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Original Research Article

EVALUATION OF INTERLEUKIN-25 LEVELS IN PATIENTS OF CHRONIC RHINOSINUSITIS WITH NASAL POLYPS

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Abstract

Background: Chronic rhinosinusitis (CRS) is a common inflammatory disease of nose and paranasal sinuses. CRS with nasal polyps (CRSwNP) was found to be associated with intereukin-25 mediated inflammation. Studies have shown beneficial effects of anti-IL-25 treatment in patients with nasal polyps. **Materials and Methods:** Twenty four patients who were classified as patients with chronic rhinosinusitis with nasal polyp (CRSwNP) and patients with chronic sinusitis, turbinate hypertrophy, deviated nasal septum and chronic dacryocystitis (CRSsNP) were included. IL-25 levels were measured in homogenized samples of nasal polyp tissues and sinonasal mucosa of both groups of patients. **Result:** IL-25 levels in patients with CRSwNP were significantly higher when compared to IL-25 levels of patients with CRSsNP (p=0.003). Ethmoid polyps were more common than antrochoanal polyps in patients with CRSwNP. Patients with ethmoid polyps had higher CT scores compared to patients with antrochoanal polyps. **Conclusion:** Nasal polyp tissue of patients with CRSwNP showed higher IL-25 levels when compared to those in patients with CRSsNP. The increased levels indicate IL-25 as a potential target in the management of patients with nasal polyps.

INTRODUCTION

Chronic rhinosinusitis (CRS) is one of the most common inflammatory diseases of nose and paranasal sinuses with local inflammation usually persisting for more than 12 weeks.[1] The prevalence of clinically based CRS was reported to range from 3% to 6.4%.[2] CRS is classified into two types based on clinical presentation and histopathology as: CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP).[3] Patients with CRSwNP usually present with symptoms of nasal obstruction and decreased sense of smell and some of the patients with CRSwNP are resistant to both surgical and medical lines of management. It has been found that CRSwNP was associated with amplification of T helper-2 (Th-2) related inflammation.[4] Cytokines such as Interleukin (IL)-25, IL-33 and TSLP (thymic stromal lymphopoietin) produced from the nasal epithelial cells are critical regulators of the Th-2 immune response which in turn enhances the inflammation through the production of IL-4, IL-5, and IL-13.[5] Hong et al demonstrated that CRSwNP with high IL-25 had more severe sinus disease on nasal endoscopy and computed tomography and thus IL-25 plays an important role in the pathogenesis of CRSwNP.[6] It was shown that anti-IL-25 therapy decreases the number of polyps and mucosal edema and hence IL-25 may be considered as a therapeutic target in treating the cases of CRSwNP.[7] In this background, the present study was conducted to measure IL-25 levels in the tissue samples of patients with CRSwNP and compare them with those of patients with CRSsNP.

MATERIALS AND METHODS

The present study was a cross-sectional observational study conducted in the Department of Otorhinolaryngology at a tertiary care center in South India after obtaining Institutional Ethics Committee approval (Lr.No.40/2021 dated 27-02-2021). The study included twenty four patients of both genders aged between 20 and 60 years and attending the Otorhinolaryngology OPD. All the patients were classified into two groups as: patients with chronic rhinosinusitis with nasal polyp (CRSwNP) [n=12] and patients with chronic sinusitis, turbinate hypertrophy, deviated nasal septum and chronic dacryocystitis (CRSsNP) [n=12]. The diagnosis of CRSwNP was made by Diagnostic Nasal Endoscopy (DNE) and Computed tomography (CT) scan of the nose and paranasal sinus. Patients with malignancy of nose and paranasal sinus, who were known

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smokers and those with history of asthma, systemic diseases and sinonasal surgery were excluded from the study.

Data was collected from all the subjects in a standardized proforma according to the European position paper on Rhinosinusitis.[1] The data included details of clinical history, complete ENT, head and neck examination, diagnostic nasal endoscopy, blood investigations including complete blood count (CBC), radiological investigations including x-ray and CT scan of the paranasal sinus. All the patients were admitted one day before the surgery. Surgical procedures such as functional endoscopic sinus surgery (FESS), septoplasty, turbinectomy, and endoscopic dacryocystorhinostomy (EndoDCR) were performed as per the indications on patients fit for surgery after a thorough pre-operative workup.

On the day of surgery, the nasal polyp tissue samples from CRSwNP patients and sinonasal mucosa samples from CRSsNP patients were collected in sample containers containing 10% formalin. The samples collected were stored at -80^{0}C until further analysis. Preparation of tissue homogenates was done by weighing 200 µg of each sample. The sample was mixed with 1800 µl of phosphate buffer saline (PBS) at pH-7.4 in cesium beads containing Precelly`s lysing tubes for homogenization. Homogenization was carried out in a Bertin–Minilys with high speed for 180 seconds. The homogenates were centrifuged at 5000 rpm (2^0-8^{0}C) for 10 minutes and the collected supernatant was stored at -20^{0}C. IL-25 levels in tissue homogenates were measured by sandwich enzyme linked immunosorbent assay (ELISA) using commercial kits.

Statistical analysis: Continuous variables were expressed as mean ± standard deviation (SD). Frequency was expressed as number (percentage), (n (%)). The difference in the means of IL-25 levels and CT scores was analysed by independent samples t-test. Data was analysed using Microsoft excel spread sheets and Statistical Package for Social Sciences (SPSS, Inc., Chicago IL) for windows version 16.0. A p value less than 0.05 was considered as statistically significant.

RESULTS

Seventeen (70.8%) of the total subjects included in the study were males and seven (29.2%) were females. There were more number of female patients in the CRSwNP group (n=6) when compared with the CRSsNP group (n=1) while males patients were more in the CRSsNP group (n=11) when compared with the CRSwNP group (n=6). Majority of patients in the CRSwNP group belonged to 50-60 years age (n=5, 41.7%) followed by 30-40 years (n=4, 33.3%) while majority of patients without nasal polyps were in 20-30 years age group (n=6, 50%) followed by 50-60 years (n=3, 25%) age group.

The most common presenting complaint in all the twenty four subjects was sneezing followed by headache and nasal obstruction, nasal discharge, postnasal drip and disturbance/loss of smell [Table 1]. The mean tissue IL-25 levels in CRSwNP patients were found to be significantly higher when compared to CRSsNP patients. [Table 2, Figure 1]. In patients diagnosed with CRSwNP, ethmoid polyps were found in 7 patients (58.33%) and antrochoanal polyps were observed in 5 patients (41.7%). Further, when the CT severity score of CRSwNP patients was evaluated according to Lund Mackay scoring system,[8] patients with ethmoidal polyps showed more disease in CT PNS compared to patients with antrochoanal polyps [Table 3].

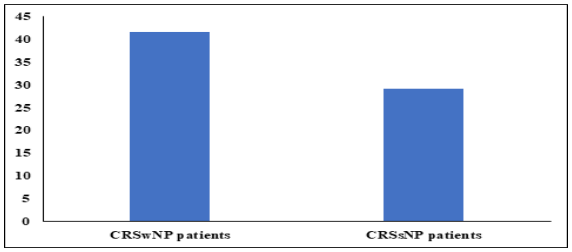

Figure 1: Mean interleukin-25 levels CRSwNP and CRSsNP patients

CRSwNP=patients with chronic rhinosinusitis with nasal polyp; CRSsNP=patients with chronic sinusitis, turbinate hypertrophy, deviated nasal septum and chronic dacryocystitis

Table 1: Frequency of the presenting complaints in the study subjects (n=24).

Complaint	Number of patients n (%)
Sneezing	22 (91.7%)
Headache	21 (87.5%)
Nasal obstruction	21 (87.5%)
Nasal discharge	16 (66.7%)
Post nasal drip	14 (58.3%)
Disturbance of Smell	08 (33.3%)

Table 2: Tissue homogenate Interleukin-25 levels in the two groups of patients

Parameter	CRSwNP patients (n=12)	CRSsNP patients (n=12)	p- value
IL-25 (pg/mL)	41.57±16.05	29.19±10.22	0.003

Data expressed as mean±standard deviation

CRSwNP=patients with chronic rhinosinusitis with nasal polyp; CRSsNP=patients with chronic sinusitis, turbinate hypertrophy, deviated nasal septum and chronic dacryocystitis; IL-25=interleukin-25

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Table 3: CT scores of ethmoid polyps and antrochoanal polyps of CRSwNP patients (n=12)

Parameter	Patients with ethmoidal polyps (n=7)	Patients with antrochoanal polyps (n=5)	p- value
CT score	15.42±2.55	6.20±1.46	<0.001

Data expressed as mean±standard deviation
CRSwNP=patients with chronic rhinosinusitis with nasal polyp; CT score=computed tomography score

DISCUSSION

Chronic rhinosinusitis is a chronic inflammatory condition of the nose and paranasal sinuses which may be associated with the development of polyps. CRS is usually associated with amplification of inflammatory markers from the nasal epithelial cells such as IL-25, IL-33, and TSLP which in turn increase the production of IL-4, IL-5, and IL-13. These further enhance the development of polyps. The pathophysiology of CRSwNP is mostly characterized by TH-2-mediated inflammation and eosinophilia.[8,9]

In the present study, it was found that nasal obstruction, sneezing, nasal discharge and post-nasal drip were the most common symptoms in CRSwNP patients, while headache and sneezing were the most prevalent symptoms in CRSsNP patients. Similarly, in a study conducted by Banerji and Colleagues on 126 CRS patients, it was found that nasal obstruction and disturbance of smell (Hyposmia/Anosmia) were the common symptoms in CRSwNP patients, while facial pain/pressure were more prevalent in CRSsNP patients.[10]

The mean IL-25 levels were significantly higher in nasal polyp tissue homogenates from patients with CRSwNP than in patients with CRSsNP (p=0.003) [Table 2, Figure 1]. When evaluated further, it was found that ethmoid polyps were more common than antrochoanal polyps in patients diagnosed with CRSwNP. Moreover, patients with ethmoid polyps had higher CT scores compared to patients with antrochoanal polyps [Table 3]. A study by Hong et al demonstrated that CRSwNP with high IL-25 levels had more severe sinus disease on nasal endoscopy and CT scan, had greater TH-2 response and more severe eosinophilia compared to CRSwNP with low IL-25 levels.[6]

IL-25, also known as IL-17E belongs to IL-17 cytokine family and is known to play an important role in inflammation through production of Th2 cytokines.[11] Experimental studies have demonstrated that nasal polyps of murine model showed an increased expression when compared to tissues from control mice. Further, anti–IL-25 treatment showed beneficial effect by decreasing mucosal thickness, polyp formation and infiltration of inflammatory cells.[7] Even in humans, it has been shown that there was an increased expression of IL-25 in the epithelial cells and infiltrating mast cells of nasal polyps which was positively correlated with inflammatory markers.[7] This might be the reason underlying the increased levels of IL-25 observed in the nasal polyp tissues of patients with CRSwNP in the present study.

The limitation of the present study was the small sample size (n=24) which was overcome by estimating the levels of IL-25 directly from the nasal polyp tissue as well as from nasal mucosa samples.

CONCLUSION

Findings of the present study show increased levels of IL-25 in the nasal polyp tissue of patients with CRSwNP when compared to those in patients with CRSsNP, suggesting the role of IL-25 as an important cytokine in the pathogenesis of polyp formation in CRSwNP patients. The increased levels further indicate IL-25 as a potential target in the management of patients with nasal polyps. In future, IL- 25 levels can be applied as a biomarker for predicting the clinical efficacy of corticosteroids both locally and systemically which are used in the management of nasal polyps.[12]

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