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Impact of aging on allergy and mucosal immunity in upper respiratory tract

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Abstract: *Objectives:* Although age-associated alterations on immune system are well described and aging is a subject of different investigations but studies did not discuss about the effect of advanced age on immunity in upper respiratory tract disorders. Therefore in this trial, we elucidated how aging imposes allergic reactions and mucosal immune responses mediated by salivary IgA and serum Total IgE in patients suffered from upper respiratory tract diseases. *Study Design:* Experimental study. *Place and Duration of Study:* Department of Otorhinolaringology, microbiology and immunology, Mazandaran university of medical sciences, sari, Iran, from September 2010 to august 2011. *Methods:* In this study, 140 patients in 7 age groups with upper respiratory tract infections underwent salivary IgA assessment by direct immunoenzymatic determination and serum Total IgE by enzyme linked immunoabsorbent assay. We compared each study arm to the youngest subjects. *Results:* There was no significant difference in salivary IgA level for patients younger than 60 but a significant change observed for patients older than 60 (p=0.01). Likewise, there was no significant change for total IgE. *Conclusion:* This research didn't provide any evidence about the minus impact of aging on allergic reactions in upper respiratory tract infections .There was an up regulation in mucosal immunity mediated by salivary IgA in patients aged over sixty which revealed secretory IgA plays an important role in mucosal defense of aged subjects.

Keywords: Aging, Mucosal immunity, Allergy, Salivary IgA, IgE.

Introduction

The number of old people is rapidly increasing in the world [1]. The cost for taking care of these old people is more expensive than young people due to higher susceptibility to infectious agents, certain types of autoimmune diseases, cancer and diminished responses to vaccination. In this regard, mortality rate to influenza viral infection in older people are higher than younger people [2-8].

Age-associated defects of immune responses have been discussed in many species. These studies wanted to say that dysregulation in host immune system happens in advanced age**.** Aging imposes both qualitative and quantitative alterations in humoral immune responses. Somatic hypermutation (SHM) has an important role in immunoglobulin production and diversity. Aging affect this process at different stages. By way of illustration, in advanced age B-cell germinal centers inside the spleen and tonsils indicate conserved SHM [9]. But aging reduces SHM in the circulating B-cell pool as well as germinal centers of Peyer's patches [10].

Different studies discussed about the impact of aging on B and T cell but these investigations didn't provide any evidence about the role of aging on immunoglobulin production in upper respiratory tract infections [2, 5, 11-12]. So, in this study, we examined the effect of aging on two crucial types of immune responses including mucosal immune responses in oral cavity and systemic immunoglobulin production (serum IgE) in patients suffered from upper respiratory tract diseases.

Material and Methods

Patients and samples: The study population included the patients with infectious and inflammatory disorders of ear, pharynx and rhinosinusitis. Patients were recruited from the Ear, Nose, Throat (ENT) section of the

university hospital. 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 investigation), renal dysfunction, vascular diseases, malnutrition or patients receiving immunosuppressive medication, chemotherapy, or radiation therapy or any other conditions that could make the participants unsuitable for the study.

Determination of Sample Size: The designed sample size of 140 patients with upper respiratory tract infections, which included 20 patients in each group, was considered suitable for measurement of immunoglobulins values and to supply statistical power appropriate for exploratory statistical data analysis. All authors read the manuscript as written and approved its integrity.

Immunoglobulin assay: We collected fasting oral cavity secretions (2 ml) of the patients and then, salivary IgA was determined by direct immunoenzymatic determination (DiaMetra, ITALY). Primary outcomes were analyzed by Neophlometric system. For IgE assay, we took fasting morning serum samples and total IgE was measured by enzyme linked immunoabsorbent assay (ELISA) (Monobind, USA).for standard analysis; all assays were performed duplicate at the time of samples collection.

Ethics: All subjects gave their consent to participate in the study. This study was conducted in accordance with the Declaration of Helsinki and good clinical practice according to International Conference on Harmonisation guidelines.

Statistical analysis: Immunoglobulins values are presented as Mean ±SEM. For statistical analysis, SPSS software (Version 15, Chicago, IL, USA) was used applying ANOVA. $P < 0.05$ was defined as significant.

Results

In this investigation, 140 patients in 7 age groups (including 20 subjects in each group) with upper respiratory tract infections underwent immunoglobulin assessment. Patients' demographic data are summarized in table-1.

Table-1: Baseline study population characteristics

Age (year)	n	Age (Mean ± SD)	male	female
0-10	20	5.25±2.67	12 (60%)	8 (40%)
10-20	20	15.05 ±3.10	8 (40%)	12 (60%)
20-30	20	24.95±2.64	10 (50%)	10 (50%)
30-40	20	34.1±2.71	10 (50%)	10 (50%)
40-50	20	44.25±2.44	8 (40%)	12 (60%)
50-60	20	53.45±2.70	10 (50%)	10 (50%)
60+	20	66.75±5.54	13 (65%)	7 (35%)

We compared different study arms to the youngest subjects. There were no significant differences in salivary IgA levels for patients younger than 60 but a significant change observed for patients older than 60 (p=0.01) (table2).

Table-2: Values of salivary IgA in patients' suffered from upper respiratory tract diseases. All values are expressed as Mean ±SEM, µg/ml, p □0.05 defined as significant

Age (year)	IgA concentration 0-10 (yr)	IgA concentration	P value
10-20	74.9±18.96	71.9±8.25	0.890
20-30	74.9±18.96	107.65±13.13	0.193
30-40	74.9±18.96	136.65±26.37	0.091
40-50	74.9±18.96	119.9±20.41	0.158
50-60	74.9±18.96	156.87±32.4	0.064
60+	74.9±18.96	177.25±29.61	0.011

Statistical analysis for IgE immunoglobulins levels didn't revealed significant difference (table 3).

Table-3: Serum total IgE concentration. All values are presented as Mean ±SEM, µg/ml, P value of less than 0.05 was considered statistically significant

Age (year)	IgE concentration 0-10 (yr)	IgE concentration	P value
10-20	132.85±40.78	143.7±30.87	0.848
20-30	132.85±40.78	115.85±33.15	0.730
30-40	132.85±40.78	113.1±28.32	0.673
40-50	132.85±40.78	139.5±33.21	0.912
50-60	132.85±40.78	93.1±27.39	0.476
60+	132.85±40.78	117.87±33.53	0.775

Discussion

In this study, we discussed how aging imposes immunity with a focus on upper respiratory tract infections. This article is divided into two broad sections. In the first part, we explained how aging might affect serum IgE level in upper respiratory tract infections. In the second section, we reviewed salivary IgA production closely implicated in upper respiratory tract diseases in various decades of life. Immunoglobulin E is correlated with hypersensitivity and allergic reactions, beside its response to parasitic worm infections [13-15]. Discussions provided by some studies suggested that allergic patients are more susceptible to upper respiratory tract infections. For instance, some investigations indicated a high rate of computed tomography abnormalities in allergic patients, and some other studies revealed higher incidence of skin prick test positivity in chronic rhinosinusitis compared to healthy controls [16-18].

In this challenge, we evaluated serum total IgE level of different decades of patients with upper respiratory tract infections including rhinosinusitis ,pharynx and ear disorders and compared them to youngest group to show that how aging influences the IgE production and allergic reaction in upper respiratory tract disorders. Busse PJ et al [19] evaluated perennial allergen-specific IgE concentrations among inner-city elderly asthmatics and revealed that allergen sensitization is not a particular interest in aged subjects with persistent asthma. But our investigation indicated there was no significant change in allergic reactions in different stages of life. In this part, we examined oral cavity mucosal immunity alterations in upper respiratory tract infections in accordance with aging. The gastrointestinal tract susceptibility to infectious diseases increases in the old people declaring that mucosal immunity is affected in aging [3, 20]. Indeed, the severity and mortality in the elderly caused by the infectious organisms entering through mucosal barrier such as the influenza virus and the bacterial pathogen Streptococcus pneumoniae are particularly increased [4, 21-22].

Mucosal inductive sites consist of the Peyer's patches or gut-associated lymphoid tissues (GALT) and the Waldeyer's ring of tonsils and adenoids as nasopharyngeal associated lymphoid tissues (NALT), which collectively comprise a mucosa-associated or MALT network for progressive supply of memory B and T cells to mucosal effectors sites [23-25]. Investigations proved that Peyer's patches have an important role in the induction of Secretory IgA and oral tolerance [26-27].

In fact, this study evaluated the effect of elderly on mucosal inductive sites in oral cavity. Crisp HC et al [28] showed that elderly patients without diseases known to affect immunoglobulins production have significantly higher serum IgA levels than younger groups. In the same way, Arranz et al [29] indicated that older patients have higher amount of salivary IgA than younger subjects. In contrast with our work we evaluated salivary IgA level in patients with upper respiratory tract diseases. Our study revealed that mucosal immunity mediated by salivary IgA will not be imposed before 60 but likewise before investigations a significant up regulation observed in the oldest group.

Conclusion

Studies claimed that aging imposes the immunity [30-31] but immunosenescence is not an unavoidable and continues decrease of all immune responses, but rather a product of progressive remodeling of different sections of the immune system over time [32]. Our trial didn't provide any evidence to prove pervious data about the minus impact of aging on B cell functions.

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The authors declare that they have no conflict of interest.

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