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# Optimizing Dry Eye Management: An Expert Consensus on the Use of Sodium Hyaluronate at Different Concentrations

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## Abstract

Background: Dry eye disease (DED) is a common, multifactorial disorder that affects ocular comfort and visual quality. Despite widespread use of sodium hyaluronate (SH) as a lubricant, the selection of appropriate SH concentration and formulation for different stages of DED has not been standardized in India.

Methods: This expert consensus was developed through a modified Delphi process with 23 renowned ophthalmologists reviewing available evidence and forming consensus statements on diagnosis, SH concentration, preservative-free options, dosing, and unmet needs.

Results: The panel recommended a stepwise approach: 0.1% SH for mild disease, 0.18% SH for moderate disease balancing efficacy and comfort, and preservative-free 0.3% SH for moderate-to-severe or post-surgical DED. The experts also emphasized the importance of preservative-free formulations, individualized dosing schedules, and patient education to ensure sustained symptom relief and adherence.

Conclusion: The purpose of this consensus is to unify practice and guide evidence-based management of DED in India.

**Categories:** Ophthalmology
**Keywords:** ded management, dry eye disease (ded), expert opinion, sh therapy, sodium hyaluronate

## Introduction

Dry eye disease (DED) is a multifactorial condition caused by factors such as tear film instability, hyperosmolarity, ocular surface injury, and inflammation. It is a common ocular surface disease and a growing cause of ophthalmic consultations worldwide [1].

The global prevalence of DED ranges from 5% to 50%, reflecting variation in diagnostic definitions [2]. A recent systematic review and meta-analysis of 119 cohort and cross-sectional studies including 15,251,528 participants estimated the global pooled prevalence of dry eye at 34.6%, with substantial variation according to region, age, sex, diagnostic criteria, and study setting [3]. Its burden is higher in older individuals and in African and Asian populations, with particularly high prevalence reported in India and East Asia [4]. A database-driven study reported an overall DED prevalence of 23.9% in Asians, with higher rates in women than men and a rising trend across age groups; East Asia showed a prevalence of 28.4% [5]. Recent Indian data also indicate a substantial burden, with a 2025 prospective study from Central India reporting a DED prevalence of 25% and identifying older age, occupation, uncorrected refractive status, smoking, ocular allergy, and contact lens use as associated factors [6]. Regional variability in India is further supported by evidence showing higher DED prevalence in extreme climatic conditions and among visual display unit users [7].

According to the Women's Health Study (WHS), prevalence among Caucasians is 4.3% in men and 12.8% in mixed populations [4], whereas the U.S. National Health and Wellness Survey identified a combined prevalence of 9.3% [8].

The Tear Film and Ocular Surface Society Dry Eye Workshop III (TFOS DEWS III) report indicates that prevalence increases with age, rising from 2.7% in women aged 20-29 years to over 30% in those aged ⩾80 years, with a steeper increase after 40 years [9].

DED is influenced by genetics, the environment, and lifestyle factors, such as digital screen use and contact lens wear, with younger populations being increasingly affected [8]. The unmet need remains substantial, as moderate-to-severe disease is associated with pain, fatigue, depression, reduced productivity, and impaired quality of life [10].

Therapeutic gaps persist, particularly in moderate-to-severe DED, where there is a need for long-lasting, preservative-free therapies, improved anti-inflammatory options, and treatments that restore all layers of the tear film [11]. Artificial tears remain first-line therapy, with sodium hyaluronate (SH) preferred for its water-retentive, tear film-stabilizing, epithelial healing, and anti-inflammatory properties [11].

However, the availability of multiple SH concentrations (0.1%, 0.18%, and 0.3%) has led to uncertainty regarding the selection and clinical use of these concentrations. Key questions include the appropriate use of different concentrations across disease severity, the role of 0.3% SH in moderate-to-severe and post-surgical conditions, and the indications for preservative-free formulations, particularly in chronic use and compromised ocular surfaces.

Currently, India lacks standardized, evidence-based recommendations for the clinical use of SH. To bridge this gap, a series of expert consensus meetings was convened with 23 ophthalmologists. The objective of this consensus was to develop practical, evidence-informed expert recommendations for the use of SH in the management of DED in Indian clinical practice. Specifically, the modified Delphi process was evaluated across the six clinical domains, including diagnosis and subtyping, severity-based management, unmet treatment needs, preservative-free formulations, dosing and practical considerations, and the selection of 0.1%, 0.18%, and 0.3% SH formulations according to disease severity and clinical context. The recommendations integrate available published evidence with real-world clinical experience and are intended to guide clinical-decision making regarding the selection and clinical use of different SH concentrations in the management of DED.

# Materials And Methods

## Methodology

The consensus was developed using a modified Delphi process, a standard approach in which high-level randomized controlled trial (RCT) evidence is limited.

*Expert Panel Selection*

Twenty-three ophthalmologists were invited to participate based on predefined eligibility criteria, including specialization in ophthalmology, a minimum of 12 years of clinical experience in glaucoma, retinal specialization, and active involvement in clinical practice, teaching, and research. The panel included ophthalmologists working in tertiary-care, teaching, and private clinical settings across India, thereby providing representation from different clinical practice environments. Experts were asked to declare relevant financial and non-financial conflicts of interest before participation.

*Consensus Development Process*

The consensus development process involved two structured in-person expert meetings held one week apart. Prior to the first meeting, all experts were provided with a comprehensive evidence review. During the first meeting, the panel discussed the evidence and 16 preliminary statements and refined them for clarity, clinical relevance, and applicability to Indian ophthalmic practice. Following this, anonymous electronic voting was conducted using a five-point scale (A = accept completely, B = accept with some reservation, C = accept with major reservation, D = reject with some reservation, and E = reject completely) [12]. Consensus was predefined as ⩾80% combined agreement (A + B). All 23 experts were invited to vote on each statement. Individual responses remained anonymous throughout the voting process and were not disclosed to other panel members. The number of responses varied slightly across statements, and consensus was calculated based on the number of valid responses received for each statement. Of the 16 statements, four were incorporated into the manuscript narrative following expert discussion, while 12 were retained for formal consensus voting (Table *1*). The Appendices document the initial and final statements, and detailed voting distributions across all five response categories. The final step involved drafting the consensus document and circulating it among experts for validation and approval. As this study was based on expert consensus without involvement of patient data or human subjects, formal ethics committee approval and informed

consent were not required.

| Statement | Consensus statement | A (%) | B (%) | A + B (%) |
|---|---|---|---|---|
| 1 | Clinical subtyping of DED (aqueous-deficient, evaporative, or mixed) is crucial for guiding appropriate therapy. | 63.6 | 31.8 | 95.4 |
| 2 | Mild DED can often be effectively managed with low-viscosity artificial tears, such as 0.1% SH, lid hygiene, and environmental modifications. | 85.7 | 14.3 | 100.0 |
| 3 | Moderate DED generally requires higher-viscosity SH, such as 0.18% or 0.3%, possibly combined with anti-inflammatory therapy and punctal plugs in select cases. | 71.4 | 28.6 | 100.0 |
| 4 | Severe DED requires preservative-free, high-viscosity SH such as 0.3%, adjunctive steroids or ciclosporin, autologous serum, and close monitoring. | 81.8 | 18.2 | 100.0 |
| 5 | Major unmet needs in DED include better diagnostic tools for early disease, longer-acting therapies, improved patient adherence, and education on the chronic nature of DED. | 81.8 | 13.6 | 95.4 |
| 6 | Long-term use of preservative-free SH formulations is strongly recommended, especially in moderate-to-severe DED, frequent users, and contact lens wearers, to avoid preservative-induced damage. | 72.7 | 27.3 | 100.0 |
| 7 | Unit-dose preservative-free SH is preferred in patients with ocular surface disease, allergy, and post-surgical DED. | 63.6 | 31.8 | 95.4 |
| 8 | Dosing frequency should be individualized: 0.1% SH often requires ≥4–6 instillations/day, while 0.3% SH may suffice at 2–3 times/day due to longer retention. | 68.2 | 27.3 | 95.5 |
| 9 | 0.1% SH is recommended for mild DED, younger patients, and those needing frequent instillations without significant blur. | 68.2 | 27.3 | 95.5 |
| 10 | 0.3% SH is particularly valuable in patients who fail to achieve relief with lower concentrations or those requiring less frequent dosing due to compliance issues. | 100.0 | 0.0 | 100.0 |
| 11 | 0.18% SH is a balanced choice for moderate-to-severe DED, providing improved retention with good tolerance. | 72.7 | 27.3 | 100.0 |
| 12 | 0.3% SH is best reserved for moderate-to-severe DED, inflammatory DED, and post-surgical ocular surface healing (e.g., PRK), where greater viscosity and longer retention are advantageous. | 90.9 | 9.1 | 100.0 |

**TABLE 1: Expert consensus statements and levels of agreement**

A: accept completely; B: accept with some reservation. Consensus was predefined as ≥80% combined A + B responses.

SH: sodium hyaluronate; DED: dry eye disease; PRK: photorefractive keratectomy

## Survey development

The initial statements were formulated directly from a comprehensive review of the literature on DED, including RCTs, meta-analyses, systematic reviews, and real-world evidence, together with recommendations from the TFOS DEWS II/III guidelines. A formal evidence-grading framework was not applied; therefore, the reported consensus levels represent the degree of expert agreement rather than the strength or certainty of the underlying evidence. These statements were then organized into six key domains: (1) diagnosis and subtyping, (2) management by severity, (3) unmet need in DED, (4) preservative-free formulation, (5) dosing and practical considerations, and (6) choosing between 0.1%, 0.18%, and 0.3% SH.

This structured process ensured that the consensus statements were evidence-informed, clinically relevant, and reflected the collective experience of Indian ophthalmologists. The complete survey instrument is provided in the Appendices, including the exact wording of the statements presented to the expert panel, the response options, and voting distribution. The five-point response scale is presented in Table *2*.

| Code | Response |
|---|---|
| A | Accept completely |
| B | Accept with some reservation |
| C | Accept with major reservation |
| D | Reject with some reservation |
| E | Reject completely |

**TABLE 2: The response scale**

Consensus was predefined as ≥80% combined A+B responses.

An overview of the modified Delphi methodology and survey development process is shown in Figure *1*.

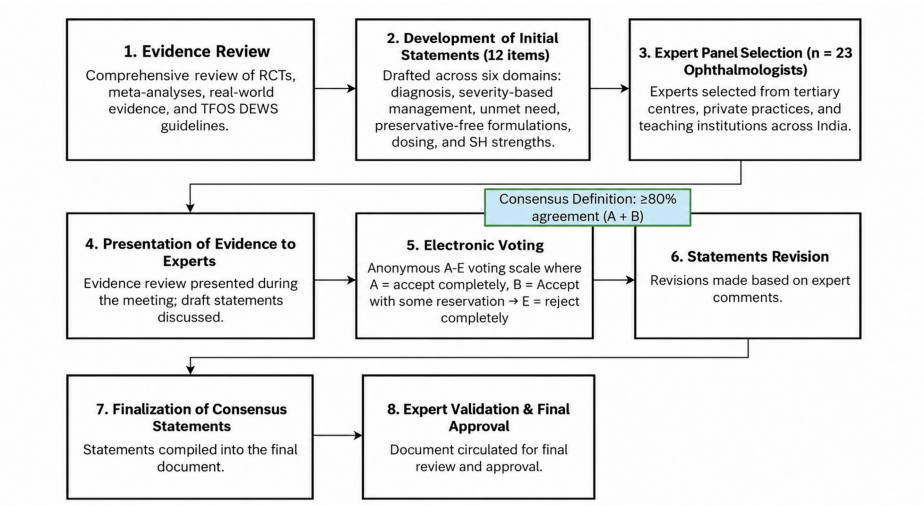



**FIGURE 1: Overview of the modified Delphi methodology and survey development process**

RCT: randomized controlled trial; TFOS DEWS: Tear Film and Ocular Surface Society Dry Eye Workshop; SH: sodium hyaluronate

# Results

## Diagnosis and subtyping

Unanimous agreement among the panel emphasized that clinical subtyping is central to the effective management of DED. Epidemiological evidence reinforces the complexity of subtyping. In a clinic-based study, only a minority of patients had pure aqueous-deficient dry eye (ADDE) (14%), while the majority presented with meibomian gland dysfunction (MGD, 50%) or mixed disease (36%) [13]. Similarly, an Indian hospital-based study reported a 29.5% prevalence of DED, distributed as 39.6% evaporative dry eye (EDE), 34.7% ADDE, and 25.7% mixed, with more advanced ocular surface changes in the mixed subtype [14].

In practice, accurate subtyping requires assessment of both tear quantity and quality using tests such as Schirmer's test, tear film breakup time (TBUT), osmolarity, ocular surface staining, and meibography [15,16]. This diagnostic approach allows for tailored therapy; for aqueous-deficient DED, options include lubricating eye drops and punctal occlusion devices. For evaporative DED, lid hygiene, warm compresses, and anti-inflammatory therapy are beneficial [17]. When both forms coexist, a combination of these approaches is required. Thus, subtyping serves as a cornerstone for personalized management.

Management of DED is a stepped-care approach that advances through basic lifestyle and environmental adjustments to advanced medical and surgical treatments depending on the level of severity.

Mild DED is managed with education, environmental changes, eyelid care, and low-viscosity tears, while moderate DED requires higher-viscosity tears with anti-inflammatory agents or punctal plugs, and severe DED may need preservative-free or high-viscosity tears combined with autologous serum, immunomodulators, and possible punctal occlusion or surgery [18].

## Management by severity

Complete consensus was achieved across all severity-based management statements, supporting the stepwise use of SH concentrations (0.1%, 0.18%, and 0.3%) with adjunctive measures tailored to disease stage and patient needs.

*Mild DED*

For mild DED, the panel reached full consensus on using low-viscosity artificial tears (e.g., 0.1% SH), along with lid hygiene, environmental modifications, and lifestyle measures such as regular breaks, increased blinking, and avoiding smoking, consistent with Indian Standard Treatment Guidelines (2016) [18] and TFOS DEWS II and III reports [17].

Hyaluronic acid (HA)-based artificial tears provide superior water retention, viscoelasticity, and lubrication, reducing friction and stabilizing the tear film [11]. Randomized trials have shown that 0.1% SH is superior to saline, improving Schirmer's test, rose bengal staining, and symptoms such as burning and grittiness [19]. Aragona et al. further showed that 0.1% SH significantly enhances ocular surface repair [20].

Comparative studies demonstrate that 0.1% SH is at least as effective as 0.5% carboxymethylcellulose (CMC) in improving TBUT and staining [21], and shows superior reductions in ocular surface damage [22]. In addition, 0.1% SH is particularly useful in young adults, where digital device usage and contact lens wear are common risk factors for the onset of disease [23,24].

*Moderate DED*

Higher-viscosity SH formulations (0.18-0.3%) have shown clear benefits in moderate DED. Multiple RCTs have reported greater ocular surface retention and lubrication with these concentrations, leading to significant improvements in patient-reported symptoms, TBUT, and corneal fluorescein staining compared with saline, carbomer, or CMC [25-27].

In one study, both 0.1% and 0.3% SH significantly improved symptoms and tear film stability versus saline, but 0.3% provided a longer-lasting effect (P=0.04) [28]. Similarly, hypotonic 0.18% SH eye drops produced a greater extension of TBUT and significantly improved corneal staining scores at three months compared with isotonic 0.1% SH ($P \leqslant 0.01$) [29].

Although direct head-to-head trial evidence for combination therapy is limited, the use of SH together with anti-inflammatory agents and punctal plugs is supported by their complementary mechanisms. SH hydrates and stabilizes the tear film, anti-inflammatory agents reduce ocular surface inflammation [30], and punctal plugs help retain natural and supplemented tears [31,32]. Together, these approaches provide a logical stepwise strategy for managing moderate DED.

*Severe DED*

In severe DED, including Sjögren's syndrome, Stevens-Johnson syndrome, ocular cicatricial pemphigoid, or post-surgical ocular surface disease, clinical studies show that 0.3% SH significantly improves TBUT, Schirmer's scores, corneal staining, goblet cell density, and patient satisfaction more effectively than saline or lower concentrations, with a good safety profile [33-35].

An Indian cross-sectional, questionnaire-based survey reported that 68.5% of respondents preferred SH eye drops for severe DED [36]. Close monitoring is critical because severe DED carries a high risk of ulceration, scarring, and vision loss [37]. Thus, preservative-free 0.3% SH may be considered as an appropriate option in severe DED, with adjunctive agents added as needed to control inflammation and ocular surface damage.

*Unmet Needs*

The panel strongly agreed on the unmet needs in DED, including improved diagnostics, longer-acting therapies, better adherence, and education on the chronic nature of DED.

Despite progress in understanding the pathophysiology and management of DED, several critical unmet needs remain unaddressed. Current methods rely on subjective symptoms and tests such as Schirmer's and TBUT, which correlate poorly with disease severity [38,39]. The absence of a pathognomonic marker and variable diagnostic thresholds further complicate clinical assessment.

DED significantly impairs quality of life, particularly in moderate-to-severe disease, affecting daily activities, productivity, and emotional well-being. Although symptom relief and treatment satisfaction are priorities [10], frequent dosing-up to 10-12 times daily reduces adherence.

There is a need for longer-acting, preservative-free therapies that provide sustained relief and improve tolerability. Personalized approaches targeting tear film deficiencies remain limited [11]. Higher-viscosity agents, such as 0.3% sodium hyaluronate, may improve retention and reduce dosing frequency.

In addition, as inflammation is central to disease pathogenesis, optimized anti-inflammatory therapies that are both effective and safe for chronic administration remain a key challenge.

Education is critical, with clinician initiatives promoting holistic management of DED and patient education on its chronic, progressive nature to improve adherence and long-term outcomes [39].

## Preservative-free formulation

Long-term use of preservative-free (PF) SH formulations is strongly recommended in moderate-to-severe DED, frequent users, and contact lens wearers, as chronic exposure to preservatives, such as benzalkonium chloride, can cause ocular surface toxicity and inflammation [40]. The TFOS DEWS II guideline also recommends PF formulations in moderate-to-severe DED and in patients unresponsive to initial therapy [17,41].

Clinical evidence supports the efficacy and safety of PF-SH formulations. Combinations such as SH 0.1% with chondroitin sulfate 0.18% [42], or SH 0.15% with trehalose 3% [43], have shown significant improvements in Ocular Surface Disease Index (OSDI) [44], dry eye questionnaire-5 (DEQ-5) [45], TBUT, corneal staining, Schirmer's scores, and goblet cell recovery, with good tolerability and patient satisfaction.

Similarly, unit-dose preservative-free SH minimizes preservative exposure and is preferred in high-risk groups, including those with ocular surface disease, allergy, and post-surgical DED, whereas preservative-free multi-dose systems are acceptable alternatives considering cost, handling, and availability [46]. All experts agreed with this statement, though 31.8% expressed some reservations, which aligns with a published study showing that patients report similar acceptance of both formats, with multi-dose bottles often perceived as more environmentally friendly [47].

## Dosing and practical considerations

The panel emphasized the need to individualize dosing regimens, as the frequency of SH dosing is an important determinant of clinical efficacy and patient adherence in DED. Although SH is available in multiple concentrations (0.1%, 0.18%, and 0.3%), its viscosity, ocular retention, and therapeutic impact vary. This directly influences the number of daily instillations required for symptomatic relief and protection of the ocular surface.

Lower-concentration SH (0.1%) has a low viscosity and clears rapidly from the ocular surface, necessitating ⩾4-6 daily instillations. Gamma scintigraphy showed that higher concentrations remained longer: 0.3% SH cleared more slowly than saline ($p<0.001$) and 0.2% SH ($p=0.033$), while 0.2% SH also persisted longer than saline ($p=0.003$). This concentration-dependent retention explains why 0.3% SH can provide effective relief with only two to three daily instillations, reducing the treatment burden while maintaining efficacy [48]. However, residence-time data alone do not establish improved adherence or long-term clinical outcomes.

Accordingly, the panel agreed that for mild DED, particularly in younger patients or those who tolerate frequent instillation without visual blur, 0.1% SH is appropriate, whereas 0.3% SH is preferred when longer retention and a reduced dosing frequency are desired. All statements achieved a full consensus.

## Choosing between 0.1%, 0.18%, and 0.3% SH

All experts (100%) agreed that 0.18% SH offers an appropriate balance of efficacy and tolerability in moderate-to-severe DED, whereas 0.3% SH was unanimously endorsed for advanced, inflammatory, or postsurgical disease requiring enhanced retention.

The choice of formulation (0.1%, 0.18%, or 0.3% SH) depends on viscosity, ocular surface retention, osmolality, preservatives, and patient tolerability rather than concentration alone. Preclinical murine studies showed that all concentrations improved TBUT and reduced corneal fluorescein staining, with greater benefits at higher concentrations [49]. A meta-analysis of 10 RCTs (n=1,796) confirmed that high-concentration HA formulations resulted in significantly greater improvements in corneal fluorescein staining, indicating superior epithelial protection and repair [50].

In moderate-to-severe DED, a randomized study comparing 0.1%, 0.15%, and 0.3% SH with cyclosporine demonstrated significant improvements in corneal staining, TBUT, LGCS, Schirmer's, and OSDI scores

across all groups, with comparable efficacy and good tolerability [51].

The positioning of 0.18% and 0.3% SH is overlapping rather than mutually exclusive. In moderate DED, 0.18% SH may offer a balance of efficacy, retention, and tolerability, while 0.3% SH may also be considered when greater ocular-surface retention, reduced dosing frequency, or inadequate response to lower concentrations is present. In more advanced, inflammatory, or postsurgical DED, the higher viscosity and longer retention of 0.3% SH may provide additional practical advantages. Thus, concentration selection should be individualized according to disease severity, treatment response, tolerability, and patient needs.

A multicenter trial reported that 0.18% HA drops with evening 0.30% HA gel effectively controlled moderate DED, while regular use of 0.30% HA was appropriate in severe cases, including postsurgical disease [52].

All 12 statements reached consensus, as shown in Figure *2*.

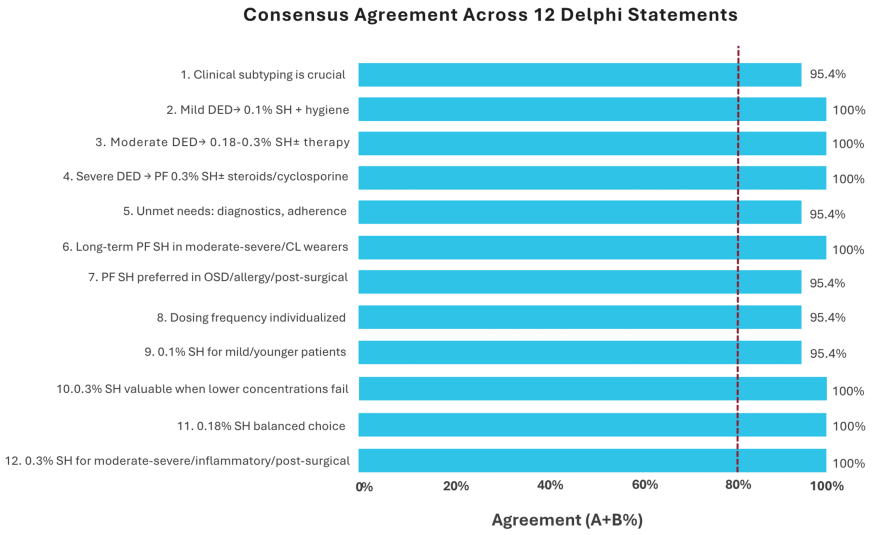



**FIGURE 2: Consensus agreement (A + B) across all 12 Delphi statements (n = 23)**

The red dashed line represents a predefined consensus threshold of ≥80%.

SH: sodium hyaluronate; PF: preservative-free; DED: dry eye disease; OSD: ocular surface disease; CL: contact lens

# Discussion

## Expert opinion

DED remains a multifactorial disorder with a significant impact on quality of life, requiring individualized therapy based on disease subtype and severity. Clinical subtyping into aqueous-deficient, evaporative, or mixed forms provides a useful framework for rational management, although overlapping mechanisms are common in practice.

According to the TFOS DEWS II framework, DED is broadly categorized into aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE) [53]. While ADDE arises from insufficient tear production, EDE is primarily linked to meibomian gland dysfunction and lipid-layer instability. Despite these distinctions, both subtypes often present with overlapping symptoms, such as irritation, burning, and visual fluctuations [54]. Recently, the ADES classification proposed a third subtype, decreased wettability dry eye (DWDE), emphasizing the role of mucins and ocular surface wettability in maintaining tear film stability [55]. Recognition of DWDE expands therapeutic options, such as strategies to enhance mucin expression or improve epithelial surface spreading, rather than focusing solely on tear volume or lipid layer quality.

Experts considered SH an important therapeutic option for all severities of DED because it relieves symptoms, protects the ocular surface, and improves tear film stability. Its effectiveness depends on its concentration and viscosity. Lower concentrations (0.1%) are suitable for mild DED, particularly in younger

patients, but require frequent instillation (4-6 times daily) due to rapid clearance.

In moderate-to-severe DED, higher-viscosity formulations (0.18-0.3%) provide greater ocular surface retention and improved symptomatic relief. Evidence supports 0.18% SH as an effective and well-tolerated option over 84 days [26]. A randomized non-inferiority trial demonstrated comparable efficacy to 0.3% SH with better tolerability and reduced risk of blurred vision [51]. However, 0.3% SH gel showed earlier conjunctival healing and improved Schirmer's test values, indicating superior water retention [52], suggesting its particular utility in severe inflammatory and post-surgical settings.

In severe DED, preservative-free 0.3% SH forms the foundation of therapy, providing sustained hydration and reducing treatment burden.

Adjunctive therapies may be added as needed. Autologous serum tears promote epithelial healing, with symptomatic improvement reported in 60% of patients within 10 days and 79% within two months, with sustained benefits up to 12 months [56]. Anti-inflammatory treatments, including short-term corticosteroids [57] and long-term cyclosporine [58,59], further improve outcomes and quality of life. These should complement, not replace, SH therapy.

Formulation choice should be individualized, considering patient profile, convenience, and adherence. Overall, the expert panel proposed a practical severity-based approach informed by the available evidence and clinical experience: 0.1% SH for mild disease, 0.18% SH for moderate disease, and 0.3% SH for moderate-to-severe and post-surgical cases. Preservative-free formulations, patient education, and adherence strategies are essential for achieving sustained outcomes in DED management.

The present consensus aligns with existing literature supporting the use of SH as an effective lubricant for DED and extends these findings by providing practical guidance on concentration selection. Previous studies have shown that 0.1% SH improves symptoms, tear film stability, and ocular surface staining in mild DED [21-24], whereas higher concentrations such as 0.18% and 0.3% offer greater ocular surface retention and may offer more sustained relief in moderate-to-severe disease [27,29,30,49]. While published studies generally evaluate individual SH concentrations, this consensus integrates the available evidence with expert clinical experience to position 0.1%, 0.18%, and 0.3% SH within a stepwise, severity-based treatment approach relevant to Indian clinical practice.

### Limitations and recommendations

This consensus has some limitations. The recommendations are derived from available published evidence combined with expert opinion and do not represent findings from a prospective clinical trial. Although the modified Delphi process allowed structured expert input, the findings may still be influenced by the clinical experience and practice patterns of the participating ophthalmologists. Additionally, the relatively small and purposively selected expert panel may not fully represent the spectrum of DED practice across India and may introduce selection bias.

The recommendations are mainly intended for the Indian clinical setting and might not be fully generalizable to other healthcare systems. Direct comparative evidence across all sodium hyaluronate concentrations remains limited and heterogeneous, particularly for specific patient subgroups; therefore, the proposed concentration-specific positioning should be interpreted as practical, evidence-informed expert guidance rather than evidence of definitive superiority of one concentration over another. Furthermore, patients, optometrists, and other ocular-surface stakeholders were not directly represented in the Delphi process, which may have limited the incorporation of broader patient and multidisciplinary perspectives. Further comparative studies and broader stakeholder involvement may help refine these recommendations.

## Conclusions

This consensus offers clear, practical guidance on the selection and clinical use of sodium hyaluronate for managing dry eye disease. By integrating current evidence with clinical expertise, the panel offers clear recommendations on diagnostic subtyping, severity-based treatment, preservative-free formulations, and individualized dosing. The structured framework links the 0.1%, 0.18%, and 0.3% concentrations to specific disease stages, highlighting safety, tolerability, and long-term adherence. It also discusses dispensing formats, patient education, and ongoing gaps such as the need for longer-acting therapies and better diagnostic tools. Overall, these consensus statements aim to promote consistent, patient-centered care and improve outcomes within the Indian healthcare environment.

## Appendices

| | Statements presented | Statements finalized | Retained as final consensus | Level of agreement |
|---|---|---|---|---|

| | | | statement | |
|---|---|---|---|---|
| 1 | Dry eye disease is a highly prevalent and underdiagnosed condition worldwide, affecting up to 10–30% of adults, with increasing incidence in ageing populations and digital screen users. | Removed. It is a fact, added in the manuscript. | No | - |
| 2 | The burden of DED is rising due to lifestyle factors, longer screen exposure, and increasing post-surgical ocular surface disease (e.g., post-LASIK, cataract surgery). | Removed and added in the manuscript. | No | - |
| 3 | Diagnosis of DED should integrate symptom questionnaires (e.g., OSDI), tear break-up time (TBUT), fluorescein staining, and Schirmer's test, rather than relying on a single test. | Removed and added in the manuscript. | No | - |
| 4 | Clinical subtyping (aqueous-deficient, evaporative, or mixed DED) is crucial to guide appropriate therapy. | S1: Clinical subtyping of DED (aqueous-deficient, evaporative, or mixed) is crucial for guiding appropriate therapy. | Yes | A- 14 (63.6%) B- 7 (31.8%) C- 1 (4.6%) D- 0% E-0% |
| 5 | First-line management for mild DED includes lifestyle modification, environmental optimization, and regular use of preservative-free artificial tears | Removed. Added in the text. | No | - |
| 6 | Mild DED can often be effectively managed with low-viscosity artificial tears (e.g., 0.1% SH), lid hygiene, and environmental modifications. | S2: Mild DED can often be effectively managed with low-viscosity artificial tears, such as 0.1% SH, lid hygiene, and environmental modifications. | Yes | A- 18 (85.7%) B- 3 (14.3%) C – 0% D - 0% E- 0% |
| 7 | Moderate DED generally requires higher-viscosity SH (e.g., 0.18–0.3%), possibly combined with anti-inflammatory therapy and punctal plugs in select cases. | S3: Moderate DED generally requires higher-viscosity SH, such as 0.18% or 0.3%, possibly combined with anti-inflammatory therapy and punctal plugs in select cases. | Yes | A- 15 (71.4%) B- 6 (28.6%) C – 0% D - 0% E- 0% |
| 8 | Severe DED (e.g., in Sjögren's or post-ocular surgery) demands intensive preservative-free high-viscosity SH (e.g., 0.3%), adjunctive steroids or ciclosporin, autologous serum, and close monitoring. | S4: Severe DED requires preservative-free, high-viscosity SH such as 0.3%, adjunctive steroids or ciclosporin, autologous serum, and close monitoring. | Yes | A- 18 (81.8%) B- 4 (18.2%) C – 0% D- 0% E – 0% |
| 9 | Major unmet needs in DED include better diagnostic tools for early disease, longer-acting therapies, improved patient adherence, and education on the chronic nature of DED. | S5: Major unmet needs in DED include better diagnostic tools for early disease, longer-acting therapies, improved patient adherence, and education on the chronic nature of DED | Yes | A- 18 (81.8%) B- 3 (13.6%) C - 0 D - 0 E – 1 (4.6%) |
| 10 | Long-term use of preservative-free SH formulations is strongly recommended, especially in moderate-to-severe DED, frequent users, and contact lens wearers, to avoid preservative-induced. | S6: Long-term use of preservative-free SH formulations is strongly recommended, especially in moderate-to-severe DED, frequent users, and contact lens wearers, to avoid preservative-induced damage. | Yes | A- 16 (72.7%) B- 6 (27.3%) C – 0% D – 0% E – 0% |
| 11 | Unit-dose preservative-free SH is preferred in patients with ocular surface disease, allergy, or post-surgical DED. | S7: Unit-dose preservative-free SH is preferred in patients with ocular surface disease, allergy, and post-surgical DED | Yes | A- 14 (63.6%) B- 7 (31.8%) C- 1 (4.6%) D- 0% E-0% |
| 12 | Dosing frequency should be individualized: 0.1% SH often requires ≥4–6 instillations/day, while | S8: Dosing frequency should be individualized: 0.1% SH often requires ≥4–6 instillations/day, while | Yes | A- 15 (68.2%) B- 6 (27.3%) |

| | | | | |
|---|---|---|---|---|
| | 0.3% SH may suffice at 2–3 times/day due to longer retention. | 0.3% SH may suffice at 2–3 times/day due to longer retention. | | C- 1 (4.6%) D- 0% E-0% |
| 13 | 0.1% SH is recommended for mild DED, younger patients, and those needing frequent instillations without significant blur. | S9: 0.1% SH is recommended for mild DED, younger patients, and those needing frequent instillations without significant blur. | Yes | A- 15 (68.2%) B- 6 (27.3%) C- 1 (4.6%) D- 0% E-0% |
| 14 | 0.18% SH is a balanced choice for mild-to-moderate DED, providing improved retention with good tolerance. | S11: 0.18% SH is a balanced choice for moderate-to-severe DED, providing improved retention with good tolerance. | Yes | A- 16 (72.7%) B- 6 (27.3%) C- 0% D – 0% E -0% |
| 15 | 0.3% SH is best reserved for moderate-to-severe DED, inflammatory DED, and post-surgical ocular surface healing, where greater viscosity and longer retention are advantageous. | S12: 0.3% SH is best reserved for moderate-to-severe DED, inflammatory DED, and post-surgical ocular surface healing (e.g., PRK), where greater viscosity and longer retention are advantageous | Yes | A- 20 (90.9%), B- 2 (9.1%) C-0% D- 0% E-0% |
| 16 | It is particularly valuable in patients who do not achieve relief with lower concentrations or who require less frequent dosing because of compliance issues. | S10: 0.3% SH is particularly valuable in patients who fail to achieve relief with lower concentrations or those requiring less frequent dosing due to compliance issues. | Yes | A- 23(100%) B-0 C-0 D- 0 E-0 |

**TABLE 3: Initial consensus statements, modifications following expert discussion, final statements submitted for voting, and detailed voting results**

DED: dry eye disease; LASIK: laser-assisted in situ keratomileusis; OSDI: Ocular Surface Disease Index; TBUT: tear film breakup time; SH: sodium hyaluronate; PRK: photorefractive keratectomy

# Additional Information

## Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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## Disclosures

**Human subjects:** Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have

declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** Dinesh Patil and Onkar C. Swami are full-time employees of Alembic Pharmaceuticals Limited, India, which actively markets sodium hyaluronate. Other authors do not have any conflict of interest.

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