**Efficacy and tolerability of anti-inflammatory drugs in the treatment of dry eye syndrome**

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ABSTRACT

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| **Aims:** The aim of our study is to evaluate the efficacy and tolerability of anti-inflammatory drugs in the treatment of dry eye syndrome.  **Study design:** This is a retrospective and comparative study  **Place and Duration of Study:** ophthalmology department of Kasserine between January 2024 and December 2024  **Methodology:** We included 100 patients with DES The patients were randomly assigned into two groups via computer-generated randomization to:  -Group 1 (G1, n=50): Carbomer gel (0.2%) + Dexamethasone 0.1% eye drops  -Group 2 (G2, n=50): Carbomer gel alone with a variable number of instillations depending on the severity of corneal damage. The mean age of our patients was 56 +/-9 years for group 1 and 60 +/- 7 years for group 2, with a higher proportion of women in both groups (47 for group 1 and 48 for group 2).The two groups were statically comparable in terms of age and sex Response to treatment was assessed by ocular surface examination and fluorescein testing, measurement of tear film break-up time and the Schirmer test, and a quality-of-life questionnaire (QSD-QOL) and compared in patient treated with carbomer gel and a steroidal anti-inflammatory eye drop (group1), and patients treated with carbomer gel alone (group2).  **Results:**  Reflex lacrimation, pruritus and sand-grain sensation symptoms improved significantly more in group 1 than in group 2, with a statistically significant difference. Evaluation of the therapeutic response according to the QOL questionnaire was also statistically better for group 1, with 66% of patients rating their improvement as satisfactory to very satisfactory, compared with 44% of patients in group 2.  **Conclusion:**  The combination of anti-inflammatory drugs and carbomer gels is an interesting way of managing dry eye, given the significant role played by the inflammatory component in the alteration of the tear film. |

*Keywords: [*dry eye syndrome, anti-Inflammatory drugs, tolerability, safety, efficacy*}*

1. INTRODUCTION

DES is one of the most frequent reasons for consulting an ophthalmologist, and its frequency increases in the elderly, in women after menopause, and in cases of autoimmune disease. DES can affect visual function and general quality of life (Britten-Jones et al., 2024; Nguyen et al., 2023). Its pathogenesis is multifactorial, involving both pathologies implicated in lacrimal hyposecretion and other conditions linked to hyper-evaporation of the tear film (McCabe & Narayanan, 2009; Rouen & White, 2018). Ocular surface inflammation is considered an important pathologic factor of dry eye (Rolando & Vagge, 2017), which is why the current therapeutic strategy aims to treat the underlying causes of lacrimal dryness and break the vicious circle of inflammation maintained by dryness, by acting on immunological, inflammatory, and hormonal mediators (Byun et al., 2012). In this prospective study, we are investigating the efficacy and tolerability of combining steroidal anti-inflammatory drugs (dexamethasone) with carbomer gels in the treatment of DES.

2. material and methods)

**Study design and settings**

A total of 100 patients with DES were included in our retrospective analysis study, which was carried out in the Kasserine ophthalmology department between January 2024 and December 2024.

**Inclusion and exclusion criteria**

Inclusion Criteria: Patients between 40 and 70 years of age whatever the etiology, with minimal to moderate dry eye, clinically diagnosed dry eye syndrome (DES) for ≥6 months, symptoms (foreign body sensation, burning, photophobia) with schirmer’s test ≤10 mm/5 min and/or tear film breakup time (TBUT) ≤10 sec, corneal fluorescein staining score ≤2 (Oxford or NEI grading scale).

Exclusion Criteria: severe DES (corneal ulcers, filamentary keratitis), active ocular infection, glaucoma (IOP >21 mmHg), or recent ocular surgery (<6 months), uncontrolled systemic diseases (, diabetes, Sjögren’s syndrome) or use of topical/systemic steroids/immunosuppressants.

**Collection of data**

The patients were randomly assigned into two groups via computer-generated randomization to:

-Group 1 (G1, n=50): Carbomer gel (0.2%) + Dexamethasone 0.1% eye drops at a rate of 4 drops per day for the first week, followed by a gradual reduction of one drop per week over 4 weeks.

-Group 2 (G2, n=50): Carbomer gel alone with a variable number of instillations depending on the severity of corneal damage (frequency adjusted per severity: mild=2x/day, moderate=4x/day).

 All patients underwent an interview to collect subjective symptoms suggestive of ocular surface abnormalities: foreign body sensation, ocular burning, photophobia, itching, and a complete ophthalmological examination performed by the same doctor, including measurement of best corrected distance and near visual acuity according to the Snellen scale, biomicroscopic examination of the anterior segment, including in particular inspection of the lacrimal meniscus, lacrimal film impregnation revealing areas of epithelial alteration within the ocular surface, such as punctate keratitis: inspection of the lacrimal meniscus, impregnation of the lacrimal film to reveal areas of epithelial alteration on the ocular surface, such as superficial punctate keratitis or corneal ulcers, evaluation of the tear film break-up time (BUT) averaged over 3 successive measurements, and a study of tear secretion using a Schirmer test performed at 5 minutes and without local anesthetic. Measurement of ocular tone by applanation and therapeutic response using quality of life assessment (QSD-QOL).

**Statistical analysis**

 Statistical analysis was performed using EPI INFO software version 6.0. The relationship between two quantitative variables was studied using the student’s t test, and the comparison between percentages was made using the Fisher's test. The significance level was set at p< 0.05.

3. results and discussion

The mean age of our patients was 56 +/-9 years for group 1 and 60 +/- 7 years for group 2, with a higher proportion of women in both groups (47 for group 1 and 48 for group 2). The two groups were statically comparable in terms of age and sex. The main etiology was Gougerot-Sjogren's syndrome (54%). This syndrome was primary in 36% of cases and secondary in 18%. Xerophthalmia due to excessive evaporation was related to meibomian dysfunction (blepharitis) in 10% of cases, and secondary to disteroidal exophthalmia in 6%. Dry eyes due to hyposecretion, unrelated to Gougerot-Sjogren's syndrome, were noted in 30% of cases. The main etiologies found were allergic conjunctivitis, degenerative keratoconjunctivitis in elderly subjects, systemic medications (mainly beta-blockers) and hepatitis C. The two groups were statistically comparable in terms of the etiology of dry eyes (*P*=0.68) (Table 1).

**Table1. Main causes of dry eyes**

|  |  |  |  |
| --- | --- | --- | --- |
| Etiology | Group 1 | Group 2 | *P* |
| ****Primary Gougerot Sjögren**** syndrome.  Secondary Gougerot Sjögren syndrome:  Rheumatoid arthritis  Systemic lupus erythematosus | 18(36%)  5(10%)  3(6%) | 19(38%)  6(12%)  4(8%) | **0,68** |
| Excess evaporation:  Meibomian gland deficiency  Exophthalmos | 6(12%)  4(8%) | 4(8%)  2(4%) |
| Aqueous deficiency no Sjogren  Degenerative  keratoconjunctivitis  Allergic conjunctivitis  Systemic medication Hepatitis C | 4(8%)  5(10%)  3(6%)  2(4%) | 3(6%)  7(14%)  2(4%)  3(6%) |

The main functional signs observed were reflex lacrimation, pruritus, sand-grain sensation, and visual fatigue. The two groups were statistically comparable for functional signs (Table 2).

**Table2. Functional signs of dry eye causing significant discomfort on initial examination**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 1 | Group 2 | *P* |
| Reflex tearing 16(32%) 19(38%) 0,040  Pruritus 28(56%) 30(60%) 0,68  Grainy feeling 10(20%) 16(32%) 0,17  Eye strain 22(44%) 25(50%) 0,54  Photophobia 26(52%) 32(64%) 0,22 | | | |

In our study, we found that some symptoms improved significantly more in group 1 than in the group 2 with a significant difference (Table 3, Tabe 4, Table 5).

**Table3. Clinical signs of dry eye causing significant discomfort on initial examination**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 1 | Group 2 | *P* |
| Schirmer test (mm/5min) 5 6 0,62  BUT average(S) 4 5 0,58  Fluorescein test (+) 40 38 0,4  No hyperemia 15 13 0,6 | | | |

**Table4. Clinical signs of dry eye inducing significant discomfort at last check-up**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 1 | Group 2 | *P* |
| Reflex tearing 4(8%) 13(26%) 0,017  Pruritus 6(12%) 15(30%) 0,016  Grainy feeling 5(10%) 16(32%) 0,007  Eye strain 20(40%) 22(44%) 0,685  Photophobia 20(40%) 25(50%) 0,229 | | | |

**Table5. Clinical signs of dry eye inducing significant discomfort at last check-up**

|  |  |  |  |
| --- | --- | --- | --- |
|  | Group 1 | Group 2 | *P* |
| Reflex tearing 4(8%) 13(26%) 0,017  Pruritus 6(12%) 15(30%) 0,016  Grainy feeling 5(10%) 16(32%) 0,007  Eye strain 20(40%) 22(44%) 0,685  Photophobia 20(40%) 25(50%) 0,229 | | | |

These were reflex lacrimation, pruritus, and sand-grain sensation (*P*<0.05). Visual fatigue and photophobia improved slightly more in group 1 than in group 2, with no statistically significant difference (*P*>0.05). On clinical examination, we found that conjunctival hyperemia was reduced at the end of follow-up in 94% of patients in group 1 versus 68% in group 2. This difference was statistically significant (*P*=0.001). We also noted a lengthening of the BUT by 1s in group 1 versus 0.5s in group 2, but with no statistically significant difference (*P*=0.15). An improvement in the Schirmer test in group 1 patients. In fact, we noted an average increase of 1 mm in group 1, whereas it was reduced by 1 mm in group 2. However, the difference was not statistically significant (*P*=0.18). A greater improvement in the fluorescein test with disappearance of the KPS was observed at the end of the control in group 1 (80%) than in group 2 (20%); the difference was statistically significant (*P*=0.01) (Table 6).

**Table6. Therapeutic response using quality of life (QOL) assessment.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Daily activities | | Group 1 | | Group 2 | *P* |
| No impact 9(18%) 2(4%) 0,025  Few impact 19(38%) 20(40%) 0,42  Moderate impact 16(32%) 21(42%) 0,032  Severe impact 6(12%) 7(14%) 0,76 | | | | | |
| Work-related disability and discomfort | |  | |  |  |
| No impact 7(14%) 1(2%) 0,027  Few impact 26(52%) 24(48%) 0,54  Moderate impact 15(30%) 20(40%) 0,29  Severe impact 2(4%) 5(10%) 0,24 | | | | | |
| Renouncing make-up | |  | |  |  |
| No impact 5(10%) 4(8%) 0,72  Few impact 30(60%) 19(38%) 0,04  Moderate impact 14(28%) 20(40%) 0,2  Severe impact 1(2%) 7(14%) 0,065 | | | | | |
| Disease recognition | |  | |  |  |
| No impact 12(24%) 4(8%) 0,029  Few impact 21(42%) 24(48%) 0,54  Moderate Impact 14(28%) 20(40%) 0,2  Severe impact 3(6%) 2(4%) 0,64 | | | | | |
| Fear of the Future |  | |  | |  |
| No impact 13(26%) 5(10%) 0,0137  Few impact 27(54%) 29(58%) 0,68  Moderate impact 6(12%) 10(20% 0,27  Severe impact 4(8%) 6(12%) 0,5 | | | | | |
| Emotional well-being | |  | |  |  |
| No impact 10(20%) 2(4%) 0,014  Few impact 19(38%) 21(42%) 0,016  Moderate impact 15(44%) 20(40%) 0,29  Severe impact 6(12%) 7(14%) 0,76 | | | | | |

Ocular surface inflammation is considered as an important pathologic factor of dry eye (dong et al., 2022). Des results from inadequate tear production or excessive evaporation (mccabe & narayanan, 2009). This evaporation increases tear hyperosmolarity, leading to discomfort and inflammation of the ocular surface (messmer et al., 2023). Hyperosmolarity triggers inflammation in human limbal epithelial cells by promoting the expression and production of pro-inflammatory cytokines and chemokines, including il-1β, tnf-α and chemokine c-x-c il-8 (li et al., 2006). The pro-inflammatory cytokines il-1 and ifn-γ inducing squamous metaplasia of ocular surface epithelial cells are increased, while decrease in the biologically inactive precursor il-1β has been found in the tear film of dry eye patients (hessen & akpek, 2014; roda et al., 2020).

Some studies suggest that chronic stimulation of the ocular surface by environmental factors such as contact lenses, low humidity, and wind disrupt neuronal transmission to the lacrimal glands. This leads to the activation of lymphocyte trafficking, the production of pro-inflammatory cytokines, and the initiation of an autoimmune response (lee et al., 2006). Several reports have highlighted the effectiveness of topical corticosteroid treatment in patients with des (nguyen et al., 2023; liu et al., 2022; gupta et al., 2024). Treating the underlying cause of disease like inflammation can be an alternative therapy to lacrimal supplementation for the signs and symptoms of des (dong et al., 2022). The positive effects of topical steroid drops in patients with dry eye may be partly due to a decrease in the number of hla-dr+ conjunctival cells (lekhanont et al., 2007). Some authors recommend using this treatment as "pulse therapy" due to the notable side effects associated with long-term use (nguyen et al., 2023). A recent study highlighted the benefits of combining topical steroids and topical cyclosporine for treating immune-based inflammation in patients with severe dry eye (byun et al., 2012).

The present study illustrated a statistically significant improvement in favor of taking steroidal anti-inflammatory drugs in combination with carbomer gels, with the variables all pointing in the same direction, showing improvement in symptoms compared with carbomer gels alone. This study revealed that the efficacy assessed by qsd-qol was statistically better for group 1. In fact, in the 7 dimensions of the qsd-qol, the number of patients who rated their improvement as satisfactory to very satisfactory (no impact and little impact) was greater in group 1 than in group 2, with a statistically significant difference (p < 0.05).

4. Conclusion

This study demonstrates that combining steroidal anti-inflammatory drugs (dexamethasone 0.1%) with carbomer gel significantly improves both subjective symptoms (e.g., reflex lacrimation, pruritus, and sand-grain sensation) and objective signs (e.g., conjunctival hyperemia, fluorescein staining) of dry eye syndrome (DES) compared to carbomer gel alone. The anti-inflammatory regimen also yielded superior patient-reported outcomes, with 66% of participants rating their improvement as satisfactory to very satisfactory on the QSD-QOL questionnaire, underscoring its clinical relevance.

These findings reinforce the pivotal role of inflammation in DES pathogenesis and support the integration of short-term, supervised anti-inflammatory therapy into management protocols, particularly for patients with moderate DES and underlying inflammatory etiologies (e.g., Sjögren’s syndrome). However, limitations such as the single-center design and short follow-up period warrant further multicenter studies to evaluate long-term efficacy and safety. Future research should explore optimal dosing strategies and biomarkers to personalize anti-inflammatory treatment in DES.

Consent (where ever applicable)

The patients have given their written informed consent on admission to use their data base and files for research work.

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Ethical approval (where ever applicable)

Ethical approval: all procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 helsinki declaration and its later amendments or comparable ethical standards.

This retrospective analysis did not require ethical approval as it involved only anonymized data from routine clinical practice, with no intervention or identifiable information disclosed

-Patients’ privacy was fully respected.

-There are no identifying details in our study

COMPETING INTERESTS DISCLAIMER:

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

References

Britten-jones, a. C., wang, m. T. M., samuels, i., jennings, c., stapleton, f., craig, j. P., et al. (2024). Epidemiology and risk factors of dry eye disease: considerations for clinical management. *Medicina (kaunas)*, \*60\*(9), 1458. [Https://doi.org/xx.xxxx/medicina60091458](https://doi.org/xx.xxxx/medicina60091458)

Nguyen, a., kolluru, a., & beglarian, t. (2023). Dry eye disease: a review of anti-inflammatory therapies. *Taiwan journal of ophthalmology*, \*13\*(1), 3-12. [Https://doi.org/xx.xxxx/tjo.1301003](https://doi.org/xx.xxxx/tjo.1301003)

Mccabe, e., & narayanan, s. (2009). Advancements in anti-inflammatory therapy for dry eye syndrome. *Optometry*, \*80\*(10), 555-566. [Https://doi.org/xx.xxxx/opt.2009.80.555](https://doi.org/xx.xxxx/opt.2009.80.555)

Rouen, p. A., & white, m. L. (2018). Dry eye disease: prevalence, assessment, and management. *Home healthcare now*, \*36\*(2), 74-83. [Https://doi.org/xx.xxxx/hhn.0000000000000018](https://doi.org/xx.xxxx/HHN.0000000000000018)

Rolando, m., & vagge, a. (2017). Safety and efficacy of cortisol phosphate in hyaluronic acid vehicle in the treatment of dry eye in sjogren syndrome. *Journal of ocular pharmacology and therapeutics*, \*33\*(5), 383-390. [Https://doi.org/xx.xxxx/jop.2017.0330383](https://doi.org/xx.xxxx/jop.2017.0330383)

Byun, y. J., kim, t. I., kwon, s. M., seo, k. Y., kim, s. W., kim, e. K., et al. (2012). Efficacy of combined 0.05% cyclosporine and 1% methylprednisolone treatment for chronic dry eye. *Cornea*, \*31\*(5), 509-513. [Https://doi.org/xx.xxxx/ico.0b013e31823f8c1d](https://doi.org/xx.xxxx/ICO.0b013e31823f8c1d)

Dong, y., wang, s., cong, l., zhang, t., cheng, j., yang, n., et al. (2022). Tnf-α inhibitor tanfanercept (hbm9036) improves signs and symptoms of dry eye in a phase 2 trial in the controlled adverse environment in china. *International ophthalmology*, \*42\*(8), 2459-2472. [Https://doi.org/xx.xxxx/s10792-022-02320-7](https://doi.org/xx.xxxx/s10792-022-02320-7)

Messmer, e. M., ahmad, s., benitez del castillo, j. M., mrukwa-kominek, e., rolando, m., vitovska, o., et al. (2023). Management of inflammation in dry eye disease: recommendations from a european panel of experts. *European journal of ophthalmology*, \*33\*(3), 1294-1307. [Https://doi.org/xx.xxxx/11206721231156730](https://doi.org/xx.xxxx/11206721231156730)

Li, d. Q., luo, l., chen, z., kim, h. S., song, x. J., & pflugfelder, s. C. (2006). Jnk and erk map kinases mediate induction of il-1β, tnf-α and il-8 following hyperosmolar stress in human limbal epithelial cells. *Experimental eye research*, \*82\*(4), 588-596. [Https://doi.org/xx.xxxx/j.exer.2005.08.019](https://doi.org/xx.xxxx/j.exer.2005.08.019)

Hessen, m., & akpek, e. K. (2014). Dry eye: an inflammatory ocular disease. *Journal of ophthalmic vision research*, \*9\*(2), 240-250. [Https://doi.org/xx.xxxx/jovr.2014.9.2.240](https://doi.org/xx.xxxx/jovr.2014.9.2.240)

Lee, h. K., ryu, i. H., seo, k. Y., hong, s., kim, h. C., & kim, e. K. (2006). Topical 0.1% prednisolone lowers nerve growth factor expression in keratoconjunctivitis sicca patients. *Ophthalmology*, \*113\*(2), 198-205. [Https://doi.org/xx.xxxx/j.ophtha.2005.09.027](https://doi.org/xx.xxxx/j.ophtha.2005.09.027)

Liu, s. H., saldanha, i. J., abraham, a. G., rittiphairoj, t., hauswirth, s., gregory, d., et al. (2022). Topical corticosteroids for dry eye. *Cochrane database of systematic reviews*, \*10\*(10), cd015070. [Https://doi.org/xx.xxxx/14651858.cd015070.pub2](https://doi.org/xx.xxxx/14651858.CD015070.pub2)

Gupta, p. K., toyos, r., sheppard, j. D., toyos, m., mah, f. S., bird, b., et al. (2024). Tolerability of current treatments for dry eye disease: a review of approved and investigational therapies. *Clinical ophthalmology*, \*18\*, 2283-2302. [Https://doi.org/xx.xxxx/opth.s429876](https://doi.org/xx.xxxx/OPTH.S429876)

Lekhanont, k., leyngold, i. M., suwan-apichon, o., rangsin, r., & chuck, r. S. (2007). Comparison of topical dry eye medications for the treatment of keratoconjunctivitis sicca in a botulinum toxin b-induced mouse model. *Cornea*, \*26\*(1), 84-89. [Https://doi.org/xx.xxxx/01.ico.0000248384.32199.16](https://doi.org/xx.xxxx/01.ico.0000248384.32199.16)

Roda, m., corazza, i., bacchi reggiani, m. L., pellegrini, m., taroni, l., giannaccare, g., et al. (2020). Dry eye disease and tear cytokine levels-a meta-analysis. *International journal of molecular sciences*, \*21\*(9), 3111. [Https://doi.org/xx.xxxx/ijms21093111](https://doi.org/xx.xxxx/ijms21093111)