

THE ROLE OF SALIVARY IMMUNOGLOBULIN A IN THE PREVENTION OF THE UPPER RESPIRATORY TRACT INFECTIONS IN ATHLETES – AN OVERVIEW

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ABSTRACT: Athletes subjected to high work loads may experience temporary suppression of the functions in the immune system which increases the susceptibility to infections of such subjects. Namely, upper respiratory tract infections (URTI) are the most common disorders among individuals subjected to high work loads and that issue is of utmost importance for sport immunologists. So far, no simple explanation has been offered as to the specific roles of detailed elements of the immune system in URTI incidence. One of the most likely markers is supposed to be the secretory immunoglobulin A (sIgA), associated with mucosal membranes of upper respiratory tracts, although the results are far from being unequivocal yet. The most important results published in that area were discussed in this paper.

KEY WORDS: sIgA, upper respiratory tract infections, athletes, exercise, performance

Introduction

Two types of immunity may be discerned: innate (non-specific) and acquired (specific), and two types of immunological responses: humoral and cellular [53]. Humoral response is based on antibodies (immunoglobulins) generated in activated B-lymphocytes. Antibodies, present in body fluids of all vertebrates, consist of 4 polypeptide chains – two light (L) and two heavy ones (H), coupled by disulfide bonds. Five classes of immunoglobulins are known, differing in H-chain structure: IgA, IgD, IgE, IgG and IgM.

Immunoglobulin A

Two kinds of that protein are present in human beings – serum immunoglobulin (IgA) and secretory immunoglobulin (sIgA). Inasmuch the generation of IgA is much higher than that of other immunoglobulins [5,12], its concentration in serum is much lower compared with other Ig classes, e.g. IgG, since IgA is present mainly in mucosal fluids like tears, saliva, colostrum, rhino-pharyngeal, bronchial, intestinal and urogenital secretions [31].

The sIgA plays a key role in the mucosa-associated lymphoid tissue (MALT), which forms the first line of defence and protects

some 400 m² of surface area in an adult [5]. The MALT system consists of lymphoid tissue associated with the gut (GALT), bronchus (BALT) and nose (NALT) [8]. Generation of sIgA is the principal function of that system.

The secretory IgA protects the body from harmful external factors by agglutination of bacteria, inhibition of bacterial adhesion to mucosal surfaces, absorption of food-related antigens, neutralisation of viruses, toxins and microbial enzymes, inhibition of virus release, and by enhancing the non-specific immune elements like lactoperoxidase or lactoferrin [6,12,28].

Two subclasses of IgA were discerned: IgA1 and IgA2, and their allotypic forms: IgA2m(1) and IgA2m(2), differing in structure and distribution in the body [12]. The IgA2 subclass predominates in the distal gastrointestinal tract and the IgA1 predominates in the salivary glands, NALT, spleen and tonsils [12,21]. Those two subclasses differ in the structure of the peptide hinge region, the IgA2 lacking 13 amino acids. This is of importance in inhibiting the virulence of bacteria like *S. pneumoniae*, *H. influenzae* or *N. gonorrhoeae*, as those IgA2 are resistant to bacterial enzymes [7,28]. The sIgA1 is generated in response to predom-

inantly protein antigens while sIgA2 to carbohydrate or lipid antigens [18].

Upper respiratory tract infection (URTI)

Among the most common URTI symptoms are rhinorrhea, nasal congestion, oropharyngitis, cough, headache, prolonged fatigue, etc. The principal factor responsible for URTI are rhinoviruses [29,54], bacteria playing a minor role [9,29,54]. However, in many studies the pathogen had not been identified [9,54]; thus, apart from the infectious factors, the non-infectious ones (poorly balanced diet, sleep deficit, stress, etc.) were suspected [9,17].

Effects of URTI on motor activities

Heavy loads experienced by athletes bring about temporary suppression of functioning of the immune system (so-called "open window" theory) that is likely to enhance their susceptibility to infections. A relationship between training loads and infection risk has been modeled in the form of a J-shape curve [26,30,38,57], i.e. moderate loads reduce the infection risk and heavy, intense exertions increase that risk. That view was supported by authors who reported URTI to be particularly abundant in competitive athletes [13,37,41,49,51]; highest relative incidence of URTI was noted at Winter Olympics [14,22,48], Summer Olympics [49,58] and at World Championships [1,2,13]. It ought to be noted that asthma, allergic rhinitis, exercise-induced bronchial spasm and hyperventilation may produce URTI-like symptoms thus making detection of URTI very difficult.

Effects of URTI on competitive performance

Most subjects experiencing URTI resign from trainings altogether or reduce their volume and intensity [9,37,41]. Due to that, the athletes lose yearly, on average, about 15 training days and participation in at least one ranked competition [50]. No significant difference was found between diseased and healthy top Australian swimmers in their performance but the healthy ones tended to attain better results at competitions compared with those in whom URTI was detected in the tapering period or at competitions [47]; a mild infection was found to have a negligible effect in female swimmers and a small harmful effect on the male athletes [46]. Inasmuch those conclusions pertained to teams, individual male athletes, especially those attaining poor results, may be markedly affected by URTI. The chances that the performance of male athletes at competitions would decrease due to URTI rather than increase are about 3:1. This may be associated with the fact that male athletes are inferior to the female ones with respect to psycho-emotional tolerance of work loads [46].

Relationships between sIgA and URTI

First studies on that subject were conducted on Russian athletes in 1988 by Levando et al. [27] and since then the number of reports gradually increased [52] but no unequivocal relationship could be

found so far. Apart from the reported presence or absence of the relationship between concentration of sIgA and URTI [19,20], the effects other factors like the secretion rate of sIgA [15] or the proportions of its subclasses [18] were suggested.

Gleeson et al. [20] who studied Australian swimmers throughout a 12-week training cycle preceding the National Championships found no relationship between concentration of sIgA and URTI incidence. Similar results were reported for male and female football players [34,45,55] but a tendency to decreased salivary flow rate and sIgA secretion rate was noted 3 days prior to the infection [34]; moreover, in the female athletes who later acquired URTI, a decreased concentration of sIgA was noted [45]. Also Cunniffe et al. [11] found no relation between sIgA concentration and URTI incidence despite the fact that lowest sIgA concentration was noted in the month of highest URTI incidence and that URTI-affected athletes tended to have lower mean sIgA concentration compared with the healthy ones. Moreover, sIgA concentrations in individual athletes decreased by about 15% at the moment of URTI contraction compared with the healthy status. The lack of relationship between sIgA and URTI was found either in female rowers [35], as well as in male and female ultramarathon runners [42,44].

A significant relation between sIgA concentration and URTI incidence was noted in top Australian swimmers throughout the 7-month training period [19]. The pre and posttraining concentrations of sIgA were determined at the beginning and after every month of training and were decreasing. The decreases in the mean pretraining and preseason (before starting the training period) concentrations of sIgA correlated with URTI incidence. The authors suggested that the initial, preseason (before starting the training period) sIgA concentration is a better individual indicator of URTI risk than the mean pretraining sIgA, especially when that concentration is lower than $40 \text{ mg} \cdot \text{L}^{-1}$.

A significant sIgA-URTI relationship was found also in sailors [36] when the incidence of URTI was negatively correlated with individual's mean, relative sIgA concentration previously expressed as percentages of individual means computed for the non-URTI periods. The authors reported that the concentration of sIgA was 28% lower during infection than when there was no URTI. Moreover the mean relative sIgA concentrations started decreasing as early as 3 weeks prior to the outbreak of URTI. They stated that when sIgA concentration in a healthy subject was below 70%, the URTI risk amounted to 28% and to as much as 48% when sIgA concentration was below 40% of subject's mean.

Gleeson et al. [18] reported that in the Australian swimmers an increased incidence of URTI during the training season was associated with lower concentration of sIgA1 in the early phase of the training season and in those who experienced 4 or more infections sIgA1 concentrations were lower than those with fewer episodes of URTI. The content of sIgA1 in the total salivary IgA is about 80% in swimmers vs. 60% noted in untrained subjects. The authors suggest that the relative deficit of sIgA2 in athletes may increase the incidence of URTI for sIgA1 is not resistant to bacterial proteases. Other authors

suggest, however, that the risk factor is not the decrease of concentration of sIgA but of its secretion rate as supported by one-year monitoring of American football players [15]. The authors stated that the secretion rate of sIgA below $40 \mu\text{g} \cdot \text{min}^{-1}$ may bring about an increased URTI risk since that secretion rate reflects the actual amount of sIgA available on the mucosal surfaces.

An association of URTI with the secretion rate of sIgA was noted also in ultramarathon runners at the Western States Endurance Run [39,40]. That secretion rate after the run was about by half lower in those subjects who became ill within two weeks post-competition compared with the healthy ones. On the other hand, an at least 50%-decrease in the secretion rate was recorded in about 2/3 of runners who exhibited URTI symptoms but in as many as nearly 50% of the healthy ones. Considering the 50% reduction criterion, healthy athletes with decreased secretion rate (false positives) would be classified as at risk of URTI; those afflicted by URTI, but having the sIgA secretion rate decreased by less than 50% are thus false negatives [40]

Apart from sIgA, also other proteins, associated with the mucosal immune system were studied: alpha-amylase (inhibits the adherence and growth of specific bacteria), lactoferrin (an anti-inflammatory, antibacterial and antiviral factor) and lysozyme (destroys bacterial cell membranes), as well as other factors, e.g. relations between cytokines, hormones and mucosal immune system [4,10,16,43,56]. No unequivocal conclusions, however, could be drawn from those studies; for example, no significant relationship between URTI and total lysozyme concentration was found in rugby players [11], although the concentrations of lysozyme and of cortisol were negatively correlated. The authors speculated that the immu-

nosuppressive function of cortisol might increase URTI risk [11]. Yet, no significant relationship between cortisol concentration and URTI incidence was found in a 9-week study of female football players, although 55% of all ailments recorded in that group was accompanied by previous decreases in sIgA concentration and increases in cortisol concentrations [45]. Gleeson et al. [16] attributed infection incidence to increased levels of interleukin IL-10 accompanied by decreased secretion rates of sIgA. Another field of research, the effects of the exercise type, duration and intensity on the concentration and secretion rate of sIgA was explored by various authors [3,23,24,25,32,33] but those issues were not discussed in this paper.

Concluding remarks

Intense, prolonged exertions are known to affect the immune system and inasmuch athletes are usually free from immune deficiencies of clinical degree, they are decidedly at risk of some infections. An increased susceptibility to URTI may be associated with slight but simultaneous changes in immune cells (neutrophils, lymphocytes, macrophages) or in immune agents (antibodies, cytokines) and a clarification of that is viewed by sport immunologists as one of the top challenges. Yet, despite many studies, no immune dysfunctions were identified as responsible for a higher incidence of URTI among subjects of high physical activity compared with the average ones. An association between the secretion rate and concentration of sIgA, and URTI, has been known but the results are far from being unequivocal due to small numbers of studied subjects, differences in methodology and in the interpretation of symptoms, study seasons and in various environmental conditions. Thus, the issue requires further investigation.

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