CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.2634396

**Available online at: http://www.iajps.com** ***Research Article***

# WHICH IS BETTER: A COMPARATIVE RESEARCH TO ASSESS THE EFFICACY OF CROMOLYN SODIUM VERSUS KETOTIFEN FUMARATE TO RELIEVE VKC SYMPTOMS

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**Abstract:**

***Objective:*** *The aim of this study was to draw a comparison of vernal keratoconjunctivitis (VKC) relief signs after taking cromolyn sodium (4%) and ketotifen fumarate (0.025%).*

***Material and Methods:*** *We conducted this comparative research at Mayo Hospital, Lahore from April to October 2018 on a total of six hundred VKC symptoms patients. Institutional ethical approval was also taken before research commencement along with the patient's informed consent about the research protocols. Data analysis was made through SPSS software (P-Value = ≤ 0.05).*

***Results:*** *Research sample was divided into Group – I & II; the respective mean age for Group – I was (17.01 ± 5.13) and for Group – II (16.72 ± 5.02) years. There were 215 patients of VKC symptomatic relief (71.67%%) who received the management of Ketotifen Fumarate than 162 patients who were treated with Cromolyn Sodium (54%). VKC symptomatic relief was better among male patients than female patients.*

***Conclusion:*** *VKC symptoms relief by using ketotifen fumarate (0.025%) is effective instead of using cromolyn sodium (4%). Males were relatively better relieved than females. We can take it as a drug of firstline choice for VKC symptoms relief among patients.*

**Keywords:** *Vernal Keratoconjunctivitis (VKC), Symptoms, Relief, Cromolyn Sodium and Ketotifen Fumarate.*

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*Please cite this article in press Sara Mateen et al.,* ***Which Is Better: A Comparative Research To Assess The Efficacy Of Cromolyn Sodium Versus Ketotifen Fumarate To Relieve Vkc Symptoms.,*** *Indo Am. J. P. Sci, 2019; 06(04).*

## INTRODUCTION:

Ocular allergies commonly affect external ocular adnexa all over the world [1]. These allergies are categorized in Type – I hypersensitivity reactions that can be mediated through "Ig-E" antibody to counter different environmental allergens which include mites, pollens, dust, moulds, weeds, grass and animals' dander [2, 3]. The onset of VKC is recurrent and bilateral disorder in which cell-mediated immune mechanism and ig-E play a very important role [2]. Initially, the body is affected and occurs normally in the first ten years of life with a mean age of seven years. Almost 95% of cases are in the bracket of late teens; whereas, remaining may develop atopic keratoconjunctivitis [2]. Its occurrence is usual in winter and jots weather (extremely hot) [2]. Regions with higher temperatures about one-third of the patients have linked atopy; whereas, two third are due to family atopy history [2]. Its symptoms include an intense feeling of itching which correlates with onset of lacrimation, photophobia, foreign body sensation, thick mucoid discharge and burning [2].

An important role of Mast cells cannot be neglected in the vernal keratoconjunctivitis pathogenesis [2]. In case of the bond of specific allergen to sensitized mast cell in conjunctiva; the outcomes if mast cells degranulation and release of inflammatory mediators (prostaglandins, histamine, PAF of all and leukotrienes). Histamine predominantly causes VKC [3]. Most repeated VKC symptomatic relief agents are antihistamine, mast cell stabilizers, ciclosporins and steroids [4]. Most repeated utilized topical agents in VKC include mast cell stabilizers, antihistamines, corticosteroids and immunosuppressive drugs [5]. More selective novel therapeutic strategies which are under testing process are anti-chemokine receptor antibodies, leukotriene receptor antagonists and specific macro-biomolecules [5].

The difference of opinion lies in the VKC symptoms relief comparison among different literary pieces of evidence. Therefore, our aim of this study was to draw a comparison of vernal keratoconjunctivitis (VKC) relief signs after taking cromolyn sodium (4%) and ketotifen fumarate (0.025%).

## MATERIAL AND METHODS:

We conducted this comparative research at Mayo Hospital, Lahore from April to October 2018 on a total of six hundred VKC symptoms patients. Institutional ethical approval was also taken before research commencement along with the patient's informed consent about the research protocols. VKC patients reported for various symptoms such as pain, intense itching, lacrimation, redness, foreign body sensation, photophobia and signs like hypertrophy, hyperemia, conjunctival chemosis, m papillae, punctate epithelial erosion and mucous deposition on papillae. Mean determination was made through the presence and absence of signs and symptoms after a through slit lamp assessment. We did not include all those patients (8 years – 25 years) who were not taking VKC drugs (steroids and mast cell stabilizers antihistamines). We also excluded all those patients who were diagnosed with diabetic retinopathy, glaucoma, ocular hypertension and corneal ulcer. Grouping was carried out randomly and both Group – I & II have respectively prescribed Ketotifen fumarate (One drop BD) and cromolyn sodium (Q.I.D). After every week there was a scheduled follow-up till four weeks of treatment. We documented treatment efficacy for both groups by using a pre-designed Proforma for VKC symptoms presence or absence. Disease recovery was established with the absence of symptoms. We also documented the demographic detail of every patient. Frequencies and Mean & SD were respectively calculated for categorical variables and age. Both groups significance symptoms relief proportion was described through the Chi-Square Test. Data analysis was made through SPSS software (P-Value = ≤ 0.05).

## RESULTS:

The research sample was divided into Group – A & B; the respective mean age for Group – A was (17.01 ± 5.13) and for Group – B (16.72 ± 5.02) years. After four weeks of treatment; there were 215 patients of VKC symptomatic relief (71.67%%) who received the management of Ketotifen Fumarate than 162 patients who were treated with Cromolyn Sodium (54%). VKC symptomatic relief was better among male patients than female patients. Group – I presented higher VKC symptomatic relief than Group – II (P-Value = 0.001). In the total research population, there were 184 males (61.33%) and 116 females (38.67%) patients. Males were significantly high for VKS symptomatic relief as 153 males (83.15%) than 62 females (53.45%) patients. There was significant involvement of the gender for VKC symptoms relief (P-Value = 0.001). Group – I was further subdivided in two different age groups i.e. (8 – 16) years including 146 patients (64.44%) and (17 – 25) years including 154 patients (51.33%). A total of 97 patients (64.44%) and 118 patients (76.62%) relieved VKC symptoms respectively in Group – I and II. Age and VKC symptoms relief were significantly correlated (P-Value = 0.034).

**Table – I:** Group-Wise Presence and Absence of VKC Symptoms

| Groups | Present | | Absent | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | Number | Percentage | Number | Percentage | Number | Percentage | |
| **Group – I** | 85 | 28.33 | 215 | 71.67 | 300 | 50 | 0.001 |
| **Group – II** | 138 | 46 | 162 | 54 | 300 | 50 | |
| **Total** | 223 | 37.17 | 377 | 62.83 | 600 | 100 | |

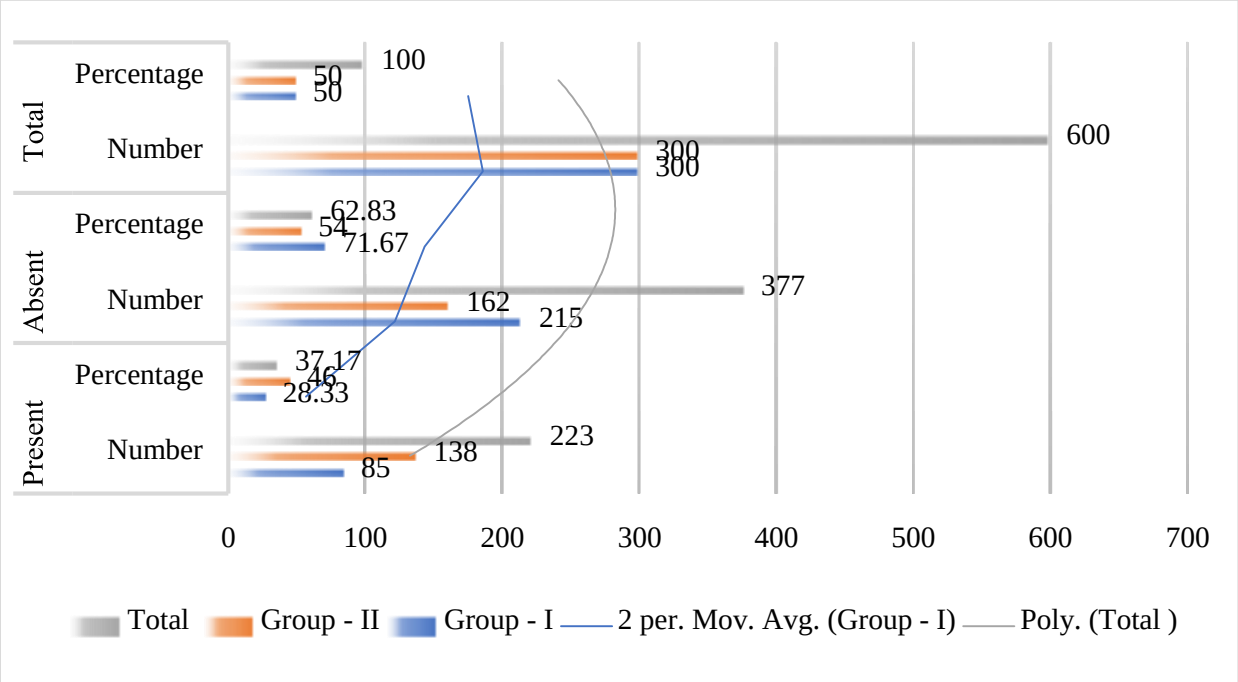



**Table – II:** Gender-Wise Presence and Absence of VKC Symptoms

| Gender | Present | | Absent | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | Number | Percentage | Number | Percentage | Number | Percentage | |
| Male | 31 | 16.85 | 153 | 83.15 | 184 | 61.33 | 0.001 |
| Female | 54 | 46.55 | 62 | 53.45 | 116 | 38.67 | |
| Total | 85 | 28.33 | 215 | 71.67 | 300 | 100 | |

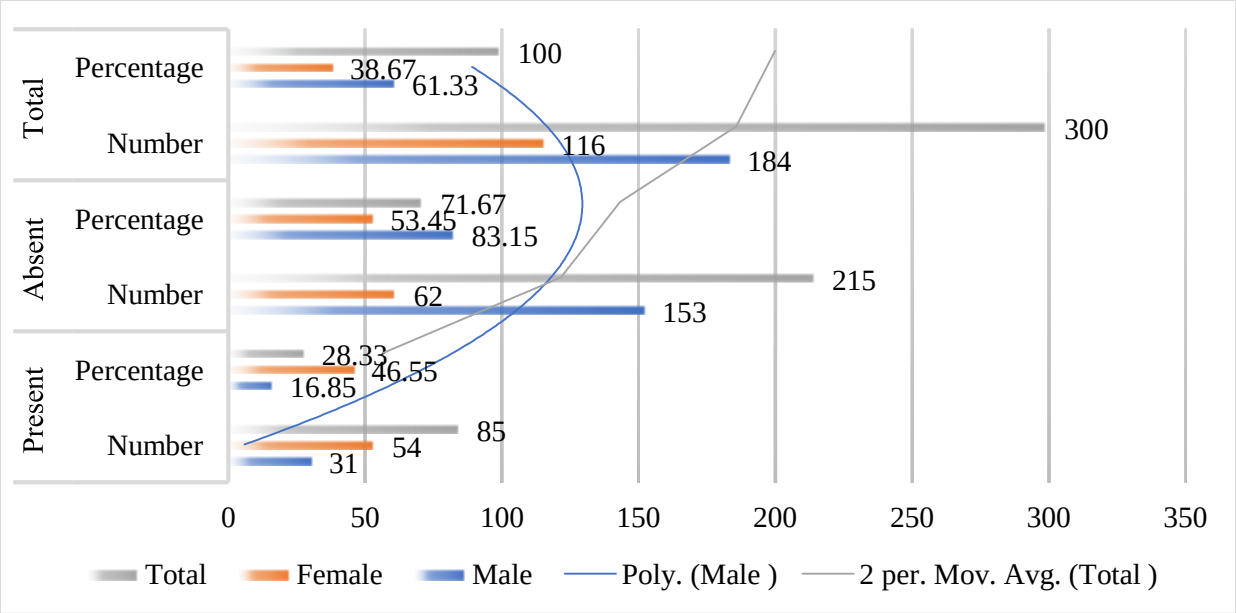
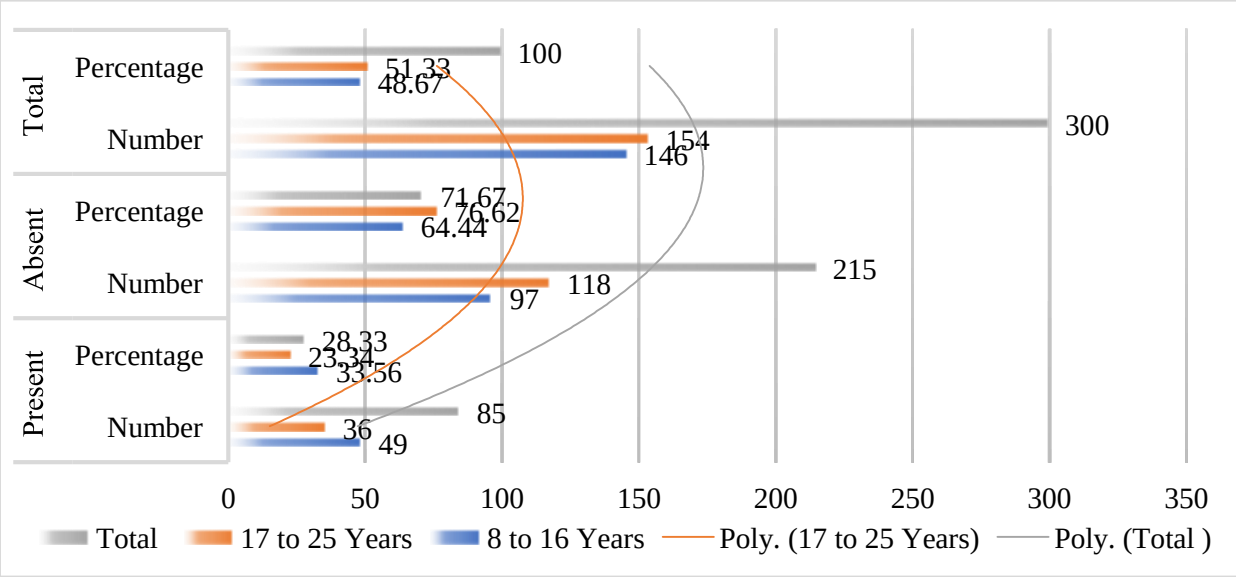



**Table – III:** Age-Wise Presence and Absence of VKC Symptoms

| Age | Present | | Absent | | Total | | P-Value |
|---|---|---|---|---|---|---|---|
| | Number | Percentage | Number | Percentage | Number | Percentage | |
| 8 to 16 Years | 49 | 33.56 | 97 | 64.44 | 146 | 48.67 | 0.034 |
| 17 to 25 Years | 36 | 23.34 | 118 | 76.62 | 154 | 51.33 | |
| Total | 85 | 28.33 | 215 | 71.67 | 300 | 100 | |



## DISCUSSION:

VKC is mostly preventable, common and hypersensitive clinical IgE mediated response. VKC refers to an immunopathological disease with an insubstantial increase in the mast cells proportion. Mast cells activation through Ig-E bound receptor crosslinking by allergen increases the release of numerous mediators such as cytokines, histamine and prostaglandins which all add to the VKC symptoms. There is an important role of mast cells in the production of VKC symptoms [6]. Presently available VKC management focuses on the immune system modulation and chemical mediators' pharmacologic inhibition which is involved in the response of the immune system. Mast cell stabilizers and antihistamines are commonly therapeutic agents' groups which utilize membranes of mast cell through prevention of calcium influx across the membranes of mast cell which resultantly inhibits the release of mediator and degranulation of cells. New antihistamines are capable enough to intervene release of mediator and allergic inflation [6]. These drugs contain multiple actions agents including Ketotifen fumarate which is mast cell stabilizer and histamine H1 – receptor antagonist. Other research studies conducted on animals also prove the inhibitory effect of Ketotifen fumarate towards the chemotaxis and activation of eosinophils into conjunctiva, which is an important stage in the later phase of the immune response [6].

Cromolyn sodium is also effective and safe to treat VKC; but there is often a need for topical steroid, glaucoma, cataract and increased bacterial keratitis chances. Therefore, our aim of this study was to draw a comparison of vernal keratoconjunctivitis (VKC) relief signs after taking cromolyn sodium (4%) and ketotifen fumarate (0.025%). Our research reports a significant decrease in the symptoms of VKC after treatment of four weeks. After four weeks of treatment; there were 215 patients of VKC symptomatic relief (71.67%%) who received the management of Ketotifen Fumarate than 162 patients who were treated with Cromolyn Sodium (54%). Shoja reported a lower symptomatic relief of VKC (61.5%) with Ketotifen fumarate with respect to our research; similarly, an Australian author also reported reduced relief as (49.5%) [6, 7]. Ganz reported a higher recovery rate with Ketotifen fumarate [8]. Clinical series also report effectivity and safety of ketotifen eye drops as it provides long-term and rapid recovery [9]. Leonardi reported the rapid response of Ketotifen fumarate than Cromolyn [10]. Relatively close outcomes were reported by Andren such as Ketotifen fumarate (91.2%) and Cromolyn (83.5%) with respect to current research [11].

Twice use of Ketotifen fumarate is significantly effective in comparison with trice use of sodium Cromolyn in a day to moderate VKC symptoms [6]. Ketotifen fumarate is valuable in terms of rapid recovery, long duration cure, safety and effectivity [6]. Canadian researcher reported the slight burning effect of the Ketotifen which causes discomfort but the effectiveness still stands undoubted [12]. Ketotifen can effectively control severe itching within fifteen minutes and the effect sustains for a period of eight hours; moreover, it reduces ocular itching, hyperemia correlated to allergic conjunctivitis [13]. Ketotifen is also safer and more effective than cromoglycate Nain in order to control the onset of severe itching, redness and tearing even with a single dose for conjunctival allergies [14].

## CONCLUSION:

VKC symptoms relief by using ketotifen fumarate (0.025%) is effective instead of using cromolyn sodium (4%). Males were relatively better relieved than females. We can take it as a drug of first-line choice for VKC symptoms relief among patients.

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