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Ischemia-modified albumin, brain natriuretic peptide, and growth differentiation factor-15 levels in patients with nasal polyps

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ABSTRACT

Objective: Nasal polyps (NP) are a chronic inflammatory disease of the nasal mucosa; their etiology is suspected to involve oxidative stress. Growth differentiation factor-15 (GDF-15), brain natriuretic peptide (BNP), and ischemia-modified albumin (IMA) are biomarkers used especially in the early diagnosis and follow-up of cardiovascular diseases. The aim of this study was to assess levels of serum GDF-15, BNP, and IMA in patients with NP and to compare them with those of healthy subjects.
Methods: This was a prospective study enrolling 41 patients with NP and 48 healthy controls, all aged 18–65 years and referred to the Department of Otorhinolaryngology, Head and Neck Surgery, between January 2014 and February 2015. After a 12-h fast, venous blood (3 mL) was drawn and centrifuged (3000 rpm, 10 min) to collect serum. Blood samples were drawn before endoscopic sinus surgery in the NP group. Serum GDF-15, BNP, and IMA levels were measured.
Results: GDF-15, BNP, and IMA levels of patients with NP were statistically significantly higher than in controls and GDF-15 values were higher than the normal upper limit. GDF-15, BNP, and IMA levels were significantly correlated in both groups.
Conclusions: As GDF-15 is a marker of chronic inflammation and oxidative stress, our finding of increased serum GDF-15 in patients with NP supports the hypothesis that its pathogenesis involves chronic inflammation and oxidative stress.

1. Introduction

Nasal polyps (NP) are an inflammatory disorder of the upper respiratory tract affecting 1–4% of the general population [1]. Although the pathophysiology of NP has not been defined clearly, inflammation is considered to be part of its etiology. Upon the development of inflammation, neutrophils migrate into the inflamed site and produce reactive oxygen species (ROS), which have bactericidal effects [2]. Any imbalance between the production of ROS and antioxidants leads to oxidative stress. As a result of oxidative overload, cell damage, apoptosis, and finally, chronic inflammation develop [3–5]. In studies on antioxidants, evidence has been found for the role of oxidative stress in the pathogenesis of NP [6].

Cardiac markers of oxidative stress, which also has an important role in the etiology of NP, include GDF-15, BNP, and IMA. Growth differentiation factor-15 (GDF-15) contributes to cardiac hypertrophy and apoptosis [7], and its release is

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increased substantially in conditions triggering oxidative stress, such as heart failure and atherosclerosis [8]. Brain natriuretic peptide (BNP), a member of the natriuretic peptide family, is an excellent indicator of subclinical cardiac stress [9]. Ischemia-modified albumin (IMA) is a biomarker of cardiac ischemia; its production is triggered by the interaction between albumin and ROS [10].

The aim of this study was to assess serum levels of GDF-15, BNP, and IMA in patients with NP and to compare them with those of healthy subjects.

2. Material and methods

This was a prospective study enrolling 41 patients with NP and 48 healthy controls, all aged 18–65 years and referred to the Department of Otorhinolaryngology, Head and Neck Surgery, between January 2014 and February 2015. Detailed ear, nose, throat and physical examinations were performed in both groups. Exclusion criteria included acute infection, cardiopulmonary disease, kidney disease, autoimmune disorders, liver dysfunction, bleeding tendencies, and pregnancy or breast feeding. Informed consent from each subject and approval of the local ethical committee were obtained.

Nasal symptoms related to nasal polyps (obstruction, anosmia, sneezing, rhinorrhea, itching) were given scores from 0 to 3: 0 for no symptoms, 1 for mild symptoms, 2 for moderate symptoms, and 3 for severe symptoms, so that the maximal nasal symptom score was 15 [11].

First, nasal polyps were detected endoscopically following examination of the nasal cavity in the study group. After endoscopic examination, paranasal sinus tomography was performed. Findings on computed tomography (CT) scans were scored in accordance with the Lund-Mackay score [12]. The mucosal abnormalities were scored as zero (no abnormality), one (partial opacification), or two (total opacification) of the frontal, maxillary, anterior ethmoid, posterior ethmoid and sphenoid sinus, bilaterally. The ostiomeatal complexes were graded bilaterally as zero (not occluded) or two (occluded). The maximal CT score was 24.

Following diagnosis of NP by endoscopic examination and tomography, all subjects in the NP group underwent functional endoscopic sinus surgery. All specimens were examined pathologically. The diagnosis of nasal polyps was finally confirmed pathologically.

After a 12-h fast, venous blood (3 mL) was drawn and centrifuged (3000 rpm, 10 min) to collect serum. Blood samples were drawn before endoscopic sinus surgery in the NP group. Serum was stored at −80 °C until assayed. Commercial enzyme-linked immunosorbent assay (ELISA) kits were used to measure human BNP (Ray Biotech, Inc., USA), GDF-15 (BioVendor, Brno, Czech Republic), and human IMA (ELABSCIENCE, Wuhan, Hubei Province, China). Measurements were performed using appropriate wavelengths on a microplate reader (Bio-Tek Instruments, ELx800, USA) following the assay instructions. All other parameters were measured using standard laboratory methods in the core laboratory.

3. Statistical analysis

Data analyses were performed using the SPSS software (ver. 18.0; SPSS Inc., Chicago, IL, USA). Data are reported as means ± standard deviation or percentages (counts) as appropriate unless otherwise specified. One-sample Kolmogorov–Smirnov test was used to test the normality of the data. Except GDF-15 and eosinophilia percentage values, all other continuous variables showed normal distribution. Comparisons of the groups in respect to normally distributed continuous variables were performed by Student's *t*-test and ANOVA while GDF-15 and eosinophils percentage were analyzed with Mann Whitney *U* and Kruskal Wallis tests accordingly; and those for categorical variables, the χ^2 test was used. Correlation coefficients were derived using Pearson's correlation test. A p value < 0.05 was considered to indicate statistical significance.

4. Results

The study included 41 patients with NP (16 females, 25 males) and 48 age- and gender-matched healthy subjects

Table 1
Demographic and laboratory characteristics of study subjects.

	Control ($n=48$)	NP group without allergic rhinitis ($n=17$)	NP group with allergic rhinitis ($n=24$)	p value for control vs NP group	p value for control vs. NP w/o AR	p value for control vs. NP with AR	p value for NP w/o AR vs. NP with AR
Age (years)	45.6 ± 8.7	43.7 ± 2.6	44.3 ± 3.7	0.923	0.182	0.359	0.607
Sex (M/F) (%)	27/21 (56/44)	10/7 (59/41)	15/9 (62/38)	0.879	0.854	0.612	0.812
GDF-15 (pg/ml)	716 ± 126	1253 ± 140	1611 ± 194	<0.001	<0.001	<0.001	<0.001
IMA (ng/ml)	4.37 ± 0.64	5.18 ± 0.80	6.35 ± 0.73	<0.001	<0.001	<0.001	<0.001
BNP (pg/ml)	7.82 ± 0.67	9.88 ± 0.48	10.15 ± 1.27	<0.001	<0.001	<0.001	0.336
Eosinophils percentage (%)	3.6 ± 1.1	3.7 ± 0.8	6.0 ± 2.4	<0.001	0.692	<0.001	<0.005
Nasal symptom score	–	7.82 ± 1.43	11.50 ± 2.19	–	–	–	<0.001
CT score	–	13.18 ± 1.78	18.54 ± 3.04	–	–	–	<0.001

AR, allergic rhinitis; BNP, B-type natriuretic peptide; CT, computed tomography; GDF-15, growth differentiation factor; IMA, ischemia modified albumin; NP, nasal polyp; M/F, male/female; w/o, without. Mann Whitney *U* test was used for the analyses related to GDF-15 and eosinophils percentage while Student's *t* test was used for the analyses related to the other continuous variables.