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The relationship between SIgA and chronic granular pharyngitis

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Abstract
A survey of the SIgA content in saliva, serum and pharyngeal mucosa with lymphoid tissue (PMLT) of chronic granular pharyngitis patients was conducted by a double antibody PEG radio-immune method. These data were compared with those from a healthy control group. Result shows that SIgA in patients with chronic granular pharyngitis had dissociation of saliva, serum and PMLY. There was low salivary SIgA level but higher levels in serum and PMLT. These data suggest that the saliva and serum immunoglobulin pools are under separate regulation.

Key words: Pharyngitis, chronic granular; Immunoglobulin A

Introduction

Secretory IgA (SIgA) is the predominant immunoglobulin in the exocrine body fluids and has an important role in immunological resistance. Early studies (Chen, 1983; Waldman, 1970) have shown that IgA-bearing cells, despite being fewer in number than IgG-bearing cells, produced five times as much immunoglobulin per unit time and per cell. This IgA was mostly of secretory type (SIgA), although variable amounts of non-secretory IgA were also detected. Even though much research on the relationship between SIgA and chronic infection has been done, no report on the relationship of SIgA to chronic granular pharyngitis could be found in the literature. Therefore, exploring the change of SIgA in chronic granular pharyngitis in various exocrine fluids, pharyngeal mucosa with lymphoid tissue (PMLT) and types of secretion will have important clinical significance. The present study was undertaken to investigate SIgA in the saliva, serum and PMLT of the posterior pharyngeal wall of chronic granular pharyngitis patients. The clinical significance and possible origination of SIgA are also discussed.

Materials and methods

Thirty cases (aged 17 to 30 years) of chronic granular pharyngitis were chosen randomly. There was no history of tonsillectomy and adenoidectomy, or upper respiratory tract disease in these patients. The control group originally consisted of 30 healthy persons, aged 16 to 20 years, with neither infectious diseases of the upper and lower respiratory tract nor general acute or chronic diseases. Considering humoral immunity, two of these 30 individuals with minor signs of tonsillitis and adenoiditis were excluded from the control group, leaving a total of 28.

Materials

The reagents used for determination of SIgA (double antibody PEG radio-immune method) were provided by the Shanghai Radio-immunity Technique Research Institute. In accordance with the instructions given by the institute, a standard curve was drawn on the basis of the combination rate. The SIgA content of the patient's specimen could be read directly from the standard curve.

Sample collection and survey of SIgA

(a) Saliva: 1.5–2.0 ml of saliva were taken from the anterior floor of the mouth with a sterilized syringe and put into a test tube. The tube was tightly plugged and preserved in a −20°C freezer. The specimens were quickly melted at 37°C before being tested. When possible, repeated freezing and thawing were avoided. The samples were centrifuged with a 3000 rpm centrifuge for 10 minutes. The supernatant was diluted 10 times with normal saline.

(b) Blood: 2 ml of blood was drawn from the vein of the forearm, put into a tube and allowed to clot at 37°C for one hour and overnight at 4°C. After being centrifuged at 3000 rpm for 10 minutes the serum was collected and preserved in a −20°C freezer. Before surveying, the frozen serum was thawed and diluted 1000 times with normal saline.

(c) Pharyngeal mucosa with lymphoid tissue: 1 per cent cocaine was sprayed twice onto the posterior wall of the pharynx. About 0.2 × 0.2 cm of the pharyngeal mucosa, with proliferated lymphoid tissue, was taken with a small bioptic forceps.The tissues were washed with cold saline immediately after removal to eliminate blood. Control group samples were taken by the same method. The bioptic tissue was put into a test tube and preserved in a −20°C freezer. When surveyed, the bioptic tissue was cut into about 0.2 × 0.2 mm, weighed, and diluted 10 times with normal saline. The tissue was made into homogenized fluid with a micro-homogenizer and centrifuged

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TABLE I
CONTENTS OF SIGA (μg/ml) IN SALIVA

Groups	Cases	$\bar{x}$	SD	SE
Pharyngitis	30	23.43	14.51	2.65
Control	28	68.89	12.51	2.43

$t = 4.94$; $p < 0.001$; x = mean; SD = standard deviation; SE = standard error.

at 3000 rpm for 10 minutes. The supernatant was used for SIgA analysis.

Results

The contents of SIgA in the saliva, serum and PMLT of the chronic granular pharyngitis patients and the control group are given in Tables I–III. The results of this study are also reported in Tables I, II and III. The levels of SIgA in saliva of the chronic granular pharyngitis patients is significantly lower ($p<0.001$) compared to the values of the healthy control group (Table I). Conversely, the SIgA in the serum and PMLT of these patients was higher than that of the healthy control group (Tables II and III). The differences between them were statistically significant.

Discussion

Relationship between salivary SIgA and pharyngeal diseases

SIgA mainly exists in secretions of the respiratory tract. It may inhibit bacterial invasion into the mucous membrane, neutralize viruses, and block large-molecule-antigens from entering the human body. The polymerized IgA may also activate the complement system, and release chemotropic factors. Thus, it plays a role in local immunity, and anti-allergic reactions. However, the origin of the protein has not been clearly demonstrated. Data derived from animal experiments are conflicting. Some authors (South *et al.*, 1966) have suggested that the antibody activity noted on various mucosal surfaces originates from serum, while others (Claman *et al.*, 1967) suggest that the serum and salivary immunoglobulin pools are formed locally and are under separate regulation. If the SIgA is derived from serum, it is difficult to explain our finding of the higher level of SIgA in the saliva of normal individuals as opposed to the serum. Secondly, the observed decrease in salivary SIgA, in light of the concomitant increase in serum SIgA of chronic granular pharyngitis patients, further argues against the production of SIgA in serum alone. Rather, our results point to a local synthesis of SIgA under separate regulatory controls.

The SIgA level in the saliva represents the immune function of the mucous membrane. It has been shown by some authors (Gu, 1982; Yao *et al.*, 1989) that the content of salivary SIgA is decreased in acute epiglottis. Others (Gu, 1982; Ma *et al.*, 1982) found that individuals with low levels of SIgA in the saliva contracted gingivitis and caries more easily. Therefore, a low level of salivary SIgA may increase susceptibility to oral and throat diseases.

This study demonstrates that the salivary SIgA content of those with granular pharyngitis is lower than that of healthy persons. Therefore, they may be prone to repeated infection and can be difficult to cure. In the treatment of such patients one should consider raising their immune function, in addition to anti-inflammatory treatment.

The role of rising SIgA in the PMLT

Mucosa associated lymphoid tissue (MALT) has been described extensively in the literature and is characterized by dense accumulations of lymphoid and non-lymphoid cells in close contact with an overlying epthelium (Van der Baan *et al.*, 1988), which are regarded as a special type of secondary lymphoid organ (Surjan, 1987). The lymphoid tissue in the respiratory tract consists of both loosely distributed lymphocytes and lymphocytes that are well organized into follicles, from which was coined the term bronchus-associated lymphoid tissue (Bienenstock, 1984). A similar structure was also found in this study within the pharyngeal mucosa. Usually MALT is involved in the uptake of particulate antigens from body lumina to present the antigens to the immune system in such a way that clones of precursor IgA B-cells are generated. These precursor IgA cells specifically return to the mucosa to become IgA-producing plasma cells. The IgA is bound to a secreting component in the epithelium to be secreted in the lumina to act as a defence mechanism. In this study PMLT were selectively taken because IgA secreting plasma cells exist in lymphoid follicles and in the mucosa itself.

Some authors (Pierce, 1959; Chen, 1983; Richtsmeier *et al.*, 1987) have shown that IgA acts locally, as first line defense system, to protect the mucous surfaces against infection. Because of its structural characteristics (polymer), SIgA is quite acid-stable and more resistant to proteinase, and therefore constitutes an important barrier of immunity. When the pharyngeal mucous membrane is repeatedly stimulated by bacteria or viruses, the SIgA content in the pharyngeal lymphoid follicles rises to strengthen its protective ability. This phenomenon may be held as a response to the infection and an attempt at resistance. It is therefore worthwhile to examine further the destruction of the lymphoid follicles as a treatment for granular pharyngitis.

Traces of SIgA (0.03 mg/ml) in serum can be determined

Now, it is generally accepted that SIgA in the blood stream is not produced by the spleen or the lymph nodes, but is produced by plasma cells in the mucous membranes

TABLE II
CONTENTS OF SIGA (μg/ml) IN SERUM

Groups	Cases	$\bar{x}$	SD	SE
Pharyngitis	30	67.95	16.7	3.05
Control	28	46.66	18.86	3.56

$t = 4.54$; $p < 0.001$; x = mean; SD = standard deviation; SE = standard error.

TABLE III
CONTENTS OF SIGA (μg/ml) IN PMLT

Groups	Cases	$\bar{x}$	SD	SE
Pharyngitis	30	48.28	19.11	3.49
Control	28	17.87	21.37	4.04

$t = 12.64$; $p < 0.001$; x = mean; SD = standard deviation; SE = standard error.

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from where it enters the blood stream. In man IgA exists in two sub-classes, IgA1 and IgA2. In the blood IgA1 is a large constituent, however an increased proportion of IgA2 secreting plasma cells was observed in mucosal surfaces (Andre *et al.*, 1978). Further studies are required to illustrate the relationship between IgA subclasses in the secretion, serum and the mucosa. In this study the increases of SIgA in the blood stream of granular pharyngitis patients may be explained by the increase of SIgA produced by plasma cells in the pharyngeal mucous membrane. There are, however, other factors which may affect SIgA content in the blood, such as the dynamics of SIgA producing cells, the SC (secretory component) produced by epithelial cells of the mucous membrane, synthesis of SIgA, and the ability of secretion. We cannot simply attribute the rise in SIgA in the blood stream to a local cause. This can only be explained as one of the general responses of the patient to granular pharyngitis.

Conclusion

The SIgA in the exocrine fluid plays a role of protective immunoglobulin. The drop of SIgA levels in the saliva might be one factor that causes repeated infection of the pharyngeal mucosa membrane. The level of SIgA in the pharyngeal mucosa is an expression of the immune response of the local mucous membrane, and has an inhibitory effect on the development of this disease. When the local mucous membrane is sensitized and SIgA antibody is produced, a general immune response might be caused in varying degrees. The determination of SIgA contents in various tissues may be used as a referential indication for diagnosis. Apart from local treatment, raising and adjusting the immune function of the organism should be taken into account.

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