperoxy- and hydroxyalkenals during thermal oxidative degradation of sesame oil monitored by proton NMR. Eur J Lipid Sci Tech 2004;106(10):680-7.
13. Yoshida H, Tanaka M, Tomiyama Y, Mizushina Y. Regional distribution in the fatty acids of triacylglycerols and phospholipids of sesame seeds (Sesamum indicum). J Food Lipids 2007;14(2):189-201.
14. Lee WJ, Ou HC, Wu CM, et al. Sesamin mitigates inflammation and oxidative stress in endothelial cells exposed to oxidized low-density lipoprotein. J Agric Food Chem 2009;57(23):11406-17.
15. Sirato-Yasumoto S, Katsuta M, Okuyama Y, et al. Effect of sesame seeds rich in sesamin and sesamolin on fatty acid oxidation in rat liver. J Agric Food Chem 2001;49(5):2647-51.
16. Zanardi I, Travagli V, Gabbrielli A, et al. Physico-chemical characterization of sesame oil derivatives. Lipids 2008;43(9):877-86.
17. Hsu DZ, Liu CT, Li YH, et al. Protective effect of daily sesame oil supplement on gentamicin-induced renal injury in rats. Shock 2010;33(1):88-92.
18. Sotnikova R, Ponist S, Navarova J, et al. Effects of sesame oil in the model of adjuvant arthritis. Neuro Endocrinol Lett 2009;30 Suppl 1:22-4.
19. Chiang JP, Hsu DZ, Tsai JC, et al. Effects of topical sesame oil on oxidative stress in rats. Altern Ther Health Med 2005;11(6):40-5.
20. Herretes S, Suwan-Apichon O, Pirouzmanesh A, et al. Use of topical human amniotic fluid in the treatment of acute ocular alkali injuries in mice. Am J Ophthalmol 2006;142(2):271-8.
21. Krachmer JH, Mannis MJ, Holland EJ, eds. Cornea. 3rd ed. Saint Louis: Mosby Elsevier Inc; 2010:1194-5.
22. Kamal-Eldin A, Moazzami A, Washi S. Sesame seed lignans: potent physiological modulators and possible ingredients in functional foods & nutraceuticals. Recent Pat Food Nutr Agric 2011;3(1):17-29.
23. Kapadia GJ, Azuine MA, Tokuda H, et al. Chemopreventive effect of resveratrol, sesamol, sesame oil and sunflower oil in the Epstein-Barr virus early antigen activation assay and the mouse skin two-stage carcinogenesis. Pharmacol Res 2002;45(6):499-505.
24. Yamada Y, Obayashi M, Ishikawa T, et al. Dietary tocotrienol reduces UVB-induced skin damage and sesamin enhances tocotrienol effects in hairless mice. J Nutr Sci Vitaminol (Tokyo) 2008;54(2):117-23.
25. Ramesh B, Saravanan R, Pugalendi KV. Influence of sesame oil on blood glucose, lipid peroxidation, and antioxidant status in streptozotocin diabetic rats. J Med Food 2005;8(3):377-81.
26. Valacchi G, Lim Y, Belmonte G, et al. Ozonated sesame oil enhances cutaneous wound healing in SKH1 mice. Wound Repair Regen 2011;19(1):107-15**.**