

A Clinical Study of Herpes Zoster Ophthalmicus

Dr. Anitha.S.Maiya¹, Dr. Sundip Shenoy².

^{1,2} (Department of Ophthalmology/ Adichunchanagiri Institute of Medical Sciences/RGUHS/ India)

Abstract: Background: Herpes Zoster Ophthalmicus(HZO) occurs from the reactivation of latent Varicella Zoster virus within the ophthalmic division of the Trigeminal nerve. Ophthalmic involvement has been considered the most important and potentially serious of all sites of Herpes Zoster. **Objectives:** 1.To study the modes of presentation and ocular manifestations of HZO. 2.To study the predisposing factors for the development of HZO. 3.To study the ocular complications of HZO after treatment with oral Acyclovir during a follow-up period of one year. **Materials and Methods:** This prospective clinical study was conducted with all patients who were clinically diagnosed to have HZO who attended the Outpatient Department of Ophthalmology. All the patients underwent a comprehensive ocular examination and were medically treated and followed up for one year. **Results:** 27 patients with HZO were studied. Advancing age was the most common predisposing factor. Acute neuralgia and skin lesions were the most common modes of presentation. Ocular involvement was seen in 16(59.25%) of the patients with HZO. Cornea was the most common ocular structure involved(62.5%). **Conclusion:** The potential ocular manifestations of HZO are numerous. Ocular complications were less frequent among patients who received prompt systemic antiviral therapy with oral Acyclovir started within 72 hours of skin rash. Among treated patients development of a serious inflammatory complication was associated with a delay in therapy.

Keywords: Acyclovir, Herpes Zoster, Herpes Zoster Ophthalmicus, Varicella Zoster virus.

I. Introduction

Both Varicella (Chicken pox) and Herpes Zoster(shingles) are caused by the Varicella-Zoster virus(VZV). Herpes Zoster (HZ) results from the reactivation of the VZV which remains latent in the primary sensory ganglion like Gasserian ganglion. HZ involving the Ophthalmic division of the Trigeminal nerve is called Herpes Zoster Ophthalmicus(HZO), irrespective of the presence or absence of ocular involvement.[1,2,3] The annual incidence of HZ is 1.2-3.4/1000 persons. Among all cases of HZ, the reported incidence of ophthalmic involvement ranges from 8-56% in various studies.[4] Upto 20% of the population will have HZ at sometime in life. HZO is second only to thoracic zoster in frequency.[5] Within the ophthalmic division of the trigeminal nerve, the frontal branch is most often involved. Approximately 50-72% of the patients with periocular zoster will have ocular involvement and sustain a moderate to severe degree of visual loss.[6] HZ is more likely to occur in older individuals who have a linear decrease in cell-mediated immunity. Immunosuppressed organ transplant recipients, immunodeficient patients with cancer, leukemia and AIDS are at increased risk of HZ.[5]

HZO usually presents with a prodrome of systemic symptoms – lancinating headache, malaise, fever, chills and occasionally stiffness of the neck – followed within days by localized neuralgic pain over the involved dermatome. Within 2-3 days of neuralgia multiple crops of clear vesicles erupt. The vesicles then become turbid and yellow and form deep eschars that commonly leave behind permanent pitted scars over the involved dermatome.[7]

The potential ocular manifestations of HZO are myriad and result from direct viral invasion, secondary inflammation and vasculitis, nerve damage and/or tissue scarring. Reported complications of HZO include lid vesicles and scarring, several forms of conjunctivitis and keratitis, episcleritis, scleritis, uveitis, secondary glaucoma, papillary abnormalities, acute retinal necrosis, optic neuritis, CRAO, cranial nerve palsies (III>VI>IV), orbital apex syndrome, localized arteritis and post herpetic neuralgia.[8]

With the above background, the present study was started with the following objectives:

1. To study the modes of presentation and ocular manifestations of HZO.
2. To study the predisposing factors for the development of HZO.
3. To study the ocular complications of HZO after treatment with oral Acyclovir during a follow-up period of one year.

II. Materials And Methods

This prospective clinical study was conducted with all patients who were clinically diagnosed to have HZO who attended the Outpatient Department of Ophthalmology. Ethical clearance for the study was obtained from the Institutional ethical committee.

A standard clinical proforma which included history, clinical findings and laboratory investigations was used in all cases. Those patients in whom diagnosis of HZO was uncertain or who refused to come for regular follow up were excluded from the study.

All patients underwent a comprehensive ocular examination which included visual acuity assessment(using Snellen's chart), detailed slit lamp examination(including fluorescein and/or Rose Bengal staining) and posterior segment examination.

The laboratory investigations included routine urine examination, complete haemogram, random/fasting blood sugar levels, Western blot test for HIV 1 and 2 and renal function tests.

All patients were treated medically. The patients were treated with oral Acyclovir 800mg 5 times/day for 10 days and systemic Non-steroidal anti-inflammatory drugs like Diclofenac or Ibuprofen. The skin lesions were treated with cool compresses, calamine lotion and topical antibiotic ointment(silver sulphadiazine). Patients with no ocular involvement or with only conjunctivitis were treated with lubricating eye drops. patients with keratitis were treated with topical Acyclovir 3% eye ointment 5 times/day, prophylactic topical antibiotics and cycloplegics(Atropine 1% or Homatropine 2% eye drops). Patients with uveitis received topical steroids(commonly Prednisolone acetate 1% eye drops) and topical cycloplegics which were tapered according to the clinical response. In patients with raised IOP, oral Acetazolamide 250mg 3 times/day for 3 days and Timolol maleate 0.5% eye drops 2 times/day was used. Patients were followed up at regular intervals for atleast one year depending on the severity of involvement and the response to treatment was evaluated.

III. Results

A total of 27 patients who fulfilled the inclusion and exclusion criteria were studied and the following observations were made:

Table 1. Age wise distribution of cases.

Age in years	Number of cases	Percentage
0-10	0	0
11-20	1	3.7
21-30	2	7.4
31-40	4	14.8
41-50	5	18.5
51-60	10	37.0
61-70	2	7.4
71-80	2	7.4
81-90	1	3.7
91-100	0	0

In this study, it was found that the maximum incidence of HZO was in the age group of 51-60 years(37%).



Fig 1. Vesicular skin eruptions of HZO showing dermatomal distribution.

Table 2. Sex distribution, predisposing factors, presenting symptoms, ocular involvement and laterality of HZO.

		Number of cases	Percentage
Gender distribution	MALE	12	44.44
	FEMALE	15	55.56
Predisposing factors for HZO	Age >50 years	15	55.56
	Diabetes mellitus	2	7.4
	HIV	3	11.1
	Malaria	1	3.7
	No predisposing cause	10	37.0
Presenting symptoms of HZO	Neuralgia	27	100
	Skin rash	27	100
	Watering	9	33.3
	Lid swelling	5	18.5
	Diminution of vision	10	37.0
Ocular involvement in HZO	Present	16	59.25
	Absent	11	40.75
Laterality of HZO	Right side involved	15	55.56
	Left side involved	12	44.44

In this study, among the 27 patients, 10 patients (37%) had no predisposing cause for the development of HZO. Among the remaining patients, age>50 years was the most common cause. In this study, skin lesions and acute neuralgia were the most common presenting symptoms which was present in all 27 of the patients studied(100%). Ocular symptoms were seen in 17 patients (62.96%). In this study, patients with HZO showed predominance of involvement in the right eye (55.56%) as compared to left eye (44.44%). No patient had bilateral involvement. In this study, 16 patients (59.25%) had some form of ocular or adnexal involvement. In 11 patients (40.75%) no ocular or adnexal involvement was found.

Table 3. Ocular structures involved in HZO.

Ocular structure involved	Number of cases	Percentage
Lids	3	18.75
Conjunctiva	2	12.5
Cornea	10	62.5
Episclera	1	6.25
Sclera	0	0
Uveal tract	6	37.5
Secondary glaucoma	3	18.75
Lens	0	0
Vitreous	0	0
Retina	0	0
Optic nerve	0	0
Extraocular muscles	0	0
Orbit	0	0

In our study, Cornea stood out as the most common ocular structure involved (62.5% of cases) followed by the uveal tract (in 37.5% cases).

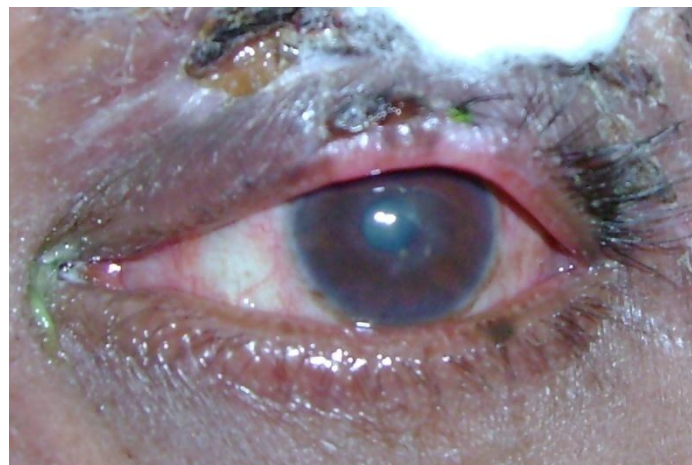


Fig 2. Resolving Disciform keratitis

Table 4. Ocular complications seen among HZO patients in the present study.

Complication	Number of cases	Percentage(%)
Lid vesicles	2	12.5
Cicatricial ectropion with ptosis	1	6.25
Follicular conjunctivitis	2	12.5
Punctuate epithelial keratitis	5	31.25
Nummular keratitis	2	12.5
Disciform keratitis	1	6.25
Keratouveitis	1	6.25
Episcleritis	1	6.25
Anterior uveitis	6	37.5
Secondary glaucoma	3	18.75
Postherpetic neuralgia	4	14.8

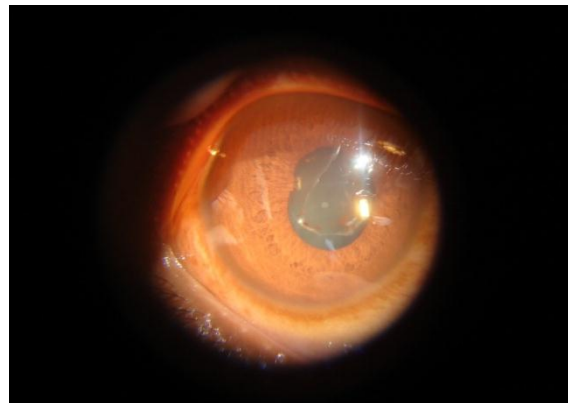


Fig 3. Showing posterior synechiae due to HZO Uveitis

In this study, 9 patients (33.3%) had a substantial visual loss(. 8 patients (29.62%)had mild visual impairment(Best corrected visual acuity of <6/18). In 5 of these patients, senile immature cataract also contributed to the visual impairment. 1 patient (3.71%) had severe visual impairment secondary to severe keratouveitis.

IV. Discussion

HZO is a severe, painful and debilitating ocular disease and is of interest to the clinician because of its potential for causing substantial visual loss and socio economic disability.

27 patients with HZO were studied and the following inferences were made:

In our study, 15 patients(55.56%) were females and 12 patients (44.44%) were males thereby suggesting a female preponderance. This correlates with the study by Womack LW et al in which there was a female preponderance.[9]

In our study it was observed that HZO occurred maximally (62.9%) in the fifth to seventh decades of life with peak incidence in the sixth decade (37%). This suggests that advancing age is the most common predisposing factor for the development of HZO, due to linear age related decrease in the cell mediated immunity. Various reports on HZO show a peak incidence in the fifth to eighth decades of life.[9,10]

3 of our patients (11.1%) tested positive for HIV infection, 2 of whom were in the 31-40 years age group. This could suggest that ophthalmologists should maintain a high index of suspicion of HIV infection in HZO patients less than 50 years of age in the absence of other predisposing factors.

In our study, of the 27 patients with HZO, 16 patients(59.25%) had ocular involvement. In the Mayo clinic and other studies of HZO, 50-72% had ocular involvement.[9,11]

Among the various ocular structures involved, corneal involvement was the most common and occurred in 10 patients(62.5%). In a study by Liesegang T., corneal complications were seen in 65% of all the cases of HZO.[4]

It was observed that in the 11 patients (40.75%) of HZO without ocular involvement, oral Acyclovir was started within 72-96 hours of onset of skin rash. This correlates with two prospective controlled clinical trials which have reported a beneficial effect of Acyclovir on ocular complications of HZO. [12,13,14,15,16]

These data may suggest that early systemic antiviral therapy for acute HZO may decrease the probability of subsequent visual loss.

The limitation of this study is the small sample size, but it can be explained by the fact that HZO is not a very commonly occurring ocular disease as understood by its low incidence in the community.

V. Conclusion

HZO is an often devastating ocular disease and may virtually involve any ocular structure. The frequency with which ophthalmologists will be asked to evaluate and treat patients with HZO is likely to increase in the near future as both the number of immunocompromised patients and the segment of population above the age of 50 years is expected to grow significantly.

In view of the potentially serious long term complications of HZO, appropriate and timely treatment is required. Antiviral medications like Acyclovir, Valacyclovir and Famciclovir remain the mainstay of therapy and are effective in preventing serious ocular complications of HZO when begun within 72 hours of onset of skin rash. Hence, timely diagnosis and prompt management of HZO are critical in limiting the ocular morbidity. In the future, a reduction in the incidence and severity of HZO may result from a more widespread use of Varicella vaccine in an effort to obtain herd immunity.

References

- [1]. Kanski JJ., Cornea, Chapter 5. In: *Clinical Ophthalmology*. 5th edition., (Edinburgh:Butterworth Heinemann; 2003).p111-114
- [2]. Wilson FI. Varicella and Herpes Zoster ophthalmicus. Chap. 25 In : Tabbara K, Hyndiuk R eds. *Infections of the eye* 2nd edition.(Bosten:Little, Brown, 1996):387-400.
- [3]. Deborah Pavan-Langston. Herpes Zoster Ophthalmicus. *Neurology* 1995;45(suppl 8):S50-S51.
- [4]. Schmader KE. Epidemiology of Herpes Zoster. In: Arvin AM, Gershon AA.Eds. *Varicella-Zoster virus: Virology and clinical management*. (Cambridge.UK: Cambridge University Press;2000).p.220-245
- [5]. Liesegang TJ. Corneal complications from Herpes Zoster Ophthalmicus. *Ophthalmology*. 1985;92:316-324
- [6]. Deborah Pavan-Langston.Viral diseases of the ocular anterior segment. Chap 14. In:Foster CS., Azar DT., Dohlman CH.eds. *Smolin and Thoft's. The cornea. Scientific foundations and clinical practice*. 4th edn.(Philadelphia:Lippincott Williams and Wilkins 2005); p297-397.
- [7]. Pavan –Langston D. Viral disease of the cornea and external eye. In: Albert D., Jakobiec F., eds. *Principles and practice of Ophthalmology*. 2nd edn. (Philadelphia : WB Saunders, 2000):846-893.
- [8]. Christopher E. Starr., Deborah Pavan-Langston.Varicella Zoster virus: Mechanisms of pathogenicity and corneal disease. *Ophthalmol Clin N Am*. 2002; 15:7-15
- [9]. Womack L., Liesegang TJ. Complications of Herpes Zoster Ophthalmicus. *Arch Ophthalmol*.1983;101:42-45.
- [10]. McLeod SD. Infectious keratitis. Chapter 62. In: Yanoff M., Duker JS eds. *Ophthalmology*, 2nd edn. (St. Louis:Mosby;2004):p 479-481.
- [11]. Miserocchi E., Waheed NK., Dios E.,Christen W., Merayo J., Roque M., et al. Visual outcome in Herpes simplex virus and varicella zoster virus uveitis : a clinical evaluation and comparison *Ophthalmology*.2002 Aug;109(8):1532-1537.
- [12]. Cobo LM., Foulks GN., Liesegang TJ.,Lass J, Sutphin JE, Wilhelmus K et al. Oral Acyclovir in the treatment of acute HZO. *Ophthalmology* 1986;93:763-770.
- [13]. Severson E., Baratz EA., Hodge DO.,Burke JP. Herpes Zoster Ophthalmicus in Olmsted county, Minn: have systemic antivirals made a difference ?. *Arch Ophthalmol* 2003;121:386-390.
- [14]. Cobo LM, Reduction of the ocular complications of Herpes zoster Ophthalmicus by oral acyclovir. *Am J Med*. 1998;85(suppl 2A):90-93.
- [15]. Wood M J., Shukla S., Fiddian AP.,Crooks RJ. Treatment of acute herpes zoster : Effect of early versus late therapy with Acyclovir and Valaciclovir on prolonged pain. *J Infect Dis* 1998;178(Suppl 1):s81-s84.
- [16]. Hoand-Xuan T., Buchi ER., Herbert CP., Denis J, Frot P, Thenault S, et al. Oral acyclovir for HZO. *Ophthalmology* 1992;99:1062-1071.