

Le linee guida in oftalmologia

Il pronto soccorso oculistico

Femtolaser Cataract Surgery

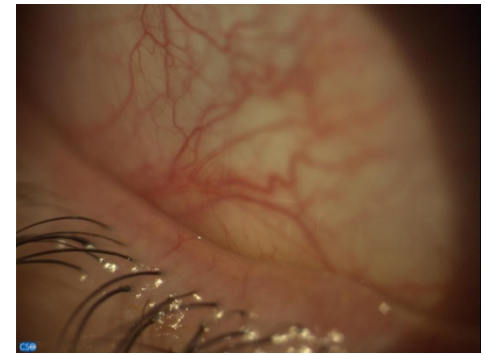


**Occhio secco e
infiammazione :
i vantaggi delle
soluzioni
nanotecnologiche**

**D. Rocca,
R. Amato, A. Messina,
C. Gagliano**

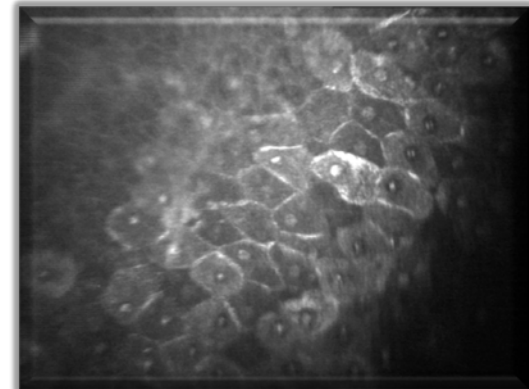
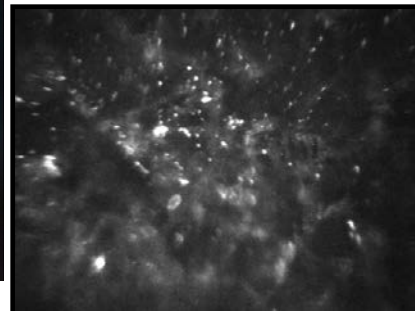
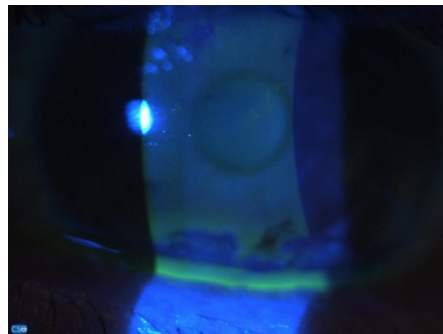
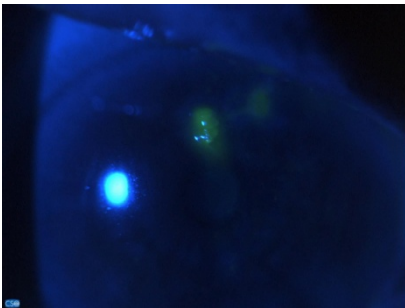
Acacia Resort
Campofelice di Roccella
14•15•16 Aprile 2016

OCCHIO SECCO



Malattia multifattoriale caratterizzata da

- Instabilità del film lacrimale
- Aumento dell'osmolarità
- **Infiammazione della superficie oculare**
- Danno palpebrale, congiuntivale, corneale

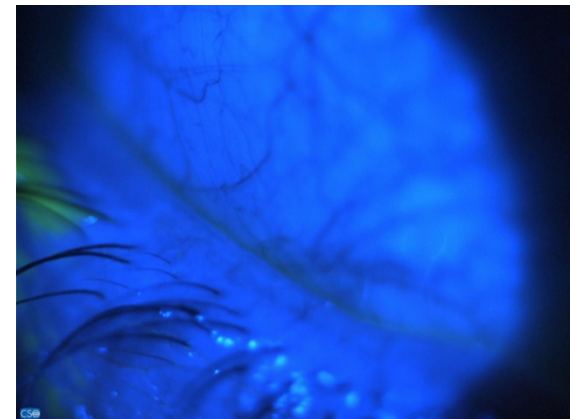
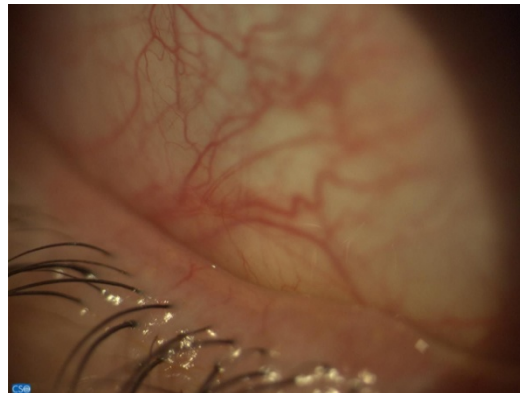


→ *La complicata struttura del film lacrimale non è facilmente comprensibile*

→ *La terapia convenzionale con lacrime artificiali non è di successo nella maggior parte dei casi*

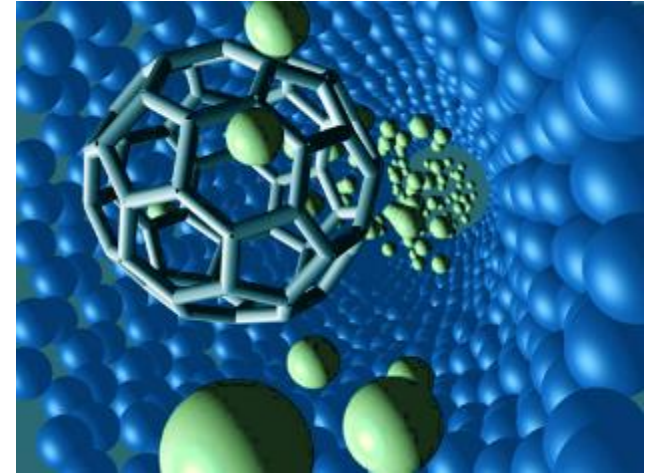
→ *Ripetute instillazioni*

→ *Tossicità*

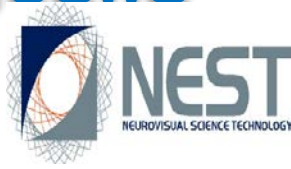


Nanotecnologia: molteplici applicazioni

- Nanomedicina
- Nanobiotecnologia
- Applicazioni industriali della nanotecnologia
- Microelettronica
- Agricoltura
- Cosmetica



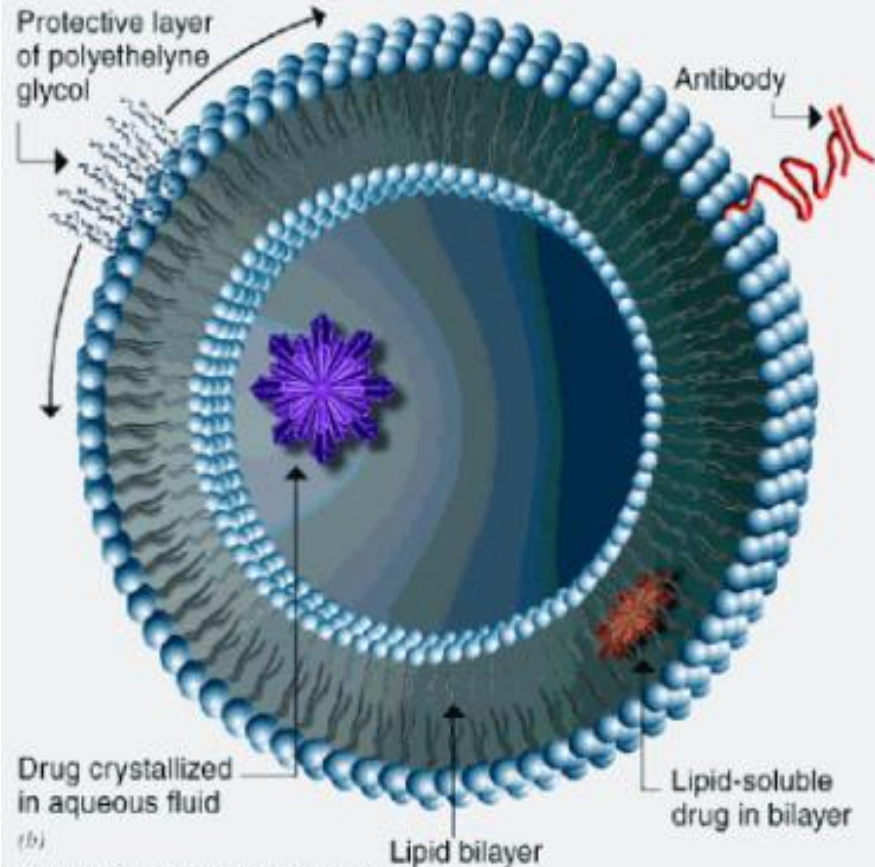
Sistemi di drug delivery con nanoparticelle usati nella ricerca oftalmologica



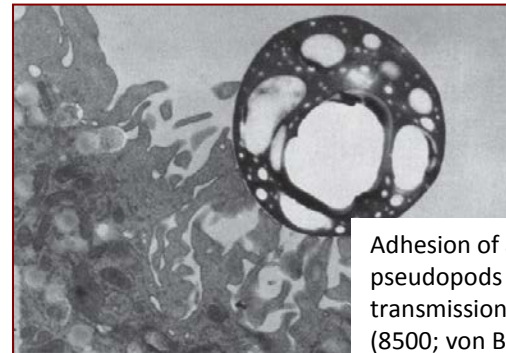
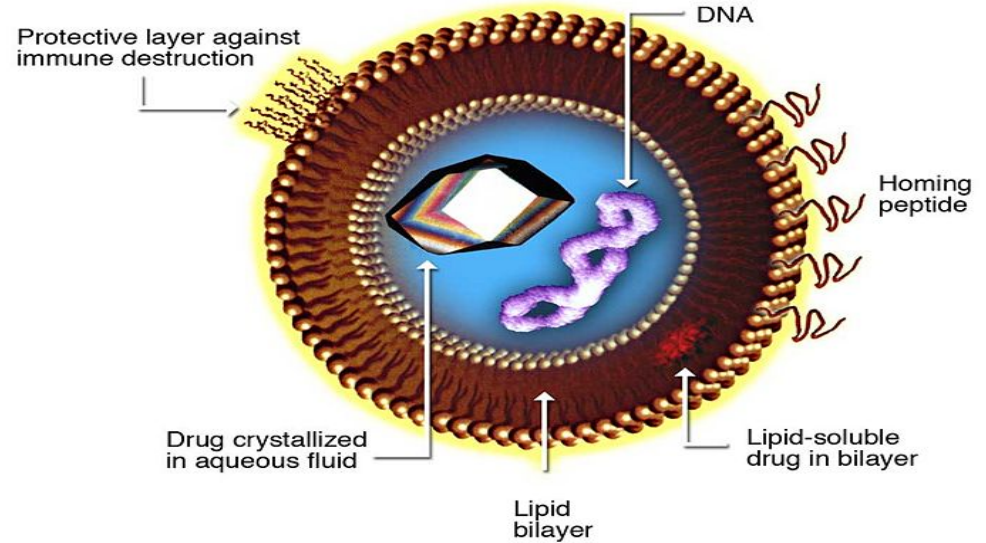
S. no	Drug	Nanoparticulate system	Result
1	Oligonucleotides	Liposomes	Better control of release rate
2	Acetazolamide	Liposomes	Produced a marked decrease in intra ocular pressure (IOP)
3	Pilocarpine HCl	Liposomes	Increased miotic response and ocular bioavailability of the drug
4	Inulin	Liposomes	Increased ocular concentration of the drug
5	Cyclopentolate	Niosomes	Promoted ocular absorption of the drug
6	Timolol maleate	Discomes	Entrapped comparatively higher amount of drug than niosomes
7	GCV	Albumin nanoparticles	Increased antiviral activity against human cytomegalovirus (HCMV) infection
8	Pilocarpine	Microemulsions	Decreased IOP by 25%
9	Amikacin	Nanoparticles	Improved delivery of drug to cornea and aqueous humor
10	Pilocarpine	Poly(butyl)-cyanoacrylate nanoparticles	Enhanced miotic response by 22% and decreased IOP
11	Flurbiprofen	Acrylate polymer nanosuspensions	Obtained higher drug levels in the aqueous humor and inhibition of Paracentesis-induced miosis
12	Cyclosporin	Chitosan nanoparticles	Enhanced delivery to external ocular tissues
13	Rhodamine	PEG and chitosan coated PECL nanoparticles	Obtained better corneal penetration
14	Dexamethasone	Microemulsions	Enhanced bioavailability in aqueous humor
15	Pilocarpine nitrate, Tropicamide	Dendrimers	Prolonged miotic activity
16	Pilocarpine nitrate	HP- β -CD	Increased miotic enhanced corneal penetration effect and by four-fold
17	Dexamethasone	HP- β -CD	Enhanced solubility, permeability, and corneal bioavailability

NanoDrugDelivery

Liposomes



Liposome for Drug Delivery

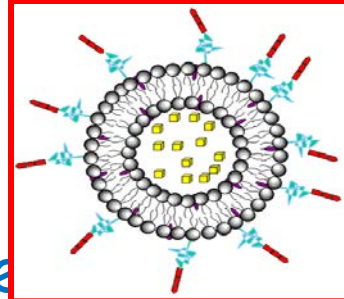


Adhesion of a nanoparticle on pseudopods of a macrophage imaged by transmission electron microscopy (8500; von Briesen et al. 2006).

Liposomi nanotecnologici

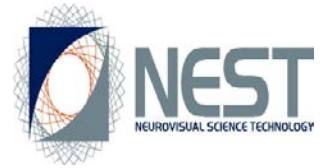
Più piccola è la dimensione dei liposomi e maggiore e più rapido sarà l'assorbimento della sostanza di interesse.

Ad una riduzione delle dimensioni corrisponde infatti un aumento dell'area superficiale disponibile al contatto con l'epitelio

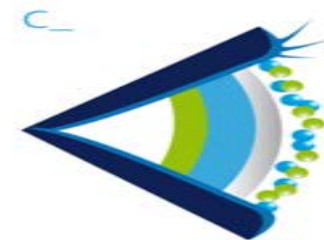


- ✓ Nuova via di somministrazione (SPRAY)
- ✓ Nuova formulazione (LIPOSOMI)

Perché utilizzare i liposomi?

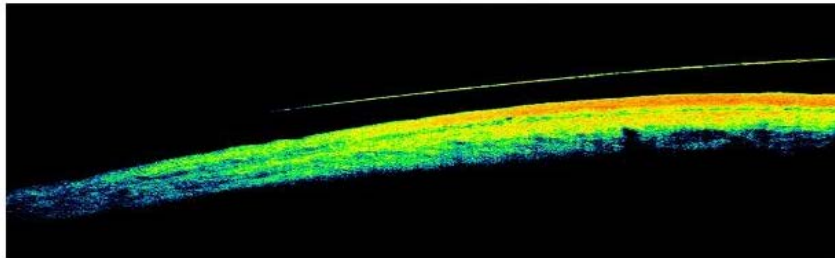


- Sono biodegradabili e biocompatibili
- Uniforme distribuzione del principio attivo
- I componenti attivi sono già solubilizzati
- La componente lipidica migliora la lubrificazione oculare e palpebrale
- Riducono l'evaporazione lacrimale
- Effetto antiinfiammatorio
- Possibilità di caricare principi attivi all'interno (es. vit. A, E)
- Facilità somministrazione (bambini, anziani)

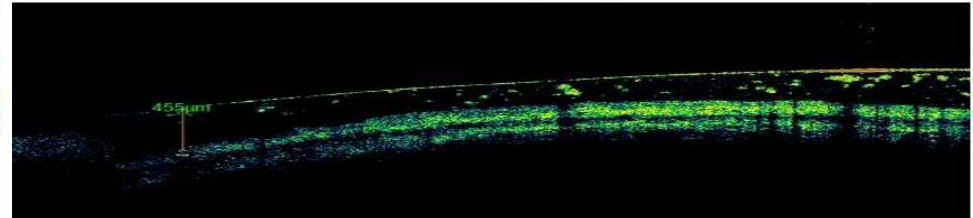


Liposomi nanotecnologici

- Sommare l'efficacia antiinfiammatoria di fosfatidilcolina, fosfatidilserina e l'attività antiossidante delle vitamine A ed E.
- Intervento diretto sul margine delle palpebre

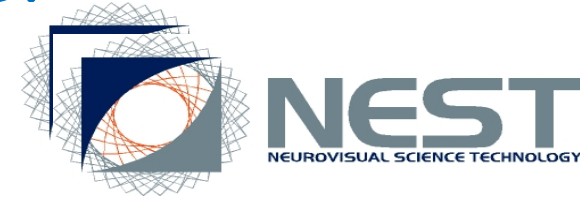


PRE



POST

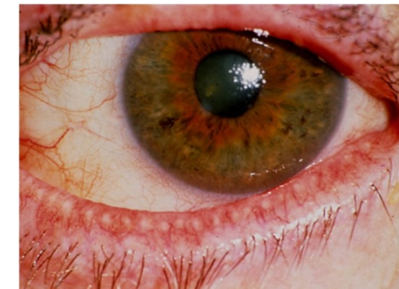
Sindromi da occhio secco nel paziente reumatologico



MALATTIE REUMATOLOGICHE

- Sindrome di Sjogren (primaria e secondaria)
- Lupus eritematoso sistemico
 - Sclerodermia
- Artrite reumatoide
 - Vasculiti
 - Connettiviti

- Grave disfunzione lacrimale su base lipidica
- Esacerbazione delle cause infiammatorie





4) Flogosi Gh. di Meibomio

6) Aumentata evaporazione

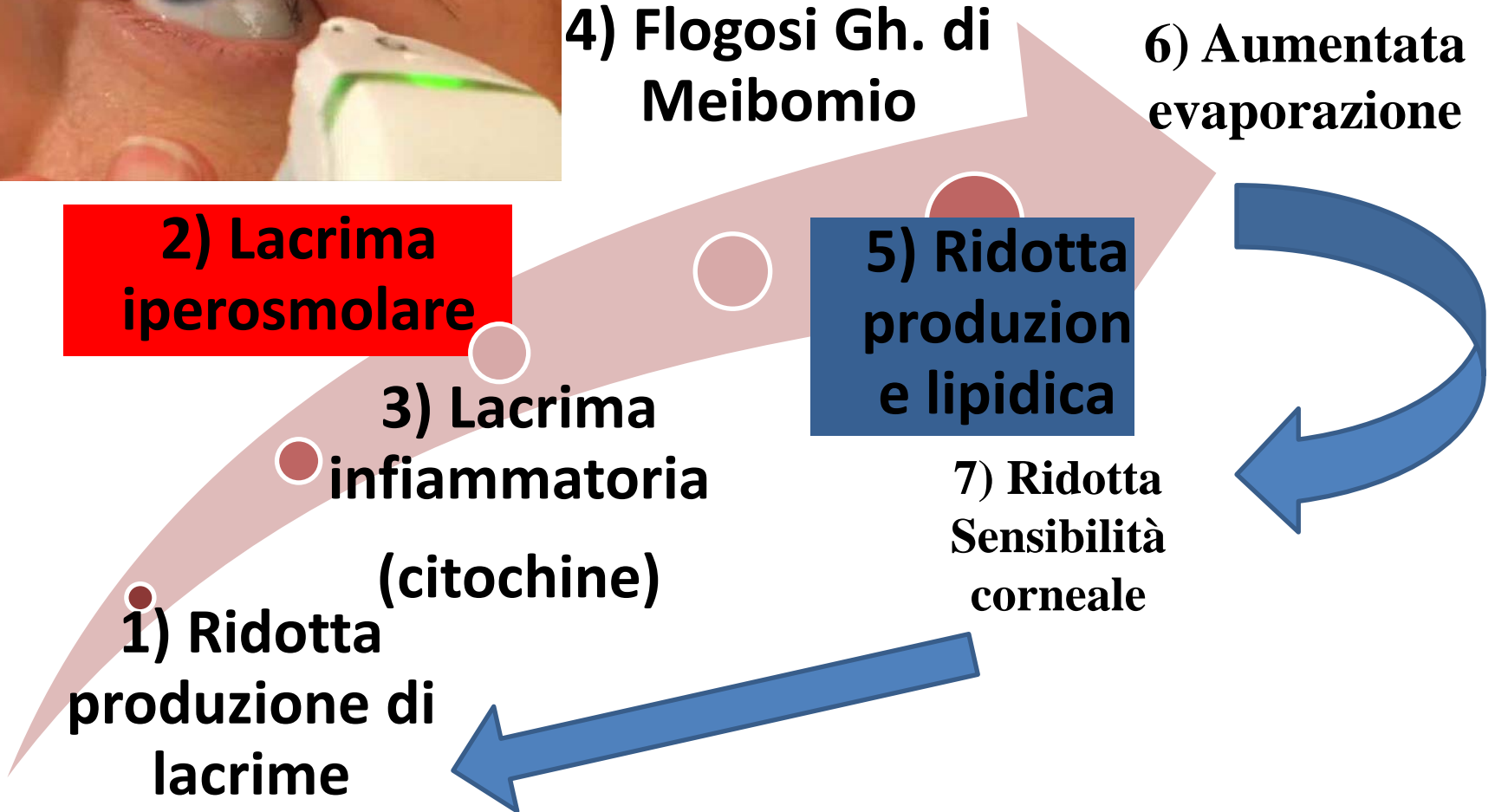
2) Lacrima iperosmolare

5) Ridotta produzione e lipidica

3) Lacrima infiammatoria (citochine)

7) Ridotta Sensibilità corneale

1) Ridotta produzione di lacrime



Meibomian Gland Dysfunction in Patients with Sjögren Syndrome

Jun Shimazaki, MD, Eiki Goto, MD, Masafumi Ono, MD, Shigeto Shimmura, MD, Kazuo Tsubota, MD

Cornea

In Vivo Confocal Microscopy of Meibomian Glands in Sjögren's Syndrome

Edoardo Villani, Silvia Beretta, Michela De Capitani, Daniela Galimberti, Francesco Viola, and Roberto Ratiglia

Tear Evaporation Rates in Sjögren Syndrome and non-Sjögren Dry Eye Patients

EIKI GOTO, YUKIHIRO MATSUMOTO, MIZUKA KAMOI, KOJI ENDO, REIKO ISHIDA, MURAT DOGRU, MINAKO KAIDO, TAKASHI KOJIMA, AND KAZUO TSUBOTA



Changes of inflammatory cytokines and tear osmolarity in systemic sclerosis after treatment with liposomes sprayed.



Author Block: Gagliano, Caterina ^{1, 2}; Amato, Roberta ^{1, 2}; Fallico, Matteo ²; Toro, Mario ²; Avitabile, Teresio ²; Foti, Rosario ³; Longo, Domenico ¹.

INSTITUTIONS (ALL): ¹ 1. NEST (Neurovisual Science Technology) srl, Catania, Italy. 2. Department of Ophthalmology, University of Catania, Catania, Italy. 3. Rheumatology Unit Policlinico Vittorio Emanuele Enterprise, University of Catania, Catania, Italy.

Purpose

The aim of this study is to investigate the effect of treatment with a liposomal spray solution in patients with systemic sclerosis (SSc) and severe dry eye by measuring the levels of inflammatory cytokines and tear osmolarity.

Methods

>Twenty-two subjects (12M, 10F), aged 45.1±7.1 years, with Ssc were enrolled in this prospective, randomised, double-masked investigation.

>Dry Eye Syndrome was identified in patients with SSc according to the classification of Dry Eye Disease of International Dry Eye Workshop (2007) and tear osmolarity values (TearLab® system) according to recommendations of the manufacturer with a cut-off value of 308 mOsm/L.

>Liposomal spray (nebulized, two sprays each, on the eyelids, 3 times per day for 15 days) with vitamin A and E was applied to one eye, and an equal volume of saline spray (control) applied to the contralateral eye.

>Expression patterns of inflammatory cytokines (IL-1β, IL6, TNF-α, IFN-γ) were evaluated at baseline and at 5, 10, 15 days after spray solution application.

>Tear osmolarity measurements, non-invasive tear film stability (TF-BUT) test and Schirmer's tests (type II) were performed. Ocular Surface Disease Index (OSDI) was used to measure the symptoms.

Results

Significant reduction ($p < 0.01-0.001$) was detected in the inflammatory cytokine levels and osmolarity in tears of eye treated with the spray liposomes solution in comparison with fellow eye treated with sprayed saline solution. There were significant differences among the 2 eyes concerning tear osmolarity ($p < .001$) and TF-BUT ($p < .001$) scores. Also, significant decrease of OSDI scores ($p < .001$) was observed. This effect could be due to the anti-inflammatory mechanism of the vitamins and also to the barrier effect of liposomes on ocular surfaces.

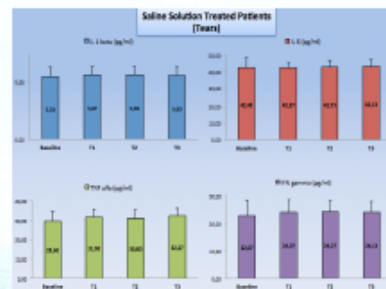


Fig. 1: Cytokine levels (IL-1β, IL6, TNF-α, IFN-γ) in tears of eye treated with saline solution at different time point.

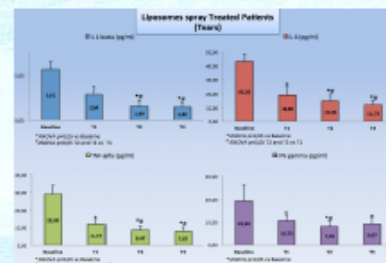


Fig. 2: Cytokine levels (IL-1β, IL6, TNF-α, IFN-γ) in tears of liposome treated eyes show a progressive decrease during five, ten and fifteen days of treatment time.

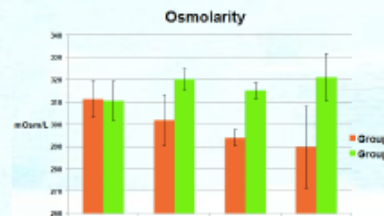


Fig. 3: Mean value of Osmolarity for the 2 eyes 5, 10 and 15 days after the treatment with liposomal spray solution (Group A) and saline spray solution (Group B). Group A shows a statistically significant decrease ($p < 0.001$) of osmolarity with respect to the Group B.

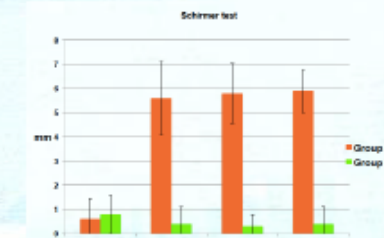


Fig. 4: Mean value of Schirmer's test (II) for the two eyes at different time point. At 5, 10 and 15 days of treatment we observed a significant increase of Schirmer in Group A compared to B ($p < 0.001$).



Fig. 5: Mean value of TF – BUT for the two eyes at different time point. At 5, 10 and 15 days of treatment we observed a significant increase of TF – BUT in Group A compared to B ($p < 0.001$).

Conclusions

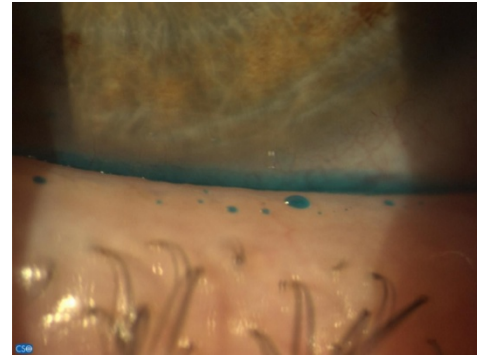
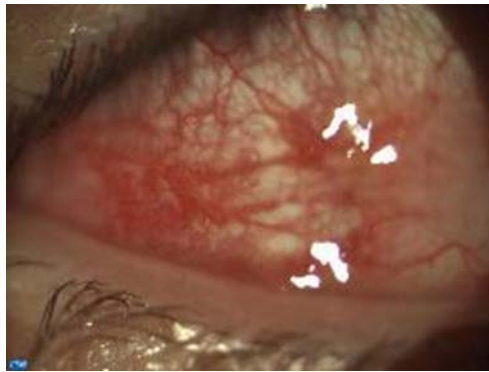
This study shows the ability of liposomal spray application to modify the pro-inflammatory cytokine profile and to increase stability characteristics of the pre-ocular tear film in severe dry eye of SSc patients. The commercially available liposomal spray represents a novel delivery system, in which the major phospholipid, phosphatidylcholine, is delivered in a stable form (liposomes) to the closed eyelid and from there, migrates across the eyelid margins to combine with the natural tear film.

Commercial disclosure: All authors have no commercial interest.

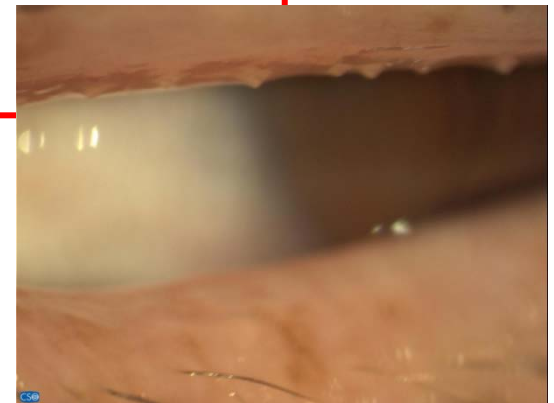
References

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- Correlation of Tear Inflammatory Cytokines and Matrix Metalloproteinases with Four Dry Eye Diagnostic Tests. *Kaet H, MacLachlan, Stephanie P, Su, Sarah W, Ward, and Jin-Chang Zhang OHSU, March 2012, Vol. 53, No. 3*
- Effect of a liposomal spray on the precorneal tear film. *Journal P. Chang, CO-MEWS Publishing, Paris J. Murphy, James S.W. Wallace, Corbett Lee & Avior Eye 20 (2012) 60-67*
- Application of Liposomes in Ophthalmology. *Shahad Shaban, MD, Ghada A. Paganis, MD, and Paul J. Lee, MD, Survey of Ophthalmology Volume 55, Number 2, March-April 2010*
- Dry Eye Disease: Treatment A Systematic Review of Published Trials and a Critical Appraisal of Therapeutic Strategies. *Monica Abreu, Silen Carolina Fonseca, Mariana Pralho Abreu, Leonardo Tarcus Matti, Gustavo Vanni Araujo, Peter S. Rabinov, and Shweta Meheri Rosta. Clinical Practice and Research, 2013, 3(1): 1-10*

Studio



Valutazione dei cambiamenti nei segni e sintomi delle disfunzioni lacrimali con deficit lipidico in pazienti affetti da patologie reumatologiche (Sclerodermia) dopo trattamento con liposomi nanotecnologici arricchiti con vitamina A ed E in formulazione spray.



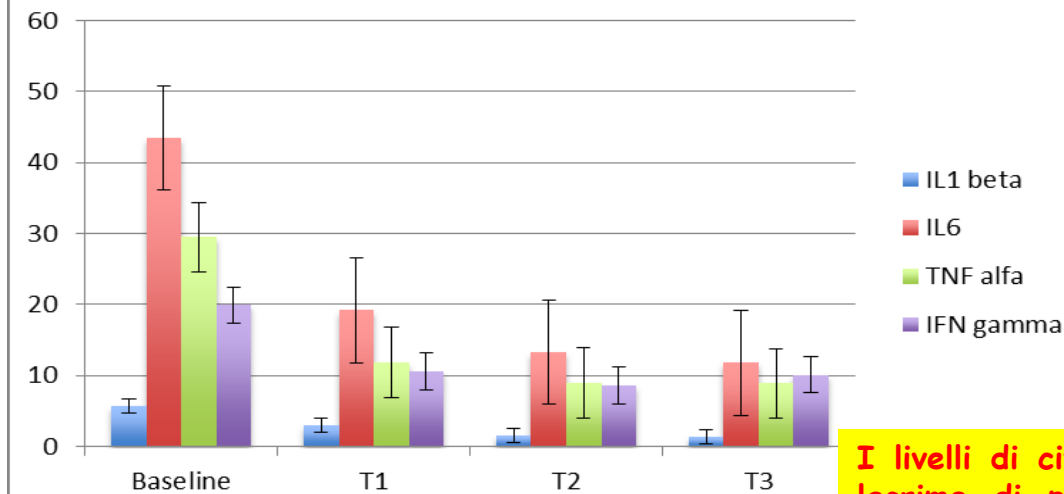
Materiali e Metodi

- Studio prospettico, randomizzato, doppio cieco
- 22 pazienti (12M, 10F), età 45.1+/-7.1 anni
- Applicazione dello spray ai liposomi arricchito di vitamina A ed E sulle palpebre 3 volte al giorno per 15 giorni in un occhio e applicazione nell'occhio controlaterale di uno spray con soluzione salina
- Valutazione livelli citochine infiammatorie (IL-1 β , IL6, TNF- α ,IFN- γ) ai tempi basale, 5, 10, 15 giorni dopo l'applicazione dello spray.

VALUTAZIONE

- ✓ Infiammazione del margine palpebrale
- ✓ Osmolarità lacrimale
- ✓ Schirmer basale
- ✓ T-BUT

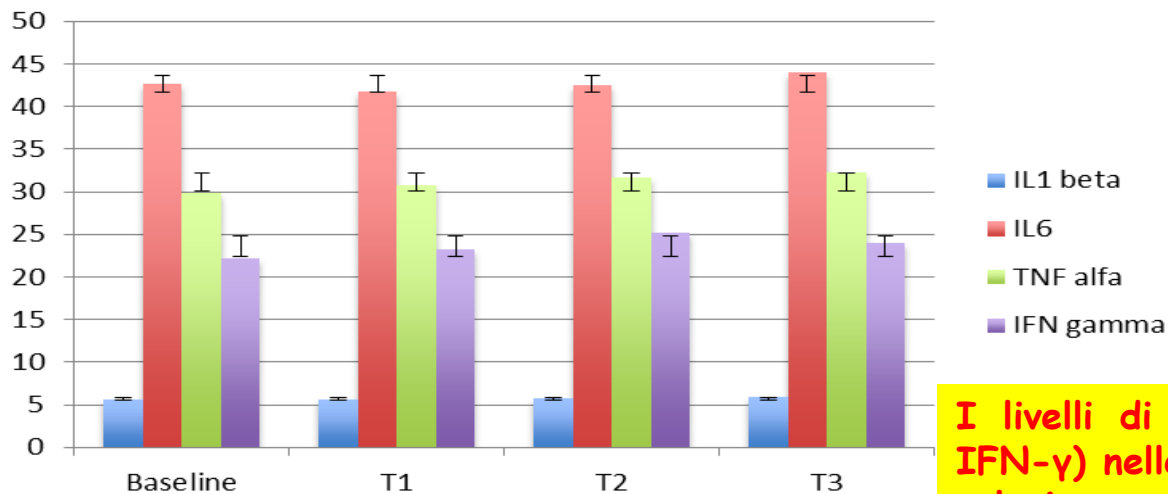
Sistemic sclerosis



Citochine

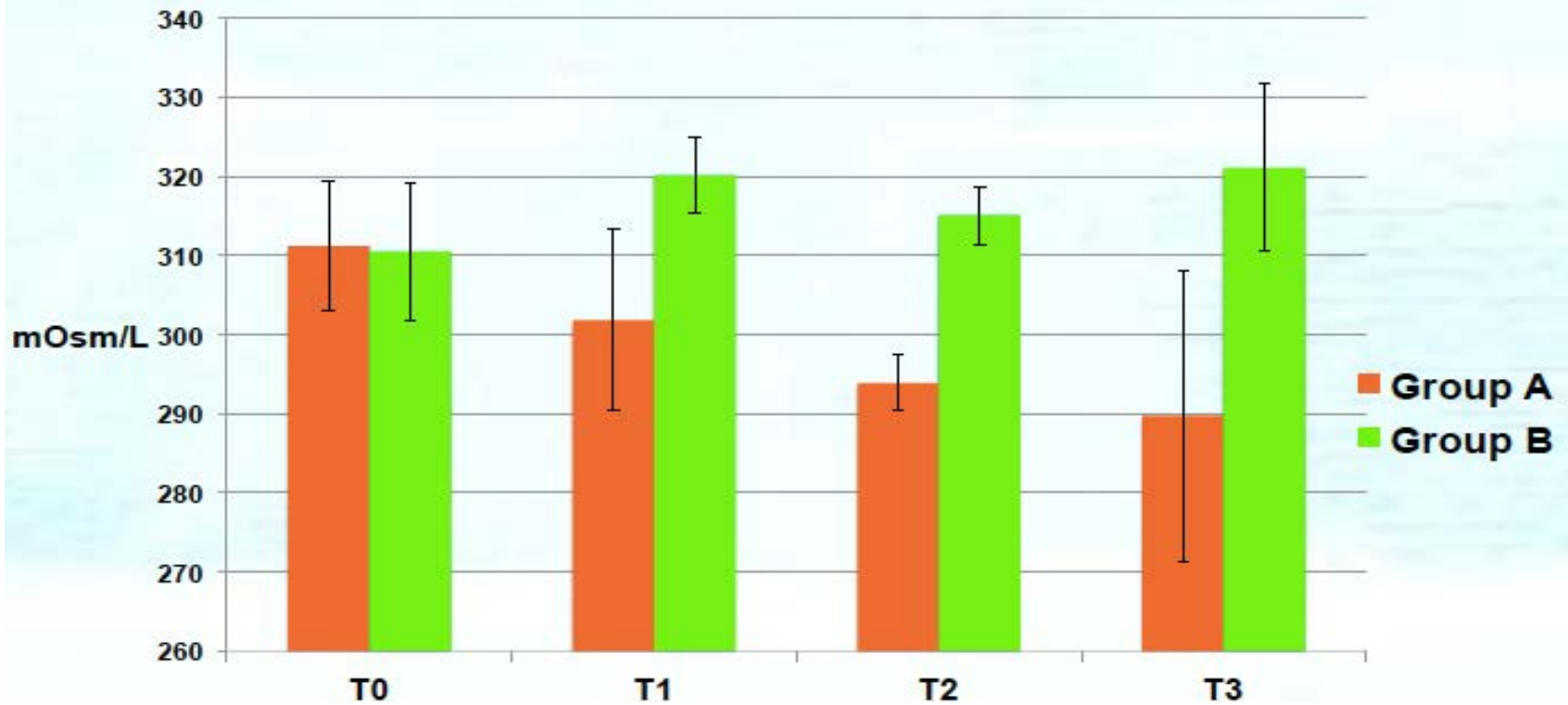
I livelli di citochine (IL-1 β , IL6, TNF- α , IFN- γ) nelle lacrime di pazienti trattati con liposomi mostrano una progressiva riduzione a 5, 10 e 15 giorni.

Controls



I livelli di citochine (IL-1 β , IL6, TNF- α , IFN- γ) nelle lacrime di pazienti trattati con soluzione salina non si modificano.

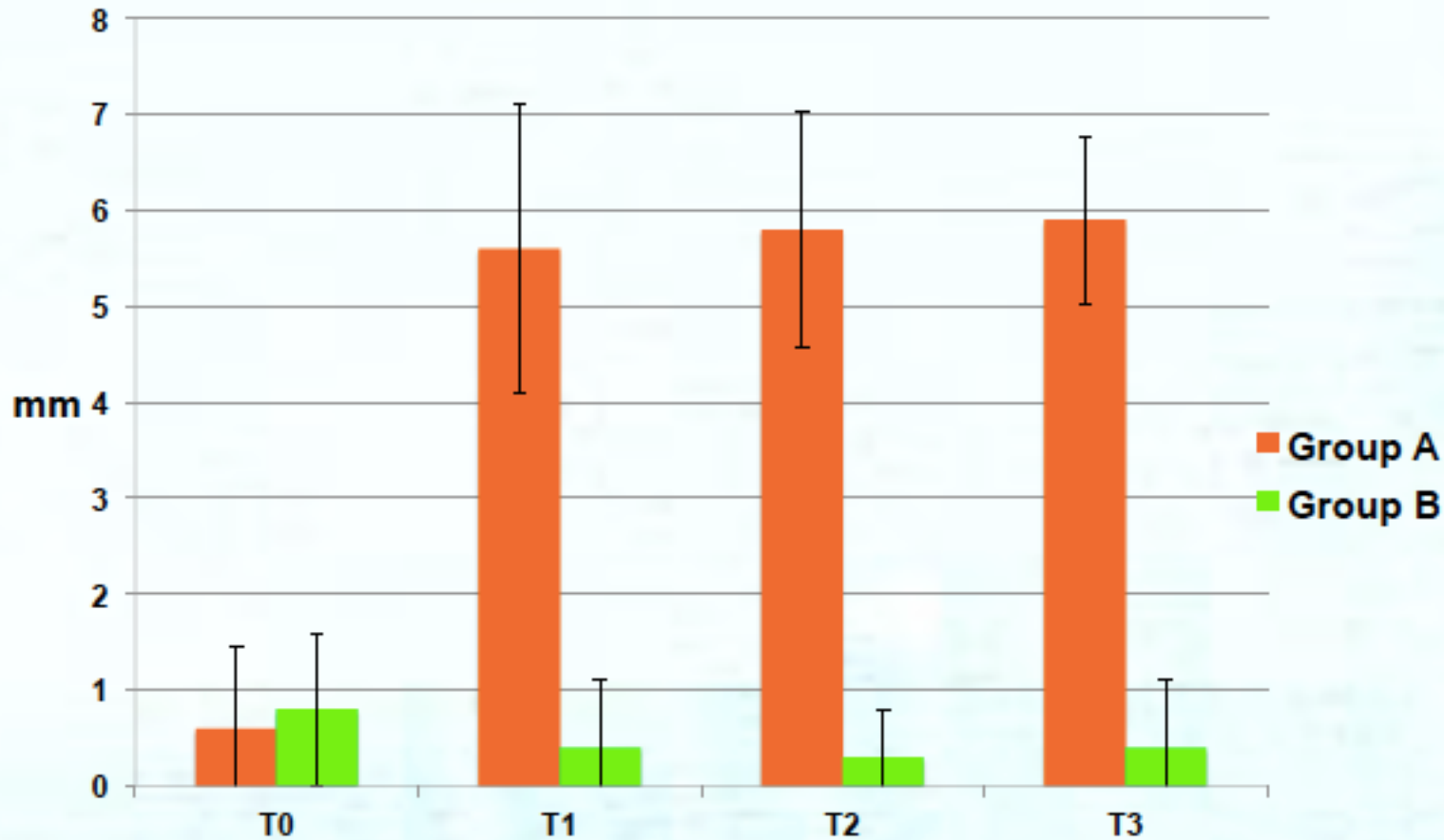
Osmolarity



Osmolarità per i 2 occhi a 5, 10 e 15 giorni dopo il trattamento con liposomi (Gruppo A) e soluzione salina (Gruppo B). Il Gruppo A mostra una riduzione statisticamente significativa di osmolarità rispetto al gruppo B ($p < 0.001$)



Schirmer test

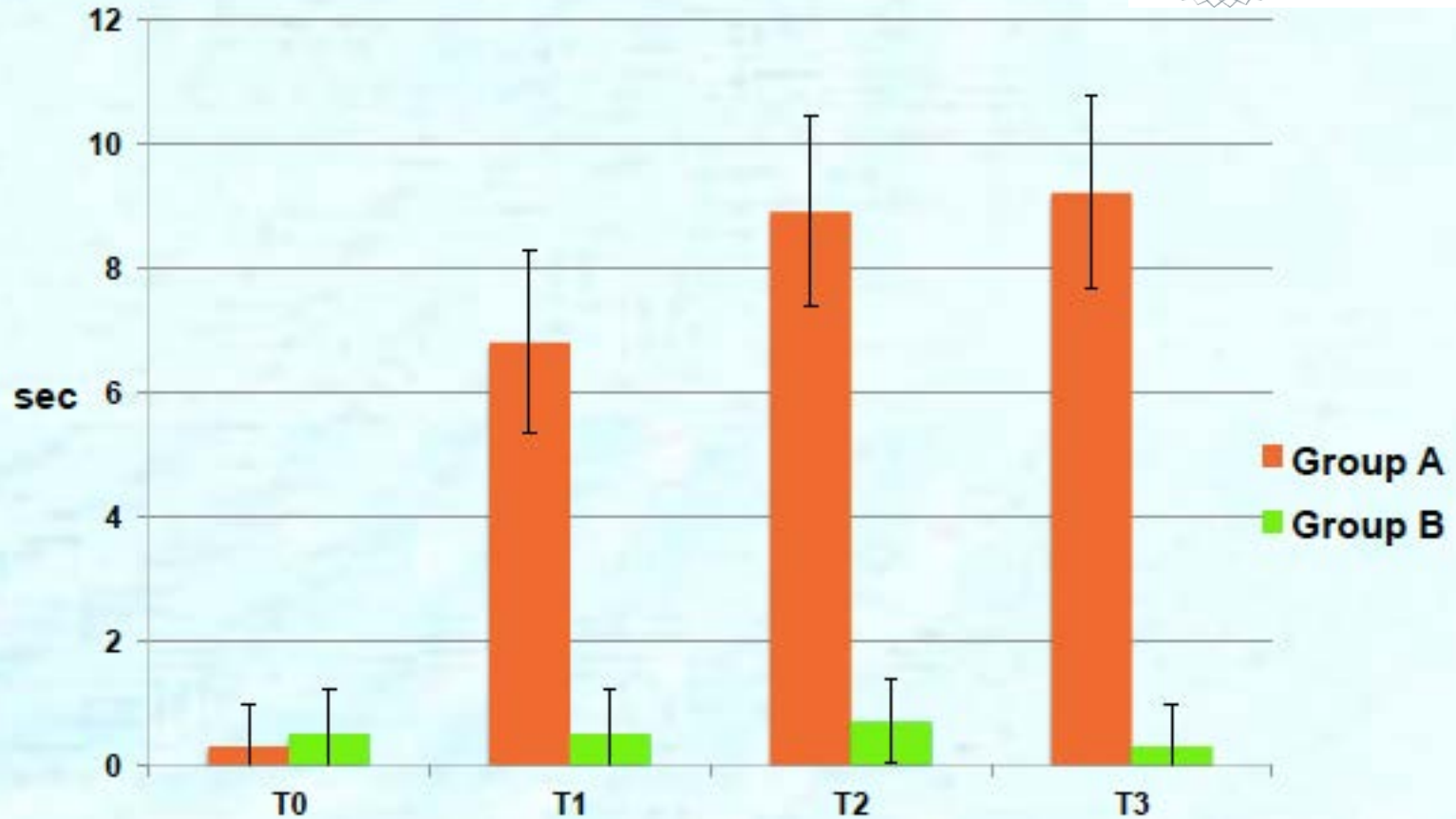


Schirmer test (II) .

A 5, 10 e 15 giorni di trattamento è stato osservato un incremento statisticamente significativo nel gruppo A rispetto al gruppo B ($p < 0.001$).



TF - BUT



BUT .

A 5, 10 e 15 giorni di trattamento è stato osservato un incremento del BUT statisticamente significativo nel gruppo A rispetto al gruppo B ($p < 0.001$).

CONCLUSIONI

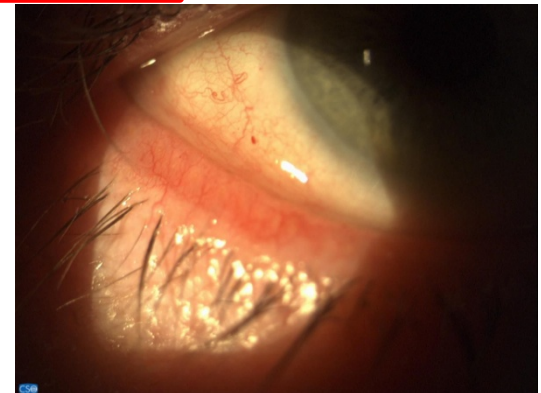
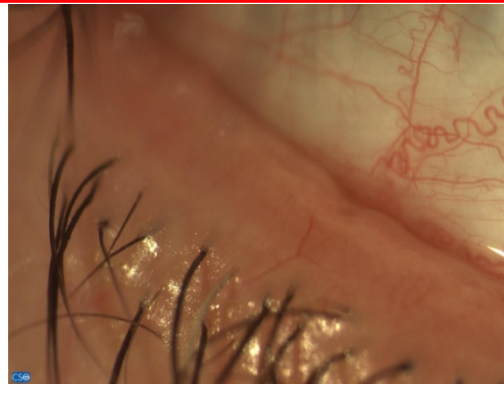
Liposomi nanotecnologici



NEST
NEUROVISUAL SCIENCE TECHNOLOGY

EFFETTO ANTIINFIAMMATORIO SULLA
SUPERFICIE OCULARE E SUL MARGINE
PALPEBRALE

SOSTITUTI LIPIDICI LACRIMALI
EFFICACI NELLE FORME DI DRY EYE
GRAVE IN PAZIENTI AFFETTI DA
PATOLOGIE REUMATOLOGICHE





GRAZIE