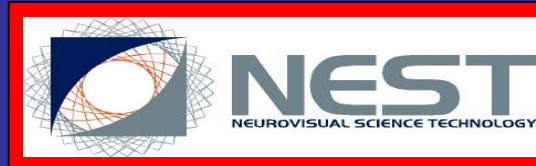




Regione Siciliana
Azienda Ospedali Vittorio Emanuele,
Ferraro e S. Bambino
Catania



UNIVERSITA' DEGLI STUDI
DI CATANIA

Azienda Policlinico - Vittorio Emanuele Catania

Clinica Oculistica II

Direttore: Prof. T. Avitabile

**UTILIZZO DEI LIPOSOMI IN FORMULAZIONE SPRAY
NELLE RINO-CONGIUNTIVITI DI ORIGINI ALLERGICHE**

G. Scollo – C. Gagliano - D. Rocca - R. Amato – T. Avitabile

XXXVI Congresso S.O.Si Santa Tecla, 14-16 Aprile 2011

Congiuntivite allergica

- 25 % popolazione USA
- 35 % causa di occhio rosso
- 90 % con rinite allergica

[Allergy Asthma Proc.](#) 2008 Nov-Dec;29(6):565-74.

Allergic rhinoconjunctivitis and differential diagnosis of the red eye.

[Granet D.](#)

University of California-San Diego/Ratner Children's Eye Center, La Jolla, CA 92037, USA. dgranet@ucsd.edu

- Manifestazione piu' comune dell'allergia in eta' pediatrica

[J Fr Ophtalmol.](#) 2007 Mar;30(3):292-9.

[Childhood allergic conjunctivitis: the allergist's point of view].

[Article in French]

[Fauquet JL.](#)

Consultation d'Ophtalmologie et Allergologie de l'enfant, Unité d'Allergologie de l'enfant, Service Pédiatrie A, Hôtel Dieu CHU, 63058 Clermont-Ferrand CEDEX 1

- Associata anche a blefarite

[Br J Ophthalmol.](#) 2005 Apr;89(4):400-3.

Blepharokeratoconjunctivitis in children: diagnosis and treatment.

[Viswalingam M](#), [Rauz S](#), [Morlet N](#), [Dart JK](#).

Corneal and External Diseases Service, Moorfields Eye Hospital NHS Trust, 162 City Road, London EC1V 2PD, UK.

Allergia e dry eye

- Flogosi cronica della superficie oculare
- Sintomi clinici spesso associati/sovrapponibili a dry eye

Przeegl Lek. 2009;66(11):967-71.

[Dry eye syndrome and allergic conjunctivitis--epidemics of XXI century--diagnostic problems and management].

[Article in Polish]

Kubicka-Trzaska A, Romanowska-Dixon B.

Katedra Okulistyki, Klinika Okulistyki i Onkologii Okulistycznej, Uniwersytet Jagielloński Collegium Medicum, Kraków. akubicka@onet.pl

- Diagnosi differenziale piu' difficile nell'adulto

Eur Ann Allergy Clin Immunol. 2004 Jan;36(1):25-9.

[Allergic conjunctivitis: diagnosis and treatment].

[Article in French]

Marmouz F, Raffard M.

Allergologue, 1, rue Thiers, 95300 Pontoise.

Br J Ophthalmol. 1996 Nov;80(11):994-7.

Allergic conjunctivitis and dry eye.

Fujishima H, Toda I, Shimazaki J, Tsubota K.

Department of Ophthalmology, Tokyo Dental College, Chiba, Japan.

- dry eye conseguenza di terapia corticosteroidea e antistaminica a lungo termine

Allergy Asthma Proc. 2008 Nov-Dec;29(6):565-74.

Allergic rhinoconjunctivitis and differential diagnosis of the red eye.

Granet D.

University of California-San Diego/Ratner Children's Eye Center, La Jolla, CA 92037, USA. dgranet@ucsd.edu

Allergia e dry eye

- riduzione goblet cell e della secrezione mucosa nelle lacrime e sulla superficie oculare
- aumento citochine infiammatorie

[J Immunol](#). 2011 Apr 1;186(7):4455-66. Epub 2011 Feb 28.

Conjunctival goblet cell secretion stimulated by leukotrienes is reduced by resolvins d1 and e1 to promote resolution of inflammation.

[Dartt DA](#), [Hodges RR](#), [Li D](#), [Shatos MA](#), [Lashkari K](#), [Serhan CN](#).

Schepens Eye Research Institute, Harvard Medical School, Boston, MA 02114;

[Ocul Surf](#). 2005 Oct;3(4 Suppl):S161-4.

Evaluation of ocular surface inflammation in the presence of dry eye and allergic conjunctival disease.

[Stern ME](#), [Siemasko KF](#), [Gao J](#), [Calonge M](#), [Niederhorn JY](#), [Pflugfelder SC](#).

Allergan, Inc., Irvine, CA 92612, USA. stern_michael@allergan.com

- aumento dell'osmolarita' associato a discomfort oculare

[J Allergy Clin Immunol](#). 2006 Oct;118(4):872-7. Epub 2006 Aug 7.

Hyperosmolar conjunctival provocation for the evaluation of nonspecific hyperreactivity in healthy patients and patients with allergy.

[Sacchetti M](#), [Lambiase A](#), [Aronni S](#), [Griqqi T](#), [Ribatti V](#), [Bonini S](#), [Bonini S](#).

Department of Ophthalmology, University of Rome, Campus Bio-Medico, Italy.

- nelle congiuntiviti allergiche dry eye con deficit lipidico (78% casi)

[Ophthalmologe](#). 1995 Feb;92(1):6-11.

[Diagnosis and and differentiation of dry eye disorders].

[Article in German]

[Heiligenhaus A](#), [Koch JM](#), [Kruse FE](#), [Schwarz C](#), [Waubke TN](#).

Universitäts-Augenklinik Essen.

[Cornea](#). 2006 Apr;25(3):277-80.

Tear film lipid layer alterations in allergic conjunctivitis.

[Suzuki S](#), [Goto E](#), [Dogru M](#), [Asano-Kato N](#), [Matsumoto Y](#), [Hara Y](#), [Fujishima H](#), [Tsubota K](#).

Department of Ophthalmology, Tokyo Dental College, Ichikawa General Hospital, Ichikawa, Japan. YR

Table 3 A classification of probability of dry eye based on fluorescein break-up time (FBUT), Schirmer's test with anesthesia (STA), and lipid layer thickness (LLT) measurements

Category	FBUT (s)	STA (min)	LLT (mm)
I	0-5	0-5	≤60
II	6-<10	6-<10	≥75-105
III	≥10	≥10	≥120

Category I=a high probability of having (significant) dry eye signs and symptoms.

Category II=an intermediate probability of having dry eye signs and symptoms.

Category III=a low or zero probability of having dry eye signs and symptoms.

Allergia e dry eye

- Collaborazione oculista-allergologo. Test allergometrici (dosaggio IgE specifiche e totali, etc.)

[Przeql Lek.](#) 2009;66(11):967-71.

[Dry eye syndrome and allergic conjunctivitis--epidemics of XXI century--diagnostic problems and management].

[Article in Polish]

[Kubicka-Trzaska A](#), [Romanowska-Dixon B](#).

Katedra Okulistyki, Klinika Okulistyki i Onkologii Okulistycznej, Uniwersytet Jagielloński Collegium Medicum, Kraków. akubicka@onet.pl

[Kathmandu Univ Med J \(KUMJ\)](#). 2009 Apr-Jun;7(26):104-8.

Tearfilm immunoglobulin E (IgE) level in vernal keratoconjunctivitis by ELISA.

[Pokharel S](#), [Shah DN](#), [Joshi SN](#), [Choudhary M](#).

Ophthalmology Department, Kathmandu Medical College, Sinamangal, Nepal. supranp@yahoo.com

[Eye \(Lond\)](#). 1998;12 (Pt 2):296-8.

Tear IgE concentrations in allergic conjunctivitis.

[Nomura K](#), [Takamura E](#).

Department of Ophthalmology, Tokyo Women's Medical College, Japan.

- Entrambe migliorano con l'uso di sostituti lacrimali a base lipidica

[Curr Opin Allergy Clin Immunol](#). 2004 Oct;4(5):421-4.

Ocular allergy and dry eye syndrome.

[Bielory L](#).

University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, New Jersey 07081, USA. bielory@mac.com

Come ripristinare la fase lipidica ?

SOLUZIONE: I LIPOSOMI

- Vescicole fosfolipidiche formate da una doppia struttura lamellare che include un compartimento acquoso e galleggiano nell'acqua

Costituiti da:

- Lecitina di soia altamente purificata
- Fosfatidilcolina (94%),
- Lipofosfatidilcolina-fosfatidiletanolamina-fosfatidilinositolo (6%)
- Diametro < 100nm



[Klin Monbl Augenheilkd. 2004 Oct;221\(10\):825-36.](#)

[A new therapy concept for the treatment of dry eye--the usefulness of phospholipid liposomes].

[Article in German]

[Lee S, Dausch S, Maierhofer G, Dausch D.](#)

Praxis Prof. Dr. Dieter Dausch, Amberg, Germany. info@asa80.com





- Si aggiungono ai lipidi della superficie oculare attraverso la rima palpebrale
- Stabilizzano e ricostituiscono l'integrità del film lacrimale apportando fosfolipidi e acqua
- La fosfatidilcolina (94%) agisce con effetto scavenger sull'infiammazione del bordo palpebrale
- Veicolano le Vitamine A ed E (liposolubili)

[Curr Eye Res.](#) 2002 Jul;25(1):55-60.

The role of different phospholipids on tear break-up time using a model eye.

[Peters K, Millar T.](#)

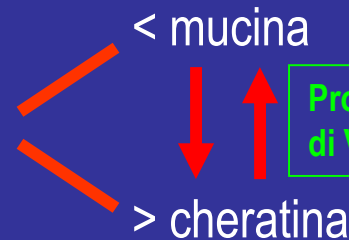
University of Western Sydney, and the Co-Operative Research Centre for Eye Research and Technology, Sydney, Australia.

NUOVA VIA DI SOMINISTRAZIONE (SPRAY) NUOVA FORMULAZIONE (LIPOSOMI)

Vitamine A ed E (liposolubili) veicolate dai liposomi

Vit. A = antinfettiva e antiallergica, utile nelle carenze localizzate:

- Infiammazioni
- infezioni,
- perdita di cellule caliciformi



Invest Ophthalmol Vis Sci. 2005 Nov;46(11):4050-61.

Effect of retinoic acid on gene expression in human conjunctival epithelium: secretory phospholipase A2 mediates retinoic acid induction of MUC16.

Hori Y, Spurr-Michaud SJ, Russo CL, Arqueso P, Gipson IK.

Schepens Eye Research Institute and the Department of Ophthalmology, Harvard Medical School, Boston, MA 02114, USA.

Vit. E = antiossidante in fase lipidica

- Migliora l'utilizzo della Vit. A
- Epitelioprotettrice (interferisce con la lipoperossidazione delle membrane cellulari)

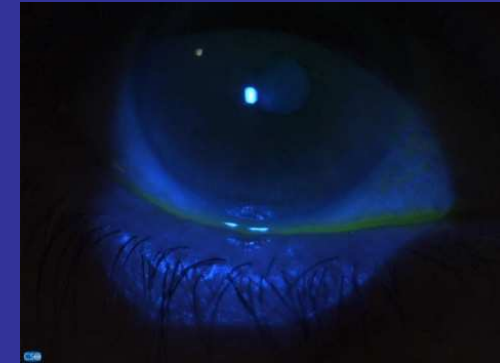
J Refract Surg. 2005 Nov-Dec;21(6):761-3.

Effect of topical vitamin E on ethanol-induced corneal epithelial apoptosis.

Bilgihan K, Konuk O, Hondur A, Akvürek N, Ozoqul C, Hasanreisoglu B.

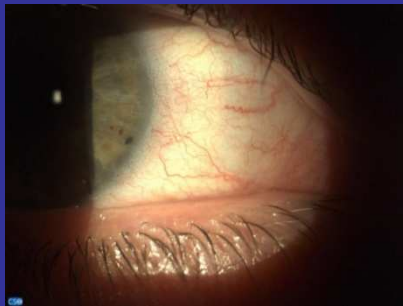
Department of Ophthalmology, Gazi University Medical School, Ankara, Turkey. bilgihan@gazi.edu.tr

NUOVA VIA DI SOMMINISTRAZIONE (SPRAY) NUOVA FORMULAZIONE (LIPOSOMI)



**RAGGIUNGE LA
SUPERFICIE OCULARE ?
AGISCE
EFFICACEMENTE ?**

- ➔ Facilità di somministrazione
- ➔ Ottima tollerabilità
- ➔ Riduce la temperatura delle palpebre



LIPOSOMAL SPRAY VS TEAR SUBSTITUTES

- CLINICAMENTE PIU' EFFICACE, MAGGIORI VANTAGGI E COMPLIANCE RISPETTO A TUTTI I TRATTAMENTI CONVENZIONALI.

[Klin Monbl Augenheilkd.](#) 2006 Dec;223(12):974-83.

[Comparative study of treatment of the dry eye syndrome due to disturbances of the tear film lipid layer with lipid-containing tear substitutes].

[Article in German]

[Dausch D.](#), [Lee S.](#), [Dausch S.](#), [Kim J.C.](#), [Schwert G.](#), [Michelson W.](#)

Abteilung Augenheilkunde, Klinikum St. Marien, Amberg. burgl.dausch@web.de

- MIGLIORI EFFETTI BENEFICI SOPRATTUTTO IN CASO DI BLEFARITI. IL BUT TEST E' RADDOPPIATO SE CONFRONTATO CON L'ACIDO IALURONICO. OTTIMO APPROCCIO L'UTILIZZO COMBINATO DI LIPOSOMI NEBULIZZATI E LACRIME ARTIFICIALI IN DRY EYE SEVERI.

[Klin Monbl Augenheilkd.](#) 2010 Feb;227(2):128-34. Epub 2009 Sep 15.

[Comparative investigation of treatments for evaporative dry eye].

[Article in German]

[Khairuddin R.](#), [Schmidt K.G.](#)

Klinik und Poliklinik für Augenheilkunde, Universitätsklinik Hamburg Eppendorf. dr.khairuddin@gmx.de

- MIGLIORE COMFORT, INSPESSIMENTO DELLO STRATO LIPIDO E STABILITA' DEL FILM LACRIMALE PER ALMENO 1 ORA DOPO SINGOLA NEBULIZZAZIONE DI LIPOSOMI.

[Cont Lens Anterior Eye.](#) 2010 Apr;33(2):83-7. Epub 2010 Jan 21.

Effect of a liposomal spray on the pre-ocular tear film.

[Craig J.P.](#), [Purslow C.](#), [Murphy P.J.](#), [Wolffsohn J.S.](#)

Department of Ophthalmology, University of Auckland, New Zealand. jp.craig@auckland.ac.nz

NOSTRA ESPERIENZA

SCOPO DELLO STUDIO

Valutare l'efficacia del trattamento delle rino-congiuntiviti allergiche con spray oculare a base di liposomi e vitamina A ed E

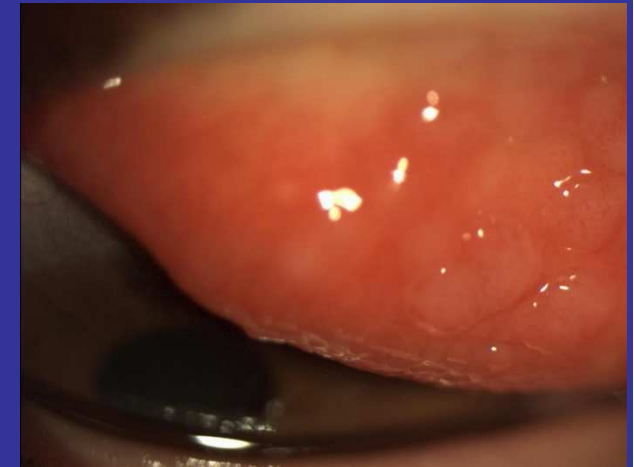
MATERIALE

Pazienti: n. 20 (7 m, 13 f)

Età media: $26,7 \pm 9,3$ anni

Follow up: 3 mesi

IgE sieriche positivi



METODI

2 GRUPPI: CASO



LIPOSOMI SPRAY

CONTROLLO



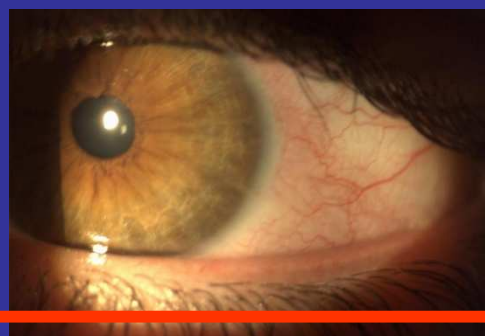
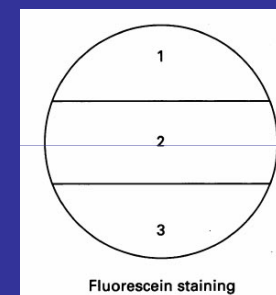
SOLUZIONE FISIOLÓGICA SPRAY

MODALITA' DI SOMMINISTRAZIONE:

1 applicazione 3 volte al dì

TEST CLINICI

- Tear break-up time (BUT)
- Tear film lipid layer (TFL)
- Test di Shirmer (TS)
- Corneal fluorescein stain scoring (0-3 punti)
- Iperemia congiuntivale (0-3punti)
- Osmolarita' (mOsm)

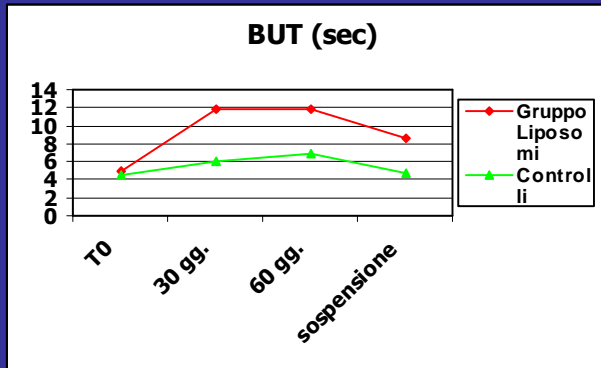


TEMPI DI OSSERVAZIONE

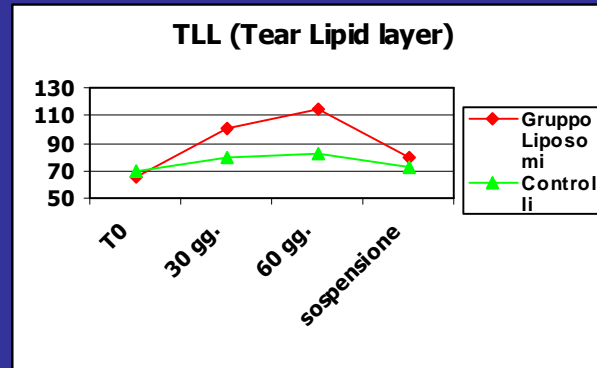
- T0
- dopo 30 giorni
- dopo 60 giorni
- dopo sospensione

ANALISI STATISTICA: Mann-Whitney test

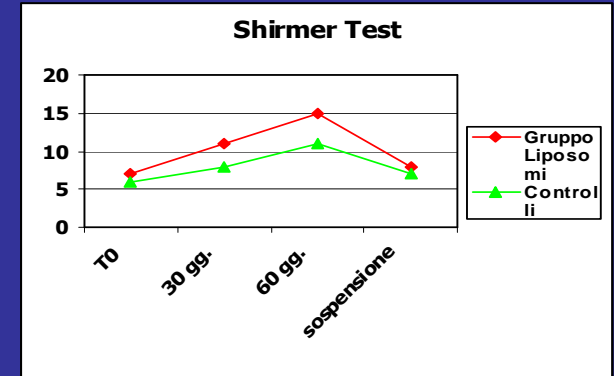
Risultati oftalmologici



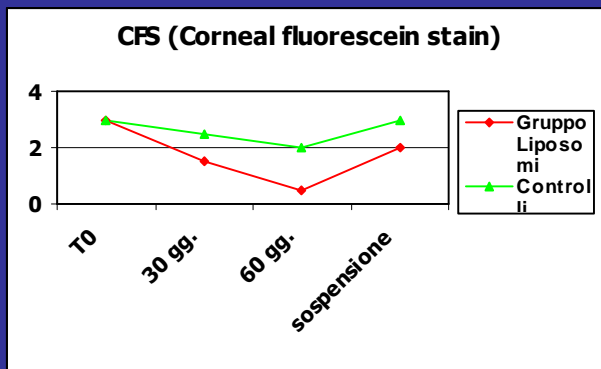
$P < 0.05$



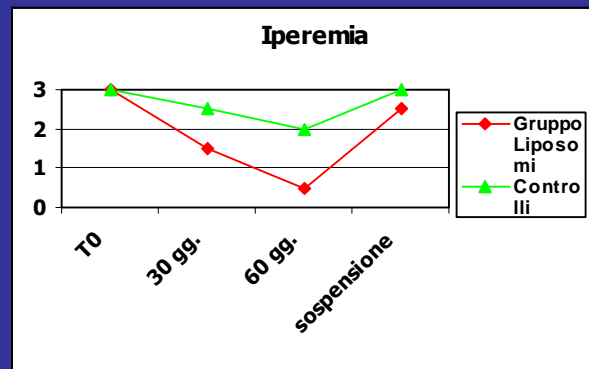
$P < 0.05$



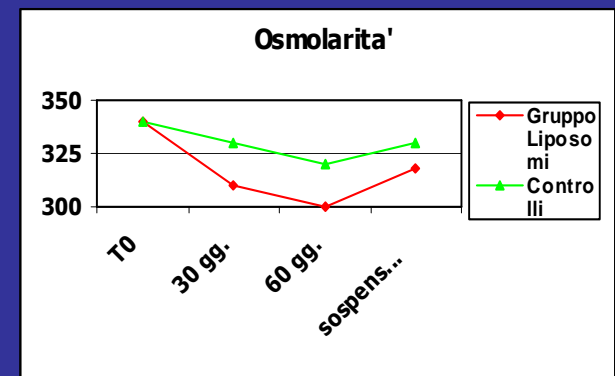
N.S.



$P < 0.05$



$P < 0.05$



$P < 0.05$

ANALISI STATISTICA: Mann-Whitney test

Osservazioni sull'apparato ORL

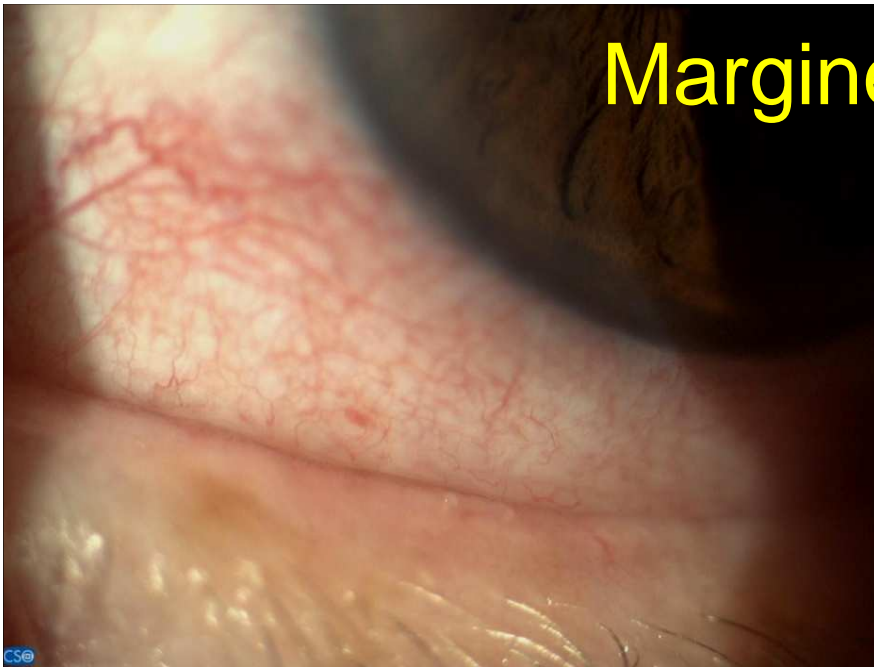
- Presenza di liposomi fluoresceinati nella mucosa e nelle secrezioni nasali dopo applicazione sulle palpebre in corrispondenza del canto interno
- Maggiore protezione della mucosa nasale
- Diluizione degli allergeni e delle citochine proinfiammatorie
- Riduzione tempo di contatto della mucosa con gli allergeni ambientali
- Miglioramento della rinite e della sintomatologia ORL



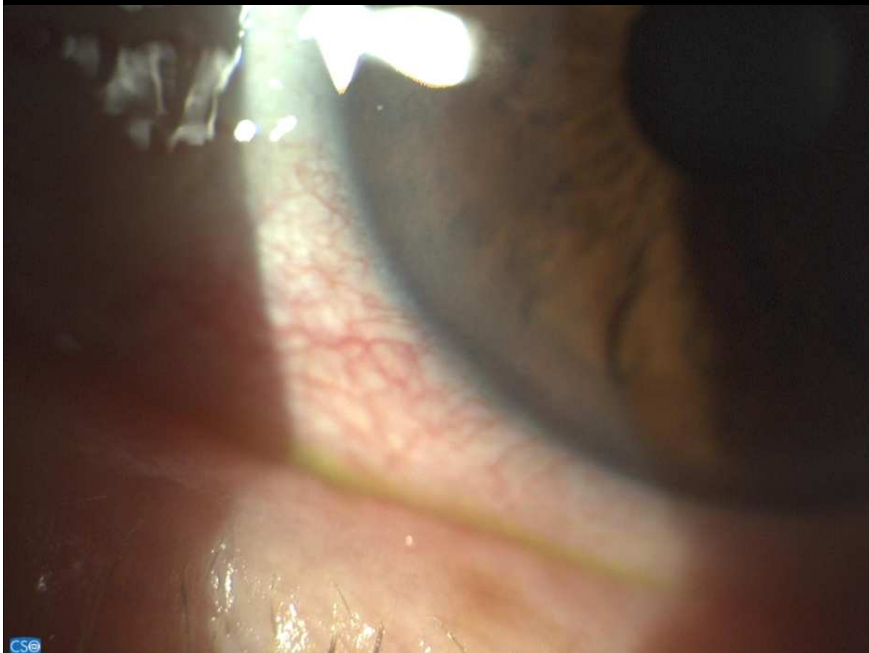
Spray liposomiale con doppio erogatore per la superficie oculare e per la cavità nasale.

Margine palpebrale

prima



Dopo



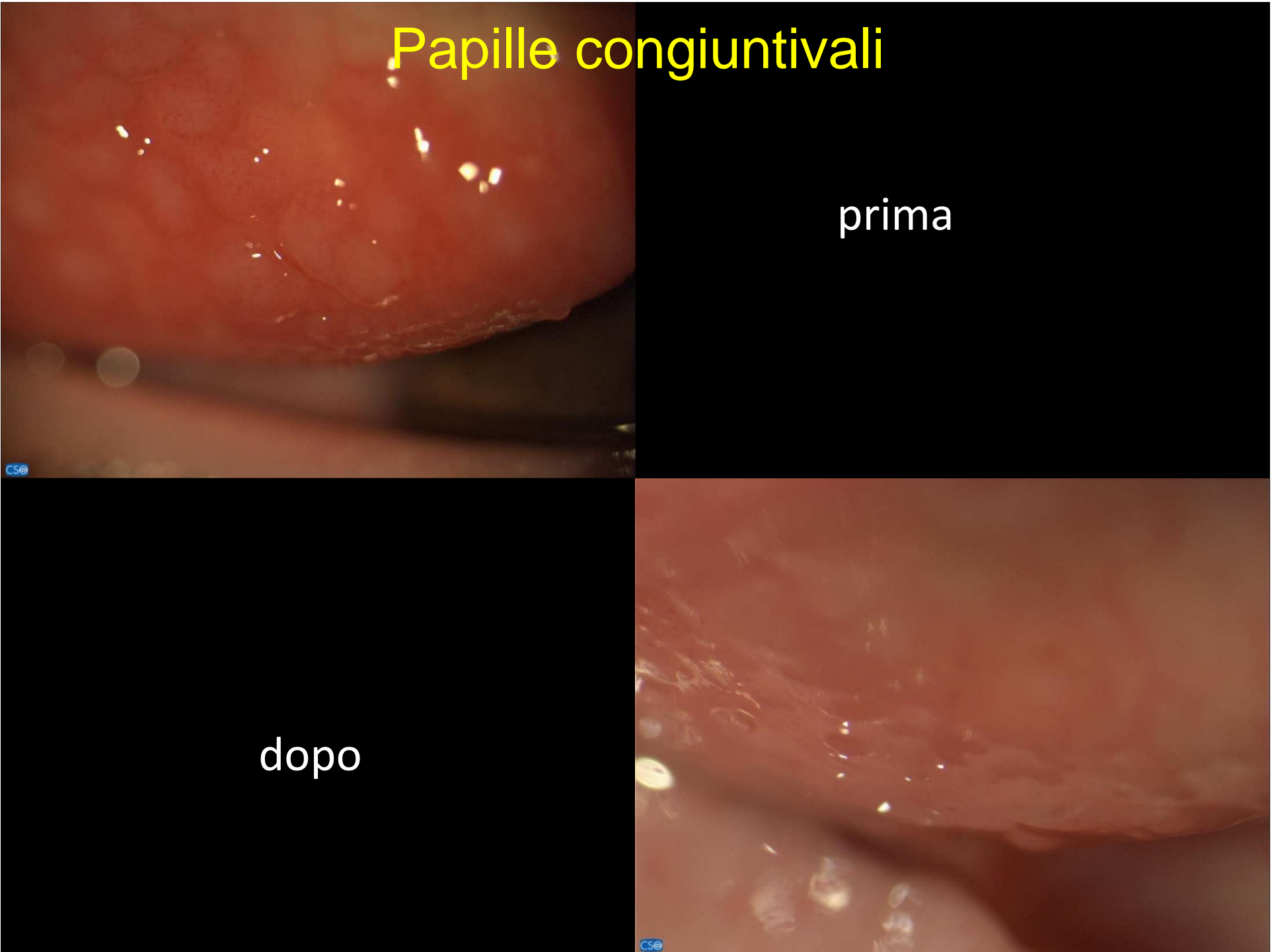
Papille congiuntivali

prima

CSE

dopo

CSE

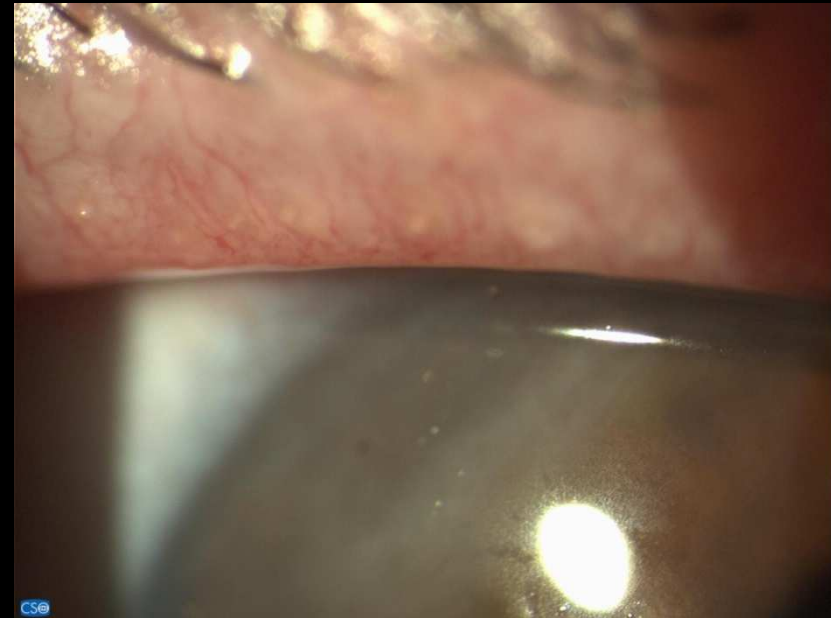


Ghiandole di Meibomio

prima

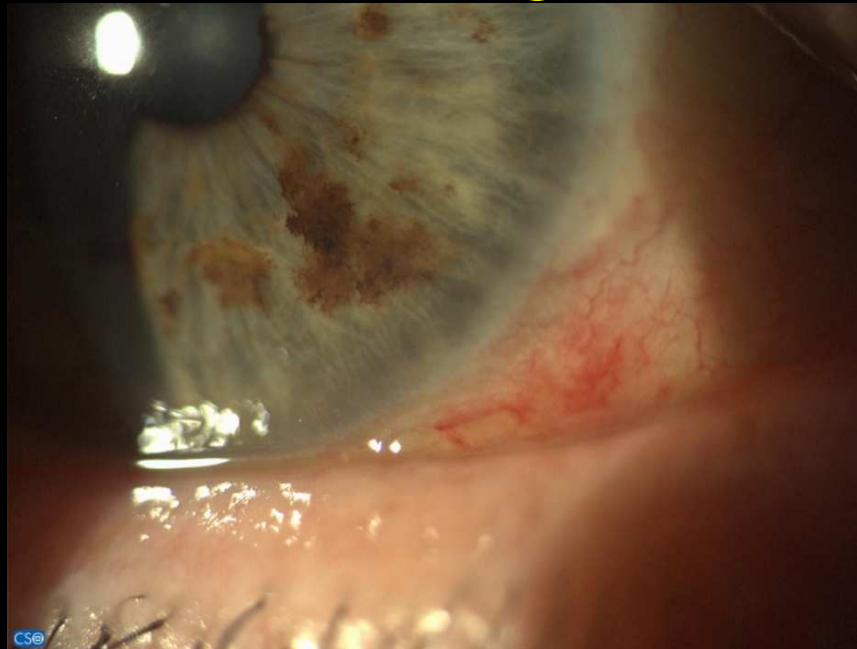


30 gg dopo



60 gg dopo

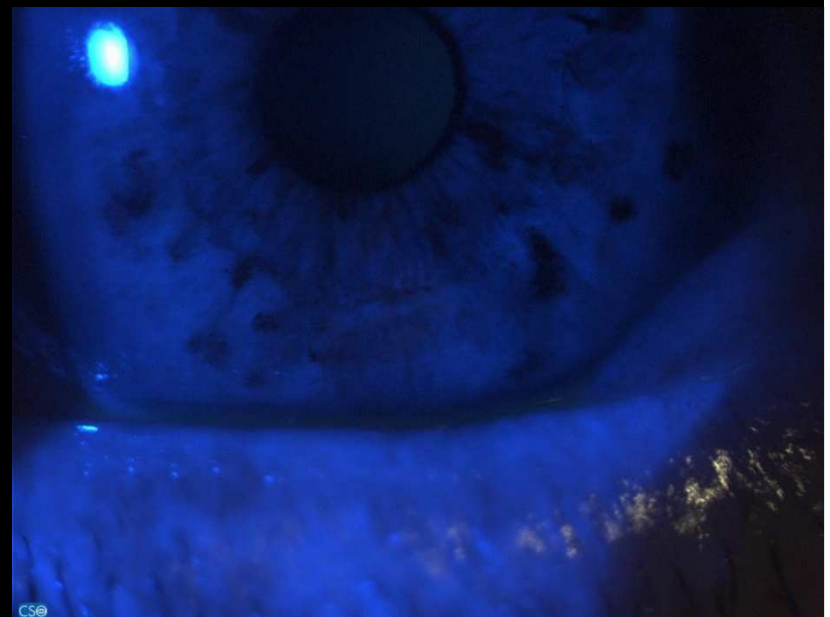
Iperemia congiuntivale



prima



dopo



Iperemia congiuntivale

prima

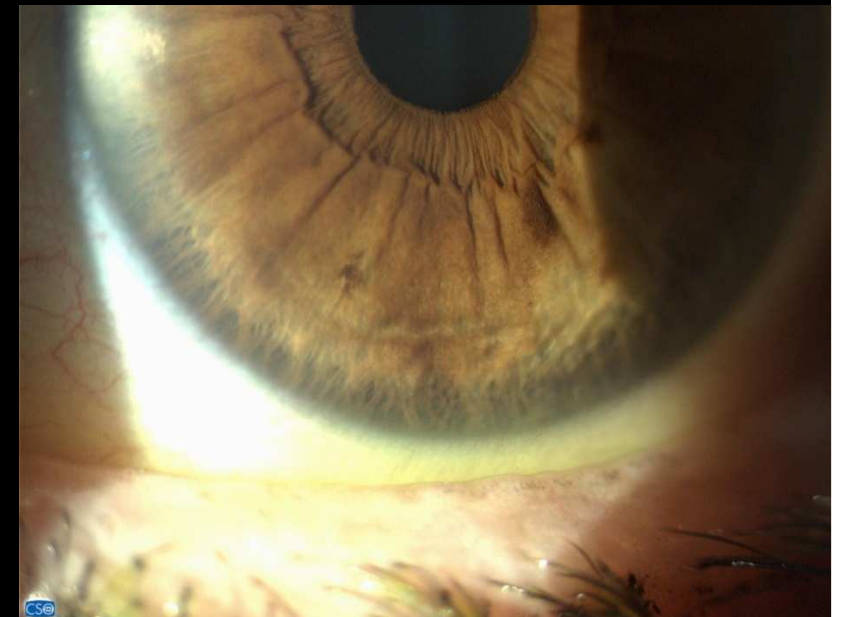
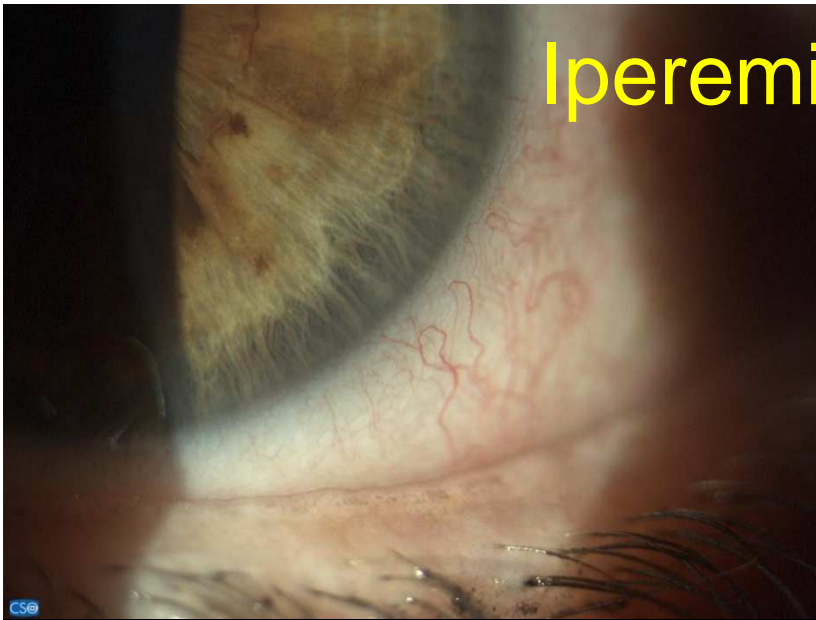
CSE

CSE

dopo

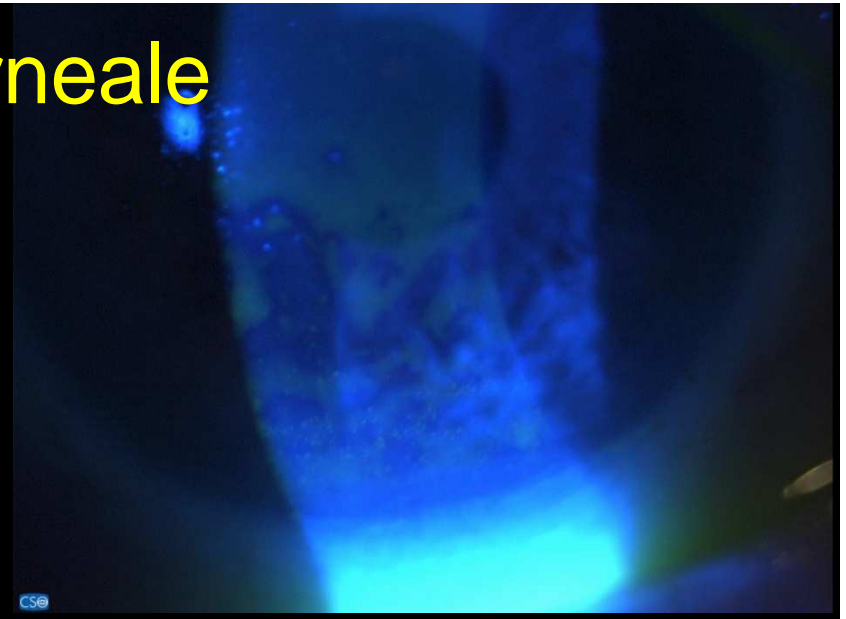
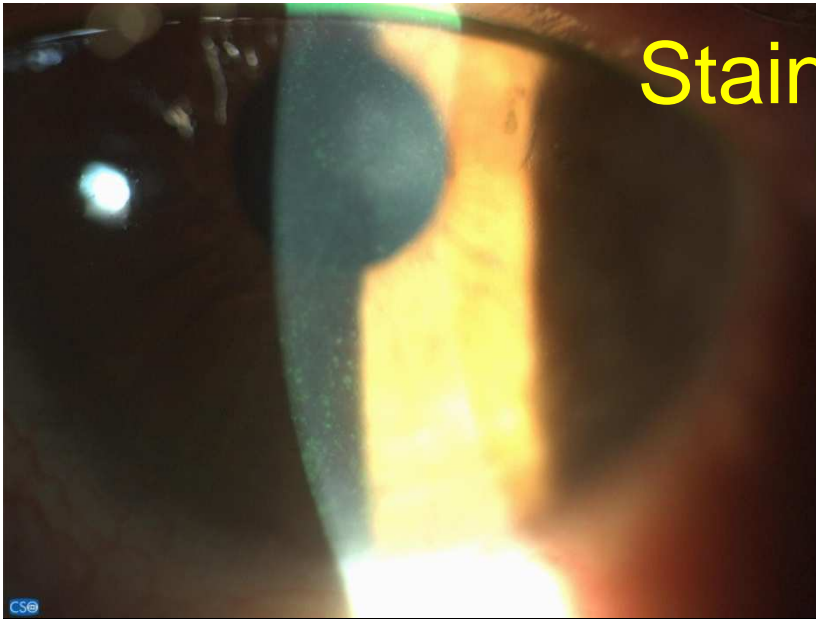
CSE

CSE



Staining corneale

prima



dopo



Conclusioni

- Vantaggi clinici statisticamente significativi sulle rino-congiuntiviti allergiche associate a dry eye
- Migliore compliance, efficacia e tollerabilità
- Nuova, rivoluzionaria procedura di somministrazione
- Effetti sull'infiammazione del margine palpebrale