

# Red eye. Ophthalmologist's and General Practitioner's point of view. Therapy with low-dose brimonidine



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## HIGHLIGHTS

This paper discusses the ocular hyperemia unconnected with specific diseases and recommendations. The priority aspect is safety of use vasoconstrictor topical medications as symptomatic treatment.

## ABSTRACT

Red eye is a symptom which may indicated different disorders. Mild hyperemia may occur without any defined aetiology and may cause esthetical and psychological problems for the patients. Diagnostics is crucial before implementing the symptomatic treatment to exclude any disease requiring targeted therapy. All cases of red eye symptom with pain and visual disturbances require special attention. Eyedrops with low-dose brimonidine are good alternative to other vasoconstrictors, as safe and well-tolerated medication not leading to hypoxia, tachyphylaxis and rebound effect.

**Key words:** ocular redness, conjunctival hyperemia, brimonidine, tachyphylaxis, rebound effect

## INTRODUCTION

Red eye is a clinical sign associated with a wide range of ocular pathologies. Most commonly, ocular redness – defined as hyperemia of vascularized structures of the ocular surface, such as the conjunctiva, episclera, or sclera – reflects an inflammatory response. The most common cause of ocular hyperemia is conjunctivitis, which may be of infectious (e.g., bacterial or viral) or non-infectious origin (e.g. allergy or dry eye disease). Patients typically experience discomfort manifested by tearing, itching, stinging, or ocular discharge.

Red eye may also result from subconjunctival hemorrhage, which can occur spontaneously, without preceding trauma, particularly in patients with arterial hypertension or coagulation disorders. Even minor trauma or the presence of a foreign body may cause transient ocular hyperemia, usually accompanied by pain. Ocular redness may also occur in contact lens users or in individuals exposed to environmental or occupational factors.

A decrease in visual acuity in a patient presenting with red eye may indicate involvement of deeper ocular structures, such as corneal ulceration, uveitis, or acute angle-closure glaucoma. Therefore, patients presenting with red eye require a comprehensive ophthalmological examination to establish the underlying cause and initiate appropriate management, including antibiotic therapy in bacterial infections, anti-inflammatory and antiallergic agents in allergic conditions, or more complex therapeutic approaches for diseases affecting deeper structures of the anterior segment. Inflammatory conditions of the conjunctiva or episclera are often self-limiting and do not typically pose a threat to vision, whereas disorders involving the cornea and deeper ocular structures carry a significant risk of visual impairment.

In clinical practice, some patients present with ocular hyperemia as the primary concern, in the absence of other accompanying signs or symptoms. Patients often report that their red eyes were first noticed by family members or acquaintances. Such individuals frequently complain of being perceived as tired, sleep-deprived, or unwell; thus, this condition is not merely a cosmetic issue but a problem affecting daily functioning, particularly in social and professional settings. For this group of patients, ophthalmic solutions containing 0.25 mg/mL brimonidine tartrate (0.025%) may represent an effective and safe therapeutic option in ophthalmological practice.

## RED EYE: WHAT SHOULD BE RECOMMENDED?

Improvement in the appearance of a hyperemic eye can be achieved with agents that induce vasoconstriction, leading to blanching of the conjunctival tissue. Topical vasoconstrictive agents in the form of ophthalmic solutions

are widely used in developed countries and are commonly recommended by primary care physicians; many of these preparations are available over the counter.

These eye drops contain compounds that stimulate  $\alpha$ -adrenergic receptors. Phenylephrine and tetrahydrozoline are selective  $\alpha_1$ -adrenergic receptor agonists, whereas naphazoline and oxymetazoline act on both  $\alpha_1$ - and  $\alpha_2$ -adrenergic receptors. Their mechanism of action involves vasoconstriction of both arterial and venous vessels, resulting in a whitening effect; however, this may also lead to tissue hypoxia due to constriction of arterioles containing  $\alpha_1$  receptors.

Lack of selectivity and activity at  $\alpha_1$ -adrenergic receptors may, over time, lead to tachyphylaxis as a result of receptor internalization and downregulation. A rebound effect (rebound hyperemia) may also occur. Adverse effects associated with  $\alpha_1$ -agonists and non-selective  $\alpha_1/\alpha_2$ -agonists include mydriasis and systemic reactions (e.g., somnolence and dizziness) [1]. Therefore, these agents cannot be considered entirely safe, and their overuse may have significant clinical consequences.

In contrast,  $\alpha_2$ -adrenergic receptor agonists induce vasoconstriction predominantly in venous vessels, with minimal effect on arterial circulation, and therefore do not cause tissue hypoxia.

Brimonidine, a third-generation selective  $\alpha_2$ -adrenergic receptor agonist, was approved in 1996 at a concentration of 0.2% as an intraocular pressure (IOP)-lowering agent for the treatment of open-angle glaucoma and ocular hypertension, and remains a well-established antiglaucoma medication used in both monotherapy and combination therapy [2]. In addition, due to its vasoconstrictive properties, brimonidine is useful in controlling conjunctival bleeding during ophthalmic procedures, such as strabismus surgery, cataract surgery, refractive surgery, and intravitreal injections [3–6].

Beyond ophthalmology, brimonidine at a concentration of 0.33% was approved in 2013 as a dermatological agent for the treatment of facial erythema associated with rosacea in adults.

A brimonidine concentration as low as 0.025% is sufficient to reduce conjunctival hyperemia. Multicenter, randomized, double-blind studies have confirmed the efficacy and safety of 0.025% brimonidine ophthalmic solution in reducing ocular redness [7]. In a study in which patients used the medication four times daily for one month, no tachyphylaxis and only a minimal rebound effect were observed. Following instillation, hyperemia was reduced rapidly (within 1–5 min) and the effect was sustained for 4–8 h.

Low-dose brimonidine was approved for the treatment of ocular redness associated with minor irritation in adults in December 2017 in the United States (Lumify) and was subsequently registered in Poland in 2023 (Lumobry).

Phase III clinical trials have shown that ophthalmic solutions containing 0.025% brimonidine are safe and effective in reducing ocular redness, with effects lasting up to 8 h. No evidence of tachyphylaxis was observed, and the rebound effect was clinically insignificant. No effect on IOP was detected. The drops were well tolerated and convenient for patient use [8].

### ADDITIONAL APPLICATIONS OF LOW-DOSE BRIMONIDINE

Adverse effects associated with higher concentrations of brimonidine include miosis and eyelid elevation; however, these effects are not always undesirable. Miosis may be beneficial in patients following refractive or cataract surgery, as it can reduce visual disturbances such as halos and dysphotopsias.

In 2021, a study evaluating the effect of 0.025% brimonidine on pupil size demonstrated a significant reduction in pupil diameter under scotopic conditions, particularly in eyes with light-colored irides. The effect was assessed 1 h after instillation. Thus, 0.025% brimonidine may serve as an alternative to higher-concentration formulations or pilocarpine in the management of postoperative aberrations and/or dysphotopsias [9].

In ophthalmic surgery, 0.025% brimonidine may also be useful in the perioperative period during procedures such as pterygium excision and other conjunctival surgeries [10]. Therefore, ophthalmic solutions containing low-dose brimonidine offer multiple advantages and potential clinical applications.

### PERSPECTIVE OF A PRIMARY CARE PHYSICIAN

Although red eye syndrome is not a leading reason for consultations in primary care, it is a relatively common finding in clinical practice. It is most often identified incidentally during consultations prompted by other medical concerns. Less frequently, ocular irritation may be sufficiently bothersome to prompt patients to seek medical attention from their primary care physician.

Red eye syndrome is commonly associated with inflammation, giving rise to classic symptoms such as redness, tearing, and, in some cases, pathological discharge. These manifestations are typically accompanied by itching, discomfort, and occasionally ocular pain. In other cases, only mild hyperemia is present, without associated discomfort. It should be noted that these features do not constitute a diagnosis per se, but rather describe a spectrum of symptoms observed across various ocular conditions.

The etiology of red eye syndrome is most commonly related to local infection or allergy, although it may also be trauma-related. In clinical practice, it frequently occurs as a consequence of activities such as renovation work or cleaning

dusty environments. It may also result from simple behaviors, such as rubbing the eye with contaminated fingers or inadequate hygiene during contact lens use or storage. Less common causes include eyelid malposition (entropion), abnormal eyelash growth (trichiasis), subconjunctival hemorrhage, and thyroid-associated orbitopathy. In primary care, a particularly important patient group consists of older adults, in whom insufficient hygiene is often accompanied by reduced vascular integrity, slower tissue regeneration, and dry eye disease.

The simplest approach after recognizing red eye syndrome would be referral to an ophthalmology clinic; however, this is often unnecessary and may be inappropriate. With a thorough medical history, appropriate assessment of the underlying cause and severity, and exclusion of red flag symptoms, treatment can be effectively managed in primary care.

At this stage, it should be determined whether symptomatic therapy with a topical vasoconstrictive agent is sufficient or whether additional treatment – such as topical antibiotic or antiallergic therapy – is indicated. Urgent specialist referral is required in patients in whom ocular redness is accompanied by any of the following: decreased or loss of vision, photophobia, perception of halos around light sources, sudden onset of diplopia, or severe ocular pain associated with headache. In such cases, specialist evaluation is necessary, including slit-lamp examination, measurement of IOP, and fundus assessment. When issuing a referral, it should be noted that there is no single ICD-10 code for red eye syndrome, as it represents a constellation of symptoms rather than a specific disease entity. Instead, coding should reflect the underlying etiology – for example, H10 for conjunctivitis.

In the majority of cases, primary care physicians have sufficient competence to manage treatment independently. However, even when referral for ophthalmological evaluation is deemed necessary, patients should be provided with symptomatic treatment in advance to alleviate discomfort and maintain an acceptable level of daily functioning.

In both scenarios, the management of uncomplicated red eye syndrome may be limited to prescribing topical ophthalmic drops, which patients can administer independently or with assistance from a caregiver. As discussed earlier; to minimize potential adverse effects, preference should be given to agents with a selective mechanism of action (predominantly targeting venous vessels), ideally at the lowest effective dose. One such agent is brimonidine, available in Poland by prescription in two concentrations (0.025% and 0.2%). The lower concentration (0.025%) is recommended for the topical treatment of isolated conjunctival hyperemia associated with mild, non-infectious ocular irritation in adults. The use of a lower concentration not only improves the appearance of the eye but also alleviates bothersome symptoms.

## CONCLUSIONS

In an era of increasing emphasis on aesthetic appearance and the widespread use of cosmetic and aesthetic medicine procedures, the eyes are also expected to appear healthy. Individuals with ocular redness often seek methods to reduce hyperemia, frequently using over-the-counter eye drops. An ophthalmologist is not always the first physician consulted. However, if red eye is accompanied by pain and/or visual disturbances, prompt referral to a specialist is re-

quired to determine the underlying cause and initiate appropriate treatment.

In cases of conjunctival hyperemia and mild ocular irritation of unclear etiology in adults, ophthalmic solutions containing 0.025% brimonidine represent an appropriate therapeutic option. Nevertheless, their use should follow medical recommendations, and regular ophthalmological follow-up should be ensured.

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## Authors' contributions:

Monika Udziela: idea and design of the article, literature review, analysis and interpretation of literature data, writing the manuscript, approval of the final version of the manuscript.

Bartosz Sapilak: literature review, analysis and interpretation of literature data, writing the manuscript.

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