

Hospital Prof. Doutor Fernando da Fonseca

Serviço de Oftalmologia

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PATOLOGIA DA SUPERFÍCIE OCULAR NOVA ABORDAGEM

20 de Abril de 2012

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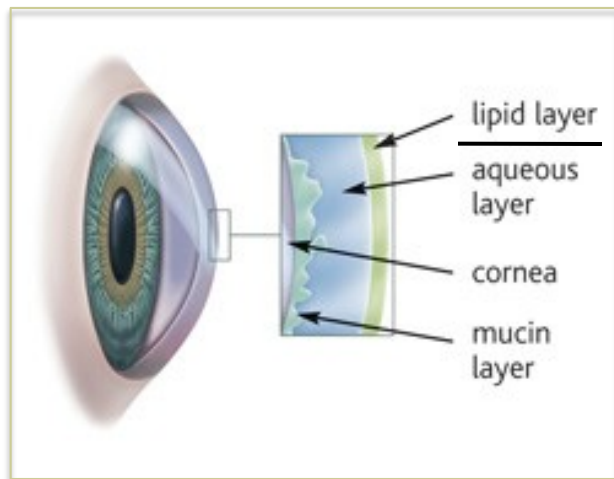
Olho seco

1. Fisiologia
2. Definição
3. Epidemiologia
4. Diagnóstico e monitorização
5. Tratamento
6. Conclusões

FISIOLOGIA

Olho Seco

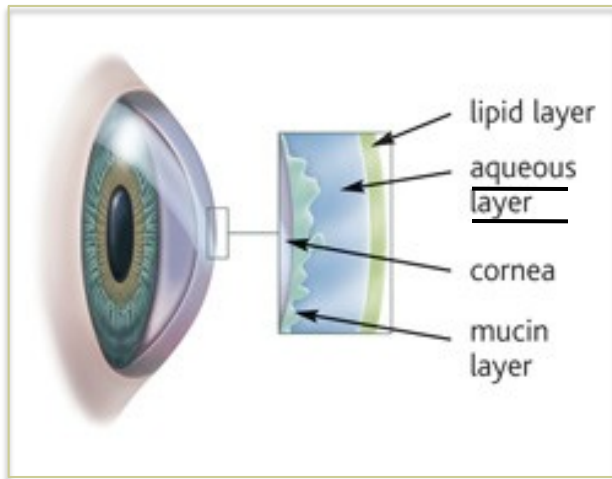
Componentes do Filme Lacrimal



Colesterol
Ácidos Gordos
Triglicéridos

- ❖ Surfactante
- ❖ Prevenir evaporação

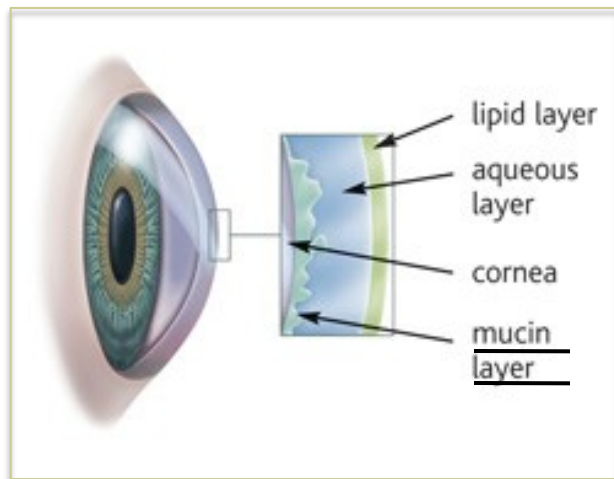
Componentes do Filme Lacrimal



Água	Ca ²⁺ , Na ⁺ , Mg ²⁺ , K ⁺
Lisozima	Albumina
Lacoferrina	Lactato
Imunoglobulinas	Glicose
Citocinas	Ureia

- ❖ Oxigenação
- ❖ Anti-bacteriano
- ❖ Neutralização de irregularidades

Componentes do Filme Lacrimal



Proteínas de alto peso molecular

Ácido hialurónico

- ❖ Matriz visco-elástica
- ❖ Superfície hidrofílica

DEFINIÇÃO

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Contexto Histórico

Andrew De Roeth
(1950)

NEI/Dry Eye
Workshop
(1995)

International Dry
Eye Workshop
(2007)



Dry eye is a disorder of the tear film due to tear deficiency or excessive evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of ocular discomfort.

Lemp MA, 1995, *CLAO J.*

Dry eye is a **multifactorial disease** of the tears and ocular surface that results in **symptoms** of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased **osmolarity** of the tear film and **inflammation** of the ocular surface.

DEWS, 2007, *The Ocular Surface*.

EPIDEMIOLOGIA

Olho Seco

Epidemiologia

?

Epidemiologia

Salisbury Eye Evaluation Self-reported assessment of dry eye in a population-based setting ¹⁰⁷	Bandeen-Roche, Munoz, Tielsch, et al. <i>Ophthalmol Vis Sci</i> 1997;38(12):2469-75	Standardized 6-question questionnaire*	Population-based prevalence survey for clinical and subjective evidence of dry eye
Dry Eye Epidemiology Projects (DEEP) Sensitivity and specificity of a screening questionnaire for dry eye ¹⁰⁸	Oden, Lilienfeld, Lemp, et al. <i>Adv Exp Med Biol</i> 1998;438: 807-20	19 questions	Screening
Women's Health Study questionnaire Prevalence of dry eye syndrome among US women ⁷	Schaumberg, Sullivan, Buring, Sullivan. <i>Am J Ophthalmol</i> 2003 Aug;136(2):318-26	3 items from 14-item original questionnaire	Women's Health Study/ Epidemiologic studies
National Eye Institute Visual Function Questionnaire (NEI-VFQ)¹⁰⁹	Mangione, Lee, Pitts, et al. <i>Arch Ophthalmol</i> 1998;116:1496-1504	25-item questionnaire: 2 ocular pain subscale questions	Useful tool for group-level comparisons of vision-targeted, health-related QOL in clinical research; not influenced by severity of underlying eye disease, suggesting use for multiple eye conditions.
Dry Eye Questionnaire (DEQ) Habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity ³⁴	Begley, Chalmers, Abetz, et al. <i>Invest Ophthalmol Vis Sci</i> 2003 Nov;44(11):4753-61	21 items on prevalence, frequency, diurnal severity and intrusiveness of sx	Epidemiologic and clinical studies
Dry Eye Questionnaire (DEQ) Use of the dry eye questionnaire to measure symptoms of ocular irritation in patients with aqueous tear deficient dry eye ¹¹⁰	Begley, Caffery, Chalmers, et al. <i>Cornea</i> 2002;21(7):664-70	As above	As above

Epidemiologia

McMonnies Key questions in a dry eye history (McMonnies) ¹⁰³	McMonnies. <i>J Am Optometric Assoc</i> 1986; 57(7):512-7	15 questions	Screening questionnaire—used in a clinic population
McMonnies Reliability and validity of McMonnies Dry Eye Index. (Nichols et al) ¹⁰⁴	Nichols, Nichols, Mitchell. <i>Cornea</i> 2004;23(4):365-71	Previously described	Screening questionnaire Dry eye clinic population
*CANDEES A patient questionnaire approach to estimating the prevalence of dry eye symptoms in patients presenting to optometric practices across Canada (CANDEES) ⁹⁵	Doughty, Fonn, Richter, et al. <i>Optom Vis Sci</i> 1997;74(8):624-31	13 questions	Epidemiology of dry eye symptoms in a large random sample
OSDI The Ocular Surface Disease Index ¹⁰⁵	Schiffman, Christianson, Jacobsen, et al. <i>Arch Ophthalmol</i> 2000;118:615-21	12-item questionnaire	Measures the severity of dry eye disease; end points in clinical trials, symptoms, functional problems and environmental triggers queried for the past week
OSDI and NEI-VFQ comparison ²⁴	Vitale, Goodman, Reed, Smith. <i>Health Quality Life Outcomes</i> 2004;2:44	Comparison of existing questionnaires	Tested in Sjogren Syndrome population
IDEEL Comparing the discriminative validity of two generic and one disease-specific health-related quality of life measures in a sample of patients with dry eye ²³	Rajagopalan, Abetz, Mertzanis, et al. <i>Value Health</i> 2005 Mar-Apr;8(2):168-74	3 modules (57 questions): 1. Daily Activities 2. Treatment Satisfaction 3. Symptom Bother	Epidemiologic and clinical studies
Salisbury Eye Evaluation Relation between signs and symptoms of dry eye in the elderly ¹⁰⁶	Schein, Tielsch, Munoz B, et al. <i>Ophthalmology</i> 1997;104:1395-1401	Standardized 6-question questionnaire*	Population-based prevalence survey for clinical and subjective evidence of dry eye

Epidemiologia

Contact Lens DEQ Responses of contact lens wearers to a dry eye survey ²³	Begley, Caffery, Nichols, Chalmers. <i>Optom Vis Sci</i> 2000; 77(1): 40-6	13 questions	Screening questionnaire for dry eye symptoms in contact lens wearers
Melbourne Visual Impairment Project The epidemiology of dry in Melbourne, Australia ¹¹	McCarty, Bansal, Livingston, et al. <i>Ophthalmology</i> 1998;105:1114-9	Self-reported symptoms elicited by interviewer-administered questionnaire	Epidemiologic studies
National Eye Institute 42-Item Refractive Error Questionnaire ¹¹¹	Hays, Mangione, Ellwein, et al. <i>Ophthalmology</i> 2003;110(12):2292-301	42-item questionnaire: 4 related questions: ocular pain or discomfort, dryness, tearing, soreness or tiredness	QoL due to refractive error
Sicca/SS questionnaire Validation of the Sicca symptoms inventory for clinical studies of Sjogren's syndrome ¹¹²	Bowman, Booth, Platts, et al. <i>Sjogren's Interest Group. J Rheumatol</i> 2003;30(6):1259-66	Inventory of both symptoms and signs of Sjogren Syndrome	Epidemiologic studies for Sjogren Syndrome
Bjerrum questionnaire Study Design and Study Populations ¹¹³	Bjerrum. <i>Acta Ophthalmologica (Scand)</i> 2000:10-3	3-part questionnaire which includes an ocular part with 14 questions	QOL due to SS dry eye, diagnosis of dry eye, epidemiology of SS
Bjerrum questionnaire Dry Eye Symptoms in patients and normals ¹¹⁴	Bjerrum. <i>Acta Ophthalmologica (Scand)</i> 2000, 14-5.	As above	Screening questionnaire
Bjerrum questionnaire Test and symptoms in keratoconjunctivitis sicca and their correlation ²⁵	Bjerrum. <i>Acta Ophthalmologica (Scand)</i> 1996:74:436-41	Dry eye tests Ocular symptom questionnaire (14 questions)	Examine correlation between dry eye test and ocular symptom questionnaire responses
Utility assessment questionnaire Utility assessment among pts with dry eye disease ²¹	Schiffman, Walt, Jacobsen, et al. <i>Ophthalmology</i> 2003;110(7):1412-9	Utility assessment	Utility assessment

Epidemiologia

Japanese dry eye awareness study Results of a population-based questionnaire on the symptoms and lifestyles associated with dry eye ¹¹⁵	Shimmura, Shimazaki, Tsubota. <i>Cornea</i> 1999; 18(4):408-11	30 questions relating to symptoms and knowledge of dry eye	Population-based, self-diagnosis study to assess public awareness and symptoms of dry eye
Sicca/SLE questionnaire Oral and ocular sicca symptoms and findings are prevalent in systemic lupus erythematosus ¹¹⁶	Jensen, Bergem, Gilboe, et al. <i>Oral Pathol Med</i> 1999;28:317-22	6-question symptom questionnaire	Screening for dry eye symptoms in SLE patients
American-European Consensus Group Classification criteria for Sjogren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group ¹¹⁷	Vitali C, Bombardieri S, Jonsson R, et al. <i>Ann Rheum Dis</i> 2002;11:554-8	6 areas of questions: Ocular symptoms; oral symptoms; ocular signs; histopathology; oral signs; auto-antibodies	Clarification of classification of primary and secondary Sjogren syndrome, and of exclusion criteria.
The Eye Care Technology Forum Impacting Eye Care ¹¹⁸	Ellwein. <i>Ophthalmology</i> 1994;101:199-201	Issues: Standardizing clinical evaluation	Decree for change

Epidemiologia

- 20 milhões de pessoas nos EUA*
- 5 milhões *
- 25%
- US\$ 320 milhões / ano

Epidemiologia

- Impacto económico directo e indirecto
- Morbilidade
 - Aumento da esperança média de vida
 - Risco de infecção e complicações da cirurgia ocular
 - Alteração dos *outcomes* da cirurgia refractiva

Epidemiologia

“Postrefractive surgery dry eye.”

- One of the most common complications of photorefractive keratectomy (PRK) and laser in situ keratomileusis (LASIK) is dry eye syndrome.
- PRK and LASIK perturb the ocular surface homeostasis by causing a decrease in corneal sensitivity, tear film instability, decreases aqueous tear production, and corneal and conjunctival epitheliopathy.

Quinto G. *et al*
Curr Opin Ophthalmol. 2008

Epidemiologia

“Postrefractive surgery dry eye.”

Identify patients at risk for dry eye
Maximize tear film stability preoperatively
Minimize dry eye through intra and postoperative interventions

Quinto G. *et al*
Curr Opin Ophthalmol. 2008

Epidemiologia

- Qualidade de vida

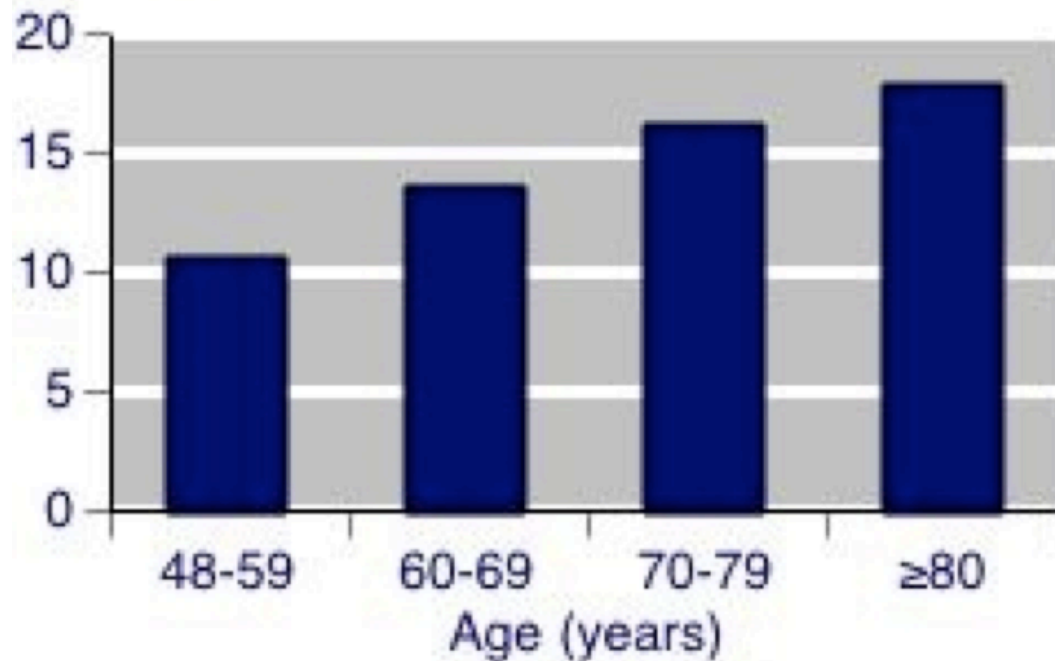
The MOS 36-Item Short-Form Health Survey (SF-36)

I. Conceptual Framework and Item Selection

JOHN E. WARE, JR., PHD,* AND CATHY DONALD SHERBOURNE, PHD†

A 36-item short-form (SF-36) was constructed to survey health status in the Medical Outcomes Study. The SF-36 was designed for use in clinical practice and research, health policy evaluations, and general population surveys. The SF-36 includes one multi-item scale that assesses eight health concepts: 1) limitations in physical activities because of health problems; 2) limitations in social activities because of physical or emotional problems; 3) limitations in usual role activities because of physical health problems; 4) bodily pain; 5) general mental health (psychological distress and well-being); 6) limitations in usual role activities because of emotional problems; 7) vitality (energy and fatigue); and 8) general health perceptions. The survey was constructed for self-administration by

Epidemiologia



Epidemiologia

Study	N	Age range	Dry eye assessment	Prevalence
US Studies				
Salisbury Eye Study ^{3,5}	2420	≥ 65 y	At least 1 of 6 symptoms (dryness, gritty/sandiness, burning, redness, crusting on lashes, eyes stuck shut in morning), occurring at least often.	14.6%
Beaver Dam ⁶	3722	≥ 48 y	"For the past 3 months or longer have you had dry eyes?" (If needed, described as foreign body sensation with itching, burning, sandy feeling, not related to allergy.)	14.4%
Women's Health Study ⁷	36995	≥ 49 y	Severe symptoms of dryness and irritation, either constantly or often, and/or the physician's diagnosis of dry eye as volunteered by the patient.	7.8%
Physician's Health Studies I and II ^{8,9,14}	25655	≥ 50, 55 y	Severe symptoms of both dryness and irritation either constantly or often and/or the physician's diagnosis of dry eye as volunteered by the patient.	
Australian Studies				
Blue Mountains ¹⁰	1075	≥ 50 y	At least 1 of 4 symptoms regardless of severity, or at least 1 symptom with a moderate to severe ranking (dryness, grittiness, itchiness, discomfort).	16.6% (at least 1 symptom) 15.3% (3 or more symptoms)
Melbourne Visual Impairment Project ¹¹	926	≥ 40 y	At least 1 of 6 "severe" symptoms, not attributed by the subject to hay fever (discomfort, foreign body, itching, tearing, dryness, photophobia).	5.5%
Asian Studies				
Shihpai ¹²	2038	≥ 65 y	At least 1 of 6 symptoms, often or all of the time (dryness, gritty/sandiness, burning, sticky, tearing, redness, discharge, eyes stuck shut in morning).	33.7%
Sumatra ¹³	1058	≥ 21 y	At least 1 of 6 symptoms, often or all of the time (dryness, gritty/sandiness, burning, redness, crusting on lashes, eyes stuck shut in morning).	27.5%

*The Ocular Surface ISSN: 1542- 0124. The epidemiology of dry eye disease: report of the Epidemiology Subcommittee of the International Dry Eye WorkShop (2007).

FACTORES DE RISCO

Olho Seco

Factores de risco

Comprovado

- Idade
- Sexo feminino
- Pós-menopausa
- Anti-histamínicos
- LASIK
- Transplante de células hematopoiéticas
- Radioterapia
- Déficit de vitamina A
- Hepatite C

Provável

- Hispânicos e asiáticos
- Medicação:
 - Anti-depressivos
 - Diuréticos
 - Beta-bloqueantes
 - Isotretinoína
- Diabetes Mellitus
- HIV
- Sarcoidose

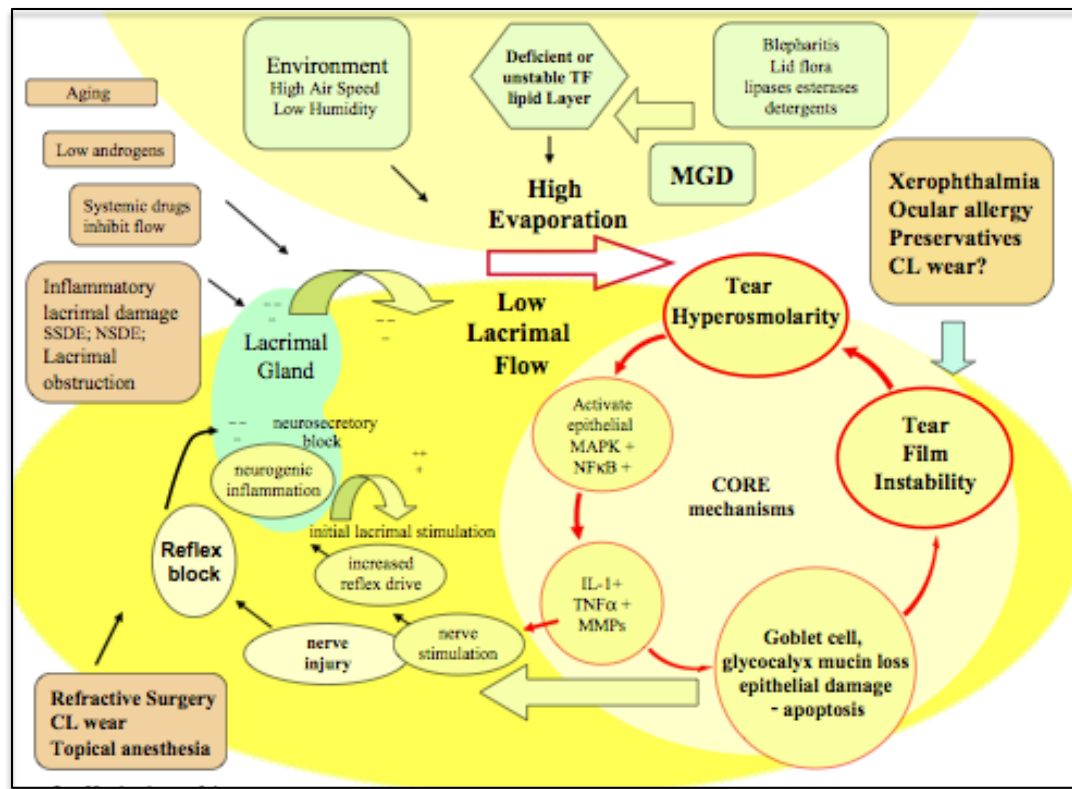
Possível

- Fumador
- Medicação:
 - Anti-colinérgicos
 - Ansiolíticos
 - Anti-psicóticos
- Hábitos alcoólicos
- Injeção de toxina botulínica
- Menopausa

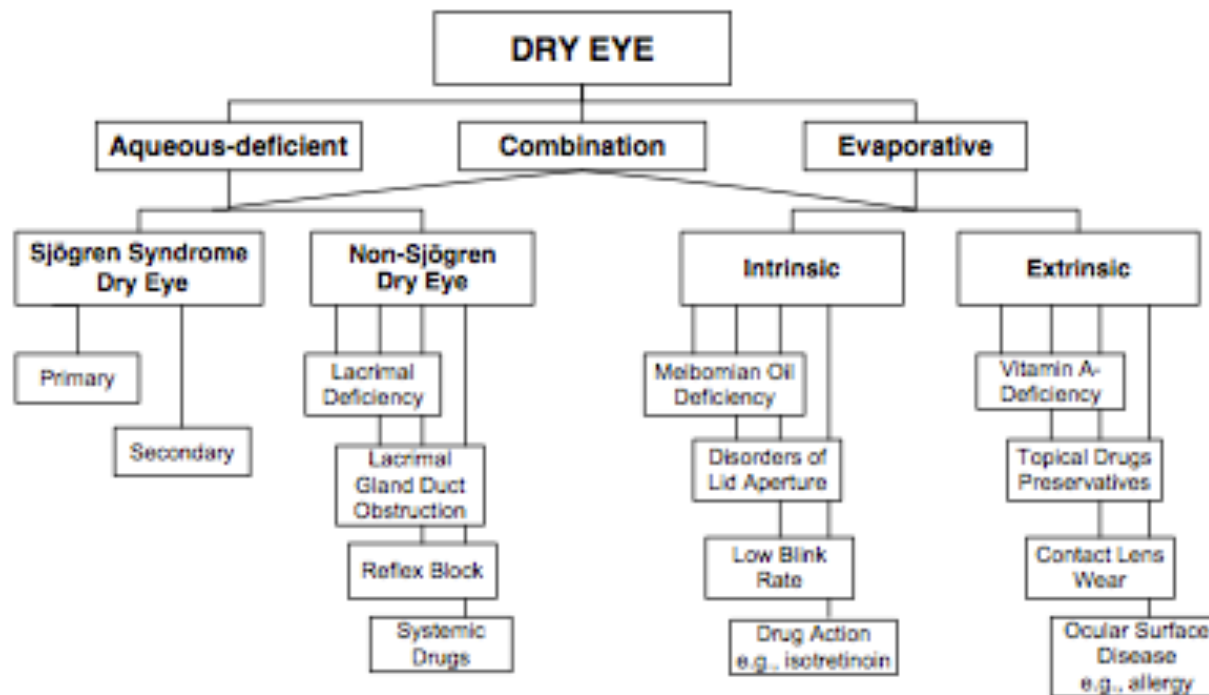
ETIOPATOGENÉSE

Olho Seco

Etiopatogénesis



Classificação



DIAGNÓSTICO

Olho Seco

Diagnóstico Objectivo

Olho Seco por Deficiência de Produção Aquosa

Exame	Resultados Característicos
Break-Up Time	< 10 seg
Corante da Superfície Ocular	Superfície interpalpebral - zona de exposição
Schirmer Test	≤ 5mm com anestesia
Teste de Clearance de Fluoresceína	< comparação com escala de cor
Função das Glândulas Lacrimais	Diminuição da concentração de lactoferrina
Osmolaridade Lacrimal	Aumentada

Diagnóstico Objectivo

Olho Seco por Evaporação

Exame	Resultados Característicos
Break-Up Time	< 10 seg
Corante da Superfície Ocular	Córnea e Conjuntiva Bulbar inferior
Osmolaridade Lacrimal	Aumentada

TRATAMENTO

Olho Seco

Tratamento

Dry Eye Severity Level	1
Discomfort, severity & frequency	Mild and/or episodic occurs under environ stress
Visual symptoms	None or episodic mild fatigue
Conjunctival injection	None to mild
Conjunctival staining	None to mild
Corneal staining (severity/location)	None to mild
Corneal/tear signs	None to mild
Lid/meibomian glands	MGD variably present
TFBUT (sec)	Variable
Schirmer score (mm/5 min)	Variable

- ✓ Alterações comportamentais (dieta/ambiente)
- ✓ Eliminação de fármacos prejudiciais
- ✓ Lubrificantes
- ✓ Tratamento das pálpebras

Tratamento

Dry Eye Severity Level	2
Discomfort, severity & frequency	Moderate episodic or chronic, stress or no stress
Visual symptoms	Annoying and/or activity limiting episodic
Conjunctival injection	None to mild
Conjunctival staining	Variable
Corneal staining (severity/location)	Variable
Corneal/tear signs	Mild debris, ↓ meniscus
Lid/meibomian glands	MGD variably present
TFBUT (sec)	≤ 10
Schirmer score (mm/5 min)	≤ 10

Tratamento Gravidade Nível 1 mais:

- ✓ Anti-inflamatórios
- ✓ Tetraciclinas (se Meibomianite, rosácea)
- ✓ Plugs
- ✓ Secretagogos
- ✓ Óculos de Câmara Húmida

Tratamento

Dry Eye Severity Level	3
Discomfort, severity & frequency	Severe frequent or constant without stress
Visual symptoms	Annoying, chronic and/ or constant limiting activity
Conjunctival injection	+/-
Conjunctival staining	Moderate to marked
Corneal staining (severity/location)	Marked central
Corneal/tear signs	Filamentary keratitis, mucus clumping, ↑ tear debris
Lid/meibomian glands	Frequent
TFBUT (sec)	≤ 5
Schirmer score (mm/5 min)	≤ 5

Tratamento Gravidade Nível 2 mais:

- ✓ Soro Autólogo
- ✓ Lentes de Contacto
- ✓ Oclusão permanente punctal lacrimal

Tratamento

Dry Eye Severity Level	4*
Discomfort, severity & frequency	Severe and/or disabling and constant
Visual symptoms	Constant and/or possibly disabling
Conjunctival injection	+ / ++
Conjunctival staining	Marked
Corneal staining (severity/location)	Severe punctate erosions
Corneal/tear signs	Filamentary keratitis, mucus clumping, ↑ tear debris, ulceration
Lid/meibomian glands	Trichiasis, keratinization, symblepharon
TFBUT (sec)	Immediate
Schirmer score (mm/5 min)	≤ 2

Tratamento Gravidade Nível 3 mais:

- ✓ Anti-inflamatório sistêmico
- ✓ Cirurgia

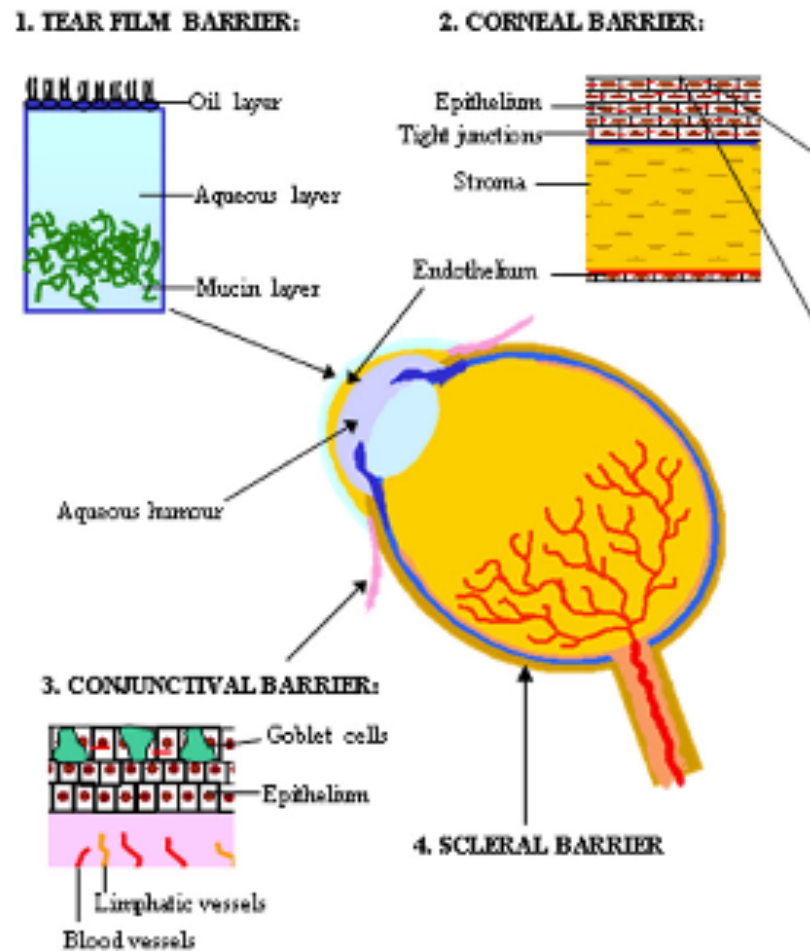
Abordagem

1. Suplementação de Lágrima

- Soluções hipo ou isotónicas (181-354 mOsm/L)
- pH neutro/ligeiramente alcalino
- Electrólitos
- Surfactantes
- Agentes de viscosidade
- Conservantes

Tratamento oftalmológico tópico

- Reduzida biodisponibilidade



Tratamento oftalmológico tópico

Compostos de Baixo Peso Molecular:

Hidrofílicos

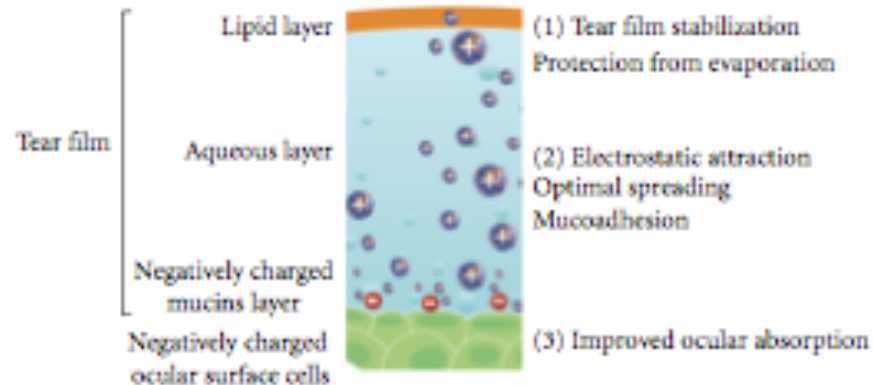
- Soluções aquosas
- Conjuntiva (via para-celular)
- 2 min após instilação 80% é eliminado via drenagem naso-lacrimal

Lipofílicos

- Emulsões e suspensões
- Maior estabilidade da substância activa
- Maior penetração ocular
- Córnea (via para-celular)

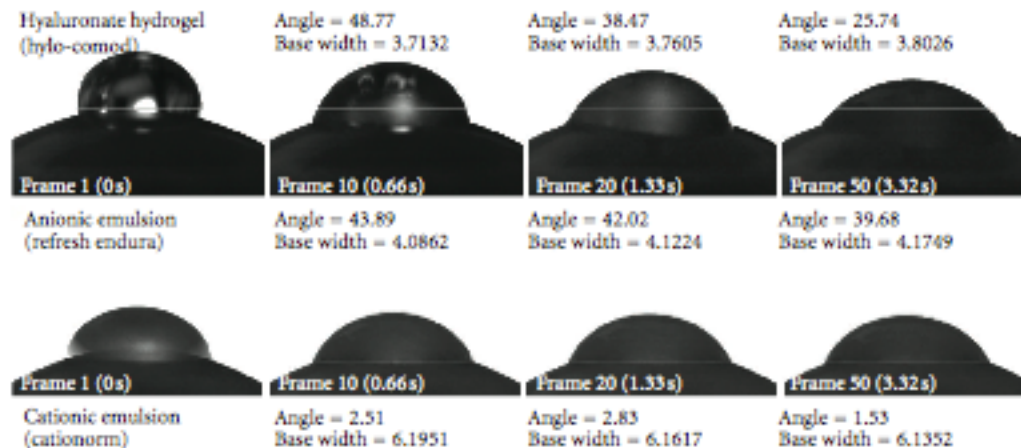
Tratamento oftalmológico tópico

Emulsões Lipofílicas Catiónicas



Tratamento oftalmológico tópico

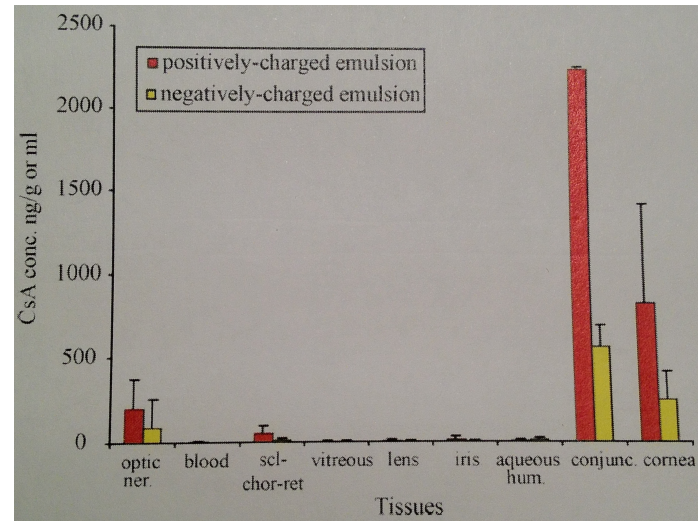
Emulsões Lipofílicas



- < ângulo de contacto (50%)
- > Dispersão na superfície ocular
- < “washout”

Tratamento oftalmológico tópico

Emulsões Lipofílicas



- > Duração de permanência na superfície ocular
- > Capacidade de humidificação e proteção da superfície ocular
- > Eficácia/Biodisponibilidade

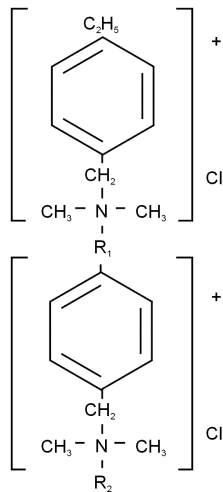
Tratamento oftalmológico tópico

Emulsões Lipofílicas

Function	Excipients
Osmotic agents	Mannitol, glycerol, sorbitol, propylene glycol, dextrose
Oils	Medium chain triglycerides, mineral oil, vegetal oil such a castor oil
Cationic agents	Benzalkonium chloride, cetylpyridinium chloride, cetrimide, benzethonium chloride
Surfactants	Polysorbates, cremophors, poloxamers, tyloxapol, vitamin E-TPGS
Buffers, salts, and anions	To be avoided if possible
Water	Water for injections
Others	Viscosifying agents: preferably neutral Preservatives: preferably nonionic and hydrophilic

Tratamento oftalmológico tópico

Cloreto de Benzalcónio



- O conservante mais utilizado em preparações oftalmológicas tópicas
- EDTA aumenta a eficácia
- Toxicidade epitelial
- Doentes com maior risco de toxicidade:
 1. Olho seco grave
 2. Secreção lacrimal muito reduzida
 3. Oclusão punctal lacrimal

Abordagem

1. Suplementação de Lágrima (cont.)

- Pomada
 - Mistura de óleo mineral e petrolato (lanolina)
 - Geralmente sem conservantes

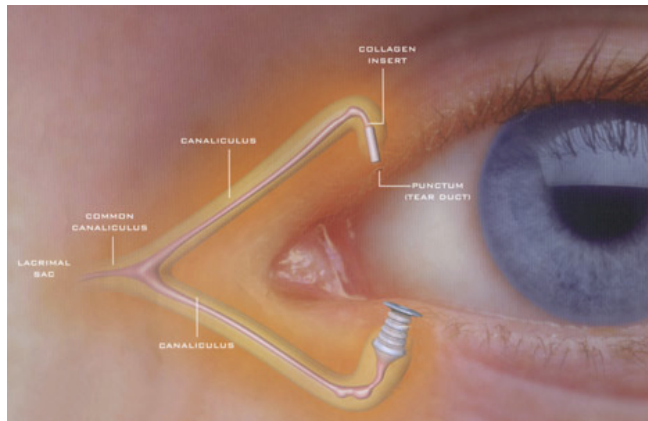
- Gel
 - Polímeros de acrilato (carbómeros)
 - Maior tempo de actuação relativamente às soluções
 - Menor turvação da visão relativamente às pomadas

Abordagem

2. Retenção de Lágrima

- Oclusão Punctal
- Óculos de Câmara Húmida
- Lentes de Contacto

Oclusão Punctal



- Freeman, 1975
- Benéfico em 74-86% dos casos
- Plugs de colagénio ou polímeros
- Contra-indicações:
 - Alergia
 - Ectropion punctal
 - Obstrução ductal naso-lacrimal pre-existente
 - Inflamação da superfície ocular
 - Infecção aguda/crónica do canalículo/saco lacrimal

Oclusão Punctal

Complicações:

- Extrusão espontânea do plug (50%)
- Desconforto
- Migração interna do plug
- Infecção
- Formação de granuloma piogénico

Oclusão Punctal

The effect of punctal occlusion on tear production, tear clearance, and ocular surface sensation in normal subjects.

Temporary punctal occlusion in normal subjects decreases tear production and ocular surface sensation. Our findings suggest that in addition to blocking tear drainage, punctal occlusion may affect the ocular surface/lacrimal gland interaction. These effects were more pronounced in subjects with both upper and lower puncta occluded. In normal subjects, there appears to be an autoregulatory mechanism to return tear production, tear clearance, and ocular surface sensation to preocclusion levels 14 to 17 days after punctal occlusion.

Yen MT et al
Am J Ophthalmol. 2001

Abordagem

3. Estimulação da produção de Lágrima

Secretagogos - secreção aquosa e/ou mucosa

- Diquafosol
- Rebamipide
- Gefarnade
- Ecabet de sódio
- 15(S) – HETE
- Agonistas Colinérgicos – Pilocarpina (Salagen[®])

Abordagem

4. Substitutos Lacrimais Biológicos

Soro Autólogo

- Tsubota, 1990s
- Mantém a morfologia e induz a proliferação do epitélio corneano
- Eficácia dose-dependente (20-100%)
- Factores epiteliotróficos

Factores de crescimento
Neurotrofinas
Vitaminas
Imunoglobulinas
Proteínas da matriz extra-celular

Abordagem

4. Substitutos Lacrimais Biológicos

Auto-transplante de glândula Salivar Submandibular

- 80% sobrevive
- Saliva hipotónica – edema microquístico da córnea

Schirmer-test \leq 1 mm

Dor persistente apesar da oclusão punctal

Deficiência absoluta de produção aquosa

Abordagem

5. Terapêutica Anti-inflamatória

- Ciclosporina (0.05%, 0.1%, 0.2%, 0.4%)
- Corticosteróides
- Tetraciclina

Ocular pharmacokinetics and safety of ciclosporin, a novel topical treatment for dry eye.

- Potent immunomodulator that acts selectively and locally when administered at the ocular surface.
- No adverse effects and only minor effects on DNA synthesis.
- No ocular or systemic toxicity was seen. Very little drug penetrates through the ocular surface to intraocular tissues.
- In 12-week and 1-year clinical safety studies the most common adverse effect was ocular burning (17%)
- No serious drug-related adverse events occurred.

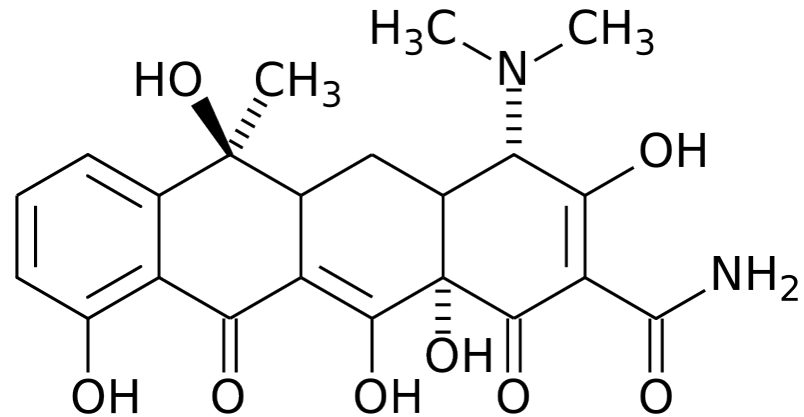
The comparison of efficacies of topical corticosteroids and nonsteroidal anti-inflammatory drops on dry eye patients: a clinical and immunocytochemical study.

Topical corticosteroids had a clearly beneficial effect both on the subjective and objective clinical parameters of moderate-to-severe dry eye patients. These effects were associated with the reduction of inflammation markers of conjunctival epithelial cells.

Abordagem

Tetraciclina

- Anti-bacterianas
- Anti-inflamatórias
- Anti-angiogénicas



- Rosácea
- Blefarite crónica posterior – Meibomianite, DGM

CONCLUSÃO

Olho Seco

Conclusões

Olho Seco...

- ✓ Patologia frequente
- ✓ Incidência e prevalência crescentes
- ✓ Avanços na compreensão da etiologia do olho seco na última década
- ✓ Novas terapêuticas que melhoram os sinais e sintomas estão disponíveis
- ✓ Melhoria da qualidade de vida



Bibliografía

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