ORIGINAL ARTICLE

Characterisation of up-regulated immunoglobulins in patients with chronic rhinosinusitis

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Abstract

Objective: To evaluate the role of immunoglobulins in patients of chronic rhinosinusitis.

Methods: Patients were recruited from the Ear, Nose, Throat, Head And Neck Surgery section of Mazandaran University of Medical Sciences, Sari, Iran, from December 2011 to August 2012. Immunoglobulin G, IgG1, IgG2, IgG3, IgG4 were evaluated. Salivary IgA was assessed by direct immunoenzymatic determination. The quantifications of serum IgG, IgG1, IgG2, IgG3, IgG4 and salivary IgA was performed through nephelometric procedure. Serum IgE was measured by enzyme-linked immunoabsorbent assay. SPSS 15 was used for statistical analysis.

Results: Of the 50 patients, 22 (44%) were males and 28(56%) were females. The overall age ranged from 1 to 67 years with a mean of 28.06±15.49. There was significant changes in levels of IgG, IgG1, salivary IgA and IgE (p=0.001). Significant difference was noted for IgG2 (p=0.03) and in IgG4 (p=0.01). There was no significant alteration in IgG3 level (p=0.3).

Conclusion: There was high prevalence of humoral immune alterations both in local and systemic response to chronic inflammation in the patients, which suggests that assessment of immunoglobulin before clinical evaluation and management could be important.

Keywords: Chronic rhinosinusitis, Immunoglobulins, IgG, IgA, IgE. (JPMA 64: 382; 2014)

Introduction

Based on the National Health Interview Survey of 1996, chronic rhinosinusitis was the second most chronic disease in the USA, accounting for 12.5% of the population or nearly 31 million Americans annually.[1,2] According to 2008 National Health Interview Survey information, rhinosinusitis affected 1 in 7 adults.[3] Since chronic rhinosinusitis was established through symptomatic criteria, the prevalence was probably overestimated in these studies. Due to co-existing inflammation of the nasal and sinus mucosa, the present terminology is 'rhinosinusitis.' If clinical symptoms exist for at least 12 weeks without complete resolution, it becomes 'chronic'.[4] It is one of the most frequent disorders of immunodeficiency, particularly affecting patients with local secretory or systemic humoral immunodeficiencies.[5,6] Various studies have indicated that patients with IgG sub-class deficiency show a higher frequency of respiratory tract disorders.[7,8] Human IgG can be split up into four subclasses; IgG1, IgG2, IgG3, and IgG4. IgG1 is the biggest section of the total IgG (66%), followed by IgG2 (24%), IgG3 (7%) and IgG4 (3%).[9,10]

The mucosal immune system improvs the adaptive anti-inflammatory defence to set homeostasis by immune exclusion mediated by secretory IgA antibodies to the clearance of pathogenic organisms from the mucosal surfaces by way of neutralising toxins and viral particles, inhibiting adherence of pathogens, colonisation and penetration of mucosal surfaces by pathogenic micro-organisms and immunosuppressive ways to limit over-reaction against inoffensive luminal antigens. The secretory immunoglobulins are the most essential section of the antibody-dependent defence of the body.[11,12] Mucosal inductive sites consist of the Peyer's patches or gut-associated lymphoid tissues as well as the Waldeyer's ring of tonsils and adenoids as nasopharyngeal associated lymphoid tissues, which collectively comprise a mucosa-associated or mucosa-associted lymphoid tissue (MALT) network for continuous supply of memory B and T cells to mucosal effector sites.[13-15] Studies have claimed that Peyer's patches play an important role in the induction of secretory IgA and oral tolerance.[16,17]

There is limited literature assessing specific immunoglobulin up-regulation in chronic rhinosinusitis. The aim of the current study was to evaluate the role of antibody up-regulation in patients with chronic rhinosinusitis to identify the possible underlying pathology.

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Patients and Methods

The study comprised 50 patients with chronic rhinosinusitis recruited from the Ear, Nose, Throat, Head And Neck Surgery department of Mazandaran University of Medical Sciences, Sari, Iran from December 2011 to August 2012. All patients were selected according to criteria for chronic rhinosinusitis as described by the Sinus and Allergy Health Partnership.[18]

Exclusion criteria comprised conditions that could influence the immunoglobulin 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 condition that could make the subjects unsuitable for the study purpose.

Informed consent from all patients, and approval from the institutional ethics committee were obtained before the study.

Fasting serum samples of the patients were collected through venepuncture and were let to clot naturally after which serum was separated.

Immunoglobulin G, IgG1, IgG2, IgG3, IgG4 were measured by MININEPHTM Human IgG Kit (The binding site Ltd., Birmingham,UK).

Besides, 2ml of fasting oral cavity secretions were collected and then, salivary IgA was determined by direct immunoensymatic determination (DiaMetra, Italy). The quantifications of serum IgG, IgG1, IgG2, IgG3, IgG4 and salivary IgA was done through the nephelometric procedure. For IgE assessment, enzyme-linked immunoabsorbent assay (ELISA) (Monobind, USA) was used. For standard analysis, all assays were duplicated at the time of sample collection.

SPSS 15 was used for statistical analysis, and p-value less than 0.05 was considered significant.

Results

Of the 50 patients, 22 (44%) were male and 28(56 %) were female. The overall age ranged from 1 to 67 years, with a mean of 28.06±15.49. The upper limit of the normal ranges was used as the cut point and immunoglobulin values were compared with the cut point level. There was statistically highly significant changes in the levels of IgG, IgG1, salivary IgA and IgE (p=0.001). Also, significant difference was observed for IgG2 (p=0.03) and in IgG4 (p=0.01). There was no significant alteration in IgG3 level (p=0.3) (Table).

Table: Immunoglobulin values.

Immunoglobulin	Cut Point	P Value	Normal range
IgG	18.37 g/l	0.000	6.58-18.37 g/l
IgG1	8550 mg/l	0.000	3150-8550 mg/l
IgG2	4950 mg/l	0.03	640-4950 mg/l
IgG3	1960 mg/l	0.3	230-1960 mg/l
IgG4	1587 mg/l	0.01	110-1587 mg/l
Salivary IgA	170 µg/ml	0.000	40-170 µg/ml
IgE	200 IU/ml	0.000	0-200 µg/ml

Discussion

The study evaluated the up-regulation of immunoglobulins in patients suffering from chronic rhinosinusitis to elucidate the potential activity of these antibodies. The study revealed that there were significant changes in all of the assessed immunoglobulins except IgG3.

Alqudah et al[19] evaluated the prevalence of humoral immunodeficiency in patients with refractory chronic rhinosinusitis, and revealed low IgG in 9%, low IgA in 3%, and low IgM in 12% of patients. Common variable immunodeficiency was noted in one subject. Common variable immunodeficiency was defined as a primary immunodeficiency disorder which is diagnosed on the basis of decreased amounts of immunoglobulins in all 3 classes and recurrent infections.[20-22] Immunoglobulin G sub-classes were examined in 31 patients and discovered low in 6 participants. Fifty-one patients underwent a dynamic evaluation of their antibody response. Sixty-seven per cent of these patients could not produce more than a four-fold increase in post-immunisation antibody titer and were considered to have functional antibody deficiency.

This study indicated an unexpectedly high prevalence of humoral immune disorders in patients with refractory chronic rhinosinusitis. These findings[20-22] provided evidences that examination of immune function should be undertaken routinely in refractory chronic rhinosinusitis. First, serum immunoglobulin levels should be evaluated and then if these immunoglobulins are normal, functional antibody responses should be examined. Likewise, the current study revealed the clinical importance of immunoglobulin levels in the diagnosis of the disease.

Franco et al[23] studied the association between IgA deficiency and respiratory atopy in young male adults. The showed IgA deficiency in 0.34% of the subjects and atopy was observed in 8.6%. Besides, 37.5 % of the IgA-deficient patients had sub-normal IgE levels. It concluded that atopy was not more common in young

male IgA-deficient, males, who rather indicated a high frequency of recurrent rhinosinusitis. Although IgE presents at the lowest serum concentration and has the shortest half-life, but it is an important antibody. IgE is correlated with hypersensitivity and allergic reactions, as well as in response to parasitic worm infections. Recently, anti-IgE antibodies, designed to target free IgE as well as B cells with surface-bound IgE, have been used as therapy for allergy and asthma.[24] The current study revealed significant alteration in serum total IgE of the patients.

Different researches have declared that plasma cell count and antigen-specific IgE levels are elevated in the polypoid sinonasal mucosal tissue from patients of chronic rhinosinusitis with nasal polyposis.[25] But these studies didn't discuss about the role of serum total IgE in such patients. In our study, the concentration of serum IgE showed significant change and this evidence elucidated that serum IgE plays a crucial role in pathogenesis of the majority of the patients.

Carr et al[26] retrospectively studied antibody deficiency in adults with medically refractory chronic rhinosinusitis. The study reported 15 (11.6%) patients with specific antibody deficiency based on an inadequate response to the pneumococcal polysaccharide vaccine. Subjects with specific antibody deficiency had significantly lower serum IgA levels when compared with those patients with normal pre-immunisation titers (138±67.3 versus 330±356; $p<0.05$). Also, it revealed that patients with specific antibody deficiency had a significantly lower number of pre-immunisation protective anti-pneumococcal titers when compared with vaccine responders (1.41 versus 2.72; $p<0.05$). Their investigation showed that patients with medically refractory chronic rhinosinusitis may have a high prevalence of low pre-immunization anti-pneumococcal titers and specific antibody deficiency. Lower serum IgA levels which was noted in these specific antibody deficiency patients showed that prospective studies are needed to evaluate the association.

Conclusion

There was high prevalence of humoral immune disorders either local or systemic in the patients, suggesting that the assessment of immunoglobulin before clinical evaluation and management could be important. Further studies will confirm the results.

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