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Original Research Paper

Ophthalmology

A COMPARATIVE STUDY OF INTRAOCULAR PRESSURE CHANGES (OCCURING AS A SIDE EFFECT) IN LONG TERM TREATMENT OF VERNAL KERATO CONJUNCTIVITIS BY TOPICAL FLUROMETHOLONE 0.1% AND TOPICAL LOTEPREDNOL ETABONATE 0.5%

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ABSTRACT

PURPOSE: The study aims to evaluate the safety of topical corticosteroids Loteprednol and Flurometholone in treating VKC keeping in mind the efficacy of the drugs. **METHOD:** A prospective study was done including 200 eyes of 107 patients with severe VKC (grade 3,4). 7 patients were lost during follow up. Patients were selected randomly. 100 eyes of 50 patients were treated with Flurometholone 1% and another 100 eyes of 50 patients with Loteprednol 0.5%. All patients were followed up over a period of 3 months. The study duration is 18 months. **RESULT:** The normal IOP ranging between 10-21 mm Hg. Out of 100 eyes receiving flurometholone in the study period of 18 months, 3 eyes (3%) showed IOP ≥ 30mm Hg and 5 eyes (5%) showed IOP between 21-30mm Hg. Out of the rest 100 eyes receiving Loteprednol, 3 eyes (3%) showed IOP between 21-30 mm Hg while none (0%) reached an IOP over 30 mm Hg. **CONCLUSION:** Loteprednol is more effective than Flurometholone and it consistently demonstrated a low propensity to elevate IOP, regardless of formulation, dosage regimen both during short term as well as long term treatment of VKC patient.

KEYWORDS : Flurometholone, Intraocular pressure, Loteprednol, VKC

BACKGROUND:

Vernal Keratoconjunctivitis (VKC) is an atopic condition of the external ocular surface. It is recurrent bilateral disorder that especially affects young boys. Itching, photo-phobia, burning, and tearing are the most common symptoms. Giant papillae (1), superficial keratitis and conjunctival hyperemia are the most common symptoms. [2].

Patients with VKC frequently have a family or medical history of atopic diseases, such as asthma, rhinitis, and eczema [3]. However, VKC is not solely an IgE-mediated disease. It has been proposed that it is a Th2-driven mechanism with the participation of mast cells, eosinophils, and lymphocytes based on challenge studies as well as immunohistochemical and mediator studies. [4]. Th2 lymphocytes (5) are important for both IgE (interleukin 4, IL-4) hyperproduction and for the differentiation as well as activation of mast cells (IL-3) and eosinophils (IL-5) (6). Other studies have shown that neural factors such as substances P and NGF are involved in VKC pathogenesis (7,8) and oestrogen and progesterone receptor over-expression. [9] in the conjunctiva of VKC patients has introduced the possible involvement of sex hormones. Thus, the pathogenesis of VKC is likely to be multifactorial, with the immune, nervous, and endocrine systems interacting.

A swift diagnosis, correct treatment, and assessment of the prognosis is needed for clinical management of VKC. The diagnosis is normally based on the signs and symptoms of the disease, but conjunctival scraping, indicating the existence of infiltrating eosinophils, can help in difficult cases. There are several treatment choices, most of them topical, which should be selected on the basis of the seriousness of the disease. However, the most powerful medications, steroids, should be administered carefully and only for short periods of time to prevent secondary glaucoma growth.

A 2% solution of cyclosporine [10] in olive oil or in castor oil should be considered as an alternative. Patients' long-term prognosis is usually strong, but 6% of patients experience corneal damage, cataract, or glaucoma.

Bonini et al identified 5 grades of VKC severity[11]:

0-quiescent: absence of symptoms, no therapy;
1-mild: presence of symptoms without photophobia, occasional use of anti-allergic eye drop;
2-moderate: presence of symptoms including photophobia, daily anti-allergic treatment;
3-severe: presence of superficial punctate keratopathy, daily anti-allergic treatment and occasional pulsed low dose steroid;
4-very severe: diffuse corneal epitheliopathy and/or ulcer, pulsed high dose topical steroid.

METHODOLOGY:

STUDY DESIGN - A prospective study was conducted in the OPHTHALMOLOGY department of Nil Ratan Sircar Medical College and Hospital, Kolkata. The study was done including 200 eyes of 107 patients with severe VKC (grade 3,4). 7 patients were lost during follow up. Patients were selected randomly. 100 eyes of 50 patients were treated with Flurometholone 1% and another 100 eyes of 50 patients with Loteprednol 0.5%. All patients were followed up over a period of 3 months. The study duration is 18 months.

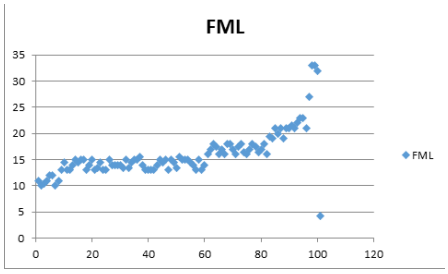
SCREENING AND TREATMENT – Children presenting to the OPD of the ophthalmology dept of NRSMCH with symptoms and signs of severe and very severe VKC (grade 3,4). After proper history taking and initial examination with a torch, slit lamp examination is performed to look for giant papillae in the palpebral conjunctiva, Horner-Trantas dots in the limbus, superficial punctate keratopathy, plaques and "shield ulcers' [12] and subepithelial scars. The baseline IOP before starting the steroid therapy is measured with the help of an Goldmann Applanation Tonometer. Then during follow up IOP measurement was done at 2 weeks, 4 weeks and 3 months post steroid therapy. The diagnosis of VKC is generally clinical, and no investigation is required as such.

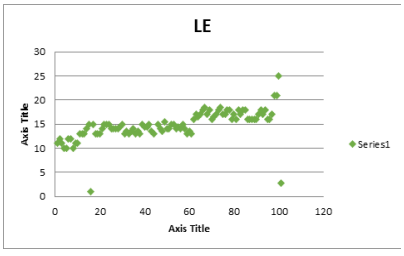
RESULT - The normal IOP ranging between 10-21 mm Hg. Out of 100 eyes receiving flurometholone in the study period of 18 months, 3 eyes (3%) showed IOP ≥ 30mm Hg and 5 eyes (5%) showed IOP between 21-30mm Hg. Out of the rest 100 eyes receiving Loteprednol, 3 eyes (3%) showed IOP between 21-30 mm Hg while none (0%) reached an IOP over 30 mm Hg

DATA ANALYSIS - Data analysis was done using **paired t-test.**

TABLE SHOWING IOP CHANGES OF ALL THE SUBJECTS

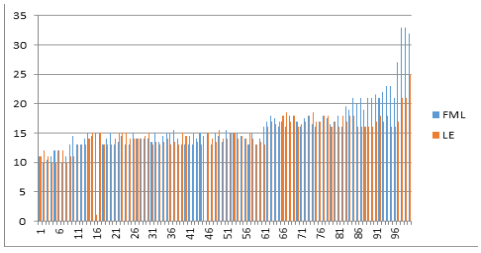
IOP RANGE (calculated at 3 months of starting therapy)	Number of Eyes receiving FLUROMETHOLONE	Number of Eyes receiving LOTEPREDNOL
10-12 mm Hg	8	10
13-15 mm Hg	52	51
16-18 mm Hg	22	29
19-21 mm Hg	10	7
21-24 mm Hg	4	2
25-30 mm Hg	1	1
30 mm Hg	3	0





X-axis showing the number of Eyes used in study
Y-axis showing IOP range

HISTOGRAM SHOWING VARIATION OF IOP CAUSED BY FML AND LE



X-axis showing the number of Eyes used in study; Y-axis showing IOP range

GROUP	GROUP ONE (FML)	GROUP TWO (LE)
Mean	16.135	14.914
SD	4.241959	2.83387
SEM	0.4241959	0.283387
N	100	100

SD = Standard deviation, SEM = Standard error of mean, N = total number of subjects

P value and statistical significance:

The two-tailed P value equals to 0.0176

This difference is considered statistically significant by conventional criteria.

Confidence interval:

The mean of Group One minus Group Two equals 1.2210000
95% confidence interval of this difference: From 0.21497999 to 2.22702001

DISCUSSION:

In this study we have found that loteprednol has a lesser propensity to elevate IOP when used both as a short term or a long-term treatment option for VKC. In a retrospective study of 159 seasonally and perennially allergic conjunctivitis patients, Ilyas et al. (13) No instances of IOP elevation identified as (5 mm Hg above baseline) were found with continuous LE usage for more than 12 months of 0.2 percent (1-4 times daily). (which is corroborating with findings of our study). In a parallel randomised study in 60 patients with vernal conjunctivitis, Oner et al. (14) recently assessed the effectiveness and safety of 0.5 percent LE suspension compared to 1.0 percent PA and 0.1 percent FML. When administered four times daily for 28 days, both PA and LE were more effective than FML in reducing the symptoms and signs of vernal conjunctivitis.

CONCLUSION:

Loteprednol is more effective than Flurometholone and it consistently demonstrated a low propensity to elevate IOP, regardless of formulation, dosage regimen both during short term as well as long term treatment of VKC patient.

LIMITATION:

It was a single-center study limited to Indian population. Study population is small. Follow up is difficult, once symptoms subside there is drop out during follow up.

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