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DRY EYE DISEASE: CURRENT GUIDELINES AND EMERGING THERAPEUTIC STRATEGIES

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ABSTRACT

Background: Dry eye disease (DED) is a chronic, multifactorial disorder of the ocular surface characterized by loss of tear film homeostasis, resulting in ocular symptoms and heterogeneous clinical signs. It affects both elderly and working-age populations, with increasing prevalence related to environmental exposure, digital device use, and lifestyle changes. Advances summarized in the TFOS DEWS II reports have substantially improved understanding of DED pathophysiology, highlighting the roles of tear film instability, hyperosmolarity, chronic inflammation, meibomian gland dysfunction, and neurosensory abnormalities.
Methods: This narrative review analyzes current international guidelines and peer-reviewed literature published between 2015 and 2025. PubMed/MEDLINE and Google Scholar were searched using keywords related to dry eye disease, ocular surface disease, TFOS DEWS II, meibomian gland dysfunction, diagnostics, and treatment. Consensus reports, randomized controlled trials, meta-analyses, and systematic reviews were included.
Results: Evidence indicates that DED is a heterogeneous condition requiring an individualized, phenotype-based diagnostic and therapeutic approach. Contemporary guidelines recommend combining symptom assessment with objective diagnostic testing to guide management. Stepwise treatment strategies emphasize patient education, environmental modification, tear supplementation, and targeted anti-inflammatory therapy. Recent advances include immunomodulatory agents, therapies for meibomian gland dysfunction, evaporation-reducing agents, neurostimulatory approaches, and biological treatments for severe or refractory disease.
Conclusion: Dry eye disease remains a complex clinical challenge. Implementation of updated diagnostic criteria and stepwise, phenotype-oriented treatment strategies enables improved disease control and quality of life. Continued research into inflammatory and neurosensory mechanisms, along with development of novel therapies, is essential for further optimization of personalized DED management.

KEYWORDS

Dry Eye Disease, Ocular Surface Disease, TFOS DEWS II, Diagnosis, Treatment, Novel Therapies

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1. Introduction

Dry eye disease (DED) is one of the most commonly diagnosed ocular disorders and represents a significant public health problem. The condition affects not only the elderly population but increasingly also younger and working-age individuals, which is associated, among other factors, with intensive use of digital devices, exposure to adverse environmental conditions, and changes in lifestyle [1]. Symptoms of DED, including burning, foreign body sensation, ocular fatigue, photophobia, and fluctuations in visual acuity, may substantially impair patients' quality of life, reduce work productivity, and limit daily functioning.

A major breakthrough in the understanding of dry eye disease was the publication of the Tear Film and Ocular Surface Society Dry Eye Workshop II (TFOS DEWS II) reports in 2017, which unified the definition, classification, and principles of diagnostic and therapeutic management of this condition [2–4]. According to TFOS DEWS II, dry eye disease is defined as a multifactorial disease of the ocular surface characterized by a loss of tear film homeostasis, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play key etiological roles [2]. This definition emphasizes the complex nature of the disease and moves away from the simplified view of DED as merely a consequence of tear deficiency.

In clinical practice, dry eye disease remains a heterogeneous condition encompassing various phenotypes and pathophysiological mechanisms, which explains the frequent discrepancy between the severity of symptoms reported by patients and objective clinical findings. The traditional classification into aqueous-deficient dry eye and evaporative dry eye, most commonly associated with meibomian gland dysfunction (MGD), remains clinically relevant; however, contemporary guidelines place greater emphasis on detailed disease phenotyping to enable individualized treatment strategies [3].

Increasing attention has also been directed toward the role of chronic ocular surface inflammation as a key mechanism sustaining and exacerbating dry eye disease. According to the "vicious cycle" concept, tear film instability and hyperosmolarity trigger inflammatory pathways, leading to epithelial damage of the cornea and conjunctiva and further impairment of lacrimal and meibomian gland function [3,5]. Consequently, effective management of dry eye disease requires not only symptomatic therapy but also targeted interventions aimed at controlling inflammation and modifying the underlying disease mechanisms.

The aim of this narrative review is to present the current state of knowledge on dry eye disease based on clinical guidelines and scientific publications from the last 10 years, with particular emphasis on contemporary diagnostic and therapeutic algorithms and novel treatment modalities that have significantly expanded clinical management options for this common yet often challenging condition.

2. Methods of the Literature Review

This narrative review was developed based on current clinical guidelines and scientific publications published between 2015 and 2025. Literature searches were conducted using the PubMed/MEDLINE and Google Scholar databases with the following keywords and their combinations: *dry eye disease*, *ocular surface disease*, *TFOS DEWS II*, *meibomian gland dysfunction*, *dry eye treatment*, and *anti-inflammatory therapy*.

Expert consensus reports, guidelines issued by scientific societies, randomized controlled trials, meta-analyses, and systematic reviews addressing the diagnosis and management of dry eye disease were included. Particular emphasis was placed on the Tear Film and Ocular Surface Society Dry Eye Workshop II (TFOS DEWS II) reports, the American Academy of Ophthalmology Preferred Practice Pattern guidelines, recommendations of the Polish Ophthalmological Society, and European consensus statements regarding the management of ocular surface inflammation in dry eye disease.

Only publications written in English or Polish, involving adult and pediatric populations, and published in peer-reviewed scientific journals were included in the analysis. The selected articles were evaluated with respect to their relevance, methodological quality, and clinical applicability in the context of contemporary diagnostic and therapeutic algorithms for dry eye disease.

3. Definition and Classification of Dry Eye Disease

According to the definition proposed by the Tear Film and Ocular Surface Society Dry Eye Workshop II (TFOS DEWS II), dry eye disease (DED) is a disease of the ocular surface characterized by a loss of tear film homeostasis and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, inflammation and damage of the ocular surface, as well as neurosensory abnormalities, play key etiological roles [2]. This definition emphasizes that DED is not merely a quantitative deficiency of tears but rather a complex functional disorder with a multifactorial pathogenesis.

Classically, two main mechanisms of dry eye disease are distinguished: aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE) [3]. In clinical practice, however, a mixed form is most commonly observed, in which both pathophysiological mechanisms coexist.

Aqueous-deficient dry eye results from insufficient tear production by the main lacrimal gland and accessory lacrimal glands. The most common cause of ADDE is primary or secondary Sjögren's syndrome; however, this form of dry eye may also be associated with other autoimmune diseases, the aging process, or the use of certain systemic medications [6].

Evaporative dry eye is primarily associated with meibomian gland dysfunction (MGD), as these glands are responsible for the production of the lipid layer of the tear film. Alterations in the quality or quantity of lipid secretion lead to increased tear evaporation and tear film instability, even in the presence of normal aqueous tear production [7].

Contemporary guidelines emphasize the importance of dry eye phenotyping, which includes assessment of the predominant pathogenic mechanism, the presence of inflammation, the extent of ocular surface damage, and potential neurosensory abnormalities. This approach allows for a more precise selection of therapy and forms the basis of modern, personalized management of dry eye disease [3,4].

4. Pathophysiology of Dry Eye Disease

The contemporary understanding of the pathophysiology of dry eye disease (DED) is based on the concept of a so-called "vicious circle," which has been comprehensively described in the TFOS DEWS II reports [3,4]. The central element of this mechanism is the loss of tear film homeostasis, which initiates a cascade of mutually reinforcing pathological processes affecting the ocular surface.

Tear film instability, resulting from abnormalities in the lipid, aqueous, or mucin layers, promotes increased tear evaporation and leads to elevated tear osmolarity. Tear hyperosmolarity is considered one of the key initiating stimuli for ocular surface inflammation [4]. It induces activation of mitogen-activated protein kinase (MAPK) pathways and the nuclear factor kappa B (NF-κB) transcription factor, resulting in increased expression of pro-inflammatory cytokines such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), as well as matrix metalloproteinases, particularly MMP-9 [8].

Chronic inflammation leads to damage of corneal and conjunctival epithelial cells, disruption of tight junctions, and a reduction in both the number and function of mucin-producing goblet cells. Consequently, tear film stability further deteriorates, perpetuating the pathophysiological vicious cycle of dry eye disease [4,9].

Meibomian gland dysfunction (MGD) also plays a crucial role in the pathogenesis of dry eye disease. Impaired gland function results in alterations in lipid composition, increased viscosity of the meibum, and obstruction of gland orifices, thereby enhancing tear evaporation and promoting the development of chronic eyelid margin inflammation [7,10]. Numerous studies have confirmed that MGD is the most common cause of evaporative dry eye disease and frequently coexists with an inflammatory component [7].

In recent years, increasing attention has been directed toward the role of ocular surface neurosensory abnormalities. In some patients, altered sensory perception may lead to severe pain symptoms despite minimal clinical signs, whereas others may exhibit relatively mild symptoms despite significant ocular surface damage [2,11]. Damage to or hypersensitivity of corneal nerve endings may result from chronic inflammation, surgical procedures, trauma, or systemic diseases such as diabetes mellitus, and it has important implications for therapeutic response.

The complexity of the pathophysiological mechanisms underlying dry eye disease underscores the need for a multidirectional therapeutic approach, encompassing improvement of tear film stability, control of inflammation, and—in selected cases—modulation of the neurosensory component.

5. Epidemiology and Risk Factors

The prevalence of dry eye disease varies depending on the studied population, applied diagnostic criteria, and methods used to assess symptoms. It is estimated that symptoms of dry eye disease affect between 5% and more than 30% of the adult population, with prevalence increasing with age and being higher in women [12]. These differences are partly attributable to the influence of sex hormones on the function of the lacrimal glands and the meibomian glands.

Among the most important risk factors are environmental conditions and lifestyle-related factors, particularly prolonged use of computers and other digital devices. Reduced blink rate and incomplete blinking lead to tear film destabilization and increased evaporation, thereby promoting the development of symptoms even in individuals without clinically apparent ocular surface disease [13]. In addition, low ambient humidity,

air conditioning, environmental pollution, and exposure to tobacco smoke exacerbate dry eye–related symptoms.

Systemic diseases also play a significant role in the pathogenesis of dry eye disease. These include Sjögren's syndrome, rheumatoid arthritis, systemic lupus erythematosus, diabetes mellitus, and thyroid disorders [6,12]. In this group of patients, dry eye disease is often characterized by a more severe clinical course, greater inflammatory activity, and the need for more intensive treatment as well as interdisciplinary management.

Systemic medications, such as anticholinergic agents, antidepressants, antihistamines, and beta-blockers, represent additional risk factors. Moreover, topical ophthalmic medications containing preservatives—particularly benzalkonium chloride (BAK)—have been shown to exert toxic effects on the ocular surface when used long term [14].

The most important risk factors for dry eye disease and their clinical significance are summarized in **Table 1**.

Table 1. Major risk factors for dry eye disease

Category	Examples	Clinical significance
Demographic	Older age, female sex, menopause	Increased risk of ADDE and MGD
Environmental	Air conditioning, low humidity, wind, pollution	Increased tear evaporation
Lifestyle	Prolonged screen use, reduced blink rate	Tear film instability
Systemic diseases	Sjögren's syndrome, rheumatoid arthritis, diabetes mellitus	Frequently severe course of DED
Medications	SSRIs, anticholinergic drugs, benzalkonium chloride (BAK)	Ocular surface toxicity
Eyelid disorders	Meibomian gland dysfunction, rosacea, demodicosis	Most common cause of evaporative DED

6. Diagnosis of Dry Eye Disease

The diagnosis of dry eye disease (DED) should be based on a combination of patient-reported symptoms, clinical examination, and tests assessing tear film function. According to the TFOS DEWS II recommendations and the American Academy of Ophthalmology guidelines, a diagnosis of DED requires the presence of both subjective symptoms and at least one objective marker of ocular surface disturbance [2,3,15].

The first step in the diagnostic process is the assessment of symptoms using validated questionnaires, such as the Ocular Surface Disease Index (OSDI) or the Dry Eye Questionnaire-5 (DEQ-5). These tools allow for quantitative evaluation of symptom severity and monitoring of treatment response [2]. However, it should be emphasized that the severity of subjective symptoms does not always correlate with the extent of clinical signs observed during ocular examination.

Clinical assessment includes evaluation of the eyelid margins, the quality and patency of the meibomian gland orifices, tear meniscus height, and the condition of the conjunctiva and cornea using slit-lamp biomicroscopy. Tear film stability tests play a key role in the diagnostic process, including tear break-up time (TBUT) or its non-invasive counterpart (NIBUT). A shortened TBUT (<10 seconds) is one of the most frequently observed objective indicators of dry eye disease [3].

Corneal and conjunctival staining with fluorescein and lissamine green enables assessment of epithelial damage and disease severity. Despite its limited specificity and variable reproducibility, the Schirmer test remains useful in the diagnosis of aqueous-deficient dry eye, particularly when Sjögren's syndrome is suspected [6].

In selected cases, the diagnostic work-up may be expanded to include additional tests, such as tear osmolarity measurement, detection of matrix metalloproteinase-9 (MMP-9) as a marker of ocular surface inflammation, and meibography, which allows structural evaluation of the meibomian glands [2,16]. The main diagnostic tests used in the evaluation of dry eye disease and their clinical significance are summarized in **Table 2**.

Table 2. Basic diagnostic tests in dry eye disease

Test	What it assesses	Abnormal values	Clinical significance
OSDI / DEQ-5	Severity of symptoms	OSDI ≥13, DEQ-5 ≥6	Screening and monitoring
TBUT / NIBUT	Tear film stability	<10 s	Key functional parameter
Corneal staining	Epithelial damage	Punctate epithelial defects	Assessment of disease severity
Schirmer I test	Tear secretion	≤5 mm / 5 min	ADDE, Sjögren syndrome
Tear osmolarity	Tear film homeostasis	≥308 mOsm/L	Marker of tear film instability
MMP-9	Inflammation	Positive result	Indication for anti-inflammatory therapy

7. Assessment of Dry Eye Disease Severity

The assessment of dry eye disease (DED) severity is a key element in treatment planning and monitoring of therapeutic response. According to the recommendations of the TFOS DEWS II reports and the American Academy of Ophthalmology, disease severity should be determined based on a comprehensive evaluation of subjective symptoms, objective clinical findings, and the impact of the disease on the patient's daily functioning [3,15].

The TFOS DEWS II guidelines move away from a rigid, stepwise classification of disease severity, instead promoting a dynamic, staged approach in which treatment intensity is tailored to the dominant DED phenotype and the individual patient's response to therapy [3]. It should be emphasized that in some patients there may be a significant discrepancy between the severity of subjectively reported symptoms and the degree of ocular surface damage observed on clinical examination, particularly in cases with a prominent neurosensory component [2].

In clinical practice, however, an approximate grading of DED severity remains useful and typically includes the following elements:

- severity of symptoms assessed using validated questionnaires (OSDI, DEQ-5),
- tear film stability (TBUT/NIBUT),
- extent of corneal and conjunctival staining,
- presence of complications such as filamentary keratopathy, recurrent epithelial defects, or corneal ulceration.

Mild and moderate forms of dry eye disease most commonly present with ocular discomfort, burning sensations, and fluctuations in visual acuity, whereas severe forms may lead to significant corneal damage, persistent visual impairment, and a substantial reduction in patients' quality of life [17].

8. Treatment Algorithms for Dry Eye Disease According to Current Guidelines

Current guidelines emphasize that the management of dry eye disease (DED) should be multimodal, individualized, and stepwise, with the primary goal of interrupting the vicious cycle of the disease, rather than providing only symptomatic relief [3,4,15]. This approach reflects the multifactorial pathogenesis of DED and the marked heterogeneity of its clinical presentation.

The *TFOS DEWS II Management and Therapy Report* and the *American Academy of Ophthalmology Preferred Practice Pattern* recommend initiating treatment with interventions associated with the lowest risk of adverse effects, such as patient education, modification of environmental factors, and the use of lubricating eye drops, followed by gradual escalation of therapy in cases of insufficient clinical improvement [3,15]. A similar stepwise strategy is also endorsed by the current guidelines of the Polish Ophthalmological Society [18].

At every stage of treatment, patient adherence and active cooperation, regular use of appropriately selected artificial tears, and elimination of factors exacerbating symptoms remain fundamental. In patients with persistent symptoms or clinical signs of ocular surface inflammation, causal treatment should be implemented, including anti-inflammatory therapy and interventions targeting meibomian gland dysfunction [3,4].

In moderate-to-severe cases, as well as in patients refractory to standard therapy, advanced treatment options may be considered, such as biological eye drops (e.g., autologous serum), scleral contact lenses, or procedural interventions, often within the framework of interdisciplinary care [17,18].

An overview of the recommended therapeutic interventions at each stage of dry eye disease management, according to the TFOS DEWS II, AAO, and Polish Ophthalmological Society guidelines, is presented in Table 3.

Table 3. Stepwise management of dry eye disease according to TFOS DEWS II, AAO, and PTO

Treatment stage	Recommended interventions	Clinical remarks
Stage 1	Patient education, environmental modifications, regular breaks during screen use, artificial tears (preferably preservative-free), eyelid hygiene	Foundation of treatment for all patients
Stage 2	Lipid-based and increased-viscosity lubricants, short-term topical corticosteroids, cyclosporine A, treatment of meibomian gland dysfunction, punctal plugs (after control of inflammation)	Indicated in patients with persistent symptoms
Stage 3	Device-based therapies (thermal pulsation, IPL), biological eye drops (ASED, PRP), neurostimulation, scleral contact lenses	Moderate to severe cases
Stage 4	Amniotic membrane transplantation, systemic immunosuppressive therapy, surgical procedures	Severe, refractory forms of dry eye disease

9. Basic and Non-Pharmacological Management

Basic management constitutes the foundation of dry eye disease therapy and should be implemented in all patients, regardless of disease severity. It includes patient education, modification of environmental factors, and regular use of lubricating eye drops, in accordance with the current TFOS DEWS II guidelines and recommendations of the American Academy of Ophthalmology [3].

Patient education should address the chronic nature of the disease, the necessity of long-term and consistent treatment, and realistic expectations regarding therapeutic outcomes. Particular emphasis should be placed on visual ergonomics, increasing the frequency of conscious blinking, and avoidance of factors that exacerbate tear evaporation, such as direct airflow from air conditioning systems, prolonged exposure to dry air, and environments with low humidity [13].

Artificial tears remain the mainstay of symptomatic treatment in dry eye disease. Current guidelines recommend selecting the formulation according to the dominant disease phenotype: lipid-based emulsions are preferred in evaporative dry eye, whereas preparations with increased water-binding capacity or hydrophilic polymers are recommended in aqueous-deficient dry eye [3,4]. In patients requiring frequent instillation, preservative-free formulations are strongly advised to minimize the risk of ocular surface toxicity.

An integral component of basic management is eyelid hygiene and the use of warm compresses, particularly in patients with signs of meibomian gland dysfunction. Regular cleansing of the eyelid margins may reduce inflammatory load, improve gland orifice patency and lipid secretion quality, and enhance the effectiveness of subsequent therapeutic interventions [7,10].

10. Anti-inflammatory treatment of dry eye disease

Chronic inflammation of the ocular surface represents one of the key pathogenic mechanisms of dry eye disease (DED); therefore, current clinical guidelines emphasize the importance of anti-inflammatory therapy in patients in whom basic treatment does not provide sufficient clinical improvement [3,4,15]. The primary goal of therapy is to interrupt the vicious cycle of the disease by reducing inflammatory mediators, improving the integrity of the corneal and conjunctival epithelium, and restoring tear film homeostasis.

Currently available anti-inflammatory treatment options differ in their mechanisms of action, efficacy profiles, and safety, allowing individualized selection based on the disease phenotype and severity. A comparison of the main anti-inflammatory therapies used in the management of dry eye disease is presented in Table 4.

10.1. Topical corticosteroids

Topical corticosteroids are effective in rapidly suppressing ocular surface inflammation and are primarily used in the management of dry eye exacerbations or as bridging therapy prior to initiation of immunomodulatory treatment [15,19]. Their mechanism of action includes inhibition of pro-inflammatory cytokine expression, reduction of inflammatory cell infiltration, and stabilization of the epithelial barrier.

Agents with a more favorable safety profile, such as loteprednol etabonate, are preferred, as they are associated with a lower risk of intraocular pressure elevation and cataract formation compared with traditional fluorinated corticosteroids. According to recommendations of the American Academy of Ophthalmology and TFOS DEWS II, topical corticosteroids should be used short-term, typically for 1–2 weeks, under close ophthalmic supervision [3,15]. Long-term use is not recommended due to the risk of adverse effects.

10.2. Cyclosporine A

Cyclosporine A (CsA) is a calcineurin inhibitor that suppresses T-cell activation and reduces the production of pro-inflammatory cytokines that play a central role in the pathogenesis of dry eye disease. The efficacy of cyclosporine A has been demonstrated in numerous randomized clinical trials and is reflected in international clinical guidelines [3,15,20].

Cyclosporine A formulations are intended for long-term use, and clinical improvement—both in subjective symptoms and objective signs—may be observed after several weeks or months of therapy. The most commonly reported adverse effect is a burning sensation upon instillation, which may negatively affect treatment adherence in some patients. In clinical practice, concomitant use of lubricating eye drops or short-term initiation of topical corticosteroids at the beginning of therapy is often recommended to improve tolerability [20].

10.3. Lifitegrast

Lifitegrast is an antagonist of lymphocyte function–associated antigen-1 (LFA-1) that inhibits the interaction between LFA-1 and intercellular adhesion molecule-1 (ICAM-1), leading to reduced activation, adhesion, and migration of T lymphocytes on the ocular surface. This mechanism allows targeted modulation of the inflammatory response without the adverse effects typically associated with corticosteroids [21].

Lifitegrast has been approved in the United States for the treatment of both signs and symptoms of dry eye disease. Clinical trials have demonstrated significant improvement in subjective symptoms, such as ocular discomfort and dryness, as well as in selected objective disease parameters [21,22]. The most common adverse effects include ocular irritation and dysgeusia. Availability of lifitegrast in Europe remains limited, which currently restricts its use in routine clinical practice.

Table 4. Anti-inflammatory treatment of dry eye disease

Therapy	Mechanism of action	Clinical indication	Remarks
Topical corticosteroids	Suppression of inflammatory response	Acute exacerbations of DED	Short-term use
Cyclosporine A	Immunomodulation (T-lymphocyte inhibition)	Chronic treatment of DED	Delayed onset of action
Lifitegrast	LFA-1/ICAM-1 pathway blockade	Inflammatory dry eye disease	Limited availability

11. Management of Meibomian Gland Dysfunction

Meibomian gland dysfunction (MGD) is the most common cause of evaporative dry eye disease and frequently coexists with chronic inflammation of the ocular surface [7]. Effective management of MGD is crucial for tear film stabilization, reduction of tear evaporation, and improvement of patient-reported symptoms.

The cornerstone of MGD management consists of non-pharmacological measures, including regular application of warm compresses, eyelid hygiene, and mechanical expression of the gland orifices. These interventions aim to liquefy thickened meibomian secretions, improve ductal patency, and reduce local inflammatory activity.

In moderate to severe cases, adjunctive therapy with anti-inflammatory antibiotics, such as doxycycline or macrolides, is recommended. In addition to their antimicrobial effects, these agents modulate matrix metalloproteinase activity, improve lipid composition, and reduce inflammatory responses within the eyelid margins and Meibomian glands [10].

11.1. Device-based therapies

In recent years, there has been increasing interest in device-based therapies for the treatment of MGD, particularly in patients who show insufficient response to conservative management. These modalities represent an important adjunct to standard therapy.

Thermal pulsation systems enable controlled heating of the eyelids combined with simultaneous evacuation of obstructed meibomian secretions, leading to improved gland patency and tear film stability. Intense pulsed light (IPL) therapy, in turn, exhibits anti-inflammatory effects, reduces eyelid margin

telangiectasia, and may improve Meibomian gland function through its influence on microcirculation and periocular bacterial flora [23,24].

Available meta-analyses indicate significant improvements in objective parameters, such as tear film break-up time, as well as reductions in subjective symptoms in a subset of patients undergoing device-based therapies. However, the effectiveness of these interventions depends on appropriate patient selection, the severity of MGD, and the specific treatment protocol applied.

12. Novel therapies for dry eye disease

12.1. Evaporation-reducing therapies

One of the most recent therapeutic approaches in the management of dry eye disease is treatment aimed at reducing tear film evaporation. **Perfluorohexyloctane** is an anhydrous fluorocarbon compound that, after instillation, forms a stable protective layer on the ocular surface, thereby reducing tear evaporation and improving tear film stability. This mechanism enables a therapeutic effect that is independent of the aqueous components characteristic of conventional lubricating eye drops.

Perfluorohexyloctane-containing formulations have been approved for the treatment of evaporative dry eye disease, particularly in cases associated with meibomian gland dysfunction [25]. Clinical studies have demonstrated improvements in both subjective symptoms, such as ocular dryness and burning, and objective parameters, including prolonged tear film breakup time. An additional advantage of this therapy is its good tolerability and preservative-free formulation, which is particularly important in patients with ocular surface hypersensitivity.

12.2. Neurostimulation and secretagogues

An emerging and rapidly developing group of dry eye therapies includes methods that stimulate natural tear secretion through activation of neural reflex pathways. Intranasal formulations containing **varenicline** act by stimulating nicotinic acetylcholine receptors of the trigeminal nerve within the nasal mucosa, leading to activation of the reflex arc responsible for lacrimal gland secretion.

This therapy has been approved for the treatment of dry eye disease in the United States and has demonstrated efficacy in improving symptoms and increasing tear volume in clinical trials [26]. Neurostimulation-based therapies may be particularly beneficial for patients who are intolerant to conventional topical eye drops, have poor adherence to topical treatment, or present with coexisting neurosensory abnormalities.

13. Biological Therapies and Advanced Management

In patients with severe forms of dry eye disease, particularly those associated with significant corneal epithelial damage and refractoriness to standard treatment, biological therapies and advanced management strategies are indicated. The most commonly used options include **autologous serum eye drops (ASED)** and **platelet-rich plasma (PRP)**. These preparations contain a wide range of growth factors, cytokines, and proteins that closely resemble the composition of natural tears, thereby promoting corneal epithelial regeneration, improving tear film stability, and reducing subjective symptoms [27,28].

Biological therapies are particularly recommended for patients with **Sjögren's syndrome**, severe ocular surface keratopathy, postoperative dry eye disease, and conditions associated with impaired epithelial healing. Limitations of their use include restricted availability, higher costs, and the need to comply with strict standards for preparation, storage, and administration.

Mechanical protection of the ocular surface also plays an important role in the management of advanced dry eye disease. **Scleral contact lenses** create a fluid reservoir over the cornea, reducing tear evaporation and shielding the epithelium from mechanical trauma, which results in improved comfort and visual function. Additionally, **amniotic membrane transplantation** exerts anti-inflammatory, anti-fibrotic, and pro-regenerative effects and is used in severe, treatment-resistant cases of dry eye disease, particularly in patients with autoimmune disorders [17,18].

14. Discussion

Advances in the understanding of the pathophysiology of dry eye disease over recent years have led to a significant shift in therapeutic strategies—from purely symptomatic treatment toward approaches targeting specific disease mechanisms. Current guidelines emphasize the necessity of dry eye disease phenotyping and the implementation of multimodal treatment strategies that simultaneously address inflammation control, tear film stabilization, and the management of meibomian gland dysfunction [3,4].

The introduction of novel immunomodulatory agents, therapies aimed at reducing tear film evaporation, and device-based interventions has substantially expanded therapeutic options for dry eye disease, particularly in patients with moderate to severe forms of the condition. However, the effectiveness of these treatments largely depends on appropriate patient selection, accurate identification of the dominant disease phenotype, and long-term cooperation between the patient and the clinician, including adherence to therapeutic recommendations and lifestyle modifications.

Despite considerable progress, the management of dry eye disease remains a clinical challenge. Particular attention is required for patients presenting with a discrepancy between the severity of subjective symptoms and the extent of clinical signs, especially in the context of neurosensory abnormalities. Further research is needed to identify reliable biomarkers of ocular surface inflammation, neurosensory dysfunction, and predictors of therapeutic response, which could enable more precise and personalized treatment strategies in the future.

15. Conclusions

Dry eye disease (DED) is a complex, chronic disorder of the ocular surface with a multifactorial pathogenesis involving disruption of tear film homeostasis, chronic inflammation, ocular surface damage, and a neurosensory component. Current international guidelines recommend a stepwise and phenotype-oriented approach, which enables more effective and personalized management and contributes to improved patient quality of life.

The dynamic development of novel therapeutic options—including anti-inflammatory agents, procedure-based treatments targeting meibomian gland dysfunction, and biological therapies—has significantly expanded the therapeutic armamentarium for dry eye disease. Nevertheless, early diagnosis, appropriate patient education, and individualized treatment strategies tailored to the dominant pathophysiological mechanisms and disease severity remain essential elements of effective long-term management.

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