Effects of Aqueous-Supplementing Artificial Tears in Wearers of Biweekly Replacement Contact Lenses vs Wearers of Daily Disposable Contact Lenses

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Purpose: To compare the effects of artificial tears (ATs) in wearers of biweekly replacement silicone hydrogel contact lenses (BW-Ws) and wearers of daily disposable contact lenses (DD-Ws) of the same material.

Materials and Methods: The aqueous-supplementing ATs, OPTOyalA and OPTOidro, were assigned to be used for 2 weeks to healthy and young subjects: 1) 20 (8 and 12, respectively) BW-Ws wearing silicone hydrogel somofilon A CLs (Clariti Elite), 2) 18 (9 and 9, respectively) DD-Ws wearing silicone hydrogel somofilon A CLs (Clarity 1 Day), and 3) a control group of 33 (16 and 17, respectively) N-Ws. Ocular symptoms and comfort, tear volume and stability, and ocular surface condition were assessed by Ocular Surface Disease Index (OSDI), 5-Item Dry Eye Questionnaire (DEQ5), tear meniscus height (TMH), non-invasive tear break-up time (NIBUT), and evaluation of ocular redness (OR). The assessment was performed before and after 15 days of use of the ATs in the 3 groups (BW-Ws, DD-Ws, and N-Ws).

Results: No clear significant difference was noted in symptoms and signs between OPTOyalA and OPTOidro irrespectively of the group of people studied. ATs use for 15 days produced a significant improvement in DEQ5 and OR in DD-Ws (Δ = −34%, p=0.006; Δ = −23%, p<0.001) and in N-Ws (Δ = −21%, p=0.001; Δ = −10%, p=0.006) but not in BW-Ws (Δ = −5%, p=0.072; Δ = −2%, p=0.257). No significant change was noted for TMH.

Conclusion: In young and healthy subjects, the aqueous-supplementing effect of the ATs under consideration is more a rinsing and tear replacement effect than an increase in tear volume, and it produces an improvement of the eye redness and ocular symptoms. Contact lens wear influenced the effectiveness of ATs in a way which is correlated with the CL replacement schedule.

Keywords: artificial tears, contact lenses, somofilon A

Introduction

In the first approximation, the tear film is typically described by a mixed inner aqueous-mucins layer with an outer lipid layer. A stable and healthy tear film provides a protective layer, which guarantees good eye comfort and vision thanks to the hydration and nutrition of the cornea and conjunctiva, the protection of the ocular surface from dust, dirt particles, and foreign bodies, and the maintenance of corneal transparency. When the quality or quantity of tears are compromised due
to some dysfunctions, tear film instability and dry eye symptoms may occur.\textsuperscript{4–9} It has been indicated that the prevalence of dry eye ranges from approximately 5\% to 50\% when the diagnosis is based on symptoms with or without signs.\textsuperscript{8} However, when the diagnosis is based primarily on signs, studies generally reported higher and more variable rates of disease, up to 75\%.\textsuperscript{5}

Artificial tears (ATs) are tear substitutes, which are available over-the-counter and are often used as the first line of treatment in order to supplement a deficient natural tear film to treat dryness and irritation.\textsuperscript{10,11} For a sustained therapeutic effect, these formulations should remain on the ocular surface for a sufficiently long time, but newly secreted tears can dilute and wash away active agents, and blinking can remove instilled tear substitutes, which flow through the main excretory ducts.\textsuperscript{10–13} Their relative short retention time leads to high frequency of instillation. Generally speaking, there are two major types of ATs, one that supplements the aqueous part of the tear and the other that supplements the lipid part.\textsuperscript{10} Aqueous-supplementing ATs are expected to provide lubrication and an enhancement of viscosity.\textsuperscript{10} Among them, there are simple saline-based solutions and other ATs containing natural and synthetic polymers.\textsuperscript{10} Ingredients are typically polyacrylic acid, carboxymethyl cellulose (CMC), dextran, hyaluronic acid (HA), hydroxypropyl guar, hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), and polyethylene glycol.\textsuperscript{10} These ingredients prolong the time that the ATs stay on the eye. Specifically, HA, a long polysaccharide with a high molecular weight which is present in connective tissue and in other parts of the human body,\textsuperscript{14,15} is a component of many ATs in the form of its sodium salt (sodium hyaluronate). Due to its viscosity-enhancing properties, some manufacturers also add sodium hyaluronate directly in the solutions of the CL blister to improve the comfort after CL insertion.\textsuperscript{15–18}

Lipid-supplementing ATs were introduced because a lipid deficit can cause a quicker evaporation of the tears leading to a condition of dry eye.\textsuperscript{10} These are typically emulsions for liquids (Atago, Japan).\textsuperscript{19} It has been indicated that the therapeutic effect, these formulations should remain on the eye for sufficiently long time, but newly secreted tears can dilute and wash away active agents, and blinking can remove instilled tear substitutes, which flow through the main excretory ducts.\textsuperscript{10–13} Their relative short retention time leads to high frequency of instillation. Generally speaking, there are two major types of ATs, one that supplements the aqueous part of the tear and the other that supplements the lipid part.\textsuperscript{10} Aqueous-supplementing ATs are expected to provide lubrication and an enhancement of viscosity.\textsuperscript{10} Among them, there are simple saline-based solutions and other ATs containing natural and synthetic polymers.\textsuperscript{10} Ingredients are typically polyacrylic acid, carboxymethyl cellulose (CMC), dextran, hyaluronic acid (HA), hydroxypropyl guar, hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), polyvinylpyrrolidone (PVP), and polyethylene glycol.\textsuperscript{10} These ingredients prolong the time that the ATs stay on the eye. Specifically, HA, a long polysaccharide with a high molecular weight which is present in connective tissue and in other parts of the human body,\textsuperscript{14,15} is a component of many ATs in the form of its sodium salt (sodium hyaluronate). Due to its viscosity-enhancing properties, some manufacturers also add sodium hyaluronate directly in the solutions of the CL blister to improve the comfort after CL insertion.\textsuperscript{15–18}

In the literature, several studies on the clinical effects of ATs and on the comparison between them are reported.\textsuperscript{13,21–29} Some of these studies concern the retention time on the ocular surface and both symptoms and signs in patients with dry eye. In rat and rabbit animal models of dry eye, sodium hyaluronate was reported to show a significantly longer retention time than other ATs, including carboxymethylcellulose and hydroxypropyl methylcellulose.\textsuperscript{13} Aragona et al found that sodium hyaluronate is also able to improve the conjunctival epithelial cell abnormalities of the ocular surface.\textsuperscript{22}

Recent studies found that more than half of the CL wearers suffer from dry eye, a much higher percentage than found in the general population matched for age.\textsuperscript{8,23} In CL wearers, a stable tear film is a requirement because it keeps the CL hydrated, ensures an adequate oxygen transmission, and reduces the chances of bacterial contamination of the CL.\textsuperscript{30–32} However, the interaction between tear film and CLs is certainly affected by the frequency of replacement of CLs for the different building up of deposits on the lens surface which is potentially reduced by the use of daily disposable CLs. Moreover, daily disposable CLs require the least amount of upkeep and have the advantage of reducing complications associated with case contamination and use of care products.\textsuperscript{33–41} However, the costs are typically higher and throwing the CLs every day means increased waste disposal due to the CL itself and its packaging.

The present work concerns CL wear combined with the use of ATs. The question that gave rise to this work was to investigate whether the efficacy of an aqueous-supplementing AT in symptoms and ocular signs is different in wearers of daily disposable CLS (DD-Ws), in wearers of CLs of the same material with lower frequency replacement, and in non-wearers (N-Ws).

Materials and Methods

Artificial Tears

OPTOyalA and OPTOidro ATs (OPTOX, Italy) were used in this work in single-dose format (0.35 mL each). They are both isotonic saline solutions buffered to pH 7.2. In addition, OPTOyalA contains, as declared by the manufacturer, sodium salt of hyaluronic acid (1.5 mg/mL), sodium salt of hyaluronic acid (0.14 mg/mL), and L-leucine (0.108 mg/mL).

The osmolarity of the ATs was measured by the TearLab™ osmosmolarity system (Tear Lab, California, USA). The measured values (mean ± standard deviation of five repetitions) were 292±2 Osm/L (OPTOyalA) and 290±2 Osm/L (OPTOidro).

The refractive index (mean ± standard deviation of five repetitions) was measured (OPTOyalA: 1.3358±0.00004; OPTOidro: 1.33543±0.00004) by a digital refractometer Atago RX3000α for liquids (Atago, Japan).
The determination of relative viscosity was carried out at 18°C by using a homemade capillary viscometer. The relative viscosity ($\eta_r = \eta/\eta_0$) was evaluated by correlating two measurements: one performed on the AT ($\eta$) and the other on an isotonic solution containing 0.9% sodium chloride without preservatives (Alcon Vision Care, USA) used as reference ($\eta_0$). The measured value of $\eta_r$ was 3.26 ±0.01 for OPTOyalA and 1.04 ± 0.01 for OPTOidro (mean ± standard deviation of five repetitions).

**Contact Lenses**

Either daily disposable or 1-month manufacturer-recommended replacement CLs of the same material were included in the study. The 1-month manufacturer-recommended replacement CLs were actually used for 2 weeks (BW-W group) in the study. Some of their properties are shown in Table 1. Daily disposable CLs (somofilcon A Clarity 1 Day, Cooper Vision, USA) were used by 18 wearers (DD-Ws), as described below, while 1-month replacement CLs (somofilcon A Clariti Elite, Cooper Vision, USA) for daily use were worn by 20 wearers (BW-Ws). The Refine One Step hydrogen peroxide solution (Cooper Vision, USA) was also given to BW-Ws for the overnight CL storage.

**Participants and Study Design**

The study was conducted according to the tenets of the Declaration of Helsinki. Before being enrolled in the study each subject expressed his/her written informed consent and gave the researchers permission to collect and treat personal and optometric data. The subjects took part in the project for free. The Optics and Optometry Board of the University of Milano Bicocca granted approval for the study (June 2018). A scheme of the study design is shown in Figure 1.

During the recruitment phase, the inclusion criteria were the absence of any known ocular and systemic pathologies, not having used any eye drops (ATs included) in the week before the study began, and, only for non-wearers, never having worn CLs.

Thirty-three N-Ws were recruited and, on the first day (Figure 1), a standard protocol was carried out (described in the clinical assessment section below) to assess ocular symptoms and the condition of tear film and ocular surface. These subjects were randomly assigned to one of two N-W subgroups based on the dispensed ATs (Figure 1 and Table 2): 16 subjects out of 33 were assigned at the OPTOyalA subgroup and 17 were assigned at the OPTOidro subgroup. All 33 subjects received an adequate number of packages of ATs in single-dose formats (0.35 mL each) to allow using the assigned AT for 2 weeks of use (3 times a day at times chosen by each subject, each application separated from the previous one by at least 3 hours). The clinical assessment was repeated on the fifteenth day (Figure 1).

Thirty-eight CL wearers (habitual or occasional wearers of CLs of different materials and different replacement modality) were recruited and randomly assigned to one of the two groups: 18 subjects in the DD-W group and 20 subjects in the BW-W group (Figure 1). All subjects received a proper number of the assigned CLs (thirty blisters of daily disposable CLs and a pair of 1-month replacement CLs of the appropriate optical power) to be used on a daily wear basis (8±1 hours a day) for 2 weeks without any AT. For the BW-W group, subjects were also provided with a package of hydrogen peroxide solution (Refine One Step, Cooper Vision, USA) as the CL care system. For CL wearers, the experimental phase of this study began at the end of these 2 weeks of preliminary wear (as shown by a dashed box in Figure 1). On the first day of the experimental phase, the standard protocol (clinical assessment) to assess symptoms, tear film, and ocular surface was carried out. Each group (DD-Ws and BW-Ws) was further divided into two subgroups depending on the randomly assigned AT (Figure 1 and Table 2). Nine out of 18 DD-Ws were included in the DD-W subgroup using OPTOyalA, the other 9 DD-Ws were included in the DD-W subgroup using OPTOidro. Eight out of 20 BW-Ws were included in the BW-W subgroup using OPTOyalA, and the other 12 BW-Ws were included in the

| Table 1 Contact Lenses |
|-------------------------|
| **Material** | **Somofilcon A** | **Somofilcon A** |
| Brand | Clarity 1 Day | Clariti Elite |
| Manufacturer | Cooper Vision, USA | Cooper Vision, USA |
| Replacement | Daily | Monthly (worn for two weeks in this work) |
| Equilibrium water content (%) | 56 | 56 |
| −3.00D central thickness (mm) | 0.07 | 0.07 |
| Elastic modulus (MPa) | 0.50 | 0.50 |

**Note:** Properties of the contact lenses used in this work.
OPTOdro subgroup. New CLs were then provided: a pair of 1-month replacement CLs were dispensed to the group of BW-Ws to be used in the following 2 weeks together with the assigned ATs and 30 blisters of daily disposable CLs were dispensed to the DD-Ws. After 2 weeks of wear, the clinical assessment was repeated (Figure 1). CLs were worn for 8±1 hours every day. ATs were instilled three times a day with the CL in-situ, at times chosen by each subject, each application separated from the previous one by at least 3 hours.

All participants of the three groups (N-Ws, DD-Ws, and BW-Ws) completed the project and stated that they had followed the instructions provided. The refractive error (spherical equivalent) of the study participants was included in the range between −12.00 D and +2.00 D (mean = 3.39 D, std dev = 2.67 D).

Clinical Assessment
The clinical assessment consisted of the ocular surface symptoms measurement gathered through the use of two

![Figure 1 Scheme of the study design showing the recruitment of non-wearers (N-Ws) and wearers of contact lenses (CLs), either daily disposable contact lenses (DD-Ws) or biweekly replacement contact lenses (BW-Ws), and the 15-day experimental phase in which artificial tears (ATs) were used.](image)

| Table 2 Groups and Subgroups |
|-----------------------------|
| Group | Subgroup | \(N_{\text{males}}\) | \(N_{\text{females}}\) | \(N_{\text{subgroup}}\) | \(N_{\text{group}}\) | Age (years) |
|------|----------|----------------|----------------|----------------|----------------|-------------|
|      |          |                |                |                |                | Mean Std Dev |
| N-W  | OPTOyalA | 10             | 7              | 16             | 33             | 25.1 23.2 3.2 |
|      | OPTOdro  | 6              | 10             | 17             |                | 2.7          |
| DD-W | OPTOyalA | 3              | 6              | 9              | 18             | 22.0 22.9 1.3 |
|      | OPTOdro  | 5              | 4              | 9              |                | 1.1          |
| BW-W | OPTOyalA | 4              | 4              | 8              | 20             | 23.5 25.0 1.2 |
|      | OPTOdro  | 4              | 8              | 12             |                | 2.3          |

Notes: Number of males/females, total number of subjects (\(N_{\text{subgroup}}\)), mean age, and standard deviation of the age for each subgroup (OPTOyalA and OPTOdro) of the three groups (non-wearers, wearers of daily disposable contact lenses, wearers of biweekly replacement contact lenses).

Abbreviations: \(N_{\text{males}}\), number of males; \(N_{\text{females}}\), number of females; \(N_{\text{subgroup}}\), total number of subjects of the subgroup; \(N_{\text{group}}\), total number of subjects of the group; N-W, non-wearers; DD-W, wearers of daily disposable contact lenses; BW-W, wearers of biweekly replacement contact lenses.
standardized questionnaire and in three objective measurements of tear film and ocular surface: tear meniscus height (TMH), non-invasive tear break-up time (NIBUT), and ocular redness evaluation (OR).

The two questionnaires to evaluate ocular surface symptoms were the Ocular Surface Disease Index (OSDI) and the 5-Item Dry Eye Questionnaire (DEQ-5).

The TMH measurement, performed to achieve a measure of tear volume, was carried by a two-step procedure as described by the Dry Eye Report (CSO, Firenze, Italy) integrated in the software platform called Phoenix (CSO, Firenze, Italy): a digital image of the inferior tear meniscus was firstly acquired, then the height of the meniscus in a central position (just under the virtual extension of the vertical axes of the cornea) was measured by the digital ruler device of the software. The evaluation was repeated three times and the mean value was taken into consideration.

The non-invasive tear break-up time (NIBUT) was performed using the Dry Eye Report (DER) (CSO, Firenze, Italy). The software allowed to detect the first tear break up through an automatic algorithm. The measurement was repeated three times and the mean value was taken into consideration.

OR was measured because considered the most common clinical sign that is suggestive of ocular surface inflammation. A snapshot of temporal bulbar conjunctiva was taken by the Dry Eye Report (CSO, Firenze, Italy) and the bulbar ocular redness. All images were saved as masked codes and OR severity was subsequently determined by comparison with the templates of Efron Grading scales.

In the clinical assessment sequence, each subject was firstly requested to complete the two questionnaires then the objective assessment was carried out in the following order: TMH, NIBUT, and OR. The two repeated clinical assessments were carried out at the same time in the morning (with a tolerance of 1 hour) in order to minimize possible effect of diurnal variation. For each subject, only the data of the right eye were analyzed.

**Statistical Analysis**

Descriptive statistics (mean, standard deviation SD) was produced for the measurements (OSDI, DEQ5, TMH, NIBUT, OR) collected on the first day and on the fifteenth day of the experimental phase. For each subject, the percentage change (Δ) of each variable was also calculated as the difference between the values measured on the first day divided by the value of the first day. Mean and SD were also calculated for these percentage changes.

For each group separately (N-Ws, DD-Ws, BW-Ws), a preliminary analysis was performed to compare the results of the two subgroups based on the type of AT (OPTOyalA or OPTOidro). Due to the small number of subjects, non-parametric statistics were used (unpaired Mann–Whitney, level of significance: p-value < 0.05). The subsequent analyses concerned (i) the three groups consisting of all N-Ws, all DD-Ws, and all BW-Ws regardless of the assigned AT, (ii) the three groups consisting of N-Ws using OPTOyalA, DD-Ws using OPTOyalA, and BW-Ws using OPTOyalA, and finally (iii) the three groups consisting of N-Ws using OPTOidro, DD-Ws using OPTOidro, and BW-Ws using OPTOidro. The comparison between the results obtained in each group on the first day and on the fifteenth day was performed by the non-parametric Wilcoxon test (level of significance: p-value < 0.05).

**Results and Discussion**

For each group separately (N-Ws, DD-Ws, BW-Ws) and for each subgroup (OPTOidro and OPTOyalA), Figure 2 shows the mean values measured on the 1st and 15th days. The values are also tabulated in Table 3, together with the mean percentage variations (Δ) for each variable, which allow to probe the effect of the ATs without the subjects’ initial individual variability influencing the data analysis.

A preliminary analysis was carried out to compare the results of the two subgroups. The p-values obtained by unpaired comparison between the Δ values of the two subgroups (OPTOyalA vs OPTOidro) are also tabulated in Table 3 for each group. Only for the TMH of BW-Ws (1 comparison out of 15), the effect of the two ATs was noted to be different (p=0.041 in Table 3). However, neither of the two corresponding TMH Δ values showed a significant variation between the 1st and the 15th day (+14% in the case of OPTOyalA showing p=0.263 and −12% in the case of OPTOidro showing p=0.195). This makes the difference between the two ATs in the unpaired comparison of little clinical significance. No significant differences were noted in the unpaired comparison between the two subgroups (OPTOyalA vs OPTOidro, p>0.05) for all other variables. Looking carefully at Table 3, some other apparent discrepancies concern OR of N-Ws, DEQ5 of DD-Ws, and NIBUT of BW-Ws. Concerning the OR of N-Ws, the variation between the
1st and the 15th day was significant only for the OPTOyalA subgroup and for the whole group of 33 subjects. Although it was not significant for the OPTOidro subgroup (p=0.130), the overall result of all the 33 N-Ws well represents this group. Indeed, all three OR Δ values of N-Ws are negative (−10%, −12%, −8%) and the unpaired comparison between OPTOyalA and OPTOidro did not result in a significant difference (p=0.416). The scenario is similar for the DEQ5 of DD-Ws. All three DEQ5 Δ values of DD-Ws are negative (−34%, −44%, −24%) and the comparison between OPTOyalA and OPTOidro did not result in a significant difference (p=0.352). Although the variation between the 1st and the 15th day was not significant for the OPTOidro subgroup (p=0.175), the overall result of all the 18 DD-Ws well represents the DD-W group. Finally, concerning the NIBUT of BW-Ws, the variation between the 1st and the 15th day was significant only for the OPTOidro subgroup and for the whole group of 33 subjects. Although it was not significant for the OPTOyalA subgroup (p=0.799), the overall result of all the 20 BW-Ws well represents this group. Indeed, all three Δ values are positive (+35%, +29%, +40%) and the comparison between OPTOyalA and OPTOidro did not result in a significant difference (p=0.160). In all the other 11 out of 15 cases of Table 3, the variations after 15 days of the OPTOyalA subgroup only, of the OPTOidro subgroup only, and of the group as a whole showed the same type of behavior and the same statistical evidence. Based on these considerations, the subsequent analyses concerned the three groups consisting of 33 N-Ws, 18 DD-Ws, and 20 BW-Ws regardless of the assigned AT.

Even if the purpose of this work was the comparison between the 1st and the 15th day, a first comment concerns the data obtained on the 1st day in the three groups. The results are compatible with the expected results for young and healthy subjects. The most interesting parameter was found to be the OR because a statistically greater average value was found for the 18 DD-Ws on the 1st day than for the 33 N-Ws (1.7±0.3 vs 1.0±0.6), as well as for the 20 BW-Ws compared to N-Ws (2.0±0.6 vs 1.0±0.6). Even if it is not reported in Table 3, an unpaired Mann–Whitney test between the data taken on the 1st day provided p<0.001 in both of these comparisons. After 15 days, a significant OR improvement was found in N-Ws (−10%) and DD-Ws (−23%). From a clinical point

**Figure 2** Mean data measured on the 1st and 15th days for the two ATs separately. 
**Abbreviations:** N-Ws, non-wearers; DD-Ws, wearers of daily disposable contact lenses; BW-Ws, wearers of biweekly replacement contact lenses; OSDI, Ocular Surface Disease Index; DEQ5, 5-Item Dry Eye Questionnaire; TMH, tear meniscus height; NIBUT, non-invasive tear break-up time; OR, ocular redness.
Table 3 Variations from the First to the Fifteenth Day

|                | N-Ws               | DD-Ws               | BW-Ws               |
|----------------|--------------------|--------------------|--------------------|
|                | All (33 Subjects)  | OPTOyalA (16 Subjects) | OPTOidro (17 Soggetti) |
|                | 11.8 (SD 5.7)      | 15.3 (SD 10.4)     | 17.0 (SD 18.3)     |
|                | 10.4 (SD 7.4)      | 11.2 (SD 9.2)      | 11.0 (SD 13.1)     |
|                | −17%               | −24%               | +2%                |
| Δ              | 0.047              | 0.391              | 0.446              |
| P (15th vs 1st)| 0.003              | 0.030              | 0.046              |
|                | 13.6 (SD 8.5)      | 15.2 (SD 15.4)     | 13.4 (SD 12.7)     |
|                | 10.8 (SD 8.3)      | 12.4 (SD 15.3)     | 13.0 (SD 18.1)     |
|                | −10%               | +2%                | −23%               |
|                | 0.047              | 0.391              | 0.446              |
| P (OPTOyalA vs OPTOidro) | 0.928          | 0.562              | 0.062              |

|                | DEQ5               |                    |                    |
|                | All 18 Subjects    | OPTOyalA (9 Subjects) | OPTOidro (9 Soggetti) |
|                | 6.0 (SD 3.0)       | 9.2 (SD 3.8)       | 8.4 (SD 4.2)       |
|                | 6.2 (SD 3.7)       | 6.1 (SD 4.4)       | 6.2 (SD 4.7)       |
|                | −27%               | −34%               | −24%               |
| Δ              | 0.014              | 0.006              | 0.010              |
| P (15th vs 1st)| 0.001              | 0.032              | 0.755              |
|                | 6.1 (SD 3.4)       | 9.9 (SD 3.6)       | 7.4 (SD 3.6)       |
|                | 4.2 (SD 2.8)       | 6.0 (SD 4.3)       | 6.0 (SD 3.2)       |
|                | −21%               | −44%               | −5%                |
| P (OPTOyalA vs OPTOidro) | 0.091          | 0.352              | 0.755              |

|                | TMH (mm)           |                    |                    |
|                | All 20 Subjects    | OPTOyalA (8 Subjects) | OPTOidro (12 Soggetti) |
|                | 0.19 (SD 0.02)     | 0.33 (SD 0.13)     | 0.23 (SD 0.08)     |
|                | 0.20 (SD 0.03)     | 0.29 (SD 0.07)     | 0.21 (SD 0.09)     |
|                | +5%                | −2%                | −2%                |
| Δ              | 0.059              | 0.342              | 0.544              |
| P (15th vs 1st)| 0.551              | 0.402              | 0.041              |
|                | 14.1 (SD 8.6)      | 11.5 (SD 4.6)      | 12.9 (SD 7.4)      |
|                | 16.6 (SD 11.3)     | 11.1 (SD 12.1)     | 15.4 (SD 5.3)      |
|                | +26%               | +22%               | +35%               |
| P (OPTOyalA vs OPTOidro) | 0.692          | 0.015              | 0.041              |

(Continued)
In patients with monthly CL wear, the mean OSDI was 1.0 (SD 0.6) in N-Ws, 1.1 (SD 0.7) in DD-Ws, and 1.0 (SD 0.5) in BW-Ws. The mean DEQ-5 was 0.5 (SD 0.4) in N-Ws, 1.2 (SD 0.3) in DD-Ws, and 1.4 (SD 0.5) in BW-Ws. The mean TMH was 2.0 (SD 0.6) in N-Ws, 1.3 (SD 0.4) in DD-Ws, and 1.4 (SD 0.5) in BW-Ws. The mean NIBUT was 1.0 (SD 0.5) in N-Ws, 1.2 (SD 0.3) in DD-Ws, and 1.4 (SD 0.5) in BW-Ws. The mean OR was 0.9 (SD 0.4) in N-Ws, 1.2 (SD 0.3) in DD-Ws, and 1.4 (SD 0.5) in BW-Ws. The mean percentage variations of the measured variables on the first and fifteenth days, mean percentage variations of the measured variables on the first and fifteenth days, and p-values for the paired comparison (Wilcoxon test) between the values measured on the first and fifteenth days for each group (N-Ws, DD-Ws, BW-Ws) and for each variable (OSDI, DEQ-5, TMH, NIBUT, OR), including all subjects, only subjects who used OPTOyalA, or only subjects who used OPTOidro. The p-values obtained by unpaired Mann-Whitney comparison between the Δ values of the two subgroups (OPTOyalA vs DD-Ws, OR of DD-Ws vs the mean OR in all subjects) are also reported. Bold font: p < 0.05.

Abbreviations: OR, ocular redness; SD, standard deviation.
wear combined with different care systems: hydrogen peroxide such as in the present work (first group in Moro et al\textsuperscript{26}), detergent solution combined with hydrogen peroxide (second group in Moro et al\textsuperscript{29}), and multipurpose solution (third group in Moro et al\textsuperscript{29}). That study was aimed at comparing the different maintenance systems. A worsening of the external-eye condition was reported only in the first group, which can be attributed to a lower cleaning efficacy of the hydrogen peroxide compared to the other two care systems or to a different effect on the CL wettability, surface friction, or on other CL properties. The present study highlights that the use of the ATs under investigation at least prevents the worsening after 2 weeks of wear of the monthly CLs treated with hydrogen peroxide. Unfortunately, ATs did not significantly improve the symptoms and ocular signs in BW-Ws.

An extension of this work could be the study of the effects of OPTOyalA and OPTOdido ATs in wearers of other types of CLs of different materials, also with the aim to shed more light on the reason why the effectiveness of ATs was not found in the case of BW-Ws. The study could also include chemical-physical analysis of the CLs used together with the ATs, eg, surface wettability and friction measurements,\textsuperscript{47,48} surface morphology and elemental characterization.\textsuperscript{49,50}

Conclusions
On young and healthy CL wearers, the aqueous-supplementing effect of the ATs under consideration was mainly a rinsing and tear replacement effect, which allowed an improvement of the ocular redness and eye comfort, without any significant increase in tear volume after 2 weeks of use. The efficacy of the ATs appeared to be correlated with the replacement schedule of the lenses. There was a less significant improvement in monthly replacement CL wearers compared with daily disposable CL wearers. Nonetheless, ATs appeared to prevent the worsening of the external eye condition that was previously reported after 2 weeks of silicone-hydrogel CL wear combined with hydrogen peroxide cleaning system. The efficacy of the ATs was observed also in the control group (non-wearers), although it is less relevant from the clinical point of view, given their initial condition of young and healthy subjects.

Disclosure
The authors report no conflicts of interest in this work.
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