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EMERGENCY OXYGEN THERAPY FOR OCULAR CHEMICAL OR THERMAL BURNS IN TEHRAN CLINICS

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Purpose: To assessment the influence of systemic oxygen therapy in the management of acute ocular chemical or thermal burns.

Design: Nonrandomized, prospective, interventional case series, comparative.

Methods

Thirty-eight eyes of 38 patients with grade III to IV acute ocular chemical and thermal burns received conventional medical therapy. The oxygen therapy group (13 eyes) furthermore received 100% oxygen using a simple mask at a flow rate of 10 L/minute for 1 hour twice daily. Keyresult measures were time for curative of the corneal epithelial deficiency and enhancement in perilimbal ischemia. Secondary resultprocedures included visual acuity, vascularization and corneal transparency, and complications.

Results

Corneal epithelial faultsured within 13.28 ± 2.54 days (range, 11 to 25 days) in the oxygen group versus 61.5 ± 25.22 days (range, 29 to 85 days) in controls ($P < .001$). Vascularization of ischemic areas was complete in 13.46 ± 2.90 days (range, 10 to 21 days) in the oxygen group versus 48.09 ± 22.20 days (range, 25 to 105 days) in controls ($P = .001$). In the oxygen group, the cornea was more transparent and less vascularized 4 and 6 months after injury. Mean final visual acuity (logarithm of the minimal angle of resolution) was 0.30 ± 0.52 (range, 0 to 1.3) versus 1.22 ± 0.73 (range, 0.2 to 3) in the oxygen and control groups, respectively ($P = .028$). In the oxygen group, symblepharon or corneoscleral

sentimental did not progress in any patient; though, in the control group, symblepharon developed in 4 eyes and corneoscleral melting advanced in 1 patient.

Conclusions

In the acute phase of ocular chemical or thermal burns, oxygen therapy advances limbal ischemia, quickens epithelialization, proliferations corneal transparency, and reductions corneal vascularization. It also may progress visual intuition and reduce difficulties. Ocular chemical and thermal burns are true ophthalmic emergencies. The severity of the injury depends on the type of offending agent, its concentration, length of exposure, and extent of contact(1). Limbal stem cells, which are the source of corneal epithelial renewal, are believed to be the most important possible targets in acute chemical burns (1). The extent of limbal ischemia is measured to be the most vital predictive factor in defining final visual consequences in these cases (2, 3) Refining perilimbal ischemia and regulatory inflammation hypothetically can reservation partially damaged limbal stem cells. Promotion of epithelial healing, control of inflammation, and prevention of tissue melting are the chief objects in the management of acute ocular burns (4). Determined corneal epithelial faults may lead to tissue thinning or melting, perforation, and secondary infections. The de-epithelialized conjunctival exteriors tend to fuse and form symblepharon bands. Early conjunctival epithelial curative may avert this difficulty.

With current medical therapies, smooth and complete conjunctivalization and vascularization of the cornea, without eyelid and adnexal physical irregularities, are the optimum and satisfactory goals in severe ocular burns. The perfect condition would be complete corneal conjunctivalization with minimal vascularization of the cornea. Conservative medical therapies, including steroids, ascorbate(5,6) tetracyclines(7) citrates(6) lubricants, and surgical processes such as application of a glued-on hard tenoplasty(4) contact lens(8) amniotic membrane transplantation(9) have been used to attain these goals. The purpose of this study was to present universal oxygen therapy as an original therapeutic technique in the acute phase of ocular chemical and thermal burns. By reducing perilimbal ischemia and decreasing inflammation, this method of treatment may simplify epithelial healing and reservation in completely damaged limbal stem cells.

Methods

This forthcoming, relative, interventional case series was done in some of Tehran clinics, Tehran, Iran. We encompassed consecutive patients with grade III and IV acute ocular chemical or thermal burns. Patients referred to the second study

center served as the control group and received conventional medical therapy. The treatment group received general oxygen therapy in addition to conservative medical therapy on recommendation to the first study center, but no later than 4 weeks after injury. Oxygen was delivered at 100% concentration by a facemask with flow rate of 10 L/minute for 1 hour twice daily in the sitting position. The 4-week gap for giving oxygen was chosen randomly to include more cases. Omission standards involved presentation later than 4 weeks after injury, insufficient treatment before performance, history of ocular surgery or use of topical medications 1 month before injury, general immunosuppressive therapy, pregnancy, and contraindications to oxygen therapy, including chronic respiratory diseases such as chronic obstructive pulmonary disease. In the oxygen therapy group, potential compensations and risks of oxygen therapy were discussed thoroughly with the patients.

All patients had received ocular irrigation with 1 to 2 L lactated Ringer solution after the injury. Conservative medical therapy included topical steroids, antibiotics, cycloplegics, artificial tears lubricating, ointments, vitamin C 500 mg every 5 hours, and systemic tetracycline 250 mg every 6 hours tapered over 2 to 3 months according to the degree of ocular surface inflammation. All patients were recommended forcefully to perform eyelid blinking, physically to separate the eyelids from the ball, and frequently to perform ductions and versions to decrease the risk of symblepharon development. Irrigation of the ocular superficial with balanced salt solution was done 5 times daily to reduce ocular surface inflammation.

Fibrinous bands and membranes in the upper and lower fornices were detached by mild movement of the end of a thermometer at each follow-up visit. Patients in the oxygen therapy group were studied by a pulmonologist (E.I.) to rule out any contraindication to oxygen treatment. The chief result procedures were development of ischemia and healing of corneal epithelial deficiencies; secondary consequence measures included corneal transparency and vascularization, development of graphic insight, and problems.

Corneal transparency and vascularization were classified individually and autonomously from 1+ to 4+ by two inspectors 4 and 8 months after surgery. If the cornea was brutally opacified and iris particulars were not noticeable, it was categorized as 1+.

If the cornea was clear and iris minutiae were clearly discernible, transparency was sorted as 4+. If there was only 1 vascularized quadrant, vascularization was classified as 1+. If all 4 corneal quadrants were vascularized, it was classified

as 4+. For superior accuracy, both slit-lamp results and numerical corneal photographs were used for classifying. Mean gradings by the two inspectors were measured as the final grade.

Patients were visited daily throughout the first week, every other day during the second week, and twice weekly afterward until wholecurative. At each follow-up visit, a complete eye inspection was performed with singularcare to perilimbal ischemia and the extent of corneal and conjunctival epithelial deficiencies. Photographic documentation of slit-lamp results was accomplished once or twice weekly.

Results

Thirty-eight eyes of 38 patients (all male) were encompassed. Twenty eyes had chemical burns (14 alkaline and 6 acidic) and 18 had thermal burns. Thirteen eyes were included for oxygen therapy and 25 eyes served as controls. Mean age was 32.58 ± 16.29 years (range, 8 to 46 years) in the oxygen remedy and 34.3 ± 14.3 years (range, 21 to 49 years) in the control group ($P = .510$). Mean follow-up period was 16.0 ± 9.27 months (range, 6 to 44 months) in the oxygen group and 15.36 ± 8.33 months (range, 7 to 27 months) in the control group ($P = .834$). Oxygen therapy was started at a mean of 9.15 ± 6.81 days (range, 6 to 21 days) after injury.

Corneal epithelial defects healed within 15.43 ± 4.94 days (range, 12 to 21 days) after oxygen therapy versus 61.91 ± 21.33 days (range, 31 to 92 days) in the control group (95% confidence interval of the difference, -58.27 to -31.09 days; $P < .001$).

Vascularization of ischemic regions began 4 days after oxygen therapy. Vascularization was complete after 14.54 ± 3.70 days (range, 11 to 21 days) in the oxygen therapy group against 45.09 ± 20.20 days (range, 25 to 105 days) in the control group (95% confidence interval of the difference, -43.38 to -17.73 ; $P = .001$). Two and 6 months afterward the injury, corneal transparency was 2.7^+ versus 1.3^+ and 2.4^+ versus 1.2^+ in the oxygen therapy and control groups, correspondingly.

Conforming values for corneal vascularization were 2.1^+ versus 3.2^+ and 2.1^+ versus 3.3^+ in the oxygen therapy and control groups, separately. At the end of follow-up, mean visual perception (logarithm of the minimal angle of resolution) was 0.30 ± 0.42 (0 to 1.4) versus 1.21 ± 0.73 (0.1 ± 3.1) in the oxygen therapy and control groups ($P = .028$).

In the oxygen group, 9 of 13 eyes (0.69%) had useful vision ($>20/200$) without need for surgery; this situation occurred in 4 (0.46%) of 18 eyes in the control group.

At final follow-up, in the oxygen therapy group, 3 (25%) of 13 eyes had corneal vascularization. Complete vascularization of the cornea advanced in 2 eyes (grade IV burns), and in 1 eye (grade III burn), vascularization complicated 1 quadrant. Oxygen therapy had been ongoing during the second week after injury in all 3 of these cases. In the control group, complete corneal vascularization advanced in all eyes with rating IV burns. In at least 1 quadrant of each eye with grade III burns, corneal vascularization industrialized. In 3 eyes with grade IV burns in the control group, symblepharon industrialized in at minimum 1 quadrant. Symblepharon and corneal thinning did not happen in any eye in the oxygen group.

One patient in the oxygen therapy group (Patient 2), in whom corneoscleral retreating or sentimentalbeforehand had advanced before oxygen therapy, recovered near-normal corneal thickness within 12 days after oxygen therapy. In the control group, corneoscleral thinning established in one patient that was modified with tenoplasty and amniotic membrane movement. Patient physiognomies in the oxygen therapy group are summarized in the Table.

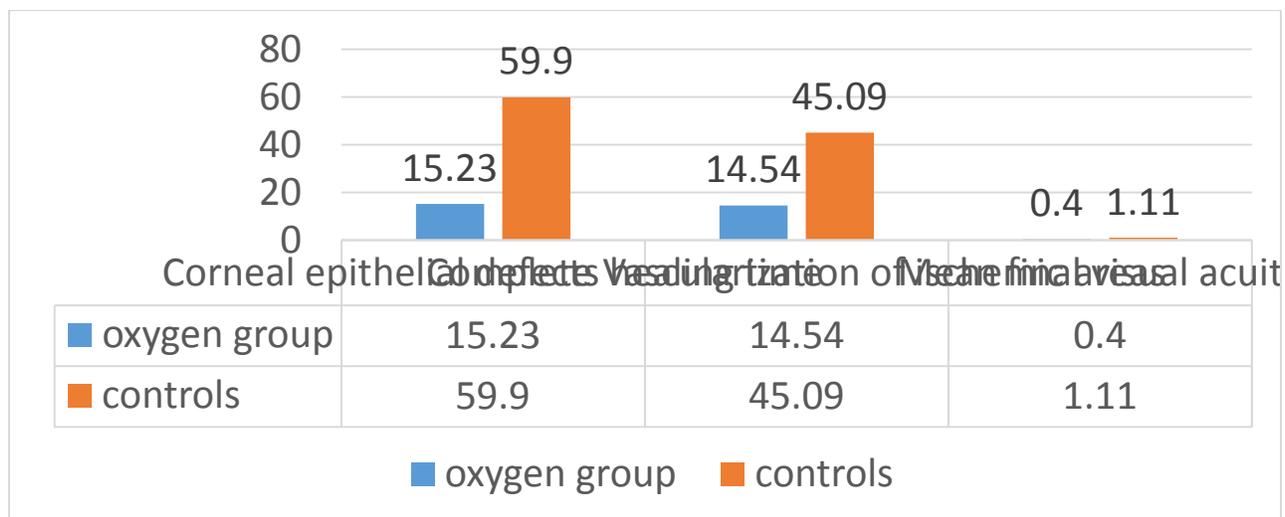


Table: Characteristics of Patients with Acute Ocular Chemical or Thermal Burns Receiving Oxygen Therapy in Addition to Conventional Medical Therapy

| Patient No. | Age (yrs) | Eye | Chemical Agent | Grade of Burn ^a | Beginning of Oxygen Therapy ^b | Epithelial Healing ^c | Improvement of Ischemia ^c | Follow-up (mos) | Final Snellen BCVA (logMAR) |
|-------------|-----------|-------|----------------|----------------------------|--|---------------------------------|--------------------------------------|-----------------|-----------------------------|
| 1 | 16 | Right | Alkali | IV | 4 | 14 | 14 | 42 | 20/30(0.18) |
| 2 | 6 | Right | Thermal | III | 20 | 10 | 10 | 30 | 20/20(0) |
| 3 | 13 | Left | Thermal | IV | 21 | 21 | 21 | 18 | 20/400(1.3) |

| Patient No. | Age (yrs) | Eye | Chemical Agent | Grade of Burn ^a | Beginning of Oxygen Therapy ^b | Epithelial Healing ^c | Improvement of Ischemia ^c | Follow-up (mos) | Final Snellen BCVA (logMAR) |
|-------------|-----------|---------------|----------------|----------------------------|--|---------------------------------|--------------------------------------|-----------------|-----------------------------|
| 4 | 40 | Right | Alkali | IV | 6 | 16 | 16 | 24 | 20/25(0.1) |
| 5 | 44 | Right | Acid | III | 8 | 14 | 14 | 12 | 20/25(0.1) |
| 6 | 15 | Left | Thermal | IV | 21 | 20 | 15 | 6 | 20/400(1.3) |
| 7 | 32 | Right | Alkali | IV | 4 | 17 | 17 | 10 | 20/25(0.1) |
| 8 | 21 | Right | Alkali | IV | 7 | 12 | 14 | 12 | 20/30(0.18) |
| 9 | 38 | Right | Acid | III | 3 | 10 | 12 | 16 | 20/20(0) |
| 10 | 18 | Right | Thermal | III | 5 | 10 | 12 | 12 | 20/25(0.1) |
| 11 | 39 | Right Left | Alkali | IIIIII | 9 | 18 20 | 14 16 | 14 | 20/40(0.3) 20/400(1.3) |
| 12 | 49 | Left | Alkali | IV | 2 | 16 | 14 | 12 | 20/30(0.18) |

BCVA = best-corrected visual acuity; logMAR = logarithm of the minimal angle of resolution; yrs = years.

a. Based on Roper-Hall classification.

b. Number of days after injury.

c. Number of days after oxygen therapy.

Case Reports

Patient 1

A 16-year-old worker with independent ammonia wound in his right eye was mentioned 5 days after injury. Initial inspection exposed visual perception of hand arrangements, 360-degree limbal ischemia, huge bulbar and palpebral conjunctival epithelial faults, and total corneal epithelial flaw with severe edema.

A gray inflammatory membrane sheltered the whole ocular surface with multiple fibrinous bands. One day after oxygen therapy, corneal edema reduced meaningfully, allowing discovery of severe forward chamber response with heavy pigment spreading and a thick anterior subcapsular cataract, representing intraocular infiltration of the chemical agent.

Three days after oxygen therapy, the gray tissue totally vanished, small vessels started to grow in the inferonasal and

inferotemporal quadrants, and early curative of the corneal epithelium was obvious. Advanced vascularization of ischemic parts and curing of the corneal epithelium occurred.

Fourteen days later, epithelial deficiencies cured with noteworthy vascularization in most parts of the ischemic conjunctiva. Six months later, the eye was quiet, the cornea was opaque with minimal vascularization, and there was no symblepharon creation. Penetrating keratoplasty organized with cataract withdrawal and intraocular lens establishment was achieved 2 years after injury. Final best-corrected visual acuity (BCVA) was 20/30.

Patient 2

A 8-year-old boy with a grade III unilateral thermal burn in his left eye was mentioned 23 days after injury (Figure). According to his doctor, rebellious and broadminded corneoscleral thinning or melting started 12 days after the burn. BCVA was 30/70 in his left eye. Corneal breadth had reduced to fewer than one third. Three days after oxygen therapy, small vessels began to grow into the ischemic area. Ten days later, complete curative with fibrovascular tissue replacement happened and the cornea recovered near normal thickness (Figure). Final BCVA was 20/20.



Patient 3

A 11-year-old boy with score IV thermal burn in his left eye was mentioned 23 days after injury. Visual insight was 20/400 and slit-lamp inspection exposed 360-degree limbal ischemia, total corneal epithelial fault, and a large conjunctival epithelial defect over the ischemic area. Four days after oxygen therapy, apparent and deep vascularization of the chronological area could be seen with a wave of branching vessels rising toward the limbus leading to conjunctivalization of the cornea. Twenty-two days after oxygen therapy, perilimbal ischemic areas were vascularized completely. Final BCVA was 20/400.

Discussion

Oxygen therapy has been used in medication for many years (11). Hyperbaric oxygen therapy (HBOT), “the intermittent administration of 100% oxygen at a weight greater than sea level,” has been used to contribution wound healing for approximately 50 years (11). It also has been used for handling of thermal burns (12). Though, there are only a few reports regarding its use in ophthalmology (13-15). The present study established that oxygen therapy may progress perilimbal conjunctival ischemia and may endorse corneal epithelial curative in the acute stage of ocular chemical and thermal burns. Such therapy may recover final visual consequences and long-term forecast by declining corneal conjunctivalization and averting adnexal difficulties such as symblepharon creation. Though a measured study in rabbits showed no helpful effect from HBOT for corneal alkali burns (16), another relative animal model of corneal alkali burns established beneficial possessions from normobaric oxygen therapy (5 L/minute) (17). It is known that oxygen is accomplished of favorably manipulating a number of cytokines and growth factors that play an significant role in wound healing (11). The effects of altering growth factor- β 1 and platelet-derived growth factor- β are synergistically improved by oxygen. When managed after wounding, oxygen may upregulate collagen synthesis. In ischemic flaps, oxygen can upregulate fibroblast growth factor, growing the effect experiential with fibroblast growth factor only (11, 18, and 19). Though, oxygen unexpectedly may cause upregulation or downregulation of cytokines under different physiological situations. For example, vascular endothelial growth factor is upregulated by both hypoxia and hyperoxia (11, 20). It is unclear how oxygen is able to motivate biological progressions such as angiogenesis, collagen production, and discharge of vascular endothelial growth factor at both hypoxic and hyperoxic concentrations, a phenomenon referred to as the *oxygen paradox*. Tissue oxygen level plays a major role in the physiology of blood flow, wound curing, and white cell function. The helpful effects of oxygen chiefly are associated to its concentration within tissues (21). Low tissue oxygen pressure (5 to 15 mm Hg) reduces the ability of white blood cells to kill bacteria and reductions collagen mixture by fibroblasts. Levitation tissue oxygen tensions to 30 to 40 mm Hg delivers the substrate essential to lay down a collagen matrix for provision of capillary ingrowth into avascular or injured areas (21). Though oxygenation of hypoxic tissue is a key mechanism in hastening wound curative, oxygen besides acts in numerous ways that affect the wound after termination of treatment. Oxygen benefits wounds by several instruments, including upregulation of growth factors, downregulation of provocative cytokines, and decrease of edema, and expansion in leukocyte function. Also, it

demonstrates antibacterial effects and at the same time supports angiogenesis and new tissue ingrowth (11, 20, and 21).

The main objects of organization for acute chemical or thermal burns are decrease of limbal stem cell damage and hastening of corneal and conjunctival epithelialization with or deprived of vascularization. Limbal ischemia, which may reproduce the extent and harshness of limbal stem cell injury, has been optional as the greatest important prognostic factor in ocular chemical or thermal wounds(4).Obliteration of limbal stem cells may be liberal in the first few days after injury. By dipping ischemia, oxygen may reduction the degree of broadminded stem cell damage and progressprediction. Though, this effect may be experientiallone if action is started early afterwardwound. Earlier epithelial curativeavoids long-term problemsrelated with determined epithelial flaws, containing bacterial superinfections, endophthalmitis, tissue melting, and symblepharon creation. In our study, epithelial curativehappened much earlier in the oxygen-treated group as related with those receiving conventional therapy. The compassion of diverse cell types to ischemia varies importantly. Before satisfyingpermanent damage, neurons stand ischemia for 5 to 10 minutes (22),while the consistent time for myocardial cells is 25minutes (23). It is thought that at least 35% to 43% of the limbal stem cell populace is obligatory to preserve corneal epithelial truthfulness (24). With acute or continued ischemia, some cells die, while others are viable but dysfunctioning (22).Rescue of as many dysfunctioning cells as likely may affect the consequence of any insult favorably. Early oxygen therapy may save incompletely injured ischemic limbal and conjunctival stem cells, may indorse corneal and conjunctival epithelialization, may avoid corneal conjunctivalization, may activate scleral vascularization, and may avoid its melting or perforation. Consequently, the cornea may become exposed by a transparent layer of epithelium. With late interference, although complete devastation of limbal and conjunctival stem cells and their niche, oxygen therapy still may be effective in persuading angiogenesis and indorsing corneal vascularization. Tissue vascularization may perform as heavy tufts of vessels ingoing the renovationstage in the following few days. In this condition, the cornea may be enclosed by conjunctival epithelium. Fascinatingly, in some eyes receiving oxygen therapy, we experiential the wave of curative corneal epithelium to leadcurative conjunctival epithelium, representivedistinctbases of corneal and conjunctival epithelial curative. Decreasing inflammation may delay limbal stem cell obliteration and may indorse corneal and conjunctival epithelialization. The role of penetrating and lengthyinteresting steroids and topical and systemic vitamin C in declining ocular superficial inflammation afterward chemical burns previously has been demonsterated (25). Amniotic membrane movement also has been shown to

decrease inflammation and to indorse epithelialization in the severestage of chemical and thermal wounds with contradictoryeffects (9, 26, and 27). It has been revealed that oxygen shows a role in reducing inflammation by downregulating inflammatory cytokines such as interleukin-6,interleukin-1, and tumor necrosis factor (11). Simple mask oxygen therapy is a low-flow oxygen distribution system that varies from HBOT in many features. It growths arterial blood oxygen pressure (PaO₂) from a standard of about 95 mm Hg to levels up to 250 mm Hg, while HBOT can rise it up to 1700 mm Hg at 2.4 atmospheric pressure (12). HBOT is contraindicated in gestation, otitis media,pneumothorax, congestive heart failure, and chronic disruptive pulmonary disease (11),while simple mask oxygen therapy can be used carefully in these conditions. Though, in patients with chronic disruptive pulmonary disease and hypercarbia (carbon dioxide pressure > 45 mm Hg), simple mask oxygen therapy must be used carefully (28). The most common difficulties of HBOT, but not humble mask oxygen therapy, myopia, oxygen seizures, are ear and sinus barotrauma, and pulmonary barotrauma (11). There are some restrictions to our study. This study was an interventional, nonrandomized, relative case series with a partial number of cases. Though some beneficial properties of oxygen therapy were well established, our study was questionable about the idealinitial time and incidence and flow rate for oxygen therapy. Though, it sensibly may be contended that oxygen therapy should be underway as soon as possible afterward chemical or thermal burns. In summary, oxygen therapy appears to be harmless and operative in ameliorating some of the overwhelmingdifficulties of acute ocular chemical and thermal burns. This technique is freely available at all hospital amenities, is economical, and is noninvasive. We commend it be combined into the early repetitive management for acute ocular chemical and thermal burns. Additional studies are necessary to confirm our explanations; to define the pathophysiologic mechanisms; to create the optimum therapeutic schedule, containing frequency, flow rate, and time for initiating oxygen therapy; and to explain better the assistances and drawbacks to oxygen therapy.

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