Original Article

Using Survey Scale to Assess the Reduction in Intensity of Vernal Keratoconjunctivitis Symptoms after Administration of Drugs in Tertiary Care Hospital

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ABSTRACT

Purpose: To establish the practicality of survey scale in estimating baseline severity at the time of diagnosis and resolution of Vernal keratoconjunctivitis (VKC) symptoms after topical medication

Study Design: Longitudinal survey design

Place and Duration of Study: Ophthalmology department of Nishtar Medical Hospital, Multan from June 2021 to November 2021

Methods: A total of 267 VKC (vernal keratoconjunctivitis) patients' data was filled in on preformed Google forms. Improvement in symptoms after follow-ups was recorded on it. Chi-squared test and Kruskal-Wallis test were employed to determine the statistical significance of the variables.

Results: There were 52.4% females and mean age of the patients was 29.52 ± 18.39 years. There was preponderance of patients falling under 20 years of age. At baseline, 63.3% patients were on topical steroids, while 5.6% of patients were using steroids at the second follow-up visit. The mean interval between patients' visits to the hospital was 7.64 ± 2.086 weeks. Nonparametric Kruskal-Wallis test was used to calculate the difference in means of radial point scale scores at the baseline examination (4.47 ± 2.321) and second follow-up (1.31 ± 1.615) visits. Z-score value was 15.266 with a significance of 0.001. For patient satisfaction and resolution of symptoms at the second follow-up visit, Chi-square values were 164.75 and 119.55, respectively, with a significance of 0.001 in each case.

Conclusion: The survey scale aided in quantifying disease symptoms, which can be useful in prescribing and adjusting the medications' dosage easier.

Key words: Vernal keratoconjunctivitis, Antihistamines, Steroids, Cyclosporine

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INTRODUCTION

Vernal keratoconjunctivitis is a bilateral cicatricial inflammatory disease of the ocular surface. People living in dry, sunny climates such as the Mediterranean, Sub-Saharan Africa, the Middle East, India, and Pakistan are more prone to it. It commonly occurs in younger age groups with male predominance, which is thought to be caused by altered levels of circulating androgens and oestrogens.[1]

In temperate climates VKC occurs seasonally, while hot humid weather keeps high load of airborne allergens thus leading to more severe symptoms in the patients.[2]

Risk factors for VKC include age, males, close animal contact, personal systemic allergy history, and dust exposure.[3] It is a severe form of recurrent allergic conjunctivitis involving both IgE and cell mediated immune mechanisms. Initially it was thought to be solely type I hypersensitivity mediated by mast cell activation. However, type IV hypersensitivity reaction occurs with T-helper 2 (Th2) cell type. Th2 cytokines inhibit matrix metalloproteinases (MMPs) which result in conjunctival collagen build-up.[4]

School-going children are mostly affected and ocular itching affects their attendance and social performance negatively.[5]

Multi-morbidities are the term coined for the conditions that share common IgE immune mediation. Allergic asthma, allergic rhinitis, rhino conjunctivitis, atopic dermatitis, vernal keratoconjunctivitis, chronic rhinosinusitis with nasal polyps, food allergies, and allergic bronchopulmonary aspergillosis.[6] A patient with VKC might have one of these conditions as well.

The disease has been classified into three types: the palpebral VKC, which presents with giant papillae on the tarsal conjunctiva of the lids; the limbal VKC, which has Horner-Trantas dots at the limbus; and the mixed VKC, which has characteristics of both the types. The terms given to them are palpebral, limbal, and mixed, respectively.[7]

Although VKC is most of the time diagnosed using an ophthalmologic examination, some studies have been conducted where conjunctival scraping and tear cytology reveal leucocytosis with an eosinophilic predominance.[8] Vernal keratoconjunctivitis in paediatric patients has led to ocular surface remodelling due to constant itching. Complications like corneal erosions, shield ulcers and scars. Despite being self-limiting condition, these changes in cornea are sight threatening and require therapeutic approach which will cut off inflammatory cascade causing histamine wave.[9] A lesser-known complication is keratoconus which occurs due to corneal epithelium rubbing resulting in apical protrusion like state.[10]

Although data is available regarding effects of different drugs used for VKC, we have used a survey scale to assess the reduction in Intensity of Vernal Keratoconjunctivitis Symptoms after administration of drugs in tertiary care hospital. There is scarcity of such surveys from Pakistan which led us to do this research.

METHODS

This study was conducted at Nishtar Medical Hospital, affiliated with Nishtar Medical University, Multan. The duration of study was from June 2021 to November 2021. Informed consent was obtained from all the participants and their parents, in case of minors. Non-probability consecutive sampling technique was employed for the enrolment of patients. Sample size was calculated according to the following formula:

$S = Z^2\ p\ (1\text{-}p)/M^2$

S is the sample size

'z' is z score its value is 1.96

'p' is the population proportion assumed to be 50% or 0.5

'm' is the margin of error that is taken 6% or 0.06

$S = (1.96)^2\ (0.5)\ (1 - 0.5)/(0.06)^2 = 266.7 = 267$

Inclusion criteria was bilateral disease clinically diagnosed by an ophthalmologist. Exclusion criteria was patients already on topical steroids, pregnant females, or suffering from any other ocular infectious or inflammatory pathology. Patients with glaucoma or diabetes or having a family history of either of the two were also not kept in the study. Anyone who did not show up on follow-up visits was not counted when considering attrition.

The ethical board of the hospital reviewed and allowed the commencement of this research. Diagnosis was established based on comprehensive history and clinical examination. History of any other skin, nasal, or respiratory allergies was considered. Patients or parents of minors were asked about symptoms of itching, redness of conjunctiva, photophobia, and discharge. A thorough slit lamp examination was done to look for papillae, Trantas spots, and the severity of redness. Fundus of the patient was also examined. IOP was checked using Perkin Tonometer on 1st and 2nd follow-ups if topical steroids were prescribed.

A radial point scale with description of numeric points was developed whereby clinical presentations of itching, redness of conjunctiva and photophobia were used to calculate the score. Ophthalmologists calculated the score on examination of patients' first and follow up visits. The score helped estimate the severity of disease and help initiate and modify medical therapy. The scale was devised with the help of four ophthalmologists. It was made in English, but the doctors explained it to the patient or underage

patient's parents in Urdu.

For each end point, "severe" meant 3 points, "moderate" earned 2 points, and "mild" was equal to 1 point.

- Score of 3 was given in case of constant itching, score of 2 in case of frequent itching (present 50% of time), score of 1 if occasional episode of severe itching, score of 0 if no itching.
- Score of 3, if vasodilation of all vessels on bulbar conjunctiva, score of 2 if many vessels were dilated, score of 1 was given in case of several vessels. If no manifestation of hyperaemia on bulbar conjunctiva, then score 0 was awarded.
- Score of 3 in alarming photophobia (present when dark glasses worn). Score 2 for moderate photophobia (requiring dark glasses). Score 1 was given in case of mild photophobia (present only in daylight). If no photophobia then score was given 0.

All the data was entered into a pre-designed Google form. Data was analysed using SPSS version 28.0. Frequencies and percentages were computed for categorical variables like gender and age. Mean ± standard deviation was computed for numeric variables like age, gender, types of conjunctivitis, symptoms at baseline visit, resolution of symptoms at consecutive follow-ups, and patient satisfaction. Mean and standard deviation were calculated for age and radial point scale scores at baseline, first follow-up, and second follow-up. Mean and standard deviation were also calculated for the intervals between the baseline examination and the first and second follow-up visits.

Non-parametric Kruskal-Wallis test was used to calculate the difference in means of radial point scale scores at baseline and second follow-up visits. The 'p' value of 0.05 was considered statistically significant.

For patient satisfaction and resolution of symptoms at the second follow-up visit, the Chi-square test was used with a p-value of less than 0.05.

RESULTS

In our study, total of 267 patients were included. For age distribution, see Table 1. There were 103 (38.6%) under 20 years of age. Age range was 3 to 64 years.

Female-to-male ratio was1.102:1. We had 127/267 male patients as compared 140/267 female patients. Mean age of males was 29.56 ± 21.265 and mean age of females was 29.48 ± 15.407. Palpebral form of VKC was the most dominant type, which accounted for 71.5% versus Limbal VKC 12.7% and Mixed VKC in 15.7%.

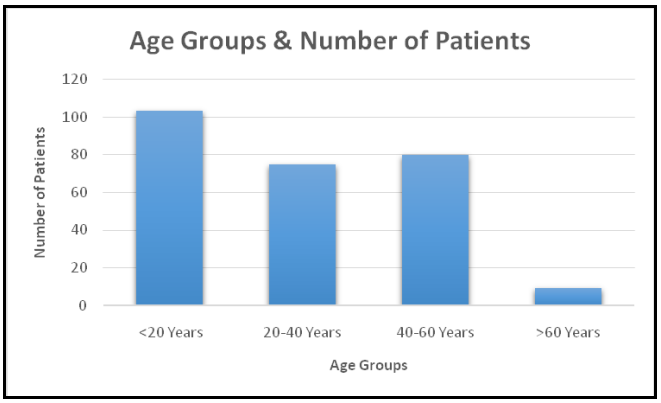

Figure 1: Distribution of VKC patients among age groups.

With the results from radial point scale, 249 (93.3%) patients were satisfied while 18 (6.7%) patients were not satisfied at the second follow-up visit. In 239 cases (89.5%) cases, VKC was controlled at the second follow-up visit. However, in 28 (10.5%) patients, VKC was not controlled at the second follow-up visit. Radial point scale mean scores and standard deviation are shown in Table 1.

Table 1: *Survey scale score.*

	Mean	Std. Deviation
Survey Scale Score baseline	4.47	2.321
Survey Scale Score first follow up	2.79	2.122
Survey Scale Score Second follow up	1.31	1.615
Disease control at 3rd follow up	1.10	.307

Table 2 shows the drug regimen at baseline visit and at second follow-up visit along with the dosage of drugs prescribed.

Non-parametric Kruskal-Wallis one way analysis of variance was used to calculate the difference in means of radial point scale scores at baseline examination and second follow-up visits. Z score value was 15.266 with significance of 0.001.

For patient's satisfaction at the second follow-up visit, Chi-square test was used. The calculated value of chi-square was 164.750 with a significance value of 0.001. For disease control at second follow-up visit,

chi-square value was 119.550 with a significance value of 0.001.

Table 2: *Drug regimen at baseline visit and 2nd follow-up.*

Drug Regimen	Baseline Visit	Second follow-up
(0) No Drugs	0	104 (39%)
(1) Olopatadine[a] twice per day	76 (28.5%)	119 (44.6%)
(2) 1 + Cyclosporine[b] twice per day	22 (8.2%)	29 (10.9%)
(3) 1+ Fluorometholone[d] four times per day	148 (55.4%)	10 (3.7%)
(4) 3 + Oral Desloratadine[e] once per day	21 (7.9%)	5 (1.9%)

Key
a = Olopatadine Eye Drops 0.2%
b = Cyclosporine Eye Drops 0.05%
d = Flouromethalone 0.25% Eye Drops
e = Desloratadine Tablet 5 mg or Desloratadine Syrup 0.5 mg/ml

DISCUSSION

The predominance of the patients who presented to us in this study were residents of South Punjab, and some of the cases were from Baluchistan, interior Sindh as well, and a few from Khyber Pakhtunkhwa.

In this study we assessed the use of different medications used for VKC. Common topical medications prescribed are antihistamines such as olopatadine and immunosuppressants like ciclosporin, but steroids are needed in cases of flare ups or resistant cases.[11]

Ciclosporin can be used for as long as 12 months with better efficacy and safety in paediatric patients.[12] Laboratory data, vital signs, slit lamp examination, best-corrected distance visual acuity, and intraocular pressure raised no safety concerns. However, patients should be instructed to protect their eyes against sunlight.[13]

Supratarsal injection of triamcinolone are also used for severe vernal keratoconjunctivitis in children.[14] There is a steroid misuse in the rural population, inciting a health crisis. Misused topical steroids are into: highly potent drugs (dexamethasone, betamethasone), B-moderate (prednisolone), C-weak (loteprednol, fluorometholone).[15] A fortnightly follow-up for visual assessment and IOP measurement is crucial to rule out steroid responders. The steroid treatment acts as a domino effect, contributing to a rise in IOP and glaucomatous optic disc damage, and eventually blindness.[16]

Recently, some trials have been conducted showing remarkable success with omalizumab.[17] Brief time duration of anti-IgE therapy is effective for steroid refractory VKC patients. It has opened new horizons for immune pharmacology.[18]

Our study had a slight female majority as compared to other studies done on VKC.[1,4,19,20,21] It could be because there are more females in the general population. However, our findings that most patients with VKC belong to the prepubescent/teen age group were consistent with numerous studies.[7,20,21] Our study's mean age was 29 years, which was higher than that of previous studies. For instance, a retrospective study done by Nagpal et al in a tertiary care hospital for 6 months, reported the highest incidence of VKC occurred in the age group of 11 – 15 years.

Palpebral form was the most frequent type found in our research, consistent with the observational study by Irfan et al.[7]

Very few studies probed into the devising of a clinical grading score system. To mention Jamil AZ and co-authors' study on the sliding scale to investigate the severity of symptoms for management of the patient with allergic conjunctivitis. A scale was printed and given to the patient to be used by both the doctor and the patient to estimate severity, which aided in the modification of the drug regimen. This caused minimal use of medicines and less frequent follow-up visits to the hospital, hence saving time and money of the patients.[22] Our study had online forms on cell phones that were only filled out by ophthalmologists in OPD. The similarity among both studies was that neither studied the efficacy of the drugs, resolution of symptoms, or patient satisfaction.

Earlier, A.M. Zicari et al tried to grade Vernal keratoconjunctivitis by devising the criteria based on presence of major symptoms (and how many) and minor symptoms. It was not uniform or agile to be used in paediatricpatients.[23]Pacci et al used serum ECP (eosinophil cationic protein) as a useful marker of disease activity in tarsal and mixed forms. Despite being subjective, it resulted in findings merging with allergic conjunctivitis.[24]

We need a reliable and valid scoring system which suits both practitioner and patient alike. Something, which benefits paediatricians in evaluation of ocular involvement during baseline diagnosis and looking through course of this disease and treating it. Limitations of our study was that only 3 symptoms

were used in the study, which did not include conjunctival discharge. The study will not be feasible in peripheral non-urban centres that do not have access to stable internet facilities. Moreover, a flare up in symptoms due to seasonal variation was not considered.

CONCLUSION

The survey scale made quantifying the severity of clinical features of VKC and the progression or regression of the disease, along with the patient's contentment during subsequent visits, computationally convenient. Drug regimens were modified using disease estimations from this scale.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval

The study was approved by the Institutional review board/Ethical review board **(Ref. No. 4121).**

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Authors' Designation and Contribution

Poombal; House Officer: *Design, Data analysis, Statistical analysis.*

Rashad Qamar Rao; Professor: *Concepts, Manuscript review.*

Waseem Sajjad; Medical Officer: *Literature search, Data analysis, Manuscript preparation.*

Wamiq Mehmood; Postgraduate Registrar: *Data acquisition, Manuscript editing, Manuscript review.*

Aiman; Final Year Student: Literature search, *Manuscript review, Final approval.*