



Research Article

Aging and Quantitative Amounts of Immunoglobulin G and its Subclasses in Patients with Chronic Rhinosinusitis

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Abstract

Aging imposes numerous immune system changes. Despite intensive researches, many disorders of age-associated immune dysfunctions have not been fully understood. Research Objective is to evaluate the effect of aging on immunoglobulin G (IgG) and its subclasses production in patients with chronic rhinosinusitis. The Study population included patients with chronic rhinosinusitis whom underwent immunoglobulins measurement. Immunoglobulin G, IgG1, IgG2, IgG3 and IgG4 were measured by MININEPH™ HUMAN IgG KIT (The binding site Ltd., Birmingham, UK). For statistical analysis ANOVA was performed. P value of less than 0.05 defined as statistically significant. The study population consisted of 65 patients with chronic rhinosinusitis including 30 female and 35 male subjects. There was significant change in IgG level of patients in category of 20 - 30 year in comparison with youngest subjects ($p=0.02$). With comparison of patients with the oldest group (more than 40 years), there was significant change in IgG2 and IgG3 in group of 20 - 30 years ($p=0.04$, $P= 0.033$, respectively). In this regard, significant difference was noted in IgG4 in group of 30-40 years ($p=0.005$). This investigation showed the defects for IgG and its subclasses could lead to the finding of procedures for improvement of humoral immune responses in chronic inflammatory diseases in the future. Further studies are needed to confirm the outcomes.

Keywords: Aging, Chronic Rhinosinusitis, Immunoglobulin G, B cell.

Introduction

Despite intensive investigations, many disorders of age-associated immune

dysfunctions have yet to be described. Aging induces numerous immune system alterations, meaning immunosenescence. These changes cause refractory responses to

vaccination or infection, reduction in previously established protective immunity and increased disease-related morbidity rate [1-6]. B cells have critical roles in the establishment and keeping of protective immunity, such as generation of protective immunoglobulins, antigen presentation, and appreciated regulatory activities [7]. Aging reduce class switch recombination and DNA recombination process which are needed for the manufacture of switched antibodies. This decrease which was noted in both mice [8] and humans [9,10], produces lower amount of immunoglobulin G (IgG) for an optimal recently generated antigen response.

Chronic and recurrent respiratory diseases, including rhinosinusitis, otitis media, and pneumonias have been correlated with antibody deficiencies. IgG and its subclasses deficiencies have been elucidated as a critical factor for chronic rhinosinusitis [11-13]. This study was conducted to evaluate the role of aging on IgG and its subclasses production in patients with chronic rhinosinusitis and to clarify the impact of these immunoglobulins in such chronic inflammatory diseases.

Methods and Material

All patients provided informed consent to participate in the study. This study was approved by the Ethics Committee of the Mazandaran University of Medical Sciences, Sari, IRAN.

The study population included 65 patients with chronic rhinosinusitis. Patients were recruited from the Ear, Nose, Throat section of the university hospital. All patients were selected according to criteria for chronic rhinosinusitis as described by the Sinus and Allergy Health Partnership [14].

In the opinion of investigators, exclusion criteria included the conditions that could affect the immunoglobulins levels such as malignancy (American Cancer Society

guidelines for benign and malignant neoplasms were used for screening the patients before the initiation of the study), renal dysfunction, vascular diseases, malnutrition or patients receiving immunosuppressive medication, chemotherapy or radiation therapy or any other conditions that could make the subjects unsuitable for the research.

We used fasting serum samples of the volunteer patients. Venous samples were collected by venepuncture and let to clot naturally then serum separated.

Immunoglobulin G, IgG1, IgG2, IgG3 and IgG4 were measured by MININEPH™ HUMAN IgG KIT (The binding site Ltd., Birmingham, UK). The quantifications of serum IgG, IgG1, IgG2, IgG3 and IgG4 had been done by nephelometric procedure. For standard analysis; all assays were performed duplicate at the time of samples collection. For statistical analysis SPSS software, Version 16, Chicago, IL, USA was used to apply analysis of variance (ANOVA). P value of less than 0.05 was considered statistically significant.

Results

The study population consisted of 65 patients with chronic rhinosinusitis including 30 female and 35 male subjects. The demographic data of participants were summarized in table1. This series was divided to four groups including patients less than 20 year, 20 to 30 years, age of 30 to 40 years and patients more than 40 years old.

The youngest patients served as control group and other groups were compared with these subjects. There was significant change in IgG level of patients in category of 20 -30 year ($p=0.02$). In this relation, there was no significant differences in other age groups (table 2).

Table1. Baseline Study Population Characteristics

Age(year)	n	Age (Mean \pm SD)	male	female
0-20	20	9.33 \pm 6.03	10(50%)	10(50%)
20-30	15	28.18 \pm 1.47	7(46.6%)	8(53.3%)
30-40	15	34.08 \pm 2.57	9(60%)	6(40%)
+40	15	51.12 \pm 9.81	9(60%)	6(40%)

Table2. Serum IgG and its Subclasses Concentrations. All Values are Presented as Mean \pm SD, P Value of Less than 0.05 was Considered Statistically Significant

	MEAN \pm SD	P value
IgG g/l	9.26 \pm2.49 (0-20 yr)	
20-30	11.43 \pm 2.09	0.02
30-40	10.67 \pm 2.62	0.1
+40	12.6 \pm 3.96	0.8
IgG1 mg/l	5024.06\pm1259.30 (0-20yr)	
20-30	6489.27 \pm 1784.01	0.2
30-40	5710.75 \pm 1704.08	0.6
+40	5663.62 \pm 1715.25	0.7
IgG2 mg/l	2599.73\pm1653.62(0-20 yr)	
20-30	4018.63 \pm 1053.05	0.92
30-40	5058.5 \pm 1659.87	0.2
+40	6113.62 \pm 1473.27	0.58
IgG3 mg/l	882.9\pm372.18 (0-20yr)	
20-30	956.63 \pm 247.24	0.79
30-40	973.25 \pm 422.16	0.77
+40	995.75 \pm 699.55	0.29
IgG4 mg/l	804.6\pm1017.86(0-20 yr)	
20-30	887.18 \pm 638.60	0.92
30-40	1686.58 \pm 2545.48	0.31
+40	854.25 \pm 667.5	0.28

With comparison of patients with the oldest group (more than 40 years), there were significant changes in IgG2 and IgG3 in group of 20 - 30 years ($p=0.04$, $P= 0.033$,

respectively). In this regard, significant difference was noted in IgG4 in group of 30-40 years ($p=0.005$).

Discussion

In the current research we examined the sera levels of immunoglobulin G and its subclasses in patients with chronic rhinosinusitis closely implicated with aging. Our study indicated there was significant change in IgG level of patients in age of 20 -30 years in comparison with youngest subjects. In comparison of patients with the oldest participants, there were significant differences in IgG2 and IgG3 in group of 20 – 30 years. Likewise, significant alteration was noted in IgG4 in group of 30-40 years. Not significantly, the amount of IgG2 and IgG3 increased with age.

B cell, T cell and other cells of the innate immune system have been showed in a suboptimal immune response in advanced age, but clarity considering the importance of intrinsic B cell contributions to this reduction and accurate biomarkers for B cell deficiencies with advance age have recently been indicated(15).Aging in mice imposes a decrease in manufacture of precursor B cells in the bone marrow [16-18], but the counts of mature splenic B cells is preserved, since to increased life-span [19].In consistent with mouse B cells, human peripheral B cell populations decrease with aging [20-22]. But there is a research [23] and a review article [24] indicating that memory B cell counts increase with age. It was revealed that in aged mice immune response to influenza has less IgG than that in young mice [25]. Despite these evidences, studies didn't discuss about the effect of aging on IgG production and chronic rhinosinusitis. Different studies have indicated a high frequency of respiratory tract disorders in patients with IgG subclass deficiencies. The age at which each of the IgG subgroups arrive at adult levels differs and every age group in childhood has its own normal values [26,27]. Human IgG could be divided into four subclasses, IgG1, IgG2, IgG3, and IgG4. IgG1 is the major part of total IgG (66%), followed by IgG2 (24%), IgG3 (7%), and IgG4 (3%) (28,29).

In the present study, there was significant elevation in IgG level of patients in group of

20 to 30 years. IgG2 and IgG3 increased with aging but IgG, IgG1and IgG4 did not indicate the same pattern. Crisp HC and Quinn JM (30) examined the sera samples of the people aged 20-89 years old to analyze for quantitative IgG. They showed IgG levels were not significantly altered in an older population. Likewise, our study revealed that there was not significant alteration in most part of the population.

In conclusion, the defects discussed in the current article for IgG and its subclasses could lead to the discovery of procedures for improvement of humoral immune responses in the future. Recognizing the autonomous B cell biomarkers of aging that impose function involve reduced IgG class switch recombination and other associated factors (31). These findings show targets for intervention to improve the humoral immune system in aging.

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