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The role of NF-κB in chronic rhinosinusitis with nasal polyps

비용을 동반한 만성 비부비동염에서 NF-κB의 역할에 대한 연구

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A thesis of the Master’s degree

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July 2017

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ABSTRACT

The role of NF-κB in chronic rhinosinusitis with nasal polyps

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Background: While the majority of nasal polyps seen in Western countries are eosinophilic, non-eosinophilic nasal polyps comprise a significant percentage in Asian countries. Given the importance of nuclear factor-kappaB (NF-κB) in the inflammatory processes and the poor description in Asian nasal polyps, the purpose of this study was to understand the role of NF-κB in the pathogenesis of chronic rhinosinusitis with nasal polyp (CRSwNPs) in Asian patients.

Materials and methods: A total of 46 patients were enrolled in this study. 22 patients were diagnosed as CRSwNPs, 10 as chronic rhinosinusitis without nasal polyps (CRSsNP), and 14 as control subjects. Nasal polyps and uncinate tissues (UTs) were obtained. The tissues were prepared for hematoxylin-eosin staining and immunohistochemistry (IHC) study. And the total RNA was isolated for real time polymerase chain reaction for p65, IL-6, IL-8, ICAM-1, IL-1β, TNFα, and eotaxin.

Results: When we analyzed histological type of nasal polyps in CRSwNPs group, eosinophilic type was 50% and non-eosinophilic type 50%. IHC revealed that the ratio of NF-κB p65-positive cells were significantly higher in the nasal polyps of the CRSwNPs group than in the UTs of the control, and
CRSsNP groups. Between eosinophilic and non-eosinophilic nasal polyps, there was no difference. The mRNA expression of p65, IL-6, IL-8, and eotaxin were significantly higher in nasal polyps of the CRSwNPs than in the UTs of the control and the CRSsNP. But eosinophilic and non-eosinophilic nasal polyps showed no difference except IL-1β.

**Conclusions:** Increased expression of NF-κB and NF-κB related inflammatory cytokine indicate that NF-κB has a pivotal role in the pathogenesis of CRSwNPs in both Caucasian and in Asian. An understanding of these mechanisms will provide a deeper insight into CRSwNPs pathogenesis and ultimately, improved therapeutic strategies. Further studies to evaluate the therapeutic possibility of NF-κB inhibition in CRSwNPs are needed.

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**Key words:** Chronic rhinosinusitis, Nasal polyp, Eosinophilic nasal polyp, Non-eosinophilic nasal polyp, NF-kappaB, Transcription factor.

**Student Number:** 2015-22003
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LIST OF ABBREVIATIONS

NF-κB: Nuclear factor-kappa B
CRSwNPs: Chronic rhinosinusitis with nasal polyps
CRSsNP: Chronic rhinosinusitis without nasal polyp
UTs: Uncinate tissues
IHC: Immunohistochemistry
IL: Interleukin
ICAM-1: Intercellular adhesion molecule-1
TNFα: Tumor necrosis factor-α
mRNA: messenger RNA
CT: Computed tomography
PCR: Polymerase chain reaction
cDNA: complementary DNA
GAPDH: Glyceraldehyde-3-phosphate dehydrogenase
VCAM-1: Vascular cell adhesion molecule-1
GM-CSF: Granulocyte-macrophage colony-stimulating factor
INTRODUCTION

Chronic rhinosinusitis with nasal polyps (CRSwNPs) is a chronic inflammatory disease of the nasal and paranasal sinus mucosa with a prevalence of 0.5-4% in the general population (1). It can lead to nasal obstruction, olfactory dysfunction, headache, and posterior nasal drip, all of which can adversely affect a patient’s quality of life (2).

Although the pathogenesis of nasal polyps has not been clearly identified, nasal polyp is generally characterized by edematous masses of inflamed mucosa and abundant inflammatory cells. However, recent studies have suggested that nasal polyps in Asian population present different immunopathological features compared with those in Western countries. Typically, while the majority of nasal polyps seen in Western countries are eosinophilic, non-eosinophilic nasal polyps comprise a significant percentage of CRSwNPs in Asian countries (3-8).

Study to identify the difference between ethnic groups should be performed and it is very important because the immunopathologic differences may come from the differences in pathogenesis and the difference in pathogenesis can bring different therapeutic approaches. In several previous studies showed that CRSwNPs patients have poor prognosis and high recurrence rate despite surgical or medical treatment. However, there are not many studies about ethnic differences in eosinophilic and non-eosinophilic nasal polyps. Several theories have been proposed to explain the pathogenesis of nasal polyps, but exact pathogenesis of CRSwNPs is still unknown. And most of the nasal polyp studies were done in Western countries.

Recent studies demonstrated that during chronic inflammation within paranasal sinuses, the growth of nasal polyp is induced and perpetuated by the complex interaction of various cytokines produced by structural and infiltrating cells (9). And it is now known that cytokine production during the inflammatory process is
induced by several transcription factors and one of the transcription factors which are the most important is the nuclear factor-kappaB (NF-κB). NF-κB is thought to play a fundamental role in the regulation of multiple pro-inflammatory genes (10). It comprises p50 and p65 subunits. When activated, NF-κB translocates to the cell nucleus and its active fraction, p65 induces the transcription of cytokines, chemokines and adhesion molecules. However, the specific roles of NF-κB in the pathogenesis of CRSwNPs are still not fully understood, especially in Asians.

Given the importance of NF-κB in the inflammatory processes and the poor description in Asian nasal polyp, the purpose of this study was to understand the role of NF-κB in the pathogenesis of CRSwNPs in Asian patients. We have investigated NF-κB expression and its relation to other inflammatory cytokines and adhesion molecules in Asian patients with CRSwNPs.
MATERIALS & METHODS

Patients

A total of 46 patients were enrolled in this study. Of the 46 patients, 22 patients were diagnosed as CRSwNPs, 10 patients had chronic rhinosinusitis without nasal polyp (CRSsNP), and 14 patients who were undergoing other rhinologic surgeries, such as septoplasty were enrolled as control subjects.

All of the patients were > 18 years of age. The sinus disease diagnosis was based on patient history, clinical examination, nasal endoscopy, and computed tomography (CT) scans of the paranasal sinuses. Preoperative CT scans were reviewed to determine the extent of the sinus disease with the Lund-Mackay scoring system. Patients were excluded if they had received systemic or topical steroids and/or had antibiotics or antihistamine medications during the 4 weeks preceding the study. Antrochoanal polyp, fungal sinusitis, and recurrent nasal polyps were excluded from the study. A written informed consent was obtained from each patient and control subject before enrollment into the study. The study was approved by the Institutional Review Board of the Seoul National University Hospital.

Tissue preparation

For histological study, nasal polyp tissues were obtained from the 22 patients with CRSwNPs and uncinate tissues (UTs) were obtained from the 10 patients with CRSsNP and 14 control subjects. Half of the samples were fixed with 10% formaldehyde solution. The tissues were embedded in paraffin, sectioned into 4-μm slices, and subsequently used for hematoxylin-eosin staining and immunohistochemistry (IHC) study. The other was placed in a Cryotube and stored
at -80°C in an ultra-low temperature refrigerator. Then total RNA from tissue specimens was isolated using a rapid extraction method (Trizol Reagent, Invitrogen, USA) for real time polymerase chain reaction (PCR). Hematoxylin-eosin-stained sections were observed by one physician who was blind to the clinical data. Nasal polyp type was identified and classified as eosinophilic (more than 10% of inflammatory cells in the studied area were eosinophils) and non-eosinophilic.

**NF-κB p65 immunohistochemical analysis**

IHC staining was performed by using the Histostain-Plus Bulk Kit (Invitrogen, Camarillo, CA). Briefly, after deparaffinization, the sections were microwave-treated in 10 mmol/L citrate buffer (pH 6.0) for heat-induced epitope retrieval and incubated in 3% hydrogen peroxide for endogenous peroxidase inhibition. The sections were incubated for overnight at 4°C with each primary antibody, which included mouse anti-human p65 monoclonal antibody (Santa Cruz Biotechnology, Inc.). Bound antibodies were visualized by 3,3′-diaminobenzidine Detection kit (Vector Laboratories, Burlingame, CA, USA). Finally, slides were counterstained with hematoxylin. Each slice was randomly taken 5 photos at 400× magnification under the microscope. The presence of brown-yellowish granules in the nucleus was considered as p65-positive. Among the total cell number, the p65-positive cells in epithelia, glands, and submucosa were counted by two independent observers, and the mean value with range was calculated. The p65-positive cell ratio was calculated according to the following formula and used as a parameter of NF-κB activity: p65-positive cell ratio = number of NF-κB p65-positive cells/total number of cells x 100 per cent.
Real time polymerase chain reaction

Total RNA was isolated from the stored frozen tissues using the TriZol reagent (Invitrogen, Carlsbad, CA, USA). Complementary DNA (cDNA) was synthesized using amfiRivert Platinum cDNA Synthesis Master Mix (GenDEPOT, TX, USA). For the analysis of p65, IL-6, IL-8, ICAM-1, IL-1β, TNFα, and eotaxin, amplification of p65, IL-6, IL-8, ICAM-1, IL-1β, TNFα, eotaxin, and GAPDH cDNA was performed using an ABI PRISM 7000 Sequence Detection System (Applied Biosystems) in conjunction with the 2 x SYBR green master mix reaction kit (Applied Biosystems). The average transcript levels of genes were then normalized to GAPDH (Table 1).

Table 1. Primer sequences for reverse transcription-polymerase chain reaction.

<table>
<thead>
<tr>
<th>Primer</th>
<th>Sequence</th>
<th>Size</th>
</tr>
</thead>
</table>
| **p65** | forward: 5’-CCA CGA GCT TGT AGG AAA GG-3’  
reverse: 5’-CTG GAT GCG CTG ACT GAT AG-3’ | 143 |
| **IL-6** | forward: 5’-ATG GCT GAA AAA GAT GGA TGC T-3’  
reverse: 5’-GCT CTG GCT TGT TCC TCA CTA CTC-3’ | 141 |
| **IL-8** | forward: 5’-GCC AAC ACA GAA ATT ATT GTA AAG CTT -3’  
reverse: 5’-AAT TCT CAG CCC TCT TCA AAA ACT T-3’ | 110 |
| **ICAM-1** | forward: 5’-TGT CCC CCT CAA AAG TCA TC-3’  
reverse: 5’-TAG GCA ACG GGG TCT CTA TG-3’ | 104 |
| **IL-1β** | forward: 5’-ACG AAT CTC CGA CCA CCA CTA-3’  
reverse: 5’-GGC AGG GAA CCA GCA TCT T-3’ | 95 |
| **TNFα** | forward: 5’-CCC AGG CAG TCA GAT CAT CTT C-3’  
reverse: 5’-AGC TGC CCC TCA GCT TGA-3’ | 85 |
| **Eotaxin** | forward: 5’-CAGAGCCCTGAGTGTGCTC-3’  
reverse: 5’-AACCCATGCCCCCTTGACTG-3’ | 85 |
| **GAPDH** | forward: 5’-GAG AAG GCT GGG GCT CAT-3’  
reverse: 5’-TGC TGA TCT GGA TGC TG-3’ | 128 |
Statistical analysis

The data are presented as means ± standard error mean. A Mann-Whitney U-test and Kruskal-Wallis test was used to compare results between groups. A P value of less than 0.05 was considered statistically significant. Statistical analysis was performed using SPSS 18.0 software (SPSS Inc, Chiago, IL, USA).
RESULTS

Patients data

Total 46 patients were enrolled in study. 22 patients (14 males and 8 females) diagnosed as CRSwNPs were evaluated, mean age 48.8 years (range, 23-79). 10 patients with CRSsNP were 6 males and 4 females, mean age 42.8 years (range, 23-67). And 14 patients were control group, 8 males and 6 females and mean age was 33.2 years (range, 19-61). The control group consisted of 14 patients submitted to septoturbinoplasty surgery with no evidence of chronic rhinosinusitis in nasal endoscopy and CT scan. Lund-Mackay CT score was 0.6 for control group, 4.8 for CRSsNP, and 8.4 for CRSwNPs. Gender and mean age were not statistically different between three groups (Table 2).

Table 2. Patients characteristics.

<table>
<thead>
<tr>
<th>Group</th>
<th>Controls</th>
<th>CRSsNP</th>
<th>CRSwNPs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total of subjects, n</td>
<td>14</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>8 (57.1)</td>
<td>6 (60.0)</td>
<td>14 (63.6)</td>
</tr>
<tr>
<td>Mean age, year</td>
<td>33.2</td>
<td>42.8</td>
<td>48.8</td>
</tr>
<tr>
<td>Mean Lund-Mackay CT score</td>
<td>0.6</td>
<td>4.8</td>
<td>8.4</td>
</tr>
</tbody>
</table>

Eosinophilic vs. Non-eosinophilic nasal polyp

When we analyzed histological type of nasal polyps in CRSwNPs group (n=22), eosinophilic type was 11 (50%) and non-eosinophilic type was 11 (50%) (Fig. 1). Eosinophilic nasal polyp group included 8 males and 3 females, mean age 53.2 years. Non-eosinophilic nasal polyp group included 6 males and 5 females, mean
age 44.5 years. Lund-Mackay CT score was 7.5 for Eosinophilic and 9.3 for Neutrophilic (p-value > 0.05) (Table 3).

Figure 1. Hematoxylin and Eosin staining (magnification x400). (A) Eosinophilic nasal polyp, (B) Non-eosinophilic nasal polyp.

Table 3. Characteristics of eosinophilic and non-eosinophilic nasal polyp.

<table>
<thead>
<tr>
<th>Group</th>
<th>Eosinophilic</th>
<th>Non-eosinophilic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total of subjects, n</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>8 (72.7)</td>
<td>6 (54.5)</td>
</tr>
<tr>
<td>Mean age, year</td>
<td>53.2</td>
<td>44.5</td>
</tr>
<tr>
<td>Mean Lund-Mackay CT score</td>
<td>7.5</td>
<td>9.3</td>
</tr>
</tbody>
</table>

**NF-κB p65 expression in immunohistochemistry**

NF-κB p65 IHC showed positive immunoreactivity in the cytoplasm and nucleus at the epithelium, subepithelial inflammatory cells, vascular endothelial cells, and glandular endothelial cells (Fig. 2).
Figure 2. Representative IHC results of NF-κB p65 expression in each group (magnification x400). (A) control, (B) CRSsNP, (C) CRSwNPs (eosinophilic), (D) CRSwNPs (non-eosinophilic). Examples of p65-positive cells (black arrows in the box).

IHC revealed that the ratio of NF-κB p65-positive cells were significantly higher in the CRSwNPs group than in the control and CRSsNP groups. The p65-positive cell ratio were 49.10% in CRSwNPs group, 9.87% in control group and 16.57% in CRSsNP group (p-value =0.041) (Fig. 3).
Figure 3. NF-κB p65-positive cell ratio in each group (Kruskal-Wallis Test; mean +/- SEM).

There was no statistical difference between Eosinophilic and non-eosinophilic nasal polyps (Eosinophilic 57.08%, non-eosinophilic 41.11%, p-value 0.340) (Fig. 4).
Figure 4. NF-κB p65-positive cell ratio in eosinophilic and non-eosinophilic nasal polyp (Mann-Whitney Test; mean +/- SEM).

**Real time polymerase chain reaction**

Expression levels of p65 mRNA in nasal tissues, IL-6, IL-8, ICAM-1, IL-1β, TNFα, and eotaxin were examined by real time PCR. The mRNA expression of p65 in the nasal polyp of CRSwNPs was higher than in the UTs of the control and the CRSsNP groups, statistically significant (p=0.045) (Fig. 5).
Expression of IL-6, IL-8, and eotaxin were significantly higher in the nasal polyp of CRSwNP than in the UTs of the control group and CRSsNP (p=0.035, 0.025, and <0.001, respectively). ICAM-1 mRNA was strongly expressed in the nasal polyps of CRSwNP patients compared with UTs in normal control and CRSsNP patients, but statistically not significant (p=0.097). IL-1β and TNFα expression showed no difference between three groups (Fig. 6).
Figure 6. IL-6, IL-8, ICAM-1, IL-1β, TNFα, and eotaxin mRNA expression level in each group (Kruskal-Wallis Test; *P<0.05; mean +/- SEM).

There were no significant differences in p65 expression between eosinophilic nasal polyp and non-eosinophilic nasal polyp (0.7564 vs. 1.3491, p-value = 0.457) (Fig. 7).
Figure 7. p65 mRNA expression level in eosinophilic and non-eosinophilic nasal polyp (Mann-Whitney Test; mean +/- SEM).

Also, no difference in IL-6, IL-8, ICAM-1, TNFα, and eotaxin were found between eosinophilic and non-eosinophilic nasal polyp. But only, IL-1β was significantly higher in non-eosinophilic (1.4166) compared to eosinophilic (0.5983) (p-value = 0.028) (Fig. 8).
Figure 8. IL-6, IL-8, ICAM-1, IL-1β, TNFα, and eotaxin mRNA expression level in eosinophilic and non-eosinophilic nasal polyp (Mann-Whitney Test; mean +/- SEM).
CRSwNPs is a chronic mucosal inflammatory disease that involves complex pathogenesis and multiple etiologies. Recently, several studies reported that the Asian nasal polyps are different from Caucasian nasal polyps. Typically, the inflammation pattern of CRSwNPs in Asians and Caucasians showed some differences, where Asian nasal polyp show Th1/Th17 dominance and neutrophilic activation, unlike the nasal polyp of Caucasians which are often associated with eosinophilic airway inflammation. Except in cystic fibrosis and primary ciliary dyskinesia, in Caucasian CRSwNPs patients, eosinophils comprise 60-90% of cell population in majority of the nasal polyps (8,11-14). However, several studies in Asian countries showed that Asian population has non-eosinophilic nasal polyps (3-7). Study done in Thailand showed that 81.9% of nasal polyp had non-eosinophilic pattern (15), Malaysian study showed that non-eosinophilic nasal polyps account for 48.75% (16). In present study, CRSwNPs patients had eosinophilic to non-eosinophilic ratio of 1:1, which is similar to other Asian studies. As shown above, in Asian nasal polyp, non-eosinophilic pattern is more common, but most of the studies have been performed in Caucasian patients. And the studies with Asian populations did not divide the nasal polyps to eosinophilic or non-eosinophilic. This histological difference of nasal polyp between Caucasian and Asian patients may come from difference in pathogenesis and mechanism of nasal polyp formation. It is very important since different therapeutic approach may be required for different pathogenesis and mechanism.

There is no doubt that nasal polyps in both Asian and Caucasian develop as a result of chronic inflammation of sinonasal mucosa with increased cytokine expression (17). Chronic inflammation in chronic rhinosinusitis is induced and maintained by a
complex interaction of various cytokines (18). Once stimulated by the cytokines, structural cells in the nasal mucosa produce a variety of other cytokines, chemokines and adhesion molecules, which once started, apparently do not depend on a causal stimulus to perpetuate itself (19, 20). Xu et al. reported that IL-5, IL-6, and IL-8 were increased in CRSwNPs than control group (21). And in another study, using in situ hybridization, reported a significant increase in IL-1β and TNFα expression in nasal polyps compared with the mucosa of the middle turbinate (22). Papon et al. observed a significantly higher concentration of the ICAM-1 protein in nasal polyps than in control mucosa, in measurements by immunochemistry methods (23). In present study, real time PCR indicated that expression of the IL-6, IL-8, and eotaxin genes was significantly higher in patients with nasal polyp when compared with normal controls and CRSsNP group. ICAM-1 showed higher tendency in CRSwNPs group, but statistically not significant. These results were similar to previous studies, this implies that IL-6, IL-8, eotaxin and ICAM-1 might play a role in the development of CRSwNPs, and stress the importance of cytokine and adhesion molecules in the polypogenesis. IL-1β, TNFα had no significant difference which is different from the previous studies. Between Eosinophilic and non-eosinophilic nasal polyp, except IL-1β, IL-6, IL-8, ICAM-1, TNFα, and eotaxin had no difference. These result implies that both eosinophilic and non-eosinophilic nasal polyp have same mechanism of polypogenesis induced by cytokine.

It is now known that cytokine production during the inflammatory process is induced by transcription factors. Once an inflammatory process is initiated, transcription factors will be activated and translocated to the cell nucleus, inducing the transcription of some genes, particularly the ones related to inflammatory cytokines, chemokines and adhesion molecules (24). One of the transcription factors which are the most important is the NF-κB. NF-κB is a heterodimer
consisting of members of the p50 and p65 families. It is a key pro-inflammatory nuclear transcription factor involved in the regulation and production of a large number of pro-inflammatory cytokines (24-26). As an inducible nuclear transcription factor, when activated, NF-κB translocates to the cell nucleus and its active fraction, p65 induces the transcription of cytokines, chemokines and adhesion molecules. Because cytokines may in turn activate NF-κB, the perpetuation of the inflammatory process in nasal polyp could be explained easily (19). NF-κB has been shown to mediate the transcription of genes for ICAM-1, VCAM-1 and for the cytokines GM-CSF, TNFα, IL-2, IL-6, and IL-8 (22,27).

There are several studies that demonstrated the relationship between CRSwNPs with NF-κB. Xu et al. reported that NF-κB expression is upregulated in CRSwNPs patient and NF-κB level has a correlation with IL-6, IL-8 cytokine expression. So they concluded that NF-κB might be one of the mechanisms for induction of IL-6 and IL-8 expression in CRSwNPs (21). Wilson (28) and Ohiri and Silvestri (29) reported that TNFα induced the expression of ICAM-1 and IL-8 in respiratory epithelial cells via NF-κB. Recently, 28 patients with NPs were analyzed through IHC by Takeno et al. (20), who observed an increase of the NF-κB in CRSwNPs patients. And the authors also reported that the increase in p50 was correlated to an increased expression of IL-8, IL-16 and eotaxin, suggesting that NF-κB may have a central role in the perpetuation of the inflammatory process in nasal polyp. In the present study, statistically higher levels of p65 mRNA, the transcriptional fraction of NF-κB, were observed in patients with CRSwNPs compared with controls and CRSsNP patients. Also, p65-positive cell ratio analyzed by IHC, were higher in CRSwNPs than in CRSsNP. But when compared between eosinophilic and non-eosinophilic nasal polyp, mRNA of p65 did not show significant difference and NF-κB positive cell ratio did not show difference in IHC.
This is the first study to analyze the role of NF-κB in Asian nasal polyp. This study is about the pathophysiology of nasal polyp whether it can be different between eosinophilic and non-eosinophilic nasal polyps. Understanding pathophysiology is important since it can change the therapeutic approach. Previous studies reported difference in nasal polyp between Asian and Caucasian, postulated that the underlying pathophysiological or immunologic mechanism of nasal polyp formation could be different in Asian and Caucasian population and may need a different therapeutic approach. In this study, non-eosinophilic polyp comprised of 50%, which is consistent with previous studies but NF-κB expression and cytokine expression had no significant difference between eosinophilic and non-eosinophilic nasal polyp. Although histologic phenotype is different, they share important common mechanism which is cytokine expression through NF-κB. In future study, inhibition of NF-κB could be explored as a novel target for therapeutics in CRSwNPs in both Asian and Caucasian. As Valera et al. reported dehydroxymethylepoxyquinomicin, a potential NF-κB inhibitor, to be effective in Caucasian CRSwNPs (30), this approach may also be effective in Asian CRSwNPs patient. Further studies are needed to determine whether NF-κB pathway can be used to inhibit the polypogenesis in CRSwNPs patients in Asian, as a therapeutic option.
CONCLUSIONS

Our study showed that expression of NF-κB p65 in both eosinophilic and non-eosinophilic nasal polyp. Increased expression of NF-κB and NF-κB related inflammatory cytokine indicate that NF-κB has a pivotal role in the pathogenesis of CRSwNPs in both Caucasian and in Asian. An understanding of these mechanisms will provide a deeper insight into CRSwNPs pathogenesis and ultimately, improved therapeutic strategies. Further studies to evaluate the therapeutic possibility of NF-κB in CRSwNPs are needed in the future.
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초 록

비용을 동반한 만성 비부비동염에서 NF-κB의 역할에 대한 연구

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의학과 이비인후과 전공
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서론: 비용을 동반한 만성 비부비동염 환자에서, 서양의 경우 호산구성 비용의 비율이 높으나, 동양의 경우에는 비-호산구성 비용이 차지하는 비율이 높다고 보고되고 있다. 비용의 발병기전으로 다양한 싸이토카인의 역할이 밝혀져 있으며, 이는 전사 인자를 통해 조절된다. NF-κB는 중요한 전사인자 중 하나로, 염증 과정에서 중요한 역할을 하고 있다. 본 연구에서는 동양의 비용을 동반한 만성 비부비동염 환자에서 호산구성 비용과 비-호산구성 비용에 따른 NF-κB의 역할에 대해 알아보고자 하였다.

방법: 비용을 동반한 만성 비부비동염 환자 22명, 비용을 동반하지 않은 만성 비부비동염 환자 10명, 그리고 14명의 대조군 환자에서 비용과 구상돌기 조직을 채취해 분석하였다. 비용은 호산구성과 비-호산구성으로 분류하였고, 면역조직화학염색법으로 NF-κB의 발현
정도를 평가하였다. p65, IL-6, IL-8, ICAM-1, IL-1β, TNFα, eotaxin 에 대해 실시간 역전사 중합효소 연쇄반응으로 비교 분석하였다.

결과: 비용을 동반한 만성 비부비동염 환자에서 호산구성 비용과 비-호산구성 비용의 비율은 1:1 이었다. NF-κB의 발현은 비용을 동반한 만성 비부비동염 환자에서 유의하게 증가한 소견을 보였고, 호산구성 비용과 비-호산구성 비용 간에는 차이가 없었다. P65, IL-6, IL-8, eotaxin mRNA는 비용을 동반한 만성 비부비동염에서 유의하게 높게 나왔으며, 호산구성 비용과 비호산구성 비용 간에는 IL-1β를 제외하고는 차이를 보이지 않았다.

결론: 호산구성 또는 비-호산구성 비용을 동반한 만성 비부비동염 환자에서 모두 NF-κB의 발현 증가와 관련된 싸이토카인의 증가를 보였다. 이러한 발병기전에 대한 이해는 치료적 접근에 도움이 되며, 비용을 동반한 만성 비부비동염 환자에 있어서 NF-κB를 차단함으로써 치료적 가능성에 대한 연구가 필요할 것으로 사료된다.

주요어: 만성 비부비동염, 비용, 호산구성 비용, 비-호산구성 비용, NF-κB, 전사인자.

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