IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A Literature Review on the Diagnostic Tool - Nasal Smear for Eosinophil

A.H. Ayshah Fazeenah

Senior Lecturer, Institute of Indigenous Medicine, University of Colombo, Sri Lanka.

Abstract: Nasal cytology directly reflects nasal inflammation and is an important tool in the diagnosis and treatment of rhinitis. There is no single test as a gold standard for the diagnosis of allergic rhinitis, but nasal smear for eosinophilia has been recommended as a tool for the diagnosis. It is a simple, cheap, non-invasive, reproducible, easy to perform and cost-effective as compared to other tests like skin prick test or radio-allergo-sorbent test, and also it is easily repeated on the same patient, which is essential in both the follow-up of the disease and to monitor the efficacy of medical and surgical interventions. Eosinophils in the nasal smear have been reported to display the best correlation with all the clinical and immunological parameters in allergic rhinitis. Despite its simplicity and proven utility in giving direction to the diagnostic study of many nasal diseases, nasal cytology paradoxically still remains underuse. There are several possible collection methods for nasal cytology, including nasal smear, swab, scraping, nasal lavage, and irrigation. The present literary review was undertaken to integrate the knowledge of nasal smear for eosinophils as the diagnostic tool in the diagnosis and treatment of nasal allergies. Details and facts on nasal smear for eosinophils were gathered from the published journals, PubMed, google scholar, research gate by using words like nasal secretion, nasal smear for eosinophil, nasal cytology, allergic rhinitis, biological markers etc., then analyzed and summarized the data. Therefore, it is concluded that the nasal smear for eosinophils is a well-known, cost effective and easy to apply diagnostic method in the diagnosis and treatment of nasal allergies.

Key words: nasal cytology, nasal cytogram, nasal smear for eosinophils, diagnostic tool, allergic rhinitis.

I. INTRODUCTION

Nasal cytology or nasal cytogram directly reflects nasal inflammation and is an important tool (Gelardi et al, 2016) or is often used as an aid in the diagnosis (Gelardi et al, 2016), (Lans et al, 1989) and treatment of rhinitis (Gelardi et al, 2016). It represents a useful, cheap and easy-to-apply diagnostic method to better detail the phenotypic characteristics of rhinitis. In fact, it allows to detect and quantify the cell populations within the nasal mucosa at a given instant, to better discriminate the different pathological conditions and also to evaluate the effects of various stimuli like allergens, infectious, irritants, physio-chemicals or the effect of treatments (Heffler et al, 2018). However, the use of nasal cytology in clinic is limited by the complicated nature of the procedure, variable results, and lack of a standardized grading system (Chen et al, 2017). But it has acquired an increasing role in the diagnosis and management of non-allergic rhinitis and mixed rhinitis; and its current day-by-day use is recommended by some authors (Bartoli et al, 2018). It has been cited as a means to distinguish allergic from nonallergic causes of rhinitis in patients whose history, physical examination, and skin test results are equivocal (Lans et al, 1989). Moreover, nasal cytology plays an important research role in the evaluation of effect of noxious stimuli, outcomes of treatments, effects of allergen immunotherapy and pathogenic aspects of comorbidities. The major unmet need, so far, is its standardization to use a reproducible methodology (Gelardi et al, 2016).

The presence of eosinophils in nasal secretions or direct nasal smears classically suggests the diagnosis of allergic rhinitis (Lans et al, 1989), also the eosinophils in the nasal smear have been reported to display the best correlation with all the clinical and immunological parameters in allergic rhinitis (Nurkic et al, 2016). Nasal smear for eosinophil is a cheap, non- invasive test that may be easily repeated on the same patient, which is essential in both the follow-up of the disease and to monitor the efficacy of medical and surgical interventions (Nurkic et al, 2016). Despite its simplicity and proven utility in giving direction to the diagnostic study of many nasal diseases, nasal cytology paradoxically still remains underuse (Heffler et al, 2018).

Though, nasal eosinophilia is not a pathognomonic, it is one of the best methods and is interpreted as an additional confirmation of nasal allergy (Sood, 2005). Mygind N (1979) had observed that after intra-nasal challenge by an allergen, eosinophilia is demonstrable from the challenged nostril and not the contralateral. The aim of the present literary review was to integrate the knowledge of nasal smear for eosinophils as the diagnostic tool in the diagnosis and treatment of nasal allergies.

2. METHODOLOGY

Related articles were collected from the published journals, PubMed, google scholar, research gate by using words like nasal secretion, nasal smear for eosinophil, nasal cytology, allergic rhinitis, biological markers etc.

3. LITERATURE REVIEW

Nasal cytology was firstly applied in the clinical practice at the beginning of the twentieth century, and it found its role in nasal diagnostic algorithm (Bartoli et al, 2018). The increase of eosinophils in nasal secretions in allergic rhinitis was first reported in 1927 (Eyermann, 1927). 20th century Eyermann identified some eosinophils in the nasal mucosa of allergic patients (Eyermann, 1927), Bickmore in the 1970s in a random manner (Bickmore and Marshall, 1976.), and from the 2000s by Gelardi more systematically (Gelardi et al, 2003).

Nasal secretions are in homogeneous fluids revealing considerable intra- and inter-individual variations in amount, composition, physical properties, biological activity and cellular content. Moreover, nasal secretions reveal spontaneous diurnal fluctuations too (Riechelmann et al, 2003). The successive wide application of nasal cytology in rhinology derives from the simplicity of normal nasal mucosa structure, which is formed by a ciliated pseudostratified epithelium, composed of mucous secreting cells and ciliated, striated, and basal cells. Therefore, on a rhino-cytogram, the presence of inflammatory cells or infectious pathogens like biofilm, bacteria, and fungi is pathologic and a marker of nasal disease (Bartoli et al, 2018).

The total count and percentage of eosinophils in a nasal smear sample (Lee et al, 2018) is accepted as a useful finding in the diagnosing allergic rhinitis (Lee et al, 2018), (Pal et al, 2017). Nasal smear for eosinophil count is simple, non-invasive and economical to diagnose allergic rhinitis than blood eosinophil count (Rudrappa et al, 2019). But the counts are poor indicators of the degree, duration, or type of upper or associated lower airway inflammation due to allergy (Pal et al, 2017).

Miller et al (1982) claimed that the nasal smear for eosinophils appears to be a reliable diagnostic test with moderately high sensitivity and high specificity. Accumulation of additional inflammatory cells such as eosinophils and T cells occurs in response to various chemokines. These inflammatory cells can be easily identified in nasal mucosa or nasal secretions by performing nasal biopsies and then, preparing nasal smears to confirm the diagnosis of allergic rhinitis. Moreover, these methods are simple, reproducible, easy to perform and cost-effective as compared to other tests like skin prick test or radio-allergo-sorbent test (RAST) (Bakhshaee et al, 2010).

Nasal cytology can give information on the activity and the efficacy of drugs used for rhinitis and it can help the physician to phenotype or in a “precision medicine” perspective (Heffler et al, 2018). Moreover, it could help the physicians, including general practitioners and allergists, in assessing the biological expression of allergic rhinitis in individual patients. Nasal smears for eosinophils are not necessary for routine use in diagnosing allergic rhinitis when the diagnosis is clearly supported by the history, physical examination, and specific IgE diagnostic studies but may be a useful adjunct when the diagnosis of allergic rhinitis is in question (Nurkic et al, 2016), (Wallace et al, 2008).

The nasal cytology represents the diagnostic gold standard tool in some diseases like cellular rhinitis, Non-Allergic Rhinitis Eosinophilic Syndrome (NARES), Non-Allergic Rhinitis with Mast cells (NARMA), and Non-Allergic Rhinitis Eosinophilic Mast Cell Syndrome (NARESMA) as these are not diagnosable without it (Heffler et al, 2018).

Eosinophils in the nasal smear have been reported to display the best correlation with all the clinical and immunological parameters in allergic rhinitis. It is a cheap, non- invasive test that may be easily repeated on the same patient, which is essential both in the follow-up of the disease and to monitor the efficacy of medical and surgical interventions (Nurkic et al, 2016).

Eosinophils are present in normal mucosa, but they appear in larger numbers in the nasal mucosa during the late phase of an atopic reaction (Klementsson et al, 1991), during natural exposure to allergen, eosinophils in nasal lavages increase 20-fold, followed closely by increasing nasal symptoms (Fazeenah et al, 2013). However, they are also found in non-allergic rhinitic noses too. The hyperreactivity of the mucosa infiltrated by eosinophils, while Mullarkey et al. (1980) described the development toward sinonasal polyps, intrinsic asthma, and acetylsalicylie acid (ASA) intolerance (Ingels et al, 1997).

Eosinophils can be demonstrated by nasal lavage tests, nasal smears, or biopsies. The problem with nasal smears and lavage tests is that eosinophils clump, and their number is extremely variable. They can be quantified by absolute numbers, or in a differential way. The finding of eosinophils in the nasal mucosa has clinical significance, since these patients more readily respond to steroids (Ingels et al, 1997).

There is no single test as a gold standard for the diagnosis of allergic rhinitis, but nasal smear for eosinophilia has been recommended as a tool for the diagnosis. In addition, it has been suggested for the diagnosis of a special type of non-allergic rhinitis called eosinophilic non-allergic rhinitis, in which the patients can be identified with many eosinophils in nasal secretions (Fazeenah et al, 2013).

3.1 Nasal sampling Methods

There are several possible collection methods for nasal cytology (Pipkorn and Karlsson, 1988), to obtain an adequate specimen, each with their advantages and disadvantages. Each sampling method may reflect inflammation of different layers of the nasal mucosa, i.e. smear or lavage - surface secretion, scraping - epithelium, brush - between secretion and epithelium, biopsy - all layers. But, according to Ingels K. et al (1997), the nasal smears and lavage tests are not very sensitive in detecting eosinophils.

At the same time, there is no consensus on how to sample and process the nasal specimen. Different techniques for sampling are described in literatures, such as nasal wash, nasal blown secretions, nasal brushing, or scraping etc. Among them, the most frequently adopted are the scraping and brushing methods, which are easy to perform and painless for the patients (Bartoli et al, 2018).

Table 01: Common techniques used to sample nasal secretions (Riechelmann et al, 2003)

	Common techniques	Methods
1.	Spontaneous secretion	• Nose blowing or collection of secretions dripping out of the nose • Suction and micro-suction • Nose blowing or suction following stimulation (methacholine, histamine)
2.	Dilution techniques	• Combined aspiration lavage • Spray blow techniques • Nasal pool lavage • Standard lavage and sequential lavage
3.	Absorption techniques	• Cotton wool • Filter paper strips or disks • Cellular materials (polyurethane foam, surgical cellulose sponges)

3.1.1 Nasal blowing

Almost identical results will be obtained by using nose-blowing method. In children with seasonal nasal symptoms, the nasal smear for eosinophils appears to be a reliable diagnostic test with moderately high sensitivity and high specificity (Miller et al, 1982).

3.1.2 Direct aspiration using micro-suction tubes

The samples are collected by repeated aspiration into a pre-weighted plastic sampling tube immediately followed by aspiration of a known volume (1.0 mL) of phosphate-buffered solution containing 10% of Mesna. The direct aspiration system combines the advantage of minimal irritation of the nasal mucosa with the facility to determine concentrations per gram of secretion. It is recommended to use only for research purpose (Heffler et al, 2018).

3.1.3 Nasal lavage

In healthy individuals the amount of spontaneously secreted or expulsed fluid from the nose is often insufficient for common investigative techniques (Riechelmann et al, 2003). It is only to study the mediators of nasal secretion and not for cytological assessment. Introduction of fluid into the nasal cavity to evaluate the proteins, cells, and cytokines like mediators in the nasal secretion. It cannot be considered as the "gold standard" method for cytological sampling since, often, the sampled cells are in apoptotic degeneration (Heffler et al, 2018).

3.1.4 Pre-weighted sinus packs or filter papers

The sinus pack or filter paper is placed on the floor of the nasal cavity between the nasal septum and the inferior turbinate for 5 minutes and then stored in a Falcon tube. The sinus pack is then washed with 3 mL of 0.9% NaCl solution and placed into a syringe and centrifuged to recover all fluid. The samples are then weighted. This technique gives reliable results but it needs the collaboration with a fully equipped laboratory to process and read the samples, with concomitant increase in costs and time to obtain the results. Therefore, it is not recommended it for clinical purpose (Heffler et al, 2018).

3.1.5 Nasal brushing

A small nylon brush is introduced in the middle meatus of the nose and turned carefully. The brush is immediately placed in a 5 mL polystyrene plastic tube containing 5 mL of phosphate-buffered solution and cut-off just above the bristles. The brush will be shaken vigorously in the solution and carefully brushed off against the wall of the tube. The tubes are centrifuged at 400 g for 10 minutes. Nasal brushing gives information on living epithelial cells, which is an advantage over nasal lavage. It is often used to study ciliary ultrastructure, even if recent studies showed better results with less prevalence of blood- derived artefacts with nasal scraping (Heffler et al, 2018).

3.1.6 Nasal scraping

It is performed with a pencil-shaped disposable nasal curette with a small distal cup. The cupped tip is gently passed over the mucosal surface of the medial aspect of the inferior turbinate. Two or three short scrapes of the epithelial layer are made to obtain a sample. The specimen is spread onto a plain slide and air-dried. Nasal scraping give information on living epithelial cells sometimes in larger lumps and it can be used to evaluate the ciliary activity if the slide is observed by a phase-contrast microscope (Heffler et al, 2018).

Smear is done by gentle scrapping of lateral nasal wall or collect blown secretions. Smear taken on to a glass is fixed in ethanol and stained with Giemsa. Microscopic examination is done for eosinophils, neutrophils, basophils, mast cells, epithelial cells and bacteria. If eosinophils are more than 10% allergy is confirmed (Rudrappa et al, 2019).

3.1.7 Nasal swab

It is an easy technique, mainly used in children, whose nasal scraping can be difficult to perform. It can be performed using an oropharyngeal swab in children and a urethral swab in newborns. Any used swab should be wet in saline and then squeezed before the use; the sample should be performed at inferior turbinate

level by “go-and-turn” rotation movements. However, the recent paediatric studies showed that the nasal scraping is still the preferable methods in children (Heffler et al, 2018).

3.1.8 Nasal biopsy

Nasal biopsy is not recommended for cytological purpose, while it is the gold standard for histological assessment of nasal mucosa (Heffler et al, 2018).

3.2 Specimen Collection and Analysis

At the end of the clinical examination, according to the methods described in literatures, two consecutive nasal scrapings are performed collecting the material from the middle third of the inferior turbinate by means of a rhino-probe (Bartoli et al, 2018).

Nasal secretion will be collected by asking the child to blow his/her nose into a plastic wrap and then placed on a glass slide. If the child is too young to do this or insufficient secretion will be obtained, cotton tipped swab will be inserted gently into the nostril and left for 60 seconds or rotated to obtain sufficient test material. Then the nasal secretion which obtained is transferred onto a glass microscopic slide is labeled with the patient's full name and date and then teased out and allowed to air dry (Rudrappa et al, 2019).

3.3 Nasal smear preparation

The collected material may be processed by direct glass smearing or by dilution of the samples with phosphate-buffered solution or dithiothreitol (DTT) coupled with cytocentrifugation (Bartoli et al, 2018).

3.4 Sample reading

The stained sample is read at optical microscopy, at 1000× magnification with oil immersion. It is recommended to read at least 50 fields. The minimum number of cells counted into the 50 fields should be more than 200 to consider the sample as adequate. The count of each cell type can be expressed as a percentage of the total cells, as an absolute value, or by a semiquantitative grading for clinical practice (Heffler et al, 2018).

3.5 Grading of nasal smear

Grading of nasal smear for eosinophils is an arbitrary measurement.

Table 2: Grading of nasal smear (Shioda and Mishima, 1966**)**

Severity	Results
0	No cells
+	Few cells or small clumps
++	Moderate number or large clumps
+++	Large clumps

Table 3: Scale to interpret nasal eosinophilia (Sood, 2005)

Severity	Number of eosinophils	Interpretation	Results
+	< 5% eosinophils	No eosinophilia	Normal
+	> 5% eosinophils	Slight eosinophilia	Doubtful
++	< 50% eosinophils	Moderate eosinophilia	Pathological
+++	> 50% eosinophils	Marked eosinophilia	Pathological

Table 4: Grading of nasal smear (Joshi et al, 2016)

Severity	Interpretation	Results
+	Less than 10 cells/hpf	Normal
2+	10-30 cells/hpf or small clumps	Mild
3+	Numerous cells or large clumps not covering the entire microscopic field	Moderate
4+	Numerous cells or large clumps covering the entire microscopic field	Marked

Table 5: Grading of nasal smear (Nurkic et al, 2016)

Severity	Results
0-3	Negative
5-10	Weak positive
10-30	Moderate positive
>30	strong positive

4. Conclusion

The nasal smear for eosinophils is a well-known, cost effective and easy to apply diagnostic method in the diagnosis and treatment of nasal allergies. Therefore, the nasal smear for eosinophils has been shown to be a pointer towards the development of subsequent nasal symptoms, and they inferred that it may be a potentially valuable test to predict prolonged or recurrent allergic rhinitis.

5. Conflict of interest

The author declares that there is no conflict of interests regarding the publication of this paper.

REFERENCES

1) Gelardi M, Iannuzzi L, Quaranta N, Landi M, Passalacqua G. 2016. Nasal cytology: practical aspects and clinical relevance. Clin Exp Allergy, 46:785-792.
2) Lans DM, Alfano N, and Rocklin R. 1989. Nasal Eosinophilia in Allergic and Nonallergic Rhinitis: Usefulness of the Nasal Smear in the Diagnosis of Allergic Rhinitis. Allergy Proc., 10(4):275-80.
3) Heffler E, Landi M, Caruso C, Fichera S, Gani F, Guida G et al. 2018. Nasal cytology: Methodology with application to clinical practice and research. Clin Exp Allergy,1–15
4) Chen J, Zhou Y, Zhang L, Wang Y, Pepper AN, Cho SH, and Kong W. 2017. Individualized Treatment of Allergic Rhinitis According to Nasal Cytology. Allergy Asthma Immunol Res. 9(5): 403–409
5) Bartoli ML, Cristofani-Mencacci L, Scarano M, Nacci A, Latorre M, Bacci E et al. 2018. Nasal Cytology: A Comparative Study of Two Different Techniques of Processing—Smeared versus Cytocentrifuged Slides. Mediators of Inflammation, 6 pages
6) Nurkic J, Al Ahmad M, Arifhodzic N, and Jusufovic E. 2016. The role of target organ diagnostic approach in seasonal allergic rhinitis: nasal smear eosinophils. Mater Sociomed, 28(2): 125-128.
7) Sood A. 2005. Diagnostic significance of nasal eosinophilia in allergic rhinitis. Indian J Otolaryngol Head Neck Surg.,57(1):13-6.
8) Mygind N. 1979. Eosinophil Leucocytes. In: Nasal Allergy. 2nd Ed. Blackwell Scientific Publications, 170-181.
9) Eyermann CH. 1927. “LXXIII Nasal manifestations of allergy”. Annals of Otology, Rhinology & Laryngology, 36 (3):808 –815.
10) Bickmore JT and Marshall ML. 1976. “Cytology of nasal secretions: further diagnostic help”. The Laryngoscope, 86 (4): 516 –523,
11) Gelardi M, Cassano P, Cassano M, and Fiorella ML. 2003. “Nasal cytology: description of a hyperchromatic supranuclear stria as a possible marker for the anatomical and functional integrity of the ciliated cell”. American Journal of Rhinology, 17 (5): 263 –268,

12) Riechelmann H, Deutschle T, Friemel E, Gross H-J, Bachem M. 2003. Biological markers in nasal secretions. Eur Respir J, 21: 600–605
13) Lee H, Yoon J, Kim K. 2018. Nasal eosinophil count and percentage in children with allergic rhinitis. Annals of Allergy, asthma and immunology, 121 (5): 100.
14) Pal I, Babu AS, Halder I, Kumar S. 2017. Nasal smear eosinophils and allergic rhinitis. ENT-Ear, Nose & Throat Journal, 96 (10-11): 17-22
15) Rudrappa S, Kumar R, Kumar V. 2019. Study of eosinophil count in nasal smear and peripheral blood smear in children with allergic rhinitis. Int J Contemp Pediatr, 6(3):1158-1162.
16) Miller RE, Paradise JL, Friday GA, Fireman P, Voith D. 1982. The Nasal Smear for Eosinophils Its Value in Children With Seasonal Allergic Rhinitis. Am J Dis Child,136:1009-1011.
17) Bakhshaee M, Fereidouni M, Farzadnia M, Varasteh AR. 2010. The Nasal Smear for Eosinophils, It's Value, and It's Relation to Nasal Mucosal Eosinophilia in Allergic Rhinitis. The Iranian Journal of Otorhinolaryngology, 22 (60): 73-78.
18) Wallace D, Dykewicz M, Bernstein D, Blessing-Moore J, Cox L, et al. 2008. The diagnosis and management of rhinitis: An updated practice parameter. JACI, 122(2): S1-S84.
19) Klementsson H, Venge P, Andersson M, Pipkorn U. 1991. Allergen-induced changes in nasal secretory responsiveness and eosinophil granulocytes. Acta Otolaryngol (Stockh), 111:776-84.
20) Fazeenah A, Quamri MA, Renuka BN. 2013. Effects of combined Unani formulations in allergic rhinitis (*Nazla Haar*) with special reference to Eosinophils in the nasal smear. Sri Lanka Journal of Indigenous Medicine, 147- 151
21) Mullarkey MF, Hill JS, Webb DR. 1980. Allergic and nonallergic rhinitis: their characterization with attention to the meaning of nasal eosinophilia. J Allergy Clin Immunol, 65:122-6.
22) Ingels K, Durdurez J-P, Cuvelier C, Cauwenberge P.V. 1997. Nasal biopsy is superior to nasal smear for finding eosinophils in nonallergic rhinitis. Allergy, 52:338-341
23) Pipkorn U, Karlsson G. 1988. Methods for obtaining specimens from the nasal mucosa for morphological and biochemical analysis. Eur Respir J,1:856–862.
24) Shioda H, Mishima T. 1966. Significance of mast cells in nasal smears from patients with food allergy. J Allergy,37(6):321-8.
25) Joshi V, Rakesh R, Silveira M. 2016. Correlation between SFAR score and nasal cytology in paediatric allergic rhinitis patients visiting OPD in Goa Medical College. J Pediatr Res, 3(12):908-913.