

Original Research Article

# Quantitative Nasal Eosinophilia: An Objective Tool to Optimize Intranasal Topical Steroid Spray in the Management of Perennial Pediatric Allergic Rhinitis

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## ABSTRACT

**Introduction:** Persistent allergic rhinitis (AR) mandates long term use of intranasal corticosteroid sprays (INS) which pose a potential risk in children, especially when administered in higher dosages. There seems to be no objective method present for dose optimization other than subjective symptomatology reduction. Quantitative nasal eosinophilia (QNE) is an objective tool where nasal mucosal eosinophil count is measured by an easily obtainable nasal smear and can be used for INS dose optimization in paediatric persistent AR. In this study we aim to correlate QNE and Total Symptom Score 6 (TSS 6) before and after 2 and 4 weeks of treatment with INS in cases of pediatric AR.

**Methods:** 300 children of age group 5-15 years, diagnosed as having AR and fulfilling the inclusion criteria were enrolled and Mometasone INS was started in appropriate dosages. TSS 6 and QNE were measured before and post Mometasone INS treatment at 2 and 4 weeks and results were then correlated and analysed.

**Results:** Pre treatment median QNE scores were +1 and +2 which decreased to less than +2 at 2 weeks and +0.5 at the end of 4 weeks post treatment. TSS 6 values decreased from 9-11 (pre treatment) to 1-3 after 4 weeks of treatment. This result was statistically highly significant.

**Conclusion:** Intranasal steroid spray in pediatric perennial Allergic rhinitis can be titrated to lower levels of optimal dosing, guided subjectively by symptom relief and objectively by applying a simple procedure of Quantitative nasal eosinophilia ideally suited in the pediatric age group.

**Key Words:** Quantitative Nasal Eosinophilia; Total Symptom Score 6, Pediatric allergic rhinitis; Intranasal corticosteroid spray

## INTRODUCTION

Allergic rhinitis (AR) is assuming alarming increase in prevalence ranging from 2-25% in children [1] and forms 55% of all allergies. [2,3] It's incidence is estimated to be around 20-30% in the Indian population. [4] International Study of Asthma and Allergy in Children (ISAAC) Phase 3 (2009) indicates an increasing trend in childhood Allergic Rhinitis and Asthma

in India. [5] Allergic Rhinitis (AR) is defined as an IgE mediated type 1 allergic response to aeroallergens by the sinonasal mucosa. The diagnosis of allergic rhinitis is primarily clinical while diagnostic testing like the skin prick tests are reserved only for inadequate symptom - control or prior to consideration of Immunotherapy. [6] AR can be confidently diagnosed purely based on history and clinical examination in patients presenting

with anterior/posterior mucoid rhinorrhoea, nasal itching, sneezing bouts and nasal obstruction. The effects of AR, especially in children, are far-reaching and its comorbidities may include chronic adenotonsillitis, otitis media with effusion, chronic rhinosinusitis, obstructive sleep apnoea, sickness absenteeism and poor scholastic performance.<sup>[7]</sup> The sheet anchor treatment for AR is intranasal topical steroid spray (INS)<sup>[8]</sup> with other adjuvant medications guided by the symptoms. Persistent AR mandates use of long-term intranasal steroid which is a potential risk, especially in children, as it may lead to inhibition of pituitary-hypothalamic-adrenal (PHA) axis, growth stunting, posterior capsular cataract, nasal mucosal irritation, epistaxis, excessive crusting and septal perforation.<sup>[8]</sup>

An algorithm for the treatment of AR with INS, H1 antihistaminics, cromolyns, mucolytics, local decongestants and immunotherapy has been propounded.<sup>[9]</sup> Mometasone hydrochloride intranasal topical spray (50mcg MDI Spray) up to 200mcg/day, shown to have the least systemic absorption, is the preferred INS in the paediatric population.<sup>[8]</sup> Patients with moderate to severe symptoms are started on maximum permissible dose INS/day which is then de-escalated to a maintenance dose after demonstrating reduction of symptom-severity two weeks post treatment. There are no objective methods to optimize the step down dose of INS presently other than subjective symptomatology reduction. There is a paucity of studies which are targeted to objectively assess the decrease in nasal mucosal inflammation. This formed the backdrop of our study which aimed to look at using a traditional method of Quantitative Nasal Eosinophilia (QNE) as an objective tool to optimize the INS dose in pediatric persistent AR.

## **MATERIALS AND METHODS**

### **Study population –**

300 children of both sexes clinically diagnosed as having Allergic Rhinitis in the

age group from 5-15years and consulting in the Otolaryngology outpatient department of a 149 bedded hospital in central India from 2006 to 2009 (3years).

**Study design -** Observational descriptive study.

### **Inclusion Criterion:**

1. Children newly diagnosed with Allergic rhinitis lasting >4weeks in terms of symptoms and clinical evaluation by an Otorhinolaryngologist.
2. Both sexes, in the age group 5-15 yrs.
3. Parental consent to partake in the study.

### **Exclusion Criterion:**

1. Children with Asthma, Chronic Rhinosinusitis, Nasal Polyposis and nasal pathologies other than AR.
2. Children with contraindications to the use of INS spray.
3. Children already being treated by any form steroids, antihistamines, antileukotrienes or intranasal medication.
4. Parents unwilling to include children in the study.

### **Methodology –**

Institutional ethical committee clearance was obtained for the conduct of the study. 300 children attending the ENT outpatient department diagnosed as having AR symptomatically and clinically, conforming to the inclusion and exclusion criterion were recruited into the study. The children underwent a thorough ENT and pediatric evaluation to rule out other comorbidities.

Total Symptom score 6 (TSS 6)<sup>[10]</sup> was used to score the severity of six diagnostic AR symptoms - Nasal symptoms: sneezing, rhinorrhoea, nasal pruritus, nasal congestion and non-nasal symptoms: ocular symptoms (including itchy, red and watery eyes) and itchy ears and/or palate. The score was in increasing grades of severity from 0-3, with Score 0 for 'No symptoms', Score 1

for ‘Mild symptoms’ (Symptoms clearly present but minimal awareness, easily tolerated), Score 2 for ‘Moderate symptoms’ (Awareness of bothersome but tolerable symptoms) and Score 3 indicating ‘Severe symptoms’ (Symptoms hard to tolerate and/or cause interference with activities of daily living, sleeping or both). Total Symptom Score 6 (TSS 6) inferences were made as below:

**Total score 1-4: Mild AR**

**Total Score 5-8: Moderate AR**

**Total score 9-12: Severe AR**

A baseline symptom scoring was performed at initial diagnosis of AR.

A 2.7mm, 0 degree, rigid nasal endoscope was used to get a pre-treatment nasal mucosal scraping from the surfaces of the middle-third of the inferior turbinates of both nostrils of the child with an atraumatic cotton tipped applicator. The applicator was smeared on glass slides and fixed with 95% ethyl alcohol and stained with modified Wright-Giemsa stain. Slides were then examined under 1000X magnification of a light microscope by an experienced pathologist for the Eosinophil counts as described by the Meltzer count (Table 1). [5,11,12] At least 10 well spread high power fields were examined. Normative data indicates that in non allergic normal individuals, Eosinophil is not seen in nasal mucosa. So any Meltzer score over 1 (0.5+) is considered pathological. The count was recorded as Quantitative Nasal Eosinophilia (QNE).

**Table 1. Meltzer Quantitative Scoring System for nasal eosinophilia** [4,5]

Number of eosinophils (per 10 high power fields)	Quantitative Nasal Eosinophilia Score
0	0
0.1 – 1 *	0.5 +
1.1 – 5.0 *	1+
6.0 – 15.0 *	2+
16.0 – 20.0 *	3+
>20.0 *	4+

(\* Mean of cells per 10 high power fields (x1000))

Subsequently, intranasal Mometasone spray (50 mcg/spray) was administered at one spray /each nostril in the morning and at night totalling 200mcg dose/day daily for two weeks. QNE and the modified Total Symptom Score (TSS 6) was repeated after the second and fourth week of initiation of Mometasone intranasal steroid spray.

In children who showed a 50% improvement in TSS 6 and reduction of QNE score at 2 weeks post treatment, the dose of Mometasone intranasal steroid spray was titrated down to one spray both nostril/once at night ( total 100 mcg/day @ 50 mcg per spray) and followed up at 4 weeks.

## RESULTS

Variables that were recorded were as follows:

- (i) QNE at start of therapy.
- (ii) QNE at second week from initiation of therapy.
- (iii) QNE at fourth week from initiation of therapy.
- (iv) TSS 6 of symptoms before onset of treatment.
- (v) TSS 6 of symptoms at 2weeks of treatment.
- (vi) TSS 6 of symptoms at 4 weeks of treatment.
- (vii) Correlation of QNE and TSS 6 before onset of treatment and at 2 weeks and 4 weeks post INS.

Children of both sexes recruited for the study: 300

Mean age group of cases was 8.16 ± 0.3 years (range 4 to 15years). 117 children were between 4 to 8 years age and 183 children were between 8 to 14 years of age.

Similarly, sex difference between subjects in the group was found to be insignificant using multivariate analysis (p =0.964).

Quantitative nasal eosinophilia (QNE) scores prior to the initiation of therapy is shown in Table 2. Median scores were 1 and 2 which was statistically

significant using Student's unpaired t test ( $p < 0.0001$ ). QNE scores in children with allergic rhinitis (with 0.5 as a lower diagnostic cut-off) were significant (Student's unpaired t test) ( $p = 0.022$ ).

**Table 2. Distribution of study population prior to initiation of therapy on the basis of Quantitative Nasal Eosinophilia Score**

Quantitative Nasal Eosinophilia score	Cases
4	15
3	36
2	150
1	60
0.5	39
0	0
<b>Total</b>	<b>300</b>

The QNE and TSS score was recorded after 2 weeks of initiation of therapy with Mometasone intranasal steroid spray (Table No 3).

**Table 3. QNE & TSS at initiation, 2 weeks and 4 weeks after start of therapy**

QNE Score	Treatment scores					
	Pretreatment		2 weeks		4 weeks	
	No of Children	TSS6 Score	No of Children	TSS6 Score	No of Children	TSS6 Score
4	15	11	3	8	0	-
3	36	9	8	6	0	-
2	150	8	69	4	16	3
1	60	6	90	3	31	2
0.5	39	4	129	2	252	1
	300		299		299	

(\*1 child was lost to follow up)

300 children were recruited for the study; however 01 child was lost to follow up before the follow up at 2 weeks. At initial presentation, 210 patients (70 %) had QNE scores at +1 or +2 and a Moderate AR category TSS 6 score ranged from 6-8. Only 51 (17%) patients had QNE scores  $> +3$  and severe TSS 6 score ranged from 9-11. All were started on Mometasone intranasal steroid spray at 200mcg/day.

On review at 2 weeks, 50% of children with QNE scores  $> +3$  shifted to lower scores and concomitant improvement in the TSS 6 scores to the Moderate AR category. 288 children (96 %) achieved QNE scores below +2 and TSS improved by 50 % of pre-treatment scores shifting to the Mild AR category with an average score of +3. All the children who had improvement of QNE and TSS score improvement  $> 50$  % were advised reduction of Mometasone intranasal steroid spray to 100mcg/ day, leaving only 11 children (3.7%) continuing with the initial starting dosage of 200 mcg/day.

At 4 weeks, all children had QNE scores below +3, with 252 (84%) of them

with values of just +0.5. All children showed remarkable and sustained improvement in symptoms with TSS scores in the Mild AR category. Student's unpaired t test was used for statistical analysis. With 95% confidence interval of mean of difference in values of two groups (QNE and TSS 6 at 2 week and 4 weeks post treatment),  $t = 2.7761$  and degrees of freedom = 8 and standard error of difference = 1.225, the two tailed p value came out to be 0.0241 which was statistically significant. Correlation of QNE and TSS 6 before onset of treatment and at 2 weeks and 4 weeks post INS was done with Spearman rank correlation which showed p value to be  $< 0.005$  which again was statistically significant.

## DISCUSSION

The International Study of Asthma and Allergies in Childhood (ISAAC) has highlighted that AR has shown an ever increasing trend in western and developing countries. The pathophysiology entails a type 1, IgE mediated persistent inflammation of the nasal mucosa. The

subject has an initial sensitization to an allergen, followed by an early phase which then cascades into the late phase reaction. The early and late phases are orchestrated by a plethora of inflammatory agents and cells. The early phase is due to allergen triggered degranulation of the IgE sensitized mast cells while the late phase is due to predominantly local mucosal Eosinophilia and the inflammatory agents secreted therein.

The mainstay of treatment of AR is presently intranasal topical steroid spray. The treatment depends on the age and weight appropriate dose of intranasal steroid spray. However, long term steroids in the pediatric age group can be fraught with risks. The aim of treatment will be to achieve an early alleviation of troublesome symptoms and to promptly titrate down to minimal required dosing in order to avoid steroid related side effects especially in the pediatric age group. Hitherto, dose titration was purely based on symptom alleviation which is purely subjective.

This study attempted giving objectivity to steroid dose titration in persistent pediatric allergic rhinitis which requires long term intra nasal steroid spray. Quantitative Nasal eosinophilia (QNE), assessing the nasal mucus eosinophil count by an easily obtained nasal smear from the pediatric subject, was found to be an ideal objective tool to assess the nasal mucosal inflammation.

Quantitative Nasal Eosinophilia, in this study had a high degree of correlation to the symptoms of AR as evaluated by an objective scale of Total symptom Score 6 (TSS 6). Mometasone nasal spray, with the least systemic absorption, ideally may be beneficial for long term pediatric use. On initial presentation, the majority of subjects had moderate severity of symptoms while severe symptoms were in a minority. A dosing of 200mcg/ day of INS Mometasone resulted in a remarkable alleviation in symptoms of 96% of subjects with a shift in QNE scores towards the lower counts centering around +0.5 to +1 from an initial

values of +1 to +2 over two weeks of treatment. There was an alleviation of 50% TSS 6 scores in the same time. The dosing of two weeks also significantly resolved symptoms in 50% subjects with severe symptoms.

The dosing on being reduced to 100mcg/day INS Mometasone continued to further reduce the QNE counts and sustained symptomatic relief from the 2<sup>nd</sup> to 4<sup>th</sup> week as signified by reduction of TSS scores. All remaining cases at 2 weeks with +3 to +4 QNE and severe TSS 6 and continuing initial dose of INS resolved to the levels of the rest of the cases by 4 weeks, thereby qualifying for dose titration to 100mcg/day.

## CONCLUSIONS

Intranasal steroid spray in pediatric perennial Allergic rhinitis can be titrated to lower levels of optimal dosing, guided subjectively by symptom relief and objectively by applying a simple procedure of Quantitative nasal eosinophilia ideally suited in the pediatric age group.

## Compliance with Ethical Standards

### *Conflict of Interest:*

The authors declare that they have no conflict of interests.

### *Ethical approval:*

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

### *Consent:*

Written informed consent was obtained from all individual participants included in the study.

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