

# Efficacy of bioflavonoid quercetin in treatment of herpetic keratitis patients with dry eye syndrome

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## Keywords:

herpetic keratitis, dry eye syndrome, Lipoflavon

**Introduction.** Dry eye syndrome has drawn a special attention of ophthalmologists not only because of its prevalence but also due to the increased frequency among patients with inflammatory processes in the cornea and conjunctiva.

**Purpose.** To study the effect of bioflavonoid quercetin on the course of the inflammatory process in patients with herpetic keratitis (HK) and dry eye syndrome (DES).

**Material and Methods.** Clinical study involved 40 patients (40 eyes) with HK (superficial keratitis) and DES; in addition, we followed up 17 patients (17 eyes) with HK-only. All patients involved in the clinical study were divided into two groups: Study Group, HK and DES patients receiving bioflavonoid quercetin, containing in Lipoflavon drug, in addition to traditional treatment, 15 patients; Control Group, HK and DES patients receiving only traditional treatment, 25 patients.

**Results.** Clinical study findings showed that the inclusion of bioflavonoid quercetin (Lipoflavon) in the complex treatment of HK patients with DES significantly decreased the intensity of clinical signs and made it possible to decrease the treatment duration. Corneal dendritic ulceration epithelization was observed significantly earlier in patients with HK and SED receiving Lipoflacon as compared to controls, at Day (4.7±0.4) vs. Day (6.8±0.6), respectively; no corneal infiltration was observed at Days (5.5±0.5) and (7.8±0.7) in Study and Control groups, respectively. Schirmer test II values were (10.47±0.83) mm/5 min and (7.36±0.28) mm/5 min in Study and Control groups, respectively. Tear break-up time equaled (6.13±0.32) and (5.24±0.19) s, in Study and Control groups, respectively.

**Conclusions.** Inclusion of bioflavonoid quercetin in the complex treatment of patients with herpetic keratitis and dry eye syndrome significantly increases the therapy efficacy, which is evidenced by accelerated corneal epithelization and infiltrate dispersion and significantly improved qualitative and quantitative characteristics of tear production.

## Introduction

Over the last years, the problem of dry eye syndrome has been of a great importance due to its significant prevalence rate. Today, dry eye syndrome is rightfully considered a disease of civilization. According to the literature, dry eye syndrome is observed in 9-18% of population [2, 5, 10, 15]. Dry eye syndrome has drawn so much attention of ophthalmologists not only because of its prevalence but also due to increased frequency among patients with inflammatory processes in the cornea and conjunctiva. The incidence rate of dry eye syndrome among patients with corneal and conjunctival diseases, according to different authors, varies within 25-96% [1, 4].

Using traditional medications for keratitis treatment does not always lead to patient's cure and recurrence prevention [3, 9, 14, 17].

In this regard, a search for a reasonable etiopathogenic therapy for keratitis and dry eye syndrome is of relevance [11, 12, 13, 16]. In our previous experimental works, bioflavonoid quercetin was found to have a significant therapeutic effect on the inflammatory process in the cornea in the presence of dry eye syndrome in correction of the metabolic state of anterior eye tissues [8]. Experimental data give the rationale for using bioflavonoid quercetin in the clinical practice for herpetic keratitis patients with dry eye syndrome. In addition, our previous studies have revealed that bioflavonoid quercetin, a natural anti-oxidant containing in Lipoflavon drug, decreases the degree of disorders in biochemical characteristics in the tear fluid of patients with herpetic keratitis (HK) and dry eye syndrome

(DES). Therefore, it decreases a destabilizing effect of DES on the corneal epithelium in keratitis [7].

**The purpose** of the present paper was to study the effect of bioflavonoid quercetin on the course of the inflammatory process in HK patients with DES.

### Material and Methods

Clinical study involved 40 patients (40 eyes) with HK (superficial keratitis) and DES; in addition, we followed up 17 patients (17 eyes) with HK-only.

All patients involved in the clinical study were divided into two groups: Study Group, HK and DES patients receiving bioflavonoid quercetin, containing in Lipoflavon drug, in addition to traditional treatment, 15 patients; Control Group, HK and DES patients receiving only traditional treatment, 25 patients.

The state of the anterior eye tissues was scored by criteria that follow: corneal and conjunctival fluorescein staining, tear meniscus, conjunctival injection score, conjunctival discharge, conjunctival folds, corneal edema, corneal infiltration, Schirmer test II, and tear break-up time.

Traditional therapy included anti-herpetic drugs locally and parenterally (aciclovir, valaciclovir, ganciclovir), antiseptics and antibiotics (if indicated), non-steroid anti-inflammatory drugs, mydriatics, tear substitutes, and corticosteroids at a proper stage of the disease.

The SPSS 11.0 package was used to statistically process the data obtained [6].

### Results

A comparative analysis of objective and subjective clinical characteristics in HK-only and HK patients with DES showed that all inflammatory signs were more expressed in HK patients with DES as compared to those in HK patients without DES.

Based on the Table 1 data, all inflammatory signs were lower in HK patients than in HK patients with DES. The difference was significant for such signs studied as: foreign body sensation ( $p=0.001$ ); photophobia ( $p=0.0049$ ); pain sensation ( $p=0.0011$ ); conjunctival discharge ( $p=0.0006$ ); dryness ( $p=0.003$ ) and burning ( $p=0.000$ ) sensation.

Based on the Table 2 data, all clinical signs of the inflammatory process were higher in HK patients with DES. The difference was significant for such signs studied as: conjunctival fluorescein staining ( $p=0.000$ ); conjunctival discharge ( $p=0.0011$ ). Also, qualitative and quantitative characteristics of tear production were significantly decreased in HK patients with DES as compared to those in HK-only patients.

The next stage of our study was to compare the effect of treatment on these signs in HK patients with DES receiving a traditional therapy and in HK patients with DES receiving a complex therapy with bioflavonoid quercetin (Lipoflavon).

The Graph 1 demonstrates the findings of clinical sign analysis in HK patients with DES receiving a traditional therapy in comparison with those receiving a complex therapy with Lipoflavon (Fig. 1).

At Day 7 of treatment, the corneal fluorescein staining score in patients with HK and SED receiving Lipoflavon was less expressed as compared to control, ( $2.33\pm0.29$ ) vs. ( $3.40\pm0.31$ ), respectively; punctate conjunctival fluorescein staining score in Study and Control groups was ( $0.27\pm0.12$ ) and ( $0.84\pm0.15$ ), respectively; the height of tear meniscus in Study and Control groups was equal to ( $1.52\pm0.10$ ) and ( $0.93\pm0.21$ ) mm, respectively; tear break-up time equaled ( $6.13\pm0.32$ ) and ( $5.24\pm0.19$ ) s, in Study and Control groups, respectively; Schirmer test II values were ( $10.47\pm0.83$ ) mm/5 min and ( $7.36\pm0.28$ ) mm/5 min in Study and Control groups, respectively; conjunctival injection in HK and SED decreased to ( $0.27\pm0.12$ ) scores after quercetin treatment compared to ( $0.80\pm0.15$ ) scores in Control group; conjunctival discharge intensity score in Study and Control groups was ( $0.13\pm0.09$ ) and ( $0.52\pm0.10$ ), respectively; the presence of conjunctival folds in HK and DES and Lipoflavon treatment was ( $0.20\pm0.11$ ) scores vs. ( $0.60\pm0.10$ ) scores in Control group; corneal edema was less apparent in Study group as compared to controls, ( $0.13\pm0.09$ ) and ( $0.52\pm0.10$ ), respectively.

Corneal dendritic ulceration epithelization was observed significantly earlier in patients with HK and SED receiving Lipoflavon as compared to controls, at Day ( $4.7\pm0.4$ ) vs. Day ( $6.8\pm0.6$ ), respectively; no corneal infiltration was observed at Day ( $5.5\pm0.5$ ) and ( $7.8\pm0.7$ ) in Study and Control groups, respectively.

### Conclusions

Clinical study findings showed that inclusion of bioflavonoid quercetin (Lipoflavon) in the complex treatment of HK patients with DES significantly decreased the intensity of clinical signs and made it possible to decrease the treatment duration.

1. Inclusion of bioflavonoid quercetin in the complex treatment of patients with herpetic keratitis and dry eye syndrome significantly increases the therapy efficacy, which is evidenced by the time of corneal epithelization and infiltrate dispersion accelerated by 30.8% and 29.5%, respectively, as compared to controls. In addition, corneal edema, epitheliopathy of the cornea and conjunctiva decreased significantly by 25%.

2. Bioflavonoid quercetin has a positive effect on the qualitative and quantitative characteristics of tear production, which is evidenced by increased Schirmer test values, increased tear break-up time, decreased conjunctival folds, increased tear meniscus height, by 29.7%, 14.5%, 66%, and 38.8%, respectively, as compared to those in patients receiving the traditional treatment without bioflavonoid quercetin

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**Table 1.** Subjective clinical signs with complaints of patients with herpetic keratitis (HK) and dry eye syndrome (DES) before treatment

Clinical signs	HK (n=17)			HK+DES (n=40)			P
	M	SD	m	M	SD	m	
Redness of the eye	1.82	0.53	0.13	2.38	0.54	0.09	0.007
Foreign body sensation	1.53	0.51	0.12	2.10	0.59	0.09	0.001
Photophobia	2.06	0.43	0.10	2.50	0.55	0.09	0.0049
Pain sensation	0.41	0.51	0.12	0.83	0.38	0.06	0.0011
Conjunctival discharge	1.47	0.51	0.12	1.88	0.33	0.05	0.0006
Dryness sensation	0.35	0.49	0.12	0.85	0.58	0.09	0.003
Burning sensation	0.71	0.47	0.11	1.65	0.48	0.08	0.000

**Table 2.** Objective clinical signs in patients with herpetic keratitis (HK) and dry eye syndrome (DES) before treatment

Clinical signs	HK (n=17)			HK+DES (n=40)			p
	M	SD	m	M	SD	M	
Corneal fluorescein staining	3.53	1.33	0.32	6.35	1.69	0.27	0.000
Conjunctival fluorescein staining	0.29	0.59	0.14	1.93	0.69	0.11	0.000
Tear break-up time	4.65	1.17	0.28	3.60	0.93	0.15	0.0007
Schirmer test II	13.41	3.08	0.75	7.08	2.97	0.47	0.000
Conjunctival injection score	2.29	0.47	0.11	2.70	0.52	0.08	0.0071
Conjunctival discharge	1.41	0.51	0.12	1.83	0.38	0.06	0.0011
Conjunctival folds	0.35	0.49	0.12	1.25	0.67	0.11	0.000
Corneal edema	1.59	0.62	0.15	2.10	0.67	0.11	0.0095
Corneal infiltration	2.06	0.90	0.22	2.75	1.01	0.16	0.0182

**Table 3.** Objective clinical signs in patients with herpetic keratitis (HK) and dry eye syndrome (DES) receiving the traditional therapy-only and the complex treatment with bioflavonoid quercetin

Clinical signs	HK + DES traditional therapy (n=25)			HK + DES traditional therapy + quercetin (n=15)			P
	M	SD	m	M	SD	M	
Corneal fluorescein staining	3.40	1.53	0.31	2.33	1.11	0.29	0.0237
Conjunctival fluorescein staining	0.84	0.75	0.15	0.27	0.46	0.12	0.0116
Tear meniscus height	0.93	0.51	0.10	1.52	0.80	0.21	0.0069
Tear break-up time	5.24	0.97	0.19	6.13	1.24	0.32	0.0157
Schirmer test II	7.36	1.38	0.28	10.47	3.23	0.83	0.0001
Conjunctival injection score	0.80	0.76	0.15	0.27	0.46	0.12	0.0195
Conjunctival discharge	0.52	0.51	0.10	0.13	0.35	0.09	0.0129
Conjunctival folds	0.60	0.50	0.10	0.20	0.41	0.11	0.0128
Corneal edema	0.52	0.51	0.10	0.13	0.35	0.09	0.0129
Інфільтрат рогівки	0.56	0.51	0.10	0.13	0.35	0.09	0.0065

