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The Effectiveness of Ganciclovir Comparing with Combination Therapy of Oxytetracycline HCl+Polymyxin B Sulfate in Herpetic Epithelial Keratitis

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Abstract

Background: Herpes simplex virus is a common keratitis agent. There are two different types of virus, type 1 and 2. Type 1 shows three main clinical pictures in cornea: epithelial herpetic keratitis, stromal keratitis, disciform keratitis.

Aims: The aim of this study is to reduce the duration of herpetic keratitis treatment, eliminate the risk of complications, minimize the cost of treatment, and increasing the quality of patients.

Study design: Prospective study.

Material and methods: Between January 2017 and January 2018, 29 patients with herpetic keratitis were included in the study. In the first group, the herpetic membrane was removed by a single shot on the herpetic lesion with the yag laser. Then topically oxytetracycline hydrochloride+polymyxin B sulfate was applied. The second group was treated with topical antiviral therapy (Ganciclovir). After treatment, daily follow-up of patients, vision, tonus, fundus diameters and recovery times were noted, and the data were compared statistically.

Results: In group I and group II, the age of the patients did not differ significantly ($p>0.05$). In group I and group II, the gender distribution of the patients did not differ significantly ($p>0.05$). In Group I and Group II, the degree of vison did not differ significantly ($p>0.05$). In group I and group II, the examination findings were not significant ($p>0.05$). In group I and group II, recovery time was significantly different ($p<0.05$).

Conclusion: In our study, the duration of herpetic keratitis treatment was very short as 4.5 days and no significant difference was observed between control vision, tonus, fundus diameter parameters and antiviral topical treatment ($p<0.05$). Although this result of the treatment showed the same efficacy as the antiviral treatment, we proved this effectiveness in a very short time.

Keywords: Herpetic epithelial keratitis; Ganciclovir; Oxytetracycline HCl + polymyxin B sulfate

Introduction

The herpes simplex virus (HSV) is a DNA virus that is a member of the herpesviridae family, and naturally it can only infect humans. Herpes simplex is an enveloped virus that contains lipid and glycoprotein structures. With this feature, envelopes can be broken with chemical factors. HSV type 1 is seen in the face and eyes, HSV type 2 causes herpetic disease in the genital area. HSV type 1 causes infection 6 months-5 years between the period of kissing. HSV is transmitted through close contact and saliva and cause primary infection. Primary infection is subclinical with general symptoms of viral diseases in 85%-99% of cases. HSV type 1 can form 3 main clinical pathologies in cornea: a) epithelial herpetic keratitis (EHK), b) stromal keratitis, c) disciform keratitis. The incidence of ocular herpes is reported as 5.9%-12% and the majority of these are EHC. Herpes simplex virus-induced keratitis (HSK) is one of the leading causes of corneal blindness in the world [1]. The primary infection occurs after direct contact of the mucosal membrane with herpes simplex virus-1 (HSV-1). Clinical pictures of the virus occur as a result of destruction of the cornea [2,3]. The virus then latent in the trigeminal ganglion and leads to recurrent infections [1,4]. There are factors such as age, poor hygiene and socioeconomic class in the etiology [5]. Ocular HSV-1 infection is associated with a wide range of ocular pathologies like conjunctivitis, keratitis, iridocyclitis and acute retinal necrosis [6]. HSV is a common viral cause of corneal disease and is one of the leading causes of infectious corneal blindness in developed countries [5]. Visual loss is most commonly seen in more severe cases with stromal opacification and corneal ulceration [6].

Antiviral agents are the most preferred treatment for HSV epithelial keratitis. Both topical and oral agents are available. Regarding topical agents, both the ganciclovir gel and the trifluridine solution were approved by the FDA [5]. Acyclovir and trifluridine ointment have similar efficacy [5] and the same efficacy has been demonstrated when acyclovir ointment compared with ganciclovir gel [5]. The recommended treatment for HSV stromal keratitis includes an oral antiviral agent in combination with a topical corticosteroid agent for at least 10 weeks.

The aim of this study is to reduce the duration of herpetic keratitis treatment and eliminate the risk of complications.

Materials and Methods

Between January 2017 and January 2018, 29 patients with herpetic keratitis were included in the study. The patients were recruited from Adana Ortadoğu Hospital. There are 14 patients in the first group and there are 15 patients in the second group. In group I, the herpetic membrane was removed by a single shot on the herpetic lesion with the yag laser. Then, topically oxytetracycline hydrochloride+polymyxin B sulfate was applied. The second group was treated with topical antiviral therapy (Ganciclovir). After treatment, daily follow-up of patients, vision, tonus, fundus diameters and recovery times were noted and the data were compared statistically. Statistical method: Mean, standard deviation, median lowest, highest, frequency and ratio values were used in descriptive statistics of the data. The distribution of the variables was measured with the Kolmogorov simirnov test. Independent samples t-test, mann-whitney u test were used for the analysis of quantitative independent data. Chi-square test was used for the analysis of qualitative independent data. SPSS 22.0 program was used in the analysis.

Results

Demographic information of the study sample is shown in Table 1.

There are 14 patients in the group I and there are 15 patients in the group II. In group I and group II, the age of the patients did not differ significantly ($p>0.05$). In group I and group II, the gender distribution of the patients did not differ significantly ($p>0.05$). Group I and group II showed no significant difference in terms of age and gender ($p>0.05$). In Group I and Group II, the vision value did not differ significantly ($p>0.05$) (Table 2 and Figure 1). In group I and group II, the diagnostic value was not significant ($p>0.05$). In group I and group II recovery time.

		Min-Max	Median	Mid ± s.s/n-%	
AGE		27.0-73.0	47.0	47.5 ± 14.1	
GENDER	Female			15	51.7%
	Male			14	48.3%
Eye Sides	Right			13	44.8%
	Left			16	55.2%
vo To Healing Days		1.0-9.0	4.0	4.3 ± 2.2 16.1 ± 2.9 9.0 ± 4.9	
		11.0-21.0	16.0		
		2.0-19.0	9.0		
Fun	Normal			29	100.0%
	1×1 mm			1	3.4%
	1×3 mm			1	3.4%
	2×1 mm			1	3.4%
Size	2×2 mm			3	10.3%
	2×3 mm			1	3.4%
	3×1 mm			4	13.8%
	3×2 mm			5	17.2%
	3×3 mm			2	6.9%
	3×4 mm			1	3.4%
	4×2 mm			5	17.2%
	4×3 mm			3	10.3%
	6×4 mm			1	3.4%
	6×5 mm			1	3.4%

Table 1: Demographic variables and examination findings.

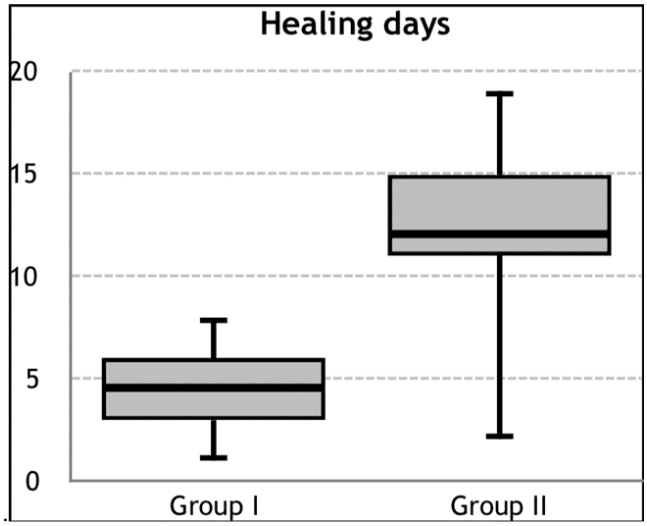

Figure 1: Treatment duration.

		Group 1		Group2		p
		Mid ± s.s/n %	Median	Mid ± s.s/n %	Median	
Age		48.1 ± 13.7	46.5	46.9 ± 14.8	47.0	0.822 ţ
Gender	Female	7	50.0%	8	53.3%	0.858 χ2
	Male	7	50.0%	7	46.7%	
Eye sides	Right	7	50.0%	6	40.0%	0.588 χ2
	Left	7	50.0%	9	60.0%	
vo		4.5 ± 2.4	4.0	4.1 ± 2.1	4.0	0.756 m
to		16.4 ± 2.4	16.5	15.8 ± 3.3	15.0	0.599 m
Healing Days		4.6 ± 1.6	4.5	13.1 ± 2.8	12.0	0.000 m

Table 2: The comparison of group I and group II.

Discussion and Conclusion

HSV is known to cause wide spectrum of medical conditions that mostly include central nervous system, eye, mouth, and genitalia. HSV-1 is the most common cause of infectious keratitis around the world and it usually impairs the quality of life [1,2]. HSV epithelial keratitis can be primary or recurrent infection. Primary eye infection may occur with or without blepharoconjunctivitis. Recurrent epithelial keratitis can be due to the reactivation of previous epithelial or nonepithelial HSV [3,4]. Primary infection is mostly seen in early childhood. HSV-1 moves into the mucous membrane and epithelial cells of patient by direct contact. The virus goes retrograde through axons to reach trigeminal ganglia and it develops latency in the ganglia. On the other hand, cornea has been reported to be an area of latency. Although there have been debates on the reactivity of the virus, fever, ultraviolet light, contact lens wear, use of prostaglandin eye drops, new eye surgery and the causes of immunosuppressive therapy, HSV has been linked to the reactivation of epithelial keratitis. Reactivation may induce different types of keratitis different from the initial presentation [7-9]. HSV epithelial keratitis is usually the most painful type of keratitis and it has vesicles and itching. Other symptoms include photophobia, blurred vision, redness, burning, foreign body sensation, tearing, conjunctival injection, and decreased vision. These findings refer the patient to an ophthalmologist. The diagnosis is made by slit-lamp examination. Dendritic and geographic ulcers are two types of HSV epithelial keratitis. They are simply recognizable with typical pattern after fluorescein staining. This characteristic feature almost always eliminates further tests like culture, PCR, immunofluorescence assay (IFA), and immunochromatographic assay, which may be used for the other types of herpetic eye disease [9]. Currently, trifluridine (TFT), ganciclovir (GCV), and acyclovir (ACV) are available topical medications, and ACV, valacyclovir (VACV), and famciclovir (FCV) are the most accessible systemic antivirals. Oral ACV, TFT, and topical GCV have been equally effective to treat HSV epithelial keratitis. After being phosphorylated and activated by viral thymidine kinase, all of these medications inhibit viral DNA replication. Based on the disease condition, either topical or systemic antivirals are used for the treatment of HSV epithelial keratitis. Topical antivirals and oral ACV have shown almost similar therapeutic effects for years. A combination of topical and systemic antivirals or even augmenting treatment with epithelial debridement was reported. It is unclear whether these modalities can fortify the treatment [9].There are different recommendations on the necessity of debridement in ophthalmology books in the treatment of the disease, which is an important cause of blindness, such as herpetic keratitis. In some books, it is recommended to start treatment with topical antiviral drugs (trifluorothymidine, acyclovir, ganciclovir, bromovinyldeoxyuridine) in the treatment of EHC. There is a consensus that tropical antiviral agents such as trifluridine, acyclovir and recently ganciclovir have improved epithelial herpetic keratitis by up to 90% within two weeks. The current treatment guidelines [5] spread the herpetic keratitis treatment over a long period of 10 weeks, but the sociocultural levels of patients were generally low for a period of 10 weeks, and the length of the treatment period reduced the rate of treatment use in patients and increased the likelihood of recurrence. Therefore, a treatment method and treatment agent is needed for herpetic keratitis to be effective in a shorter time [7,8]. In our study, the duration of herpetic keratitis treatment was very short as 4 days and no significant difference was observed between control vision, tonus, fundus diameter parameters and antiviral topical treatment. Although this result of the treatment with the same efficacy as the antiviral treatment, we proved this effectiveness in a very short time.

References

1. Darougar S, Wishart MS, Viswalingam ND (1985) Epidemiological and clinical features of primary herpes simplex virus ocular infection. Br J Ophthalmol 69: 2-6.
2. Liesegang TJ, Melton LJ, Daly PJ, Ilstrup DM (1989) Epidemiology of ocular herpes simplex: incidence in Rochester, Minn, 1950 through 1982. Arch Ophthalmol 107: 1155-1159.
3. Tang Q, Chen W, Hendricks RL (1997) Proinflammatory functions of IL-2 in herpes simplex virus corneal infection. J Immunol 158: 1275-1283.
4. Tsatsos M, MacGregor C, Athanasiadis I, Moschos MM, Hossain P, et al. (2016) Herpes simplex virus keratitis: an up- date of the pathogenesis and current treatment with oral and top- ical antiviral agents. Clin Exp Ophthalmol 44: 824-837.

5. White ML (2014) Chodosh J Herpes simplex virus keratitis; A Treatment Guideline.
6. Farooq AV, Shukla D (2012) Herpes simplex epithelial and stromal keratitis: an epidemiologic update. Surv Ophthalmol 57: 448-462.
7. Miserocchi E, Modorati G, Galli L, Rama P (2007) Efficacy of valacyclovir vs. acyclovir for the prevention of recurrent herpes simplex virus eye disease: A pilot study. Am J Ophthalmol 144: 547-551.
8. Chong DY, Johnson MW, Huynh TH, Hall EF, Comer GM, et al. (2009) Vitreous penetration of orally administered famciclovir. Am J Ophthalmol 148: 38-42.
9. Roozbahani M, Hammersmith KM (2018) Management of herpes simplex virus epithelial keratitis. Curr Opin Ophthalmol 29: 360-364.