


# **MEDICAÇÃO TÓPICA SEM CONSERVANTES NO GLAUCOMA**

## **1º Parte - DOENÇA DA SUPERFÍCIE OCULAR NO GLAUCOMA**

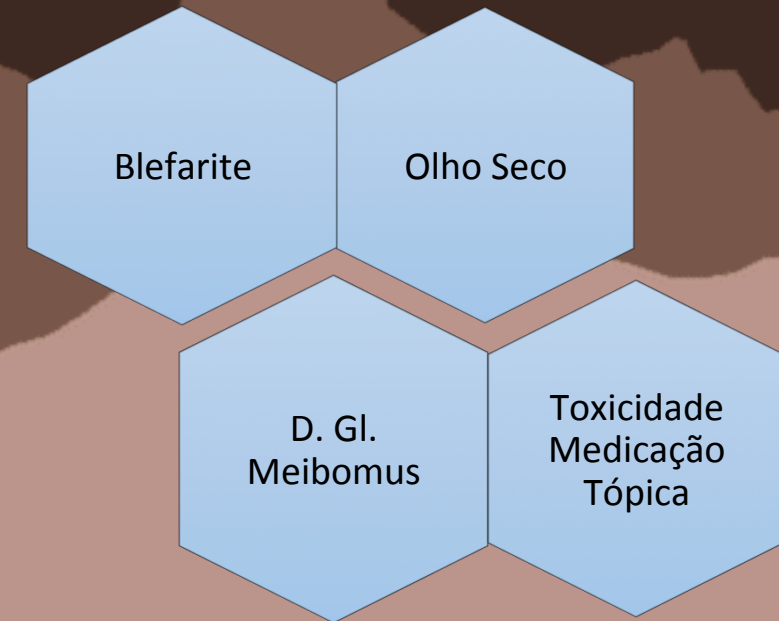
- 
- A close-up photograph of a person's eye, showing the iris and pupil. A hand is visible near the eye, holding a small object, possibly a contact lens or a piece of paper. The background is a soft, out-of-focus landscape with mountains and a body of water.
- **INTRODUÇÃO**
  - **OSD**
  - **OSD – SINTOMAS E SINAIS**
  - **OSD NO GLAUCOMA**
  - **GLAUCOMA – MEDICAÇÃO TÓPICA**
  - **CONSULTA DE GLAUCOMA**
  - **CONCLUSÃO**

# INTRODUÇÃO

- Neuropatia Ótica **Crónica Progressiva**
  - Fator de risco major: Aumento da PIO → Medicação tópica hipotensora
- 
- 60,5 milhões de pessoas no Mundo
  - 4,5 a 5 milhões de pessoas cegas devido à doença
  - Atinge maioritariamente idosos

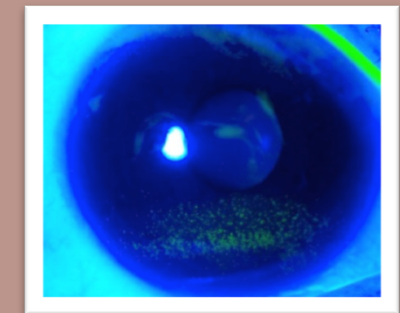
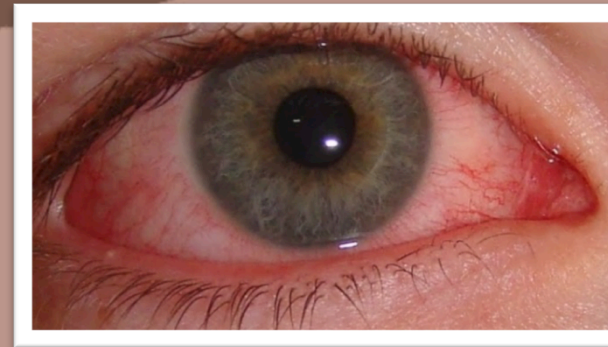
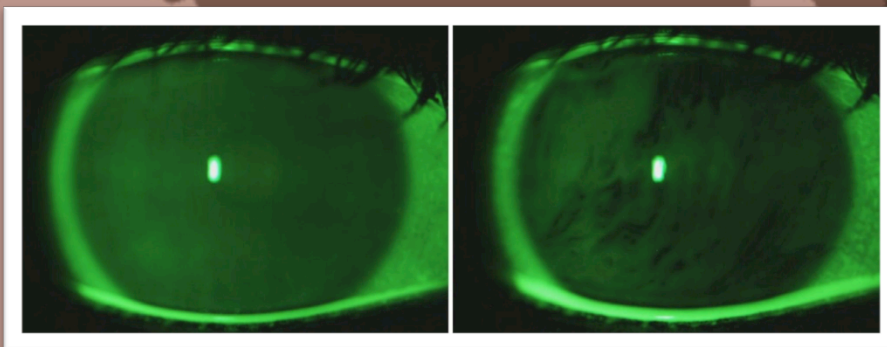
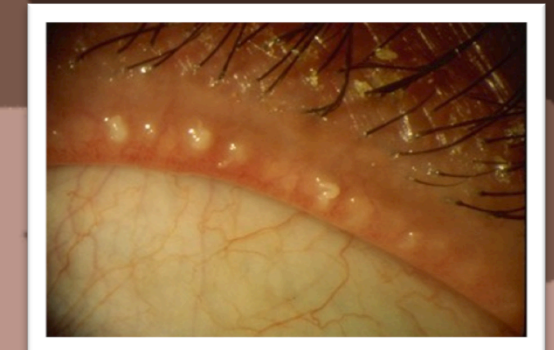
# DOENÇA DA SUPERFÍCIE OCULAR (OSD)

- “Doença multifatorial da superfície ocular e da lágrima que resulta em sintomatologia como desconforto, visão turva e instabilidade do filme lacrimal com potencial dano na superfície ocular. Acompanha-se de aumento da osmolaridade do filme lacrimal e inflamação da superfície ocular.”
- Influenciado por:
  1. Idade
  2. Sexo
  3. Raça
  4. Uso de LC
  5. Deficiências vitamínicas ou alterações hormonais
  6. D. Auto-imunes
  7. Med. Sistémica
  8. **Med. Tópica**



# OSD – SINTOMAS E SINAIS

| Sintomas                           | Sinais                                    |
|------------------------------------|---|
| Visão turva                        | Teste de Schirmer alterado                |
| Sensação de olho seco              | Alteração da osmolaridade da lágrima      |
| Epífora                            | Alteração do TBUT                         |
| Sensação de corpo estranho         | Disfunção das glândulas de meibomius      |
| Prurido                            | Secreção das gl. mais espessa             |
| Fotofobia                          | Vascularização do bordo palpebral         |
| Ardor                              | <i>Staining</i> corneano e/ou conjuntival |
| Aumento do frequência do pestanejo | Hiperémia conjuntival                     |



# OSD NO GLAUCOMA

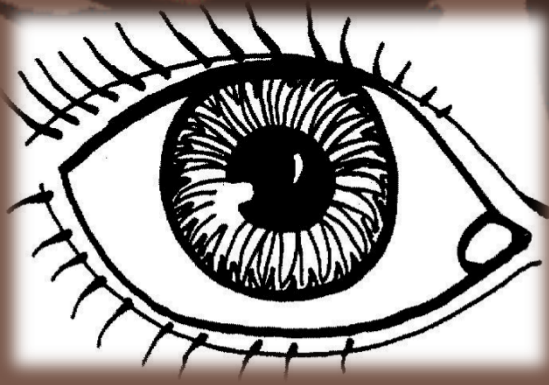


TABLE 1: Topical glaucoma medications: systemic and ocular side effects.

|                               | Systemic side effects   | Ocular side effects  |
|-------------------------------|---|--|
| Nonselective beta-blockers    | Decreased heart rate, bradycardia, arrhythmias, exacerbation of heart failure, masking of hypoglycemic symptoms, and depression | Burning, redness, decreased ocular blood flow, and decreased corneal sensation                   |
| Alpha-2 agonists              | Hypotension, respiratory depression (in infants), central nervous system depression (in infants), sedation, and fatigue         | Redness, itching, pupillary dilatation, and lid retraction                                       |
| Carbonic anhydrase inhibitors | Allergy, bitter taste, and low blood counts   | Stinging, irritation, and red eyes   |
| Prostaglandin analogs         | No significant side effects   | Hyperemia, changes in particularly skin pigmentation, changes in iris color, and eye-lash growth |

# OSD NO GLAUCOMA

- OSD em 48 a 59% dos doentes com glaucoma a realizarem medicação tópica.
- 1 em 6 doentes com glaucoma refere sintomas graves que necessitam de tratamento.
- Fatores que influenciam o risco de OSD:
  1. Glaucoma
  2. Valor de PIO
  3. Número de colírios e de gotas por dia
  4. História prévia de OSD
  5. História de alergia/intolerância à medicação



# GLAUCOMA – MEDICAÇÃO TÓPICA



## Cloreto de Benzalcônio (BAK)

- Prevenção da contaminação microbiana e da biodegração.
- Manutenção da atividade do medicamento.
- Quebras nas junções intercelular → Medicamento na CA
- Disrupção da camada lipídica do filme lacrimal → Evaporação do componente aquoso.
- Tóxico para o epitélio da córnea e da conjuntiva e estroma da córnea.
- Toxicidade: > 0,005% (Colírios: 0,015 a 0,02%)
- Aumento das citocinas pró-inflamatórias e dos seus recetores (CCR4 e CCR5), infiltração de linfócitos (TH1 E TH2), proliferação fibroblástica, perda das microvilosidades corneanas, diminuição das células de goblet, queratinização epitelial, metaplasia escamosa.



**Inflamação ocular e hiperosmolaridade da lágrima com instabilidade do filme lacrimal.**



**Conservantes**

Subs. ativa

Sol. Tampão

# GLAUCOMA – MEDICAÇÃO TÓPICA



## Outros conservante:

- **Complexo Estabilizado de Oxiclora (SOC):** Disrupção das membranas celulares. Criação de stress oxidativo → Ação fungicida e bactericida.
- **SofZia (*ionic buffer solution*):** atividade microbiana.
- **Poliquaternium-1 (PQ-1):** Solução de LC e lágrimas artificiais. Atividade tipo detergente semelhante ao BAK, mas menos tóxico.

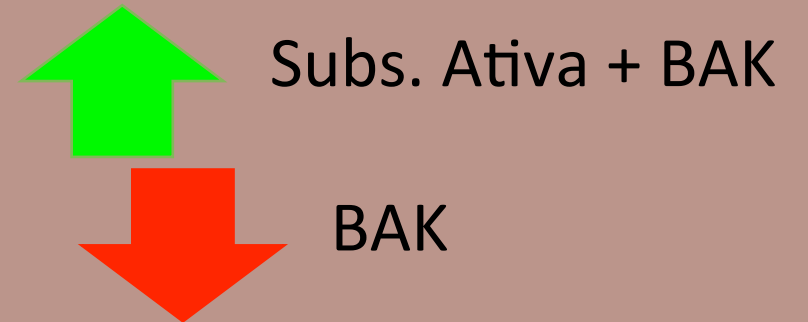
## Colírios sem conservantes:

- Mais caros.
- **Unidoses:** uso mais difícil.

# GLAUCOMA – MEDICAÇÃO TÓPICA



- A Subs. Ativa não é a causa principal de OSD e pode muitas vezes ser protetor do efeito do BAK.
- Carteolol, Timolol, Betaxolol e Latanoprost não ativam o sistema de complemento (SC).
- Timolol e Betaxolol têm um efeito anti-inflamatório (prevenção da ativação do SC).
- Os beta-bloqueantes não têm um efeito pró-apoptótico.

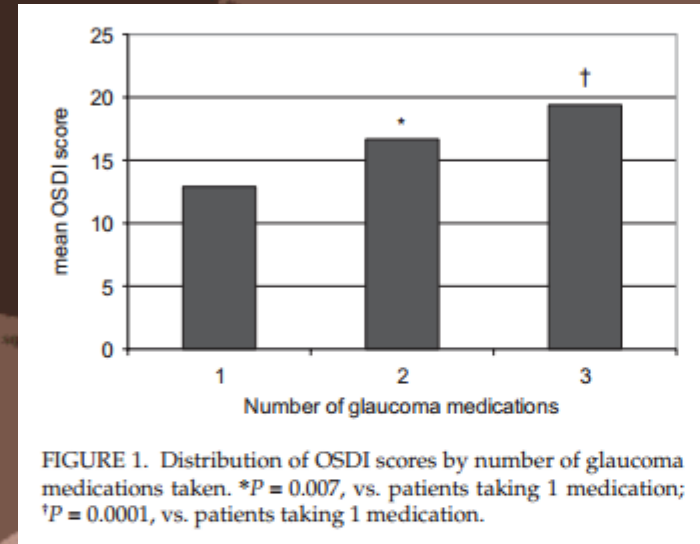


# CONSULTA DE GLAUCOMA

- OSD é mais frequente em doentes a realizarem medicação hipotónica tópica.
- Cuidado especial: doentes a realizarem vários colírios e mais idosos.

TABLE 3: Evaluation of the ocular surface.

|  |
|--|
| Subjective assessment  |
| Questionnaires:<br>OSDI: ocular surface disease index<br>GQL-15: glaucoma quality of life-15 |
| Clinical testing   |
| Visual acuity  |
| Assessment of morphology of the eyelid and meibomian gland                                   |
| Assessment of meibomian gland secretion  |
| Tear break-up time test (TBUT)   |
| Corneal and conjunctival staining (fluorescein/lissamine green/rose bengal)                  |
| Schirmer test  |
| Tear film osmolarity   |



- OSDI: OSD leve em 21%, moderada 13%, grave 14%
- Alteração do TBUT: 78%
- Impregnação conjuntival: 22%
- Teste de Schirmer alterado: 61%

## Ocular Surface Disease Index® (OSDI®)<sup>2</sup>

Ask your patients the following 12 questions, and circle the number in the box that best represents each answer. Then, fill in boxes A, B, C, D, and E according to the instructions beside each.

| Have you experienced any of the following during the last week? | All of the time | Most of the time | Half of the time | Some of the time | None of the time |
|---|-----------------|------------------|------------------|------------------|------------------|
| 1. Eyes that are sensitive to light? ..                         | 4               | 3                | 2                | 1                | 0                |
| 2. Eyes that feel gritty? .....                                 | 4               | 3                | 2                | 1                | 0                |
| 3. Painful or sore eyes? .....                                  | 4               | 3                | 2                | 1                | 0                |
| 4. Blurred vision? .....  | 4               | 3                | 2                | 1                | 0                |
| 5. Poor vision? .....   | 4               | 3                | 2                | 1                | 0                |

Subtotal score for answers 1 to 5 (A)

| Have problems with your eyes limited you in performing any of the following during the last week? | All of the time | Most of the time | Half of the time | Some of the time | None of the time | N/A |
|---|-----------------|------------------|------------------|------------------|------------------|-----|
| 6. Reading? .....   | 4               | 3                | 2                | 1                | 0                | N/A |
| 7. Driving at night? .....  | 4               | 3                | 2                | 1                | 0                | N/A |
| 8. Working with a computer or bank machine (ATM)? .....   | 4               | 3                | 2                | 1                | 0                | N/A |
| 9. Watching TV? .....   | 4               | 3                | 2                | 1                | 0                | N/A |

Subtotal score for answers 6 to 9 (B)

| Have your eyes felt uncomfortable in any of the following situations during the last week? | All of the time | Most of the time | Half of the time | Some of the time | None of the time | N/A |
|--|-----------------|------------------|------------------|------------------|------------------|-----|
| 10. Windy conditions? .....  | 4               | 3                | 2                | 1                | 0                | N/A |
| 11. Places or areas with low humidity (very dry)? .....                                    | 4               | 3                | 2                | 1                | 0                | N/A |
| 12. Areas that are air conditioned? ..   | 4               | 3                | 2                | 1                | 0                | N/A |

Subtotal score for answers 10 to 12 (C)

Add subtotals A, B, and C to obtain D (D = sum of scores for all questions answered) (D)

Total number of questions answered (do not include questions answered N/A) (E)

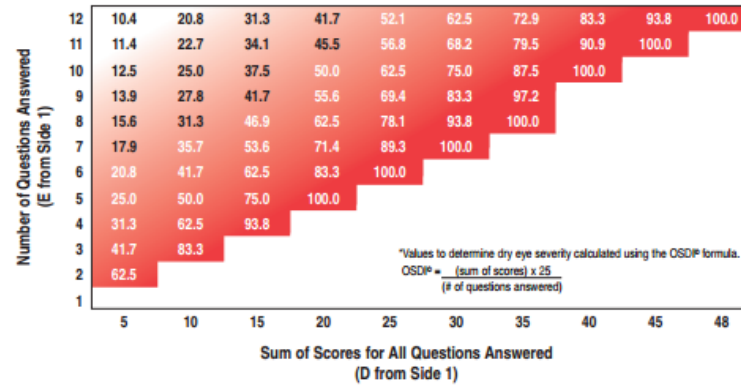
Please turn over the questionnaire to calculate the patient's final OSDI® score.

## Evaluating the OSDI® Score<sup>1</sup>

The OSDI® is assessed on a scale of 0 to 100, with higher scores representing greater disability. The index demonstrates sensitivity and specificity in distinguishing between normal subjects and patients with dry eye disease. The OSDI® is a valid and reliable instrument for measuring dry eye disease (normal, mild to moderate, and severe) and effect on vision-related function.

## Assessing Your Patient's Dry Eye Disease<sup>1, 2</sup>

Use your answers D and E from side 1 to compare the sum of scores for all questions answered (D) and the number of questions answered (E) with the chart below.\* Find where your patient's score would fall. Match the corresponding shade of red to the key below to determine whether your patient's score indicates normal, mild, moderate, or severe dry eye disease.



Normal Mild Moderate Severe

Patient's Name: \_\_\_\_\_ Date: \_\_\_\_\_

How long has the patient experienced dry eye disease? \_\_\_\_\_

Eye Care Professional's Comments: \_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

\_\_\_\_\_

1. Data on file, Allergan, Inc.  
 2. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol.* 2000;118:615-621

**Table 3: The glaucoma quality of life (GQL-15) questionnaire<sup>24</sup>**

| APPENDIX   |             |                     |             |                    |               |   |
|--|-------------|---------------------|-------------|--------------------|---------------|---|
| <i>The Glaucoma Quality of Life—15 questionnaire: List of daily activities with the strongest relationship with visual field loss in glaucoma</i>  |             |                     |             |                    |               |   |
| Patient instruction: Please, circle the correct answer on the scale ranging from 1 to 5 where [1] stands for no difficulty, [2] for a little bit of difficulty, [3] for some difficulty, [4] for quite a lot of difficulty, and [5] for severe difficulty. If you do not perform any of the activities for other than visual reasons, please circle [0]. |             |                     |             |                    |               |   |
| Does your vision give you any difficulty, even with glasses, with the following activities?  |             |                     |             |                    |               |   |
|  | <i>None</i> | <i>A little bit</i> | <i>Some</i> | <i>Quite a lot</i> | <i>Severe</i> | <i>Do not perform for nonvisual reasons</i> |
| Reading newspapers   | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Walking after dark   | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Seeing at night  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Walking on uneven ground   | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Adjusting to bright lights   | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Adjusting to dim lights  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Going from light to dark room or vice versa  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Tripping over objects  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Seeing objects coming from the side  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Crossing the road  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Walking on steps/stairs  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Bumping into objects   | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Judging distance of foot to step/curb  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Finding dropped objects  | 1           | 2                   | 3           | 4                  | 5             | 0   |
| Recognizing faces  | 1           | 2                   | 3           | 4                  | 5             | 0   |

# CONSULTA DE GLAUCOMA

## OSD moderada a grave:

- 38% - 1 colírio
- 54% - 2 colírios
- 71% - 3 ou mais colírios.

## Limitações dos estudos:

- Curta duração
- Diferenças na quantidade de colírios/gotas por dia
- Período de *washout*
- Exclusão de doentes com outras patologias concomitantes
- Exclusão de doentes com alergia/hipersensibilidade à medicação tópica

# CONSULTA DE GLAUCOMA

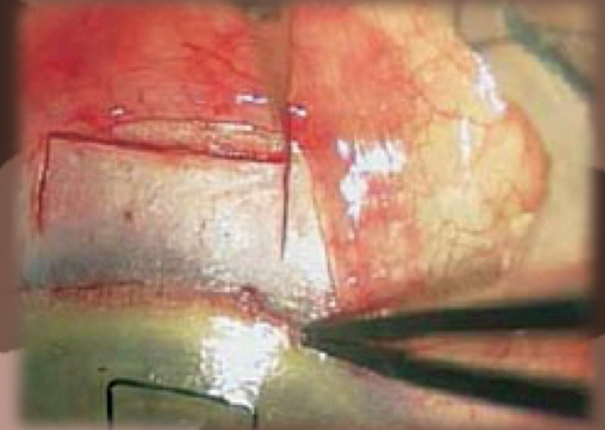
**Importância para a adesão à terapêutica.**

**OSD leve:**

- Manter Tx e vigiar
- Lubrificantes ocular

**OSD moderada a grave:**

- Alteração da medicação
- Tx laser
- Tx cirúrgico



Cirurgia mais exigente  
Mais complicações pós-operatórias

TABLE 1 Clinical studies.

| Ref. | First author | Glaucoma/OHT patients        | BAK-preserved drugs                   | Non-BAK-preserved drugs                                 | Key findings   |
|------|--------------|------------------------------|---------------------------------------|---|--|
| 3    | Leung        | 101                          | Any                                   | N/A   | A large proportion of glaucoma/OHT patients had OSD signs and/or symptoms.   |
| 7    | Tsai         | 108                          | Any                                   | N/A   | Higher prevalence of glaucoma in patients with severe OSD  |
| 8    | Fechtner     | 630                          | Any                                   | N/A   | Prevalence among glaucoma patients and severity increases with number of medications.                                    |
| 9    | Rossi        | 61                           | Any                                   | N/A   | Glaucoma patients present with dry eye more than controls. The presence of dry eye reduces QoL.                          |
| 10   | Erb          | 20,506                       | Any                                   | N/A   | Anti-glaucoma eye drops containing BAK compromises patient compliance.   |
| 11   | Schmier      | 629 glaucoma (7000 controls) | Any                                   | N/A   | Dry eye prevalence is more in glaucoma than controls. Use of glaucoma adjunctive therapies may increase rate of dry eye. |
| 20   | Henry        | 691                          | No                                    | Travoprost BAK free                                     | Patients previously treated with a BAK-preserved PTG who changed to travoprost BAK-free have improved OSD.               |
| 21   | Uusitalo     | 158                          | Latanoprost                           | Iafluprost  | Iafluprost was better tolerated in patients having fewer signs or symptoms, which resulted in improved QoL,              |
| 27   | Levrat       | 919                          | Yes, N/A                              | Yes, N/A  | Patient complaints and damage to the ocular surface are more frequent with preserved meds.                               |
| 28   | de Jong      | 21                           | Timolol                               | Timolol BAK free  | BAK-free timolol improves corneal epithelial barrier function and reduced complaints.                                    |
| 29   | Jaenan       | 9,658                        | Yes, N/A                              | Yes, N/A  | Preservative-free eye drops are significantly less associated with ocular symptoms and signs.                            |
| 52   | Horsley      | 20                           | Latanoprost                           | Travoprost BAK free                                     | BAK increases OSD by disrupting tear film and increasing conjunctival inflammation.                                      |
| 53   | Mundorf      | 20                           | Brimonidine                           | Brimonidine purite                                      | Brimonidine purite is more comfortable than brimonidine with BAK in patients with irritated eyes.                        |
| 54   | Shedden      | 261                          | Dorzolamide/timolol fixed combination | Dorzolamide/timolol fixed combination preservative free | Both drugs had equivalent efficacy for change in trough and peak intraocular pressure and similar tolerability.          |
| 55   | Godfrey      | 54                           | Latanoprost                           | Travoprost BAK free                                     | Following a single drop, latanoprost and travoprost BAK-free exhibit similar comfort.                                    |

OHT = ocular hypertension; BAK = benzalkonium chloride; OSD = ocular surface disease; QoL = quality of life; PTG = prostaglandin; TBUT = tear break up time; OSDI = ocular surface disease index.

# CONCLUSÃO

- O OSD é mais frequente em doentes com Glaucoma.
- Tem grande impacto na adesão à terapêutica.
- Relação estreita entre OSD e a quantidade de medicação tópica.
- Implicações na terapêutica cirúrgica.
- Menor com medicação tópica sem conservantes.

# MEDICAÇÃO TÓPICA SEM CONSERVANTES NO GLAUCOMA

## 1º Parte - DOENÇA DA SUPERFÍCIE OCULAR NO GLAUCOMA