OCULAR DISCOMFORT IN PROFESSIONAL POLO-WATER PLAYERS: A PRACTICAL EXPERIENCE WITH TOPICAL HYALURONIC ACID AND GLYCURONATE ENOXOLONE

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SUMMARY

Aims: Professional polo-water athletes are exposed to chlorine in the swimming pool. Chlorine is an irritant agent, so polo-water athletes commonly experience irritative eye symptoms. Hyaluronic acid and glycuronate enoxolone exert anti-inflammatory and cytoprotective activity. Therefore, the present practical experience explored the efficacy and safety of eye drops containing both components.

Material and Methods: The current study included 59 professional polo-water athletes. The ocular surface disease index (OSDI) and dry eye-related quality of life (QoL) score (DEQS) questionnaires were used to assess the efficacy. Subjects took the eye drops for one month. The study consisted of a baseline visit (T0) and an end-treatment one (T1).

Results: Athletes experienced a significant improvement in symptoms and QoL as assessed by OSDI and DEQS scores ($p < 0.001$ for both).

Conclusion: The present study showed that professional polo-water athletes frequently experience ocular discomfort associated with swimming pool attendance. Eye drops with hyaluronic acid and glycuronate enoxolone can significantly relieve eye symptoms and improve the quality of life in these athletes.

Key words: swimming pool, chlorine, irritation, polo water athletes, ocular discomfort, hyaluronic acid, glycuronate enoxolone

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INTRODUCTION

Ocular surface inflammation, including irritative conditions and dry eye disease (DED), is a prevalent eye problem worldwide [1,2]. The prevalence of ocular surface irritation is also growing as there is increasing exposure to irritants for the eyes, such as visual display terminals, pollutants, and chemicals [3]. In this regard, exposure to chemicals causes an ocular surface injury that damages the mucosa [4]. For example, chlorine is a chemical component in many disinfection products used to sanitize swimming pools. As a result, chlorine disinfectants contribute to eye, cutaneous, and respiratory irritation [5].

Patients with ocular surface irritation commonly report eye discomfort and reduced health-related quality of life (HRQL) [6-12]. The diagnosis in patients with ocular irritation consists of quantifying subjective symptoms and dry eye examinations. In addition, they include tear film breakup time (TFBUT), ocular surface staining, tear secretion volume measurement using Schirmer's test and tear osmolarity assessment [12,13]. Therefore, a balanced consideration of the quantitative measures of subjective symptoms and HRQL (using patient-reported outcome questionnaires) and clinical findings are required to accurately assess and treat ocular surface inflammation. In this regard, two questionnaires are very popular and commonly used: the ocular surface disease index (OSDI) and dry eye-related quality of life score (DEQS) in daily practice [14,15].

It is well known that attending swimming pools involves exposure to chlorine-containing vapors causing ocular surface irritation [16]. Therefore, professional polo-water athletes frequently complain of eye symptoms, including itching, irritation, redness, and impaired quality of life [17].

There is evidence that hyaluronic acid (HA) eye drops are helpful in patients with ocular discomfort [18]. Namely, HA exerts anti-inflammatory, cytoprotective, and lubricant activity that positively restores conjunctival mucosa. Consistently, an open-label study reported that topical treatment with HA and coenzyme Q10 significantly improved ocular symptoms in professional water polo athletes [5]. In addition, a pilot study demonstrated that eye drops containing HA, magnesium alginate, and *Camelia sinensis* extract significantly improved ocular discomfort in patients with dry eyes [19].

The high mobility group protein box 1 (HMGB1) is an alarmin molecule, and plays a relevant role in inflammatory events [20]. HMGB1 promotes the macrophage proliferation and activation, so in turn increases the release of some pro-inflammatory cytokines, including IL-1β, TNF-α, GM-CSF [21]. Also, HMGB1 affects endothelial cells as increases expression of adhesion molecules (ICAM-1 and VCAM-1) so allowing the inflammatory cells transmigration from blood to inflamed tissues, induces the secretion of fibrinolysis regulators (e.g., plasmin) associated with inflammatory pathways, and cytokine secretion, such as TNF-α, IL-1β, and MCP-1 [21]. HMGB1 also activates eosinophils and prolongs their survival [21].

Glycyrrhizin (or glycuronate enoxolone) is a triterpene saponin extracted from the root of *the Glycyrrhiza glabra* plant. Glycuronate enoxolone (GE) exerts a broad mechanism of action, including anti-inflammatory, antioxidant, cortisol-like, antiallergic, and antiviral activity [22]. Interestingly, GE blocks, by binding, HMGB1 and, therefore, may significantly dampen inflammation [21].

Recently, a new medical device containing HA and GE has been formulated as eye drops and proposed to manage patients with ocular discomfort.

Therefore, the current study explored the efficacy and safety of HA and GE eye drops in professional polo-water athletes.

MATERIAL AND METHODS

This study was mono-center and open-label. The study included professional polo-water athletes from the Nuoto Catania sport association, playing in the A1 series. The participants visited the trial site because of routine examinations. A complete ophthalmological assessment, including administering questionnaires, was performed during the investigation.

The study protocol was approved by the Institutional Review Board- Ethics Committee of the University of Catania (n. 592/20). The participants signed informed consent.

The participants took two drops twice a day of the medical device Enoxoftal (hyaluronic acid, glycuronate enoxolone manufactured by DMG, Italy). The treatment lasted one month. The participants were visited at baseline (T0) and after treatment (T1). In addition, the participants completed two questionnaires: OSDI and DEQS.

The OSDI is a 12-item questionnaire to investigate ocular symptoms. Further, reliability and validity were confirmed (14). OSDI questionnaire is of low burden to the patient as approximately 5 minutes occur to be completed. The OSDI scoring was performed according to the reference reports [24,25]. This questionnaire has three subscales: ocular symptoms (three questions), vision-related functions (six questions), and environmental triggers (three questions), with each question being answered on a five-point scale ranging from "None of the time" (no points) to "All of the time" (four points) (N/A is selected when the question is not applicable). The OSDI total score ranges from 0 to 100 points and is obtained by multiplying the total score of all the questions by 25 and dividing the result by the number of valid answers. A maximum score of 100 points can be obtained per subscale. The total score is positively correlated with DED severity and the impact on activities of daily living. The OSDI total score can be used to classify the respondent's dry eye symptoms as normal (0–12 points), mild (13–22 points), moderate (23–32 points), or severe (33–100 points).

The DEQS questionnaire is a 15-item instrument developed in 2013 for assessing subjective dry eye symptoms and their effects on activities of daily living within the previous week [15]. The DEQS questionnaire comprises six questions on eye symptoms and nine on the dry eye effects on activities of daily living. Each question has columns A and B for frequency and severity, respectively. Responses to the frequency portion in column A are based on a five-point scale ranging from "None of the time" (no points) to "All of the time" (four points). Here, a score of 1 to 4 points prompts the respondent to proceed to column B to answer the questions regarding severity on a four-point scale.

A QoL score ranging from 0 to 100 points is calculated by multiplying the total points in column B by 25 and dividing the result by the number of valid responses. The QoL score positively correlates with the severity of subjective dry eye symptoms and dry eye effects on daily life. The cutoff value is 15 points [26].

Descriptive data are expressed as counts with percentages for categorical variables or mean with standard deviation and median (range) for continuous variables, as appropriate.

Differences between pre- and post-scores are analyzed with Wilcoxon Signed Ranks Test for paired data. The significance level is set at 0.05.

RESULTS

Globally, 59 participants completed the study and were evaluated. All of them were male professional water polo athletes. The mean age was 23.7 ±5.81 years.

Symptoms severity

The athletes perceived a significant improvement in symptoms as assessed by the OSDI questionnaire score changes over time (Table 1 and 2). In particular, the mean total score significantly ($p < 0.001$) diminished from 66.2 (±21.38) to 20.9 (±11.24). Consistently, the mean change was – 45.3 (±19.24).

Tables 1 and 2 detail the subscale scores concerning symptoms, visual function, and triggers.

Quality of Life

The perception of quality of life measured by the DEQS questionnaire significantly ($p < 0.001$) improved. In detail, the mean baseline score was 30.9 (± 9.08), and the mean end score was 9.6 (±5.55), as reported in Table 1. In addition, the mean absolute change was – 21.3 (±8.59), as reported in Table 2).

Safety

The subjects did not report any clinically relevant adverse event.

DISCUSSION

Chlorine is an irritant widely used for disinfecting swimming pools. As a result, the subjects who remain in such environments for a long time often experience ocular discomfort. However, treating ocular discomfort due to irritants can be unsatisfactory in many patients, mainly if the cause persists. In this regard, a previous experience employed eye drops with HA and CoQ10 [5]. That pilot study

Table 1. General characteristics and questionnaires' outcomes

Sex, males %		59 (100.0)
Age, years		23.7 ±5.81 23.0 (15.0–37.0)
DEQS questionnaire (T0)		30.9 ±9.08 34.0 (5.0–41.0)
DEQS questionnaire (T1)		9.6 ±5.55 8.0 (0.0–28.0)
OSDI questionnaire grade (T0) Number of subjects (percentage)	*Normal*	1 (1.7)
	Mild	2 (3.4)
	Moderate	5 (8.5)
	Severe	51 (86.4)
OSDI questionnaire total score (T0)		66.2 ±21.38 70.8 (6.3–93.8)
Subscale: Symptoms (T0)		66.1 ±24.12 66.7 (0.0–100.0)
Subscale: Visual Function (T0)		65.6 ±21.73 70.8 (12.5–95.8)
Subscale: Environmental Triggers (T0)		67.5 ±25.22 75.0 (0.0–100.0)
OSDI questionnaire grade (T1) Number of subjects (percentage)	*Normal*	13 (22.0)
	Mild	28 (47.5)
	Moderate	10 (16.9)
	Severe	8 (13.6)
OSDI questionnaire total score (T1)		20.9 ±11.24 18.8 (0.0–60.4)
Subscale: Symptoms (T1)		24.2 ±16.35 25.0 (0.0–75.0)
Subscale: Visual Function (T1)		20.5 ±11.25 16.7 (0.0–54.2)
Subscale: Environmental Triggers (T1)		18.7 ±13.73 16.7 (0.0–66.7)

Results are expressed as count (%) or mean ± standard deviation and median (range), as appropriate.
OSDI – ocular surface disease index, DEQS – dry eye-related quality of life score

Table 2. Absolute change in OSDI and ocular discomfort questionnaire after treatment

	Mean differences (Δabs_{T1-T0})	p value
OSDI total score	-45.3 ±19.24 -47.9 [(-79.2)–(-6.3)]	< 0.001
Subscale: symptoms	-41.9 ±20.64 -50.0 (-91.7–0.0)	< 0.001
Subscale: visual function	-45.1 ±20.01 -50.0 [(-83.3)–(-8.3)]	< 0.001
Subscale: environmental trigger	-49.1 ±23.96 -50.0 (-91.7–0.0)	< 0.001
DEQS total score	-21.3 ±8.59 -23.0 [(-33.0)–(-4.0)]	< 0.001

Differences between pre and post scores were investigated with Wilcoxon Signed Ranks Test for paired data. Results are expressed as mean ± standard deviation and median (range), as appropriate.
OSDI – ocular surface disease index, DEQS – dry eye-related quality of life score

showed that a two-month treatment improved ocular symptoms and signs in professional polo-water athletes.

The present study considered the same disease model, such as male professional polo-water athletes.

The first outcome demonstrated that a very high percentage (near the totality) of professional polo-water athletes suffer from dry eye disease. In particular, 86% of participants experienced severe discomfort, as documented by the OSDI questionnaire. This finding underscores the relevant impact of chlorine exposure in a frequent-player swimming pool.

The results showed that one-month treatment with eye drops containing HA and GE significantly reduced the severity of ocular discomfort and improved patients' quality of life.

It may be speculated that these positive findings might depend on the mechanism of action of the two components. HA in the lacrimal fluid guarantees optimal lubrication and moistening of the ocular surface and provides anti-inflammatory activity [26]. Glycyrrhizin also exerts an effective anti-inflammatory activity by blocking HMGB1-mediated inflammation [20]. As a result, hyaluronic acid and glycuronate enoxolone can restore a physiological tear film and dampen inflammatory events.

Moreover, these outcomes were consistent with the previous study conducted in the same setting, such as swimming pool players [5].

However, this study had limitations, including the open design, the need for a control group, and objective tests. In particular, the lack of evaluation of inflammatory parameters does not allow an objective assessment of the results of this study. Therefore, it will be necessary to design further studies that precisely and objectively measure inflammatory parameters of the ocular surface.

On the other hand, the study's strength was the homogeneous population, characterized by the same exposure level to chlorine.

In conclusion, the present study showed that professional polo-water athletes frequently experience ocular discomfort associated with swimming pool attendance. Eye drops with hyaluronic acid and glycuronate enoxolone can significantly relieve eye symptoms and improve the quality of life in these athletes. Thus, using well-known components with anti-inflammatory, immune-modulatory, lubricant, and moistening activity could represent a practical approach in subjects exposed to irritants.

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