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# Efficacy and tolerability of esculin and digitalis glycosides eye drops versus sodium hyaluronate in pediatric digital screen-related visual fatigue and dry eye

**Jun Wu*, Jili Wen and Daodian Tao**
Ophthalmology Department, Jinhua Municipal Central Hospital, No. 365, Renmin East Road, Jinhua 321000, Zhejiang Province, China

**Abstract**: **Background**: Visual fatigue and dry eye are prevalent pediatric ophthalmic conditions. Esculin-digitalis glycosides and sodium hyaluronate eye drops are widely used, yet their specific clinical value remains unclear. **Objectives**: This study compared esculin and digitalis glycosides eye drops with sodium hyaluronate eye drops for pediatric digital screen-related visual fatigue and dry eye, assessing efficacy and tolerability. **Methods**: In the observational retrospective study, 126 patients were initially screened from December 2022 to December 2024 and 122 were enrolled after exclusions. They were divided into two groups according to the treatment plan: the sodium hyaluronate group (n=60) and the esculin-digitalis glycosides group (n=62). After propensity score matching (PSM), 50 patients were included in each group. The primary outcome measures included the Ocular Surface Disease Index (OSDI) score, Tear Film Breakup Time (TBUT), tear secretion volume and Corneal Fluorescein Staining (CFS) score. The secondary outcome measures included Functional Visual Acuity (FVA) accuracy rate, Tear Meniscus Height (TMH), Meibomian Gland Function Score (MGFS), incidence of adverse events and the Scale of Quality of Life for Diseases with Visual Impairment score (SQOL-DVI). **Results**: After PSM, baseline data showed no significant between-group differences (all $P > 0.05$). Following 3 months of treatment, the esculin-digitalisglycosides group had greater reductions in OSDI, CFS and MGFS scores (all $P < 0.001$), longer TBUT, higher tear secretion, improved FVA accuracy and increased TMH than the sodium hyaluronate group (all $P < 0.001$). The esculin-digitalisglycosides group also had a higher SQOL-DVI total score. Adverse event rates were 4% (esculin-digitalisglycosides) and 8% (sodium hyaluronate), with no significant difference ($P = 0.400$) and no serious adverse events reported. **Conclusion**: Esculin and digitalis glycosides eye drops show superior efficacy to sodium hyaluronate eye drops in treating pediatric digital screen-related visual fatigue and dry eye, with good tolerability and clinical value.

**Keywords**: Children; Dry eye disease; Esculin and digitalisglycosides eye drops; Sodium hyaluronate eye drops; Visual fatigue

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## INTRODUCTION

In the 21st century, marked by rapid advances in digital technology, electronic devices have become indispensable tools for children's learning, entertainment and social interaction. While the frequent use of digital screens has driven innovations in educational models and facilitated easy access to information, it has also led to a range of eye health issues among children. Among these, the incidence of visual fatigue and dry eye syndrome has shown a significant upward trend, becoming the primary reason for visits to pediatric ophthalmology clinics (Kaur *et al.*, 2022). In 2024, the incidence of digital screen-related visual fatigue among Chinese children was 42.8% and that of dry eye syndrome was 29.3%. Notably, the younger the age, the greater the growth rate of incidence, presenting a clear trend of younger onset (Hecht *et al.*, 2025, Zhang *et al.*, 2025).

Prolonged fixation on digital screens exposes children's ocular tissues to multiple adverse stimuli, including blue light radiation, flicker effects and sustained visual focus (Soundari *et al.*, 2025). Additionally, studies have confirmed that long-term exposure to digital screens can induce visual fatigue and dry eye syndrome, reducing the efficiency of visual signal transmission and leading to inattention, memory decline and even affecting refractive development. This increases the risk of myopia onset and progression, posing a serious threat to children's physical and mental health as well as their future development5. Therefore, finding a therapeutic regimen that can both alleviate ocular surface dryness and improve ocular regulatory function and microcirculatory status has become a key focus of current clinical research in pediatric ophthalmology.

In the clinical treatment of children's visual fatigue and dry eye syndrome, drug therapy is a main approach. Among the commonly used medications, sodium hyaluronate eye drops and esculin and digitalis glycosides eye drops are the two most widely used. As a representative of artificial tear preparations, sodium hyaluronate eye drops have hyaluronic acid as their main component, boasting excellent biocompatibility and moisturizing properties. They can quickly supplement ocular surface tears, form a stable artificial tear film, reduce tear evaporation and thereby relieve symptoms such as dryness and foreign body

**Corresponding author:* e-mail: chenchen18030899@hotmail.com

sensation (Hynnekleiv *et al.*, 2022, Wang *et al.*, 2025). As a compound preparation, esculin and digitalisglycosides eye drops contain esculin and digitalisglycosides as their primary ingredients, which exert multi-dimensional regulation of ocular function through synergistic effects. Modern pharmacological studies have shown that digitalis glycosides can enhance contractility and regulatory sensitivity of the ciliary muscle, alleviate fatigue and spasm of the ciliary muscle caused by prolonged close-range viewing and improve symptoms such as blurred vision and eye distension (Wang *et al.*, 2025). Esculin, on the other hand, can inhibit vascular endothelial cell apoptosis, increase blood flow to the retina and choroid, improve oxygen and nutrient supply to ocular surface tissues and promote corneal epithelial repair and the recovery of lacrimal gland secretion function(Li *et al.*, 2022). While esculin and digitalisglycosides eye drops have demonstrated favorable clinical efficacy in treating visual fatigue and dry eye syndrome in adults, specialized research targeting the pediatric population remains scarce.

This study aims to conduct a comparative analysis of the clinical efficacy of esculin and digitalis glycosides eye drops (esculin and digitalisglycosides eye drops) and sodium hyaluronate eye drops in the treatment of digital screen-related asthenopia and dry eye syndrome in children, comprehensively evaluate the clinical efficacy and tolerability of esculin and digitalis glycosides eye drops in the pediatric population and provide evidence-based medical evidence for clinically optimizing the treatment regimens for such ophthalmic diseases in children.

## MATERIALS AND METHODS

### *Patient selection*

Children with visual fatigue and dry eye syndrome who visited Jinhua Municipal Central Hospital between December 2022 and December 2024 were screened. Among them, 126 patients had conditions related to digital screen use. After exclusions (2 cases of blepharitis, 1 cases of cognitive impairment and 1 cases of corneal lesion), a total of 122 patients were enrolled and divided into two groups based on the treatment plans documented in their medical records, the sodium hyaluronate group (60 patients treated with sodium hyaluronate eye drops) and the esculin-digitalisglycosides group (62 patients treated with esculin and digitalisglycosides eye drops). Following 1:1 Propensity Score Matching (PSM), 50 patients per group were ultimately included in the analysis (Fig. 1).

*Inclusion criteria*: (1) Aged 3-14 years; (2) Daily digital screen exposure of ≥3 hours; (3) Clear temporal association between visual fatigue/dry eye symptoms and screen use; (4) Presence of at least 2 of the following symptoms for ≥2 weeks: dryness, eye distension, blurred vision, foreign body sensation, or burning sensation; (5) Ocular Surface Disease Index (OSDI) score ≥16 and tear film breakup time (TBUT) <10 seconds(Lu *et al.*, 2022); (6) Received standardized treatment with either esculin and digitalisglycosides eye drops or sodium hyaluronate eye drops after diagnosis, with complete and traceable clinical data.

*Exclusion criteria*: (1) Pre-existing ocular conditions, including uncorrected refractive errors, congenital eye diseases, corneal lesions, blepharitis, severe meibomian gland dysfunction and other organic ocular disorders; (2) Comorbid systemic diseases such as diabetes mellitus, autoimmune diseases and allergic diseases; (3) Use of other anti-dry eye medications, ciliary muscle modulators, glucocorticoid eye drops, or oral drugs affecting tear secretion during treatment; (4) Concurrent receipt of ocular physical therapy, traditional Chinese medicine physical therapy, or other related interventions during treatment; (5) Participation in other ophthalmic drug clinical trials during the same period; (6) Cognitive or communication impairments (Salim *et al.*, 2023).

### *Sample size calculation*

The sample size calculation of this study was based on the findings of relevant previous research. A prior study involving 52 pediatric patients aged 9–14 years with dry eye complicated by allergic conjunctivitis demonstrated that both treatment groups receiving eye drops containing 0.2% hyaluronic acid and 0.1% arnica extract achieved a significant reduction in the Ocular Surface Disease Index (OSDI) scores after treatment (study group: 25.11±1.52; control group: 17.12±1.50)(Buzzonetti *et al.*, 2022). Cohen's d effect size was estimated to be 0.79 according to the formula. In this study, G*Power 3.1.9.7 was used to calculate sample sizes. With the significance level (α) set at 0.05 (two-tailed) and the type II error rate (β) set at 0.05, the calculation results indicated that a minimum of 43 patients per group was required to ensure sufficient statistical power. Given the inherent risk of data loss in retrospective studies and the actual number of eligible pediatric patients at our hospital, 50 patients per group were included in the analysis after PSM. This final sample size not only met the requirements of statistical estimation but also enhanced the robustness of the study results.

### *Data collection*

The collected data include baseline information, efficacy indicators and safety indicators. With the hospital's electronic medical record system as the core data source, data extraction and verification were independently completed by two uniformly trained ophthalmic researchers to ensure reliable data quality (Amer *et al.*, 2024). Data were collected at baseline (the day of the child's first visit and initiation of medication) and 3 months after medication administration.

### *Treatment regimens*

The determination of treatment regimens was based on actual clinical diagnosis and treatment records. All children received standardized medication in accordance with the

Expert Consensus on the Diagnosis and Treatment of Dry Eye in Children (2024)(Cornea Group of Ophthalmology Branch of Chinese Medical and Cornea Group of Chinese Ophthalmologist, 2024) and clinical pathways. Grouping was established based on the therapeutic drugs selected by physicians after evaluating the children's conditions during consultation. Specific medication details are as follows:

*Esculin-digitalisglycosides group*: Esculin and digitalisglycosides eye drops (Stulln, Pharma Stulln GmbH, Germany; 0.4ml/vial) were administered via instillation into the conjunctival sac, with a dosage of 1 drop per eye, 3 times daily (Wang *et al.*, 2021).

*Sodium hyaluronate group*: Sodium hyaluronate eye drops (Hylo Comod, URSAPHARM Arzneimittel GmbH, Germany; 10ml/bottle) were administered via instillation into the conjunctival sac, with a dosage of 1 drop per eye, 3 times daily (Sharma *et al.*, 2025).

***Outcome measures***

***Primary outcome measures***

(1) *OSDI score*: The OSDI has been verified in previous studies to exhibit good test-retest reliability (ICC = 0.90) and repeatability. It can effectively assess dry eye symptoms in children, achieved through targeted revisions to its items: refining the wording of descriptors (e.g., revising "a gritty sensation in the eyes" to "a foreign body sensation in the eyes"), eliminating items irrelevant to children's daily experiences (e.g., "night driving") and adding items associated with digital device usage (e.g., "using computers or tablets"). Meanwhile, relevant validation studies on the OSDI scale have demonstrated that following cross-cultural adaptation(Temelturk *et al.*, 2024, Riascos *et al.*, 2025), the scale yields a high internal consistency coefficient of up to 0.91 and demonstrates robust construct validity, thereby providing a methodological foundation for its application in the pediatric population.

For toddlers as young as 3 years old, this study used scale assessments administered by ophthalmologists and parental reporting. Specifically, ophthalmologists explained the meaning of each item using child-friendly language, while parents supplemented feedback based on the toddlers' day-to-day behavioral manifestations. The specific measurement procedure was as follows: ophthalmologists guided children and their parents to complete the scale; each item was scored on a 5-point Likert scale, with ratings ranging from "no impact (1 point)" to "severe impact (5 points)". The total raw score was subsequently standardized and converted to a range of 0–100, where higher scores indicate more severe functional impairment related to ocular surface diseases.

(2) *TBUT*: Measurements were performed in accordance with the standardized operating protocols specified in the Expert Consensus on the Diagnosis and Treatment of Pediatric Dry Eye (2024)(Cornea Group of Ophthalmology Branch of Chinese Medical and Cornea Group of Chinese Ophthalmologist, 2024). This operational guideline serves as an authoritative reference in pediatric ophthalmology in China and the associated measurement procedures have been validated in clinical practice to yield high consistency. As a core parameter for evaluating tear film stability, this indicator has a normal reference value of ≥10 seconds. The specific measurement procedure was as follows: the child was positioned in a seated posture and following topical anesthesia administration, an ophthalmologist applied a fluorescein sodium strip to the inferior fornix conjunctiva of the child's eye; after uniform tear film staining was achieved, the child was instructed to blink three consecutive times and the time to initial tear film breakup was then observed using a slit-lamp microscope (cobalt blue light mode; SLM-2000, Suzhou 66 Vision Tech Co., Ltd., Suzhou, China). The measurement was repeated three times consecutively and the mean value was calculated as the final result.(Serino *et al.*, 2023).

(3) *Tear secretion volume*: The measurement was conducted using the Schirmer I test method in accordance with the standardized operating procedures specified in the Expert Consensus on the Diagnosis and Treatment of Pediatric Dry Eye (2024)(Cornea Group of Ophthalmology Branch of Chinese Medical and Cornea Group of Chinese Ophthalmologist, 2024), with a normal reference value of ≥10 mm/5 min. As a classic approach for evaluating tear secretion function, this method has been validated in long-term clinical practice and is widely recognized for its accuracy and repeatability. The specific measurement procedure was as follows: the child was positioned in a seated posture and without topical anesthesia, one end of a Schirmer filter paper strip (ST-100, Jinan Euroimmun Medical Devices Co., Ltd., Jinan, China) was folded 5 mm and inserted into the outer one-third of the inferior palpebral conjunctival sac, with the remaining portion hanging outside the eyelid margin. The child was then instructed to keep their eyes gently closed; after 5 minutes, the filter paper strip was removed and the wetting length from the folded end was measured and recorded precisely (Serino *et al.*, 2023, Huang *et al.*, 2025).

(5) *Corneal Fluorescein Staining (CFS) score*: The specific measurement procedure was identical to that employed for the TBUT test. As an internationally recognized tool for assessing corneal injury, this method has been validated in multicenter studies and is characterized by well-defined grading criteria and high operability. Following fluorescein sodium staining, the distribution and density of staining spots in each corneal quadrant were observed under a slit-lamp microscope, with findings categorized using a 0–3 grading scale. Grade 0 denotes no staining; Grade 1 indicates scattered punctate staining (≤ 5 spots); Grade 2 represents diffuse punctate staining (> 5 spots without

fusion); and Grade 3 corresponds to patchy fused staining or corneal epithelial defect. The total score is calculated as the sum of scores across 5 corneal regions, ranging from 0 to 15, where higher scores reflect more severe corneal epithelial damage (Huang *et al.*, 2025).

***Secondary outcome measures***

(1) *Functional Visual Acuity (FVA)*: This indicator is defined as the visual recognition accuracy rate of children under simulated daily digital screen exposure scenarios. Specifically, it refers to the percentage of correctly identified optotype lines relative to the total number of optotype lines on a standard logarithmic visual acuity chart, following 3 minutes of continuous viewing of dynamic visual targets that simulate the flicker frequency and brightness of electronic screens. Relevant literature (Sargent and Yule, 2025) has demonstrated a significant negative correlation between this indicator and the severity of digital eye strain symptoms in children ($r = -0.72$, $P < 0.01$), confirming its robust discriminative validity. The accuracy rates of two consecutive visual acuity tests were recorded (calculated as: [number of correctly identified optotype lines / total number of optotype lines] × 100%) and the difference between the two values was used as the core evaluation index. A rate ≥ 90% is considered normal; 80%–89% indicates mild reduction; 70%–79% denotes moderate reduction; and < 70% signifies severe reduction, reflecting substantial visual function impairment induced by the condition(Walha *et al.*, 2025). For the younger pediatric population (aged 3–6 years), the reliability of measurements and children's compliance were ensured via the following strategies: replacing traditional optotypes with engaging visual targets (e.g., cartoon-patterned optotypes) to minimize resistance; conducting all measurements by two fixed, trained pediatric ophthalmologists who adhered to standardized instructions and operational protocols; implementing a 5-minute adaptive observation period prior to testing to familiarize children with the environment; providing encouraging guidance (e.g., "You're doing great, try one more!") throughout the process to sustain their attention; and for children with poor compliance during a single measurement session, completing the test in 2–3 separate intervals and calculating the mean value to eliminate errors associated with a single assessment.

(2) *Tear Meniscus Height (TMH)*: Measurements were conducted in accordance with the Expert Consensus on the Diagnosis and Treatment of Pediatric Dry Eye (2024)(Cornea Group of Ophthalmology Branch of Chinese Medical and Cornea Group of Chinese Ophthalmologist, 2024). This guideline serves as the core basis for the diagnosis and management of dry eye in China and the recommended anterior segment optical coherence tomography (OCT) measurement protocol has been clinically validated. Tear meniscus height was detected non-invasively using an anterior segment OCT device (RS-3000, Topcon Corporation, Tokyo, Japan). A value ≥ 0.3 mm is defined as the normal reference range; 0.2–0.29 mm indicates mild reduction in tear meniscus height; and < 0.2 mm denotes a significant decrease, suggestive of insufficient basal tear secretion (Hou *et al.*, 2023). The specific measurement procedure was as follows: an anterior segment OCT device was employed, with the scanning probe aligned to the tear meniscus region of the child's lower eyelid margin to acquire a clear cross-sectional image. The vertical distance from the corneal epithelial surface to the tear film surface was measured using the device's built-in software. The measurement was repeated three times consecutively and the mean was calculated as the final result.

(3) *Meibomian Gland Function Score (MGFS)*: Meibomian gland assessment was performed using a meibomian gland imaging system (MGI-100, Shenzhen Motic Imaging Technology Co., Ltd., Shenzhen, China). Scoring was conducted in accordance with the Expert Consensus on the Diagnosis and Treatment of Meibomian Gland Dysfunction (2022), based on three dimensions: meibomian gland loss (0–3 points), secretion characteristics (0–3 points) and orifice obstruction (0–2 points). The total score ranges from 0 to 8, with higher scores indicating more severe meibomian gland dysfunction(Hou *et al.*, 2023). This consensus standard has been validated in international multicenter studies, confirming its reliability and applicability across populations. The specific measurement procedure was as follows: the child was placed in a supine position; after local disinfection of the eyelid margins, the ophthalmologist gently compressed the orifice regions of the upper and lower meibomian glands using meibomian gland compression forceps, recorded the glandular secretion characteristics and calculated the total Meibomian Gland Function Score (MGFS) as the sum of scores for the upper and lower eyelids.

(4) *Scale of Quality of Life for Diseases with Visual Impairment (SQOL-DVI)*: This scale comprises 25 items across five dimensions: visual dependence in daily activities, psychological status, social function, treatment concerns and visual symptoms(Ocansey *et al.*, 2023). Validated in domestic multicenter clinical studies, the scale exhibits robust reliability and validity, supporting its application in pediatric ophthalmic research. The specific measurement procedure was as follows: An ophthalmologist instructed the children and their parents to complete the scale collaboratively; each item was rated on a 5-point Likert scale, with scores ranging from "no impact" (1 point) to "severe impact" (5 points). Raw scores were summed, then standardized and converted to a 0–100 scale, where higher scores indicate better quality of life related to visual health.

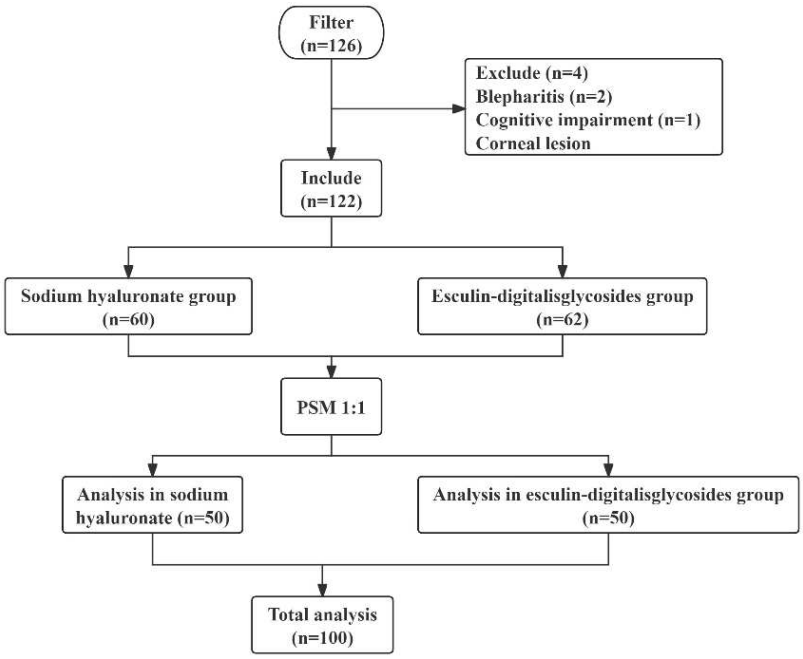


**Fig. 1**: Research flow chart.

(5) *Adverse events*: All procedures were conducted in accordance with the relevant standards specified in the Good Clinical Practice (GCP) for drug clinical trials, with rigorous monitoring of adverse drug reactions (ADRs). ADRs were classified into three grades: Mild—mild ocular tingling or itching, requiring no special treatment and not affecting continued medication; Moderate—mild conjunctival congestion, requiring a reduced medication frequency to once daily; Severe—obvious ocular redness and swelling accompanied by photophobia, requiring immediate drug withdrawal and symptomatic treatment with artificial tears. Causality assessment was performed independently by two attending ophthalmologists using a causal relationship evaluation method, encompassing four dimensions: the temporal association between medication administration and ADR onset, consistency with the drug's known adverse reaction profile, alleviation of symptoms following drug withdrawal and recurrence of symptoms upon re-administration. Assessment results were categorized into six grades: "definite", "probable", "possible", "possibly unrelated", "pending evaluation" and "unassessable". Only ADRs graded as "definite", "probable" and "possible" were included in the statistical analysis of this study(Molero Senosiain *et al.*, 2025). The ADR incidence rate was calculated as (number of cases with ADRs / total number of enrolled cases) × 100% and the severity of each ADR and corresponding management measures were recorded in detail.

***Ethical statement***

All research procedures in this study strictly adhered to the Declaration of Helsinki (World Medical, 2025) and the protocol was approved by the Medical Ethics Committee of Jinhua Municipal Central Hospital. For retrospectively collected historical cases, the Ethics Committee waived informed consent (approval number: 2025-340). This is because the study only uses existing clinical data without imposing additional risks on children and all data are de-identified throughout processing. The Ethics Committee formulated strict, operational safeguard guidelines to minimize trial-related risks to pediatric subjects. Specific measures include data desensitization and privacy protection, risk assessment and threshold limitation, conflict of interest review, as well as process supervision and regular reporting, so as to ensure that all operations are conducted in strict compliance with the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice (ICH-GCP)(Yang *et al.*, 2023).

***Statistical analysis***

SPSS 27.0 software was used for statistical analysis. PSM was performed using the nearest-neighbor matching method with a caliper of 0.02. After matching, the standardized mean difference (SMD) was used to assess the balance of baseline characteristics between groups; SMD < 0.1 indicated good balance. Normality tests (Shapiro-Wilk test) and homogeneity-of-variance tests (Levene test) were performed on the data. For normally distributed measurement data, paired t-tests were used for intragroup comparisons and independent-samples t-tests for intergroup comparisons, expressed as mean ± SD (Okoye and Hosseini, 2024). For measurement data not conforming to normal distribution, data were presented as median (interquartile range) [M (Q1, Q3)], with Wilcoxon tests for intragroup comparisons and Mann-Whitney U

tests for intergroup comparisons. Categorical data were expressed as n (%) and intergroup comparisons were performed using chi-square tests. All statistical tests were two-tailed and P < 0.05 was considered statistically significant.

## RESULTS

***Baseline characteristics of patients***

A total of 126 pediatric patients with digital screen-related visual fatigue and dry eye syndrome were initially screened in this study. After exclusion of the exclusion criteria, 122 patients were finally enrolled in the primary analysis, including 60 cases in the sodium hyaluronate group and 62 cases in the esculin and digitalis glycosides eye drops group. To reduce the impact of confounding factors in the baseline data on the study results, the baseline characteristics presented in table 1 were incorporated into the 1:1 PSM model. After matching, patients with imbalanced baseline data were excluded and 50 patients from each group (100 cases in total) were included in the subsequent statistical analysis. See table 1, Before matching, significant differences were observed between the two groups in age, average daily screen usage duration, TBUT, CFS score, FVA accuracy rate and TMH (all $P < 0.05$). After PSM, no significant differences were found in all general baseline characteristics (all $P > 0.05$), resulting in two cohorts with highly balanced baseline features and good comparability.

***OSDI score and CFS score***

The OSDI score reflects patients' subjective symptom experience, while the CFS score indicates the degree of objective ocular surface damage. A comparison of OSDI and CFS scores between the two groups (Table 2) showed that both scores decreased significantly after treatment compared with baseline (all $P < 0.05$), suggesting that both therapeutic regimens exert curative effects by alleviating dry eye symptoms and repairing ocular surface damage. Among them, the post-treatment OSDI score ($P < 0.001$) and CFS score ($P < 0.001$) in the esculin and digitalisglycosides eye drop were both lower than those in the sodium hyaluronate group. These results demonstrate that esculin and digitalis glycosides eye drops offer greater advantages in relieving dry eye symptoms, reducing the impact on visual function and repairing ocular surface damage.

***TBUT and tear secretion volume***

After treatment, both TBUT and tear secretion volume in the two groups were significantly increased compared with baseline (all $P < 0.05$). However, the esculin and digitalisglycosides eye drop showed a greater improvement in TBUT ($P < 0.001$) and tear secretion volume ($P < 0.001$) than the sodium hyaluronate group (Table 3). These findings indicate that both therapeutic regimens can improve tear film stability and tear secretion capacity. At the same time, esculin and digitalis glycoside eye drops are more effective in prolonging tear film breakup time, promoting tear secretion and achieving better supplementation of total tear volume.

***FVA accuracy rate***

As shown in table 4, the FVA accuracy rate in both groups was significantly higher after treatment than at baseline (all $P < 0.05$), indicating that both therapeutic regimens can effectively enhance uncorrected visual function and improve visual acuity accuracy in patients with dry eye syndrome. Among them, the post-treatment FVA accuracy rate in the esculin and digitalisglycosides eye drop was higher than that in the sodium hyaluronate group ($P = 0.036$). These results demonstrate that esculin and digitalis glycoside eye drops offer greater advantages in restoring uncorrected visual acuity and enhancing visual function.

***TMH and MGFS***

After treatment, both TMH and MGFS were improved in both groups compared with baseline (all $P < 0.05$). Moreover, the increase in TMH in the esculin and digitalisglycosides eye drop was greater than that in the sodium hyaluronate group ($P < 0.001$), indicating that esculin and digitalisglycosides eye drops are more effective in increasing tear meniscus height and enhancing tear storage capacity. The reduction in MGFS in the esculin and digitalisglycosides eye drop was more significant than that in the sodium hyaluronate group ($P < 0.001$), demonstrating that esculin and digitalisglycosides eye drops exert a more prominent improvement on meibomian gland function and better restore meibomian gland secretion. (Table 5)

***SQOL-DVI Score***

As shown in table 6, the SQOL-DVI scores in both groups were significantly higher after treatment than at baseline (all $P < 0.05$), indicating that both therapeutic regimens can effectively improve quality of life in patients with visual fatigue and dry eye syndrome. Among them, the increase in SQOL-DVI score in the esculin and digitalisglycosides eye drop was more pronounced than that in the sodium hyaluronate group ($P < 0.001$). These results further confirm that the esculin and digitalisglycosides eye drop has greater advantages in improving patients' subjective quality of life.

***Adverse events***

During the entire treatment cycle, the incidence of adverse events was low in both groups, with no severe adverse reactions reported. In the esculin and digitalis glycosides eye drop, only 2 cases (4.0%) experienced itching and the symptoms resolved spontaneously within 1–2 days without discontinuing medication. In the sodium hyaluronate group, 4 cases (8.0%) of adverse events occurred, including 2 cases of stinging, 1 case of worsening foreign body sensation and 1 case of blurred vision.

**Table 1**: Baseline clinical data [mean±SD, n (%)]

| Indicators | Before PSM | | | | After PSM | | | |
|---|---|---|---|---|---|---|---|---|
| | Sodium hyaluronate group (n=60) | Esculin-digitalisglycosides group (n=62) | *P* | Effect size | Sodium hyaluronate group (n=50) | Esculin-digitalisglycosides group (n=50) | *P* | Effect size |
| Age (years) | 8.40±1.40 | 7.85±1.39 | 0.032 | 0.393 | 8.39±1.37 | 8.45±1.37 | 0.844 | -0.039 |
| Gender | | | | | | | | |
| Male (n %) | 36 (60.00%) | 35 (56.50%) | 0.691 | 0.036 | 27 (54.00%) | 26 (52.00%) | 0.841 | 0.020 |
| Female (n %) | 24 (40.00%) | 27 (43.50%) | | | 23 (46.00%) | 24 (48.00%) | | |
| Average daily screen usage duration (h) | 7.42±1.77 | 6.25±1.78 | <0.001 | 0.657 | 6.90±1.70 | 6.81±2.37 | 0.813 | 0.048 |
| BMI (kg/m2) | 17.45±1.45 | 17.10±1.42 | 0.184 | 0.242 | 17.46±1.44 | 17.50±1.45 | 0.885 | -0.029 |
| Screen usage purpose | | | | | | | | |
| Study (n %) | 37 (61.70%) | 30 (48.40%) | 0.141 | 0.133 | 31 (62.00%) | 30 (60.00%) | 0.838 | 0.021 |
| Entertainment (n %) | 23 (38.30%) | 32 (51.60%) | | | 19 (38.00%) | 20 (40.00%) | | |
| OSDI (scores) | 39.34±1.57 | 40.26±5.36 | 0.201 | -0.230 | 39.32±1.58 | 39.39±1.54 | 0.833 | -0.042 |
| TBUT (s) | 6.01±0.31 | 6.13±0.30 | 0.035 | -0.387 | 6.01±0.32 | 6.06±0.27 | -0.168 | 0.404 |
| Tear secretion volume (mm/5min) | 7.72±0.32 | 7.61±0.37 | 0.099 | 0.301 | 7.72±0.32 | 7.68±0.36 | 0.560 | 0.117 |
| CFS (scores) | 2.30±0.15 | 2.22±0.23 | 0.035 | 0.384 | 2.30±0.15 | 2.28±0.18 | 0.626 | 0.098 |
| FVA Accuracy (%) | 74.34±1.63 | 73.27±2.25 | 0.003 | 0.541 | 74.34±1.61 | 74.27±1.69 | 0.837 | 0.041 |
| TMH (mm) | 0.19±0.02 | 0.19±0.02 | 0.026 | 0.410 | 0.20±0.02 | 0.19±0.02 | 0.541 | 0.123 |
| MGFS (scores) | 3.22±0.18 | 3.15±0.28 | 0.086 | 0.312 | 3.22±0.18 | 3.20±0.23 | 0.562 | 0.116 |
| SQOL-DVI (scores) | 59.38±1.58 | 59.18±1.66 | 0.491 | 0.125 | 59.37±1.58 | 59.32±1.61 | 0.866 | 0.034 |

Note: BMI: Body Mass Index; PSM: Propensity Score Matching; OSDI: Ocular Surface Disease Index; TBUT: Tear Film Break-Up Time; CFS: Corneal Fluorescein Staining; FVA: Functional Visual Acuity; TMH: Tear Meniscus Height; MGFS: Meibomian Gland Function Score; SQOL-DVI: Scale of Quality of Life for Diseases with Visual Impairment.

**Table 2**: Comparison of OSDI and CFS scores [mean±SD]

| Indicators | | Sodium hyaluronate group (n=50) | Esculin-digitalisglycosides group (n=50) | *P* | Effect size | *95%CI of the difference* |
|---|---|---|---|---|---|---|
| OSDI (scores) | Before Treatment | 39.32±1.58 | 39.39±1.54 | 0.833 | -0.042 | -0.69,0.55 |
| | After Treatment | 22.20±1.49* | 13.82±1.82* | <0.001 | | |
| CFS (scores) | Before Treatment | 2.30±0.15 | 2.28±0.18 | 0.626 | 0.098 | -0.05,0.08 |
| | After Treatment | 1.20±0.17* | 0.58±0.18* | <0.001 | | |

Note: **P*<0.05 vs. Before Treatment; 95%CI: 95% Confidence Interval; OSDI: Ocular Surface Disease Index; CFS: Corneal Fluorescein Staining.

**Table 3**: Comparison of TBUT and tear secretion volume [mean±SD]

| Indicators | | Sodium hyaluronate group (n=50) | Esculin-digitalisglycosides group (n=50) | *P* | Effect size | *95%CI of the difference* |
|---|---|---|---|---|---|---|
| TBUT (s) | Before Treatment | 6.01±0.32 | 6.06±0.27 | -0.168 | 0.404 | -0.17,0.07 |
| | After Treatment | 7.82±0.21* | 9.39±0.53* | <0.001 | | |
| Tear secretion volume (mm/5min) | Before Treatment | 7.72±0.32 | 7.68±0.36 | 0.560 | 0.117 | -0.10,0.18 |
| | After Treatment | 10.15±0.22* | 12.18±1.06* | <0.001 | | |

Note: *$P$<0.05 vs. Before treatment; 95%CI: 95% Confidence interval; TBUT: Tear film break-up time.

**Table 4**: Comparison of FVA accuracy [mean±SD]

| Indicators | | Sodium hyaluronate group (n=50) | Esculin-digitalisglycosides group (n=50) | *P* | Effect size | *95%CI of the difference* |
|---|---|---|---|---|---|---|
| FVA Accuracy (%) | Before Treatment | 74.34±1.61 | 74.27±1.69 | 0.837 | 0.041 | -0.59,0.72 |
| | After Treatment | 84.07±1.13* | 92.25±1.41* | 0.036 | | |

Note: *$P$<0.05 vs. Before treatment; 95%CI: 95% Confidence interval; FVA: Functional visual acuity.

**Table 5**: Comparison of TMH and MGFS [mean±SD]

| Indicators | | Sodium hyaluronate group (n=50) | Esculin-digitalisglycosides group (n=50) | *P* | Effect size | *95%CI of the difference* |
|---|---|---|---|---|---|---|
| TMH (mm) | Before Treatment | 0.20±0.02 | 0.19±0.02 | 0.541 | 0.123 | -0.01,0.01 |
| | After Treatment | 0.26±0.01* | 0.30±0.03* | <0.001 | | - |
| MGFS (scores) | Before Treatment | 3.22±0.18 | 3.20±0.23 | 0.562 | 0.116 | -0.06,0.11 |
| | After Treatment | 2.02±0.15* | 1.21±0.21* | <0.001 | | |

Note: *$P$<0.05 vs. Before Treatment; 95%CI: 95% Confidence Interval; TMH: Tear Meniscus Height; MGFS: Meibomian gland function score.

**Table 6**: Comparison of SQOL-DVI score [mean±SD]

| Indicators | | Sodium hyaluronate group (n=50) | Esculin-digitalisglycosides group (n=50) | *P* | Effect size | *95%CI of the difference* |
|---|---|---|---|---|---|---|
| SQOL-DVI (scores) | Before Treatment | 59.37±1.58 | 59.32±1.61 | 0.866 | 0.034 | -0.58,0.69 |
| | After Treatment | 71.40±0.82* | 81.20±3.45* | <0.001 | | |

Note: *$P$<0.05 vs. Before Treatment; 95%CI: 95% Confidence Interval; SQOL-DVI: Subjective quality of life in dry eye visual index.

**Table 7**: Comparison of adverse events [n (%)]

| Indicators | Adverse Events | | | | |
|---|---|---|---|---|---|
| | Itching | Stinging | Worsening foreign body sensation | Blurred vision | Total |
| Esculin-digitalisglycosides group (n=50) | 2 (4%) | / | / | / | 2 (4%) |
| Sodium hyaluronate group (n=50) | / | 2 (4%) | 1 (2%) | 1 (2%) | 4 (8%) |
| *P* | / | / | / | / | 0.400 |
| *Effect size* | / | / | / | / | -0.084 |

All symptoms were relieved within 3 days of continuous medication, without affecting the treatment process. The incidence of adverse events was slightly lower in the esculin and digitalisglycosides eye drop than in the sodium hyaluronate group, but the difference was not statistically significant ($P = 0.400$) (Table 7).

## DISCUSSION

### *Research objective*

Visual fatigue and dry eye syndrome often co-occur in children, forming a vicious cycle. Due to the immature development of children's ocular surface tissues, their lacrimal gland secretion function, meibomian gland function and corneal epithelial barrier function are all in a fragile state. The pathogenesis of visual fatigue and dry eye syndrome in children is more complex and their treatment responses differ significantly from those in adults. Therefore, targeted clinical treatment regimens are urgently needed(Chen *et al.*, 2024). This study systematically compared the clinical efficacy and tolerability of sodium hyaluronate eye drops and esculin and digitalis glycosides eye drops, aiming to provide evidence-based medical support for the clinical management of digital screen-related visual fatigue and dry eye syndrome in children.

### *Visual fatigue*

From the perspective of visual fatigue pathogenesis, the core mechanisms of digital screen-related visual fatigue lie in periorbital blood circulation disorders and visual regulatory dysfunction. When children engage in prolonged close-range viewing, the ciliary muscle remains in a state of sustained contraction, leading to periorbital vasospasm, slowed blood flow and insufficient blood supply and oxygenation to the retina, resulting in symptoms such as blurred vision and eye distension. The esculin component in esculin and digitalisglycosides eye drops has an apparent vasoactive effect. It can dilate periorbital capillaries by inhibiting endothelin-1 release, improve blood perfusion to the ciliary muscle and retina and relieve ciliary muscle spasm, thereby fundamentally alleviating visual fatigue symptoms(Ryu *et al.*, 2024). Meanwhile, the digitalisglycosides it contains can enhance the metabolic activity of retinal photoreceptor cells, improve the efficiency of visual signal transmission and enhance functional visual acuity—an essential reason for the significant improvement in FVA accuracy rate in the esculin and digitalisglycosides eye drop. In contrast, sodium hyaluronate eye drops relieve ocular surface discomfort solely through moisturizing and lubricating effects, without interfering with periorbital blood circulation or visual regulation. Thus, their impact on reducing visual fatigue is inferior to that of esculin and digitalis glycosides eye drops(Hynnekleiv *et al.*, 2022).

### *Dry eye*

In terms of pathological intervention for dry eye syndrome, digital screen-related dry eye syndrome in children is mainly of the evaporative type, with core pathological changes including meibomian gland dysfunction, decreased tear film stability and corneal epithelial damage. The esculin component in esculin and digitalisglycosides eye drops can promote the secretory function of meibomian gland acinar cells and increase the secretion of meibomian gland lipids by improving the blood supply to the meibomian glands. As an important component of the tear film's outer layer, increased meibomian gland lipid content can significantly reduce tear evaporation rate and prolong TBUT(Zemanova, 2021). In a randomized controlled study(Wang *et al.*, 2021), the esculin and digitalis glycosides eye drops treatment group showed a greater extension of TBUT after one month of treatment compared to the sodium hyaluronate group, consistent with the results of this study. Additionally, esculin has an anti-inflammatory effect, inhibiting the expression of ocular surface inflammatory factors, reducing ocular surface inflammatory responses and promoting the proliferation and repair of corneal epithelial cells. Therefore, the esculin and digitalis glycosides eye drop exhibited better performance in improving CFS and MGFS scores. Although sodium hyaluronate eye drops can alleviate dry eye symptoms by supplementing tear moisture, they cannot improve meibomian gland function or ocular surface inflammatory status. Consequently, their therapeutic effect duration is shorter and the overall treatment effect is not as good as that of esculin and digitalis glycoside eye drops.

### *Comprehensive therapeutic efficacy and safety*

The differences in the improvement of TMH and tear secretion volume also reflect the distinct mechanisms of action of the two drugs. Esculin and digitalisglycosides eye drops promote the functional recovery of tear-secreting cells by improving the blood supply to the lacrimal glands and accessory lacrimal glands, thereby increasing the secretion of physiological tears and significantly elevating tear meniscus height. In contrast, sodium hyaluronate eye drops mainly exert their effects through exogenous supplementation of artificial tears, with a weak impact on improving the body's own tear secretion function. Thus, the magnitude of improvement in tear secretion volume and tear meniscus height in the sodium hyaluronate group was smaller than that in the esculin and digitalisglycosides eye drop (Koppe *et al.*, 2024). The difference in SQOL-DVI scores is due to the comprehensive effect of therapeutic efficacy. Patients in the esculin and digitalis glycosides eye drop group experienced greater improvements in ocular surface discomfort, visual function and psychological status, leading to a more pronounced enhancement in their quality of life. In terms of safety, both drugs had a low incidence of adverse events with no severe adverse reactions reported, meeting the safety requirements for pediatric medication. A study exploring the use of esculin and digitalisglycosides eye drops in children with video terminal-related abnormal blinking found that the total effective rate of esculin and

digitalisglycosides eye drops was higher than that of sodium hyaluronate eye drops, with no significant difference in the incidence of adverse events, consistent with the overall results of this study (Xie, 2023).

***Comparison with previous studies***

The review (Venugopal and Bhaskar, 2025) indicated that the screen time of children has increased significantly since the COVID-19 pandemic and the prevalence of dry eye syndrome has risen from 6%-10% before the pandemic to 20%-25%. Given that children's visual systems are not yet fully developed, their tolerance to eye fatigue and dry eye syndrome is relatively low, underscoring the urgent need for safe and effective interventions. This study specifically enrolled a high-risk population and verified the efficacy and safety of esculin and digitalis glycosides eye drops, which aligns with the demand proposed in the review for developing eye intervention regimens suitable for children. Compared with other treatment protocols, this study selected Sodium Hyaluronate Eye Drops as the control, which is consistent with routine clinical practice. A meta-analysis (He *et al.*, 2024) found that autologous serum eye drops are more effective than artificial tear substitutes in the treatment of dry eye syndrome, but their clinical application is limited due to complex preparation processes and high costs. As a commonly used artificial tear substitute in clinical practice, Sodium Hyaluronate Eye Drops were used for comparison in this study, which confirmed that esculin and digitalisglycosides eye drops have superior efficacy. This finding provides a more optimal and convenient therapeutic option for clinical practice.

***Research necessity and innovation***

The incidence of digital screen-related visual fatigue and dry eye syndrome in children is increasing year by year, becoming a significant public health issue affecting children's visual health. However, current clinical practice lacks clear medication guidelines for pediatric patients and physicians mostly rely on experience when selecting drugs. High-quality clinical studies are urgently needed to provide evidence, making this study highly clinically relevant (Belalcazar-Rey *et al.*, 2021). Its innovation lies in establishing a comprehensive efficacy evaluation system that includes visual function, meibomian gland function and quality of life—breaking the limitation of previous studies that focused only on dry eye symptoms and better aligning with actual clinical needs. Additionally, this study clarifies the therapeutic advantages and tolerability of esculin and digitalis glycosides eye drops in the pediatric population, providing targeted, evidence-based medical evidence for clinical practice.

***Study limitations***

Despite PSM to control confounding factors, selection and information bias were not eliminated. The 3-month observation period precluded assessment of long-term efficacy and safety. No subgroup analyses by age, disease severity, or screen use type were performed, leaving treatment response differences unclarified(Munoz-Villegas *et al.*, 2023, Li *et al.*, 2025). Moreover, the study lacked basic research support for drug mechanisms, with only clinical efficacy analyzed and no exploration of laboratory indicators such as ocular surface inflammatory factors.

***Future recommendations***

Future research should employ large-sample, multi-center, prospective randomized controlled designs, integrate laboratory data and conduct subgroup analyses to provide evidence for individualized pediatric treatment.

## CONCLUSION

Esculin and digitalis glycosides eye drops can be recommended as preferred drugs for the treatment of digital screen-related visual fatigue and dry eye syndrome in children and are worthy of clinical promotion and application.

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***Authors' contributions***

Jun Wu: Conceived and designed the research and analyzed data. Drafted and revised the manuscript critically for important intellectual content. Participated in the conception and design of the study. Played a key role in data interpretation and manuscript preparation; Jili Wen, Daodian Tao: Contributed to the acquisition, analysis and interpretation of data. Provided substantial intellectual input during the drafting and revision of the manuscript. All authors have read and approved the final version of the manuscript.

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***Data availability statement***

All data generated or analysed during this study are included in this published article [and its supplementary information files].

***Ethical approval***

All research procedures in this study strictly adhered to the Declaration of Helsinki and the protocol was approved by the Medical Ethics Committee of Jinhua Municipal Central Hospital. (Approval number: 2025-340). This study was performed in adherence with the STROBE guidelines. See Supplementary file for the STROBE checklist.

***Conflicts of interest***

The authors affirm that they have no financial conflicts of interest.

***Supplementary data***

https://www.pjps.pk/uploads/2026/04/SUP1775374198.pdf

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