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Original Research Article

A Prospective Study to Observe Ocular Outcome and Clinicoepidemiological Pattern in Herpes Zoster Ophthalmicusat District Hospital in Hilly Area in India

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Abstract: The pattern of ocular involvement in patients of Herpes Zoster Ophthalmicus (HZO) is varied presenting from blepharo conjunctivitis seen most frequently to acute retinal or progressive outer retinal necrosis seen rarely which can also be sight threatening. To study the various ocular manifestations in patients of herpes zoster ophthalmicus presenting to skin opd in a District Hospital set up. a longitudinal cross sectional study of patients diagnosed of HZO, referred from Skin ODP, was done over a period of two years and their pattern of ocular involvement studied after a complete ophthalmological check up. There were 81 patients of HZO who presented to skin OPD over a period of two years and all of them were referred to eye OPD, where 73 were included in the study. 48 patients were male and 25 patients were female. The mean age at presentation was 55.2 ± 10.5years.Out of these 65 (89.04%) patients had some form of ocular involvement. The commonest presenting symptom was pain seen in 52 (72.23%) patients. The commonest form of ocular involvement was blepharo conjunctivitis followed by keratitis and uveitis. Regular and complete ophthalmological checkup of all patients of HZO presenting to skin OPD needs be done in order to prevent or timely treat any ocular involvement and also to detect sight threatening complication at the earliest.
Keywords: Herpes zoster, Blepharo conjunctivitis, Keratitis.

INTRODUCTION

Herpes Zoster Ophthalmicus (HZO) (also known as Shingles) is caused by the reactivation of the herpes virus type 3 lying dormant in the trigeminal ganglia. HZO occurs when the ophthalmic division of the trigeminal nerve is affected. The risk of reactivation is increased with advancing age, immunosuppression, HIV, tuberculosis and malignancy. Stress either physical or emotional can also precipitate an attack. The onset of HZO is as with other forms of herpes zoster characterized by a prodrome of malaise fever or fatigue lasting for a week or so after which the typical rash appears which strictly obeys the midline. The rash goes through the typical phase of macule, papule, vesicle and later pustule which forms a crust and heals completely over a few weeks. The ocular manifestations of HZO arise from involvement of either of the branches of ophthalmic division of the trigeminal nerve namely the supraorbital(frontal), lacrimal or nasociliary. The virus damages the eye and surrounding structures by secondary intraneural and perineural inflammation of sensory nerves. The aim of the present study was to study the pattern of ocular involvement in patients of HZO presenting to skin OPD and also to emphasize the need of complete ophthalmological check up in patients of HZO so that visual threatening complications could be avoided or treated at the earliest.

MATERIAL AND METHODS

A longitudinal cross sectional study was conducted at a District Hospital (Deen Dayal Upadhyay Hospital, Shimla) w.e.f 1st January 2015 to 31st December 2016. During this time period all patients of herpes zoster ophthalmicus (HZO) were selected out of total patients of herpes zoster who were subjected to detailed clinical examination. Patient was diagnosed to be having HZO when there was unilateral predominantly, grouped vesicular lesions associated with dysesthesia involving the ophthalmic dermatome. the division of ophthalmic nerve involved was labelled according to distribution as

shown in Fig.1. Frontal branch involvement was labelled if lesions were found on scalp, conjunctiva upper eyelid, medial part of upper eyelid, medial part of forehead or root of nose. Lacrimal branch involvement showed lesions on superior lacrimal gland, lateral part of superior eyelid. Involvement of nasociliary branch was labelled if lesions on medial angle of eye, upper and lower half of nose were present.

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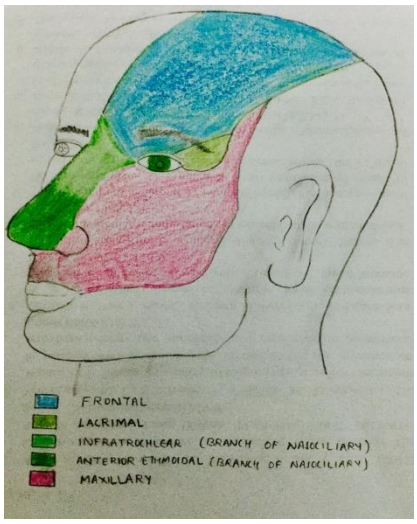

Fig-1: Depicting the distribution of various divisions of ophthalmic branch of trigeminal nerve.

Comorbidities like diabetes, hypertension, human immunodeficiency virus infection, etc were noted. Detailed history of the patients was taken and complete examination (general and local) was done. Relevant tests were carried out wherever necessary. Patients were referred for ophthalmological examination. Adenexal examination, ocular motility assessment, Snellen best corrected visual acuity, visual axis, pupillary reaction, fluorescein test, slit lamp examination for veiwing anterior segment and slit lamp biomicroscopy for posterior segment. In adnexal examination lid edema, rash, conjunctival injection, blepharo conjunctivitis was recorded. Corneal sensation were tested by cotton wisp and graded as normal, reduced or absent in comparison to contralateral uninvolved eye. Non contact tonometry was done for all patients. Intraocular pressure was labelled as raised if it was ≥22 mm Hg. Uveitis was defined as presence of free cells in anterior chamber. All patients received oral acyclovir in a dose of 800mg 5 times a day. Patients were reviewed after 1 ,3 and 6 month. Patients with healed lesions of herpes zoster ophthalmicus and with previous history suggestive of eye disease like keratitis, chronic uveitis , cataract and glaucoma were excluded from the study

RESULTS

A total of 368 patients of herpes zoster presented to the skin OPD during the period of study of which there were 81(22.01 %) patients of HZO. Of these 8 patients were excluded 2 patients had healed lesions, two had glaucoma, three had associated cataract. There was a single patient of post traumatic corneal opacity and congenital blindness. A total of 73 patients who were included in the study.Of these 48were males and 25 females as summarised in Table 1.

Table-1: Age and sex distribution of patients

Age group in years	male	female	Total	%age
<40	4	3	7	9.5
41-50	8	5	13	17.8
51-60	20	9	29	39.7
61-70	9	3	12	16.4
71-80	5	4	9	12.3
>81	1	1	2	2.7
total	48	25	73	

The mean age of the patients was55.2 ± 10.5 years. Maximum patients were above 50years. The youngest patient was 34 years old and the eldest 85 was years old. The patient distribution was as presented in Table 1.The various branches of ophthalmic division of trigeminal nerve involved in decreasing order of frequency were frontal in all patients followed by nasociliary and lacrimal. The results are presented in Table 2.

Table-2: Distribution of branches of ophthalmic nerve involved

Dermatome involved	number	percentage
frontal	73	100
lacrimal	26	35.6
nasociliary	29	39.7

There were 38.3%(28cases) of the patients who presented to us within 5 days of onset of vesicular lesions, 54.8%(40cases) presented in 6-9 days of onset of lesions and 6.8 % (5cases) presented after 9 days but before healing of lesions. HZO had comorbid conditions in 28 (38.35%) patients as shown in table 3 . Diabetes was found to be the commonest association seen in 19.2 %cases. There was one patient of chronic liver disease. The various co-morbid conditions are as depicted in table3.

Table 3: Co-morbid conditions

Diseases	number	percentage
diabetes	14	19.2
HIV	3	4.1
Tuberculosis	6	8.2
malignancy	1	1.4
Immuno supressive drugs	3	4.1
others	1	1.4

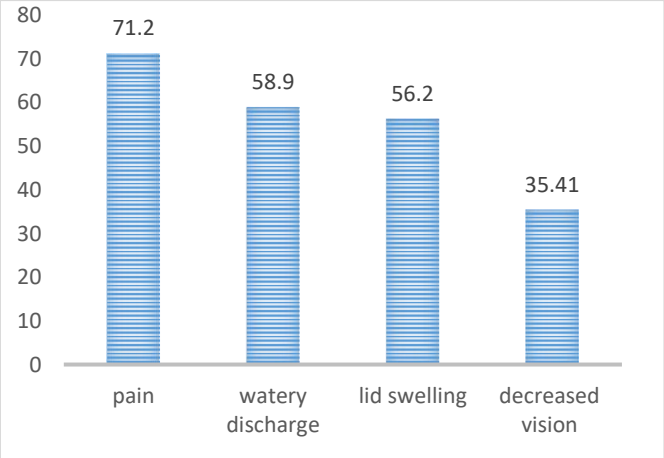

Fig.2: Distribution of ocular symptoms

The commonest ocular complaint was pain seen in 52 (71.23%) patients, followed by watery discharge in 43 (58.90%),lid swelling in 41 (56.16%) patients and diminution of vision seen in 26 (35.61%) patients in that order. The ocular symptomatology is summarised in Fig.2. The pain was typically described as unilateral, lancinating and burning. Majority of the patients had good visual acuity at presentation. Their visual acuity was as summarised in Fig.3 which shows that 51(69.86%) patients had visual acuity greater than 6/18 at the time of presentation. Only 2.7 % cases had severe impairment in vision.

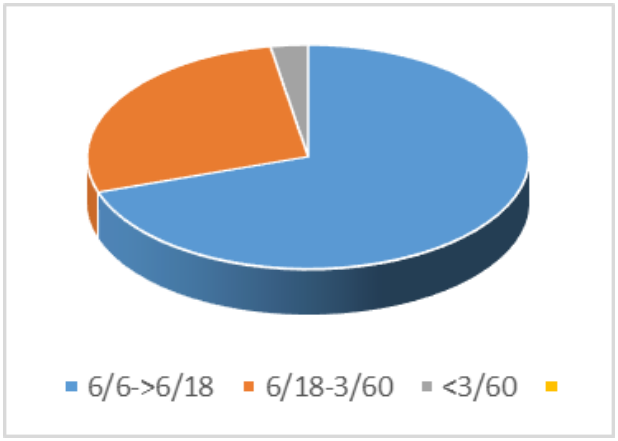

Fig.3 Visual acuity

Of the total, 65 (89.04%) patients had some form of ocular signs. The ocular signs at presentation was as described in fig. 4 which shows that ocular adenexal involvement was most common as seen in 61 (83.56%) cases and cornea was the next common tissue involved, seen in 22 (30.13%) patients. There were two cases of oculomotor nerve palsy**.** No patient showed optic neuritis, disc edema or retinal involvement. Adnexal involvement was seen in the form of edema in 40 patients (54.7%), vesicular lesions on lids in 32(43.8%), conjunctival injection in 23 (31.5%)patients. Among 22 patients having keratitis 12 showed corneal hypoesthesia, stromal keratitis was seen in 6 and epithelial in 2 and combinedin2patients.There was no case of endothelitis or neurotrophic keratopathy.

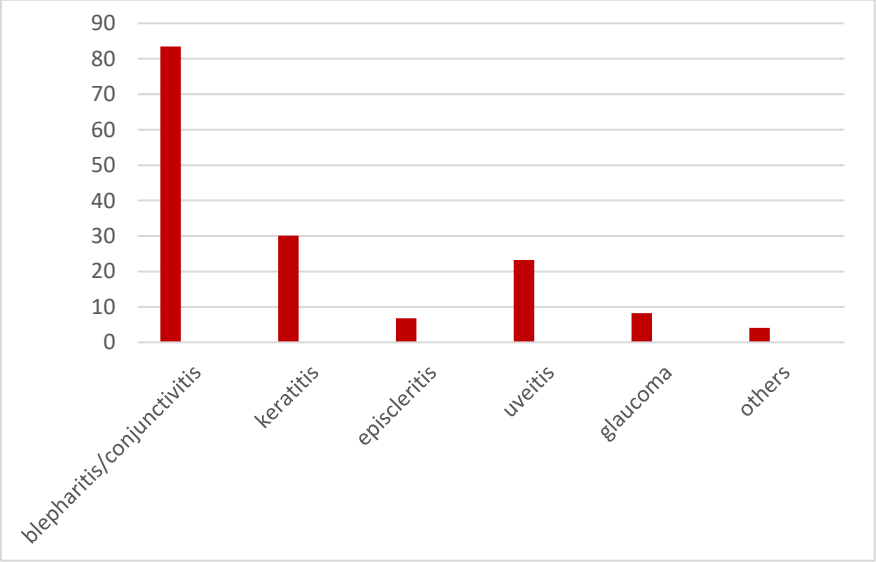

Fig.4 Ocular signs

Out of total of 73 patients 8 patients did not turn up for follow up. Patients examination after 1 month showed oculomotor paralysis in both the patients had improved. Residual corneal changes were seen in 4 out of initial 22 patients having corneal changes. One patient had persistent uveitis and in one patient intraocular pressure was increased After 3 months of examination post herpetic neuralgia was seen in 16 patients(24.6%) and after 6 months in 20.0% .Residual corneal involvement was seen in 4 patients. Patient with chronic uveitis and the other with secondary glaucoma persisted.

DISCUSSION

Herpes Zoster Ophthalmicus (HZO)is caused by reactivation of the herpes virus lying dormant in the trigeminal ganglion. Herpes zoster involving ophthalmic division is 20 times more common when compared with either mandibular or maxillary infection, being exceeded only by thoracic zoster [1]. In previous studies HZO constituted 10-25% of all cases of Herpes Zoster [2], while in our study it comprised of22.01% . A good clinical acumen can aid the diagnosis of Herpes Zoster Ophthalmicus (as with other forms of herpes zoster) even before the characteristic rash appears as the patient complains of burning pain in the area of distribution of the one or more branches of the ophthalmic division of the trigeminal nerve. The ocular involvement commonly accompanies the dermatomal involvement and can vary from mild blepharo conjunctivitis by direct invasion to occlusive vasculitis by secondary inflammation to neurotrophic keratitis by reactivation with inflammation affecting sensory ganglia.

In our study age distribution showed maximum patients were in the age group 51-60 years comprising of 39.7 % cases. A large percentage (50.7%) of patient was between 40-70 years this is similar to study by Ghaznavi *et al* [3]. Most of other studies report that incidence increases with age.[2]Elderly are more prone to develop herpes zoster because of reduced cell mediated immunity which leads to reactivation of the latent virus. In our set up this was not seen because number of patients in the more elderly group (>60 years) find it difficult to reach district hospitals due to difficult terrain of our area. Advancing age is considered the most common predisposing factor of HZO.

In ourstudy we had males outnumbering females(1.92 :1) Male gender dominance has been reported in earlier studies also [4]. This could be because males seek medical care more often than females. Female preponderance has been reported by Maiya etal and Womack [5-6]. Though there are few studies which show no gender variation [7].HZO is caused by reactivation of varicella zoster virus in the ophthalmic division of the fifth cranial nerve. Ophthalmic division further divides into frontal, lacrimal and nasociliary branches .The nerve supply of these branches is as depicted in Figure 1. The involvement of nasociliary branch is a marker of ocular involvement in HZO [8]. Nasal tip involvement is known as positive Hutchison's sign and requires immediate eye consultation. Nasal tip is supplied by anterior ethmoidal branch of nasociliary. Negative Hutchison's sign does not rule out ocular involvement as the other branches of nasociliary nerve supply cornea, sclera, iris, and even the frontal branch of ophthalmic nerve does supply upper eyelid and conjunctiva [8] Lacrimal branch supplies lacrimal sac, conjunctiva and lateral part of upper eyelid [9]. Nerve supplying the nasal tip supplies parts of anterior as well as posterior chambers of eye and may lead to serious ocular sequel. In our study we had all our patients having frontal branch involvement, while nasociliary was involved in 39.7 % cases and lacrimal in 35.6 % patients. There were many patients showing involvement of 2 or even all three branches of ophthalmic nerve. Frontal nerve involvement as observed by Puri *et al* [4] though being commonest branch involved(57.35 %) was quite less than our study. Such a large presentation difference lacks any explanation. Puri *et al* had 35.29% of patients with nasociliary involvement and 16.17% of patients with lacrimal nerve involvement. Frontal nerve involvement in 94% cases was seen in a study by Hoang-Xuan et al followed by lacrimal nerve 59% and nasociliary nerve involvement 35 %.[10]Patients presenting within 5 days and from 6-9 days after onset of cutaneous lesions was approx. 38.3% and 54.8% respectively. There were 6.8 % patients who presented after 9 days but before drying up of lesions. Late presentation in our patient is due to certain misbelief where they first resort to some religious activities and later seek medical advice. Also the difficult terrain restricts patients from seeking immediate medical guidance. In a study by Kahloun majority of the patients (60%) presented within 5 days of the onset of the disease.[7] There were less patients who presented late 28% patients presented between 6 to 9 days of onset and 12% patients presented after 10 days. The very late presentation of patients presenting after lesions healed were not included in our study.

Co- morbidities with HZO which could cause worsening of disease were seen in38.35%.Diabetes was the most common co-morbid condition seen in 19.2 % . HIV was found in only 4.1 %This is lower than in other studies, this could be because of low prevalence of HIV infection in our state. Kahloun reported co morbidities as 20 %diabetes mellitus, systemic hypertension in 17.8%, use of immunosuppressive in 6.6 % and dyslipidemia in 4.4 % cases. HIV positive serology was seen in 4.4 % cases[7]. Maiya et al reported similar co morbid states in 37 % patent; diabetes (7.4% %), HIV (11.1 %) [5].This study considered age >50 years also in the co-morbid conditions. Though increasing age is a

risk factor for herpes zoster we did not include it in diseases .In our study, herpes zoster ophthalmicus was present in 4.1 % of patients taking immunosuppressive drugs, 1.4 % of patients with alcoholic liver diseaseand in 8.2%% of patients with tuberculosis .Incidence of tuberculosis in our state is slightly higher and also patients present late in the disease when they have decreased immunity to other infections, which can explain higher percentage of tuberculosis as a co-morbid condition of HZO in our study.

Catron has a view that eye is involved in 100% cases when nasociliary branch is infected and in one third of cases in other divisions of ophthalmic nerve [11]. He assumed that on an average 50% of HZO patients will have ocular complications [11]. A total of 81 patients who presented to skin OPD with HZO were referred to eye OPD, 8 of these did not meet inclusion criteria so a total of 73 patients underwent ophthalmic evaluation. Ocular involvement was seen in 68 patients (93.15%).Similar observation was made in few previous studies [7]. The higher percentage in our study as well as study at Tunisia can be because of easy accessibility of eye care so even trivial eye involvement could be observed. Various other studies have found a much lower ocular involvement (70-80%) [4,12]. There were many patients having two or more complaints or signs. The commonest presenting symptom was pain seen in71.2 % patients, followed by watery discharge, lid swelling. Various studies report pain as commonest complaint seen in 70-80 % patients [4, 12]. Pain in herpes zoster can precede, be simultaneous or appear after onset of lesions. Altered sensation is severe lancinating pain, tingling, burning itching, etc. Increased watery discharge was seen in 58.9 % this is because of lid, conjunctival or corneal involvement. Lid swelling was seen in 54.7 % of our patients. This is higher than previous studies. All of our patient had frontal division involvement which can be the cause of more common lid swelling. Gupta et al in their study of eye involvement in young adults observed lid swelling in all their patients [13]. While most of other studies concluded that lid swelling was seen in 45-51 % cases [4, 12]. Diminution of vision was in 35.4% cases in our study. Most of the patients had mild diminution of vision, which could be due to hyperemia and inflammatory activity. Topical application of allergens can further aggravate the problem. Kahloun observed markedly decreased visual acuity in 7.8 % patients.[7]They also observed that vision was severely impaired when Hutchison's sign was positive. Visual outcome was good in 56.3% patients in a study by Nithyanandam and only 4.7% had markedly decreased vision [14]. In our studyonly 2.7 % patients had severe impairment of vision. Severe and persistent impairment is normally secondary to corneal involvement. In a study in HIV positive patients 12 % had visual acuity <20/200.[15]Persistent visual impairment was seen in 5.5 % of our patients, out of whom 2.7 % had severe impairment and 2.7 % moderate .

Of the total 65 (89.04%) patients had some form of ocular signs. Puri etal observed eye changes in77.94%.[4]A study at Tunisia showed adnexal involvement in 58.8%, uveitis in 60.7%, keratitis in 31.4%, oculomotor nerve palsy 5.8%, and optic neuritis with optic discedema 1.9% [7]. No case of retinal involvement was seen. The ocular signs at presentation was as described in Table 5 which shows that ocular adnexal involvement was most common as seen in 61 (83.56%) cases and cornea was the next common tissue involved, seen in 22 (30.13%) patients. There was two cases of oculomotor nerve palsy. No patient showed optic neuritis, disc edema or retinal involvement. Adnexal involvement was seen in the form of edema in 40 patients (54.7%), vesicular lesions on lids in 32(43.8%), conjunctivalinjection in 23 (31.5%)patients. While in study at Tunisia all cases of adnexal involvement showed lid edema, subconjunctival hemorrhage was seen in 45.1%, and vesicular conjunctivitis 25.8% [7]. Conjunctivitisin patients of HZO was seen in 41.17 % and 54 % in a study by Puri et al and Hoang –Xuan et al respectively [4, 12]. Episcleritis was seen in only 6.8 % patients, there was no case with scleritis. Both these conditions are trivial and do not cause much discomfort. Corneal involvement in HZO can be by direct viral infection, antigen-antibody reactions, delayed cell-mediated hypersensitivity reactions, and neurotrophic damage. Epithelial keratitis is the earliest damage seen, punctate lesions appear within 1-2 days while dendrites are seen after4- 6 days. Stromal keratitis is visible as granular deposits in stroma appear after 2 weeks and is thought to be secondary to antigen antibody reaction [16]. Among 22 patients having keratitis (30.12%), 12 showed corneal hypoesthesia(16.4%), stromal keratitis was seen in 6(8.2%) and epithelial in 2(2.7%) and combined in 2 patients. There was no case of endothelitis or neurotrophic keratopathy. Kahloun *et al* reported corneal hypoesthesia was recorded in 31.4%.stromal keratitis in 15.6%, epithelial keratitis in 5 eyes 9.8%, and concomitant superficial and stromal keratitis in5.8% [7]. Gupta et al in his study on young subjects reported corneal involvement in 89 % cases

[13]. Such high differences cannot be explained. In another study of HZO in HIV positive patients have shown corneal involvement from 52 % of these 12 % had stromal keratitis [15].

Uveitis was seen in 23.2 % of our patients. Uveal tract involvement has been observed in 17-19.1 %[4, 17] In other studies uveal tract has been reported to be involved in 40-60 % cases [7,18,19]. A very low incidence of 6 % has been seen in a study in Pacific [18]. This difference can be due to less number of immunosuppressed patients in our study. Of the 17 patients showing uveitis, 14(82.3%) had acute involvement, chronic in one (5.8%) and posterior synechia were seen in two patients(11.7%). We had 7 (41.1%)patients presenting with keratotic precipitates. In a study at Tunisia uveitis was acute in 26 eyes (83.8%), recurrent in 2 eyes (6.4%), and chronic in 3 eyes (6.9%). Granulomatous keratotic precipitates were found in 18 eyes (58.1%). Focal iris atrophy was recorded in 8 eyes (25.8%), Koeppe's nodules in 2 eyes (6.5%), pupillary distortion in 2 eyes (6.5%), and posterior synechiae in 5 eyes (16.1%) [7]. In our study there were 35.29 % of uveitis who developed secondary glaucoma. Kahloun had 23.5 % patients with secondary glaucoma in his study [7]. The higher percentage of glaucoma in our study was probably due to delay in presentation and hence starting of antiviral therapy. Secondary glaucoma can be due to combination of open- angle and angle closure disease.

Two of our patient had oculomotor nerve palsy which had resolved in subsequent visit. Extraocular muscle palsies has been reported in 7-31 % cases but it is usually transient [20]. Both of our patients had no residual palsy in follow up after 1 month.

In our study PHN was seen in 24.6% and after 6 months in 20.0 %. In a studies by Ghaznawi, Kahloun and Borker PHN was seen in 13.3 %, 17.8%, 20.9% respectively [2,7,18]. Puri *et al* reported PHN in 80 % patients after the age of 80 years [21]. The main risk factor for PHN is advancing age; other risk factors include severity of acute zoster pain and rash, a painful prodrome, and ocular involvement. It has been also shown that patients with keratitis, conjunctivitis, or uveitis had a higher risk of developing PHN compared with patients who did not have these ocular features [18]. Gupta *et al* in their study on HIV patients observed PHN in 75 % cases [13]. A study in Africa reported no difference in PHN incidence in HIV positive and negative group [22].

CONCLUSION

Ocular involvement is common in all patients of HZO. All patients of HZO presenting to Skin OPD should have their complete ophthalmological check up so that ocular morbidity could be timely prevented or treated. Ophthalmic examination of the patients should not only be done at time of diagnosis but also follow up ophthalmic examination is required at 2,4,12 and 36 weeks to improve the visual outcome.

Acknowledgement-nil

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