OCULAR TOLERANCE AND EFFICIENCY OF TWO SOLUTIONS APPLIED ON NON-INFECTIOUS BLEPHARITIS

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INTRODUCTION

Blepharitis is one of the most frequent ocular pathologies[1] inducing inflammation of the palpebral margin. Alterations of the ocular tear film, dysfunction of the Meibomius glands as well as conjunctivitis, keratitis and secondary infections[2,3] are complications often encountered in this pathology.
These complications are inducing result in permanent palpebral inflammation. There are two main alterations related to blepharitis:

- Hypertrophy of the Meibomius gland orifices[4];
- Lipid hypersecretion on the palpebral edge which leads to free fatty acids release in the lacrimal tear film, development of bacterial proliferation[4,5] and induction of eye surface inflammation[6].

BLEPHARITES

This study is intended to evaluate the therapeutic effect of two solutions on this peripheral ocular pathology:

- An isotonic 0.1% zinc sulfate solution;
- A natural selenium-rich thermal water*.

The anti-inflammatory and anti-free radical efficiency of the two products have already been demonstrated in previous clinical studies [6, 7, 8].

MINERAL COMPOSITION OF THERMAL WATER UNDER STUDY

ANIONS IN MG/L		CATIONS IN MG/L		OLIGOELEMENTS IN µG/L	
Bicarbonate	387	Calcium	149	Selenium	53
Sulfate	56.1	Magnesium	4.4	Copper	< 5
Chlorides	26.2	Potassium	1.9	Zinc	< 5
Nitrates	1.6	Sodium	8.3		
Nitrites	< 0.02	Lithium	< 0.1		
Fluorides	0.2	Iron	< 0.005		
Bromides	0.3	Manganese	0.003		
Phosphates	< 0.1	Strontium	0.3		

MATERIAL AND METHODS

Volunteers were divided into two groups:

VOLUNTEERS AND CONDITIONS OF APPLICATION:

	Zinc sulfate group		Thermal water group	
Number of subjects	30		29	
	Female	29	Female	27
	Male	1	Male	2
Inclusion parameters	- Seborrheic blepharitis, - and/or anterior blepharitis, - and/or posterior blepharitis with conjunctival irritation.			
Application area	Both eyes			
Quantities applied	1 solution impregnated compress on each eye			
Application frequency	Twice a day (morning and evening)			
Duration of treatment	29 days (4 weeks)			
Special requirement	No eye make-up throughout the study			

CLINICAL, BIOLOGICAL AND SUBJECTIVE EVALUATIONS:

Subjects had ophthalmic tests:

- Prior to the study, on day 1 and 10 minutes after the first application;
- Upon completion of the study, on day 29 and 10 minutes after the last application.

Clinical and biological tests distribution between both groups:

Objective signs	Number of subjects tested in zinc sulfate group	Number of subjects tested in thermal water group
Cutaneous periocular tests	30 (100%)	29 (100%)
Ocular tests with biomicroscope	30 (100%)	29 (100%)
Cornea and conjunctiva colorimetric tests	30 (100%)	29 (100%)
Lacrimal tear film examination with Tearscope	22 (73%)	29 (100%)
Lacrimal albumin dosage	15 (50%)	15 (52%)
Lacrimal pH measurement	9 (30%)	10 (34%)
IL8 cytokine lacrimal content	10 (33%)	10 (34%)
Palpebral edge microbiological analysis	21 (70%)	20 (69%)
Palpebral edge photographs	5 (17%)	5 (17%)
Mebometric tests	21 (70%)	19 (66%)

Subjective signs were recorded by the volunteers.

RESULTS

* Clinical tolerance:

	Zinc sulfate group	Thermal water group
Clinical tolerance: in both groups	- No functional irritation signs, no physical signs, not irritant for conjunctiva or cornea. Lacrimal tear film conservation Excellent eye comfort indices: > 98.5% No effect on ocular structures	

* Biological tolerance:

Zinc sulfate group	Thermal water group
INFLAMMATION MARKERS DOSAGE (Mean values +/- Sd)	
Albumin (mg/L): Day 1 : 43.72 +/- 48.3 Day 29: 26.9 +/- 37.9 (t = -0.99) **Marked decrease in albumin level**	Albumin (mg/L): Day 1 : 25.3 +/- 52.7 Day 29: 1.9 +/- 5.0 (t = 1.68) **Marked decrease in albumin level**
→ *No intraclinical irritancy*	
STATISTICAL ANALYSIS: Values were assessed before and after solution application with a test comparing means of matched, low number samples. (α risk = 5%)	
IL8: Day 1 : 0 Day 29: 0	IL8: Day 1 : 0 Day 29: 0
→ *No corneal toxicity detected*	
PH MEASUREMENT (Mean values +/- Sd)	
Day 1 : 7.25 +/- 0.18 Day 29: 8.33 +/- 0.21 P = 1.11*10^{-5}, **significant increase**	Day 1 : 7.39 +/- 0.38 Day 29: 8.50 +/- 0.14 P = 3.4*10^{-5}, **significant increase**
→ *Alkalinization explained by the decrease in lipid secretion*	
STATISTICAL ANALYSIS: Values were compared before and after solution application with a parametric Student's test in matched samples (α risk = 5%)	
SUBJECTIVE TOLERANCE ASSESSED BY SUBJECTS	
9.5/10	**10/10**

* Efficiency:

Zinc sulfate group	Thermal water group
MEBOMETRIC MEASUREMENTS: RESULTS EXPRESSED AS A PERCENTAGE OF SUBJECTS IN ARBITRARY UNITS (OPTICAL DENSITIES)	
Day 1 : 14 out of 21 group subjects had a fatty palpebral edge (mebum > 25). Day 29: 6 out of those 14 subjects (42.9%) presented a **not significant** reduction of the mebum excretion rate	Day 1 : 14 out of 19 subjects had a fatty palpebral edge (mebum > 25). Day 29: 10 out of those 14 subjects (71.4%) presented a **significant** reduction of the mebum excretion rate
→ *Palpebral edge lipids reduction*	
MICROBIOLOGICAL ANALYSIS:	
Mean number of colonies for both most common bacteria: Staphylococcus Aureus and Staphylococcus Epidermidis	
Staph. Aureus: Day 1: 10 +/- 26.26 Day 2: 6.57 +/- 26.22 P= 0.5, **not significant reduction**	**Staph. Aureus:** Day 1: 7.70 +/- 19.37 Day 9: 0 P= 0.034, **significant reduction**
Staph. Epidermidis: Day 1 : 11.57 +/- 16.42 Day 29: 4.38 +/- 8.77 P= 0.038, **significant reduction**	**Staph. Epidermidis:** Day 1 : 9.14 +/- 15.4 Day 29: 36.34 +/- 71.14 P= 0.23, **not significant increase**
ANALYSIS OF MEIBOMIUS GLAND ORIFICE DIAMETER (mm +/- Sd)	
Measurement over 17 glands (5 subjects) Day 1 : 0.17 +/- 0.02 Day 29: 0.11 +/- 0.03 P= 1.46 *10^{-4}, **significant reduction**	Measurement over 20 glands (5 subjects) Day 1 : 0.14 +/- 0.03 Day 29: 0.07 +/- 0.03 P= 6.59 *10^{-5}, **significant reduction**
→ *Reduction of meibomius gland hypersecretion*	
STATISTICAL ANALYSIS: Values were compared before and after solution applications with a non-parametric Wilcoxon test in matched samples (α risk = 5%)	

CONCLUSION

The zinc sulfate and selenium-rich thermal water solutions used in this study, showed a highly satisfactory clinical as well as biological tolerance in subjects with inflammatory palpebral edge pathologies:

- No functional irritation signs;
- No potential conjunctiva and cornea irritancy;
- Lower lacrimal pH acidity rate;
- Preservation of the lacrimal lipid layer.

Good tolerance was confirmed when measuring corneal and conjunctival inflammation markers.

The solutions also corrected the pathogenic cycle efficiently through:

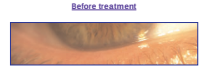
- Palpebral edge lipids reduction;
- Meibomius glands orifice diameter reduction;
- Preservation of the saprophyte conjunctival flora.

Consequently, both solutions tested have highly interesting properties regarding the induction and development of palpebral edge physiopathologies and their application is now being extended to eyelid condition.
However, better results were obtained in terms of efficiency with thermal water which provides a most reliable alternative to the only available treatment up to now for small ophtalmic inflammatory lesions.
The therapeutic properties of the thermal water under study could be related to its unique mineral composition which include selenium, strontium and large amounts of calcium.

Before treatment

Before treatment

After treatment with thermal water



After treatment with thermal water

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* La Roche-Posay thermal water

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L'ORÉAL RECHERCHE