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REVIEW

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Aspects of physical training related with upper respiratory tract infections: a review

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ABSTRACT

Background: The upper respiratory tract infections (URTI) are characterized by symptoms present, mainly, in the nose and pharynx. Physical exercise is one of the factors that can lead to development of URTI, causing a state of immunosuppression during a small-time interval, making the athlete susceptible to development of acute infectious states. Besides its influence in athlete's quality of life and healthy, the progression of URTI seems to be associated with overtraining state, inducing reduction on physical performance. Several authors have been discussing how the variables of exercise training can alter the incidence and prevalence of URTI, and the present study was developed to present the current knowledge about this tissue, discussing how the modulation in the exercise training variables may interfere in the URTI. **Methods**: This is a review study. **Results**: Athletes with different levels of training and different categories in most diverse modalities seem to suffer from symptoms of URTI in training and competitive periods. Increasing of URTI symptoms seems to be related to internal training load and evidence has pointed out that suppression of serum and salivary immunoglobulin concentrations appear to be a factor which influences appearance of these symptoms and may even be used as markers of immune status of athlete. **Conclusion**: In point of view of reviewed articles, athletes with different levels of training and different categories in most diverse modalities seem to suffer from symptoms of URTI in training and competitive periods. Increasing of URTI symptoms seems to be related to internal training load and evidence has pointed out that suppression of serum and salivary immunoglobulin concentrations appear to be a factor which influences appearance of these symptoms and may even be used as markers of immune status of athlete. However, studies that verify and provide "cutoff points" that indicate a higher risk for URTI onset is still needed.

Key Words: Physical Training; Immunology; Respiratory Infections.

INTRODUCTION

Moderate regular or alternate exercises may benefit their practitioners; for example, helping them to be less susceptible to infections (e.g. upper respiratory tract) compared to sedentary subjects[(1-3)]. On the other hand, the acute and/or chronic increase in physical demand resulting from changes in physical training variables (volume and/or intensity) throughout a session of training, or even a competition, may exert an opposite-to-expected effect, and triggering symptoms related to infections[(4)]. Such outcomes are more often studied and observed in the upper respiratory tract, including nasal and pharyngeal symptoms (e.g., stuffy nose, runny nose, and sore throat). This phenomenon is commonly characterized as upper respiratory tract infection (URTI)[(4)].

In fact, the rate of URTI is small in recreational athletes, moderate in sedentary and elevate in high-performance athletes[(5)]. Exercise performed in vigorous intensity may cause a decrease in the immune system surveillance[(1,4)] leading the athlete susceptible to infections that can last from 3 to 72 hours after a training session (2.4). This state is called the "Window Open"[(1)]. The model in curve J expresses the relationship between the domain of intensity of the exercise and its effect on the immunological functionality[(6)] (Figure 1).

Symptoms of URTI have been observed in athletes of different sport modalities (e.g. marathon runners, triathletes and boxers), which may present themselves at different moments of physical training, mainly reported during periods of overarching/overtraining and after competitions at different levels[(5,7-9)]. However, physical exercises that predominately are under aerobic metabolism and performed exhaustively (≥ 90 minutes and ≥ 70% VO_2 MAX) appear to have a greater influence on the function of the immune system[(10)].

In addition, URTI frames are not exclusive to training stages and competitive events but may also appear during world championships (e.g. Olympics Games)[(9)]. The incidence

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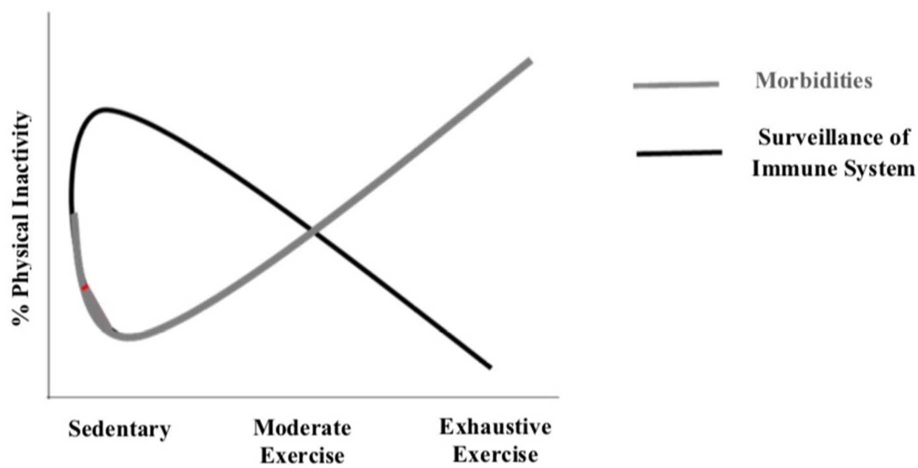

Figure 1. "J" curve model expressing the inverse relationship between intensity of physical exercise and domain in exercise which performed.

of URTI has been significantly higher than other conditions known to affect elite athletes, such as: joint injuries and muscular pain(9,11). Specifically, in the 2000 Olympic Games in Sydney, URTI symptoms were the main diagnosis made by physicians in New Zealand team athletes (101 diagnoses), being much higher than the second condition (dermatological lesions; 49 diagnoses)(9). In addition to compromising the athlete's health, the presence of URTI may cause changes in training routine (e.g. change in volume and intensity), or even discontinuation(12). The higher incidence of URTI in athletes is related to the loss of points in international rankings, general decrease in physical performance, fatigue symptoms and fewer of gold medals in international competitions(13-15). In this sense, the higher prevalence of diseases of the upper respiratory tract during pre-competitive and competitive periods can increase up to 3 times the chance of impairment of physical performance, so for those with lower incidence of URTI present higher results in international competitions, when compared to the "unhealthy"(13).

PHYSICAL TRAINING VARIABLES AND RELATIONSHIPS WITH URTI

Intensity vs Volume: Acute protocols

Acute stress from a competition is an agent related to the appearance of URTI symptoms. However, when we think about physical exercise, it is necessary to take into account that the physiological stress caused by a competitive test, also most probably could be added to the stress accumulated by the training period, especially when it is not well organized.

Generally collective sports do not have minimum distances that must be covered by the practitioner, so volume of the exercise becomes a product of the playing conditions. However, race events (e.g. marathon, ultra-marathon) have predetermined distances and intensity, coupled with stress of the training, are probably the most influential factors in the appearance of URTI in this type of competition. In this sense, the variation in athletes' test time is also studied as a measure of intensity and has been significantly correlated with the incidence of URTI symptoms in weeks after the tests(16,17). In faced with these limitations inherent in competition types, there is an interruption in the literature, regarding to specific impact of intensity and volume of competition on the symptoms of URTI in athletes.

Peters and Bateman(16) studied a classic and seminal experiment among 174 athletes who participated in the Two Oceans Marathon (56 km). The volunteers were asked to answer a questionnaire to assess their self-perception regarding URTI symptoms and characteristics of the physical training performed before their competition. In addition, for the control group, athletes should invite someone close to the race to participate in the race, to be submitted to the same questionnaire. After two weeks of the end of the race, the questionnaire was again applied in both groups. The results showed that 33% of the athletes who finished the race had URTI symptoms, while the control group showed an incidence of 15.3%. When relationship of intensity to incidence of URTI symptoms after the race was evaluated, observed athletes that completed the race in a shorter time presented a higher frequency of URTI symptoms.

On the other hand, in a recent study, Ekblom et al.(17), presented same results with Peter and Bateman(16). After studying 1,694 athletes (majority recreational) competitors of the Stockholm Marathon (42km), they observed that during the training period 17% of athletes already had symptoms of URTI, and higher prevalence in younger individuals. After the race, 33% of the athletes who had URTI symptoms later reported symptoms in the 3 weeks that accompanied the race. On the other hand, among the subjects who did not report symptoms of URTI in the previous weeks, 16% presented symptoms later. Regarding associated factors, adult subjects (30-59 years old) who had completed the test, a standard deviation above mean in time of runners, and who had no symptoms of pre-competition URTI, had higher prevalence of URTI after. In addition, athletes who performed the test were a standard deviation below the mean of time presented and a lower prevalence of URTI. An important question in relation to this experiment is that the researchers did not observe a relationship between training volume and incidence of URTI symptoms before and/or after the competition.

Pacque et al.[18] investigated incidence of URTI, concentrations of salivary and serum IgA antibodies, and influence of physical training variables during the pre-race training period on seventeen Cradle Mountain Run athletes (82 km). The results demonstrated significant decreases in serum and salivary IgA concentrations, in relation to the pre-race. The researchers also observed that there was an inverse relationship between salivary IgA concentrations and running time. In addition, leukogram showed a significant increase in total leukocyte counts, neutrophil and monocyte family; as well as decreases in the number of circulating lymphocytes. Although there have been significant changes in the cells of immune system, symptoms of URTI were not dissimilar between pre- and post-marathon periods. Despite significant results in work of Pacque et al.[18] in relation to a possible mechanism associated with running intensity and mucosal immunosuppression status, sample size (n = 17) is a factor that limits the conclusions about work. Still in relation to this bias, authors argue that the lack of results regarding prevalence of URTI may also be associated with this factor.

Another experiment that did not verify relation in variables of physical training and/or intensity of race with the symptoms of URTI was work of Nieman et al.. The authors studied a significant sample of participants in Los Angeles Marathon (n = 4,926) and found that one week before the race, 342 runners had at least one episode of URTI. Number of 38.6% of athletes which continued to present symptoms in a week after the race. In turn, 1,828 of athletes were free of disease before the race. However, after the competition, 12.9% had URTI symptoms. The authors considered 134 runners who had no symptoms a week before the race, who decided not to compete, which only 3% had symptoms in the following week. The authors did not observe relationship between intensity and incidence of URTI symptoms after the test in this experiment. Therefore, the only study that studied this phenomenon from acute protocols that showed influence of distance covered during a test on the increase and/or onset of URTI symptoms after the race was the work of Peters and Bateman[16], which inferences about the actual dependence of these variables.

A summary of the articles cited above can be seen in Table 1

Intensity vs. Volume: Physical Training

Most of experiments evaluated in this review are observational; thus, the researchers only followed periodization of the coaches without intervening. In addition, assessing impact of changes in volume and/or intensity of training on URTI symptoms is difficult because of training programs which change both variables.

Linear periodization is characterized by sessions composed of high volume low intensity at beginning of the physical training program. Since, these variables will undergo proportional changes with the progression of training, they presented at the end of high intensity and low volume program[20]. This type of approach could facilitate observation of impact of training variables on the URTI symptoms. Gleeson et al.[22] studied 22 elite swimmers were submitted to 12 weeks of training with linear periodization prior to a national competition. The researchers observed that 45% of athletes had at least one symptom of URTI lasting more than 3 days during training period. In addition, biweekly athletes had saliva collected before and after training session to assess IgA and IgM concentrations. The center value results showed there was a significant decrease in salivary concentrations of proteins after the training sessions of each period of micro cycle (e.g. aerobic resistance and polishing phase). However, there were no significant differences between groups with and without URTI symptoms, as well as significant relationships between immunoglobulins and self-report of infectious symptoms.

Similarly, Brunelli et al.[22] did not observe a relationship between increasing of incidence of URTI symptoms in the first

Table 1. Primary and secondary results of acute experiments evaluating URTI

Authors	Samples	Competition features	Primary results	Secondary results
Peters e Bateman, 1983	174 ▲; 124▼ adults	Two Oceans Marathon (56km)	33% ▲ URTI 15.3% ▼ URTI	r= *f* URTI and test time
Niemanet *al.,*1990	4926 ▲ athletes	Los Angeles Marathon (42 km)	12.9% ▲ URTI 3% ▼ URTI	r= URTI and training volume
Ekblomet *al*, 2006	1694 ▲ adults	Stockholm Marathon	33% ▲ URTI	Higher prevalence among youngers
Pacqueet *al*., 2007	17 ▲ beginners	Cradle Mountain Run (82 km)	3 ▲ URTI	(30-59) and faster

Note: URTI = Upper Respiratory Tract Infections; ▲ = Athletes group; ▼ Control group; r = Pearson's correlation; *f* = Frequency.

weeks of training and variables of physical training (tension, monotony and load) in 12 adolescent basketball players during the preparatory period (9 weeks).

Interestingly, the same group evaluated the young basketball practitioners (n=12) for a longer period (18 months). However, this time, Brunelli et al.[23] accompanied athletes during preparatory and competitive period. At that moment, incidence of URTI symptoms in the competitive period (61.7%) was significantly higher in comparison to preparatory period (28.8%). In turn, it was related to training monotony, which is a parameter that may be related to overtraining. In addition, during competitive period, pro-inflammatory cytokines (IL-6, TNF-α), C-reactive protein (CRP) and cortisol hormone showed a significant increase. In contrast, IL-10 levels were decreased after competitive period compared to preparatory period, suggesting a decrease in anti-inflammatory environment.

Regarding to the individual impact of volume and intensity of physical training on incidence of URTI symptoms, Nieman and et al.[24] compared impact of increased training intensity immunological variables and also incidence of URTI in runners and cyclists. A priori, both groups trained continuously with equalized volume for 4 weeks (~ 410 minutes/week) in usual intensity. However, during the fifth week, both groups underwent, for 3 consecutive days, an exercise protocol with a higher intensity than performed for 12 weeks (2.5 hours at 70% VO2max) on treadmill or on their own bicycle. The results showed that both groups showed an increase in concentration of proinflammatory cytokines after exercise, with higher values in the group of runners. However, the URTI symptoms were not different between the groups and showed no correlation with cytokine concentrations.

Likely, during 50 weeks of training, Neville et al.[25] followed 38 weekly men on incidence of URTI and collected their saliva to assess IgA concentrations. Athletes were divided to their physical demand in the sport, being then stratified in groups of high and low intensity. During training period, there were 102 incidences of URTI, but no differences between the groups. At times of higher incidence of URTI, IgA concentrations were decreased. In addition, these values began to decline in 3 weeks after appearance of URTI. Thus, researchers suggested that salivary IgA could be used to monitor athletes in order to prevent URTI frames. However, there was no relationship between URTI and effort intensity.

Fricker et al.[26] in a study evaluated impact of race training intensity on URTI symptoms. Researchers studied 20 medium and long-distance runners during 16 weeks of training. Athletes were monitored daily for training variables (e.g. intensity, volume). During the period, 75% of athletes presented at least one symptom of URTI with an average duration of eight days. However, first evaluation did not show a significant relationship between incidence of URTI and physical training variables. At second moment, when researchers separated athletes into two groups (healthy and URTI), the URTI group had shorter distance covered and higher training intensity during the 16 weeks evaluated. Unlike the intensity, which was not shown to be main impact factor in URTI symptoms, two studies which modulated volume of training period, verified a positive relationship between this variable and URTI[27,28].

Gleeson et al.[27] followed four months on ninety volunteers who practiced physical exercise in three different volumes: low (3-6 hours/week), moderate (7-10 hours/week) and high (> 11 hours/week). The authors observed, there were more episodes and a higher proportion of subjects with URTI in the moderate and high training groups compared to the low volume group. In addition, authors did not observe significant differences between immunological variables (e.g., leukocyte and subgroup counts, proinflammatory cytokines). In addition to general immunological variables, IL-10 concentrations were higher in the high-volume group compared to the low volume group. These results are interesting, whereas IL-10 has anti-inflammatory activity inhibiting the activity of histocompatibility molecules (MHC) and antigen-presenting cells.

In another study, evaluating high-performance athletes, Ferrari and colleagues[28] followed 9 cyclists who competed at national level for 29 weeks. The athletes underwent 3 different mesocycles during periodization which included: preparatory (9 weeks), competitive phase 1 (10 weeks) and competitive phase 2 (10 weeks). During these steps, athletes were monitored for URTI symptoms using the WURSS-44 questionnaire, which evaluated symptoms, associated with URTI and collected blood for immunological evaluation. Results showed during preparatory phase, characterized by high training volume and lack of intensity control, there was an increase in total score and number of URTI symptoms in athletes compared to rest phase (pre-study) and competitive phases. In addition, results evaluated by the questionnaire showed a positive and significant relationship between tension of preparatory and competitive phase. Although prescription of preparatory phase aimed at increasing volume that athletes were resting before this phase. Thus, increase intensity in compared with resting moment may have contributed to result found by the researchers. Therefore, general tension demonstrated in athletes indicates both factors interfered in the result. Discussion about the above study, and question of total load being a determinant of incidence of URTI symptoms, confirmed by several studies[29-32].

Fahlamn and Engels[29] studied 100 volunteers were for 12 months, which 75 participants were athletes of the American university league, while 25 were physically active college students. Results showed during moments of greater physical (pre-season and competition) overload, IgA concentrations and secretion were lower in athlete groups compared to control group. At the same time, incidence of URTI was significantly increased in athletes group. Interestingly, researchers also assessed rate of IgA secretion that could serve as a predictor of incidence of URTI in college athletes. Although results indicate that increase in physical demand represents is cause of an increase in incidence of URTI, it is not possible to distinguish influence of volume and intensity of training phases individually.

Results of Fahlamm and Engels[29] study are repeated in studies of various sports, such as field soccer[30], futsal[31], basketball[32] and volleyball[33], which also evaluated internal training load, had a great influence on the URTI symptoms.

Increasing of internal training load, which represents physiological response and individual's perception of stress which generated by physical exercise, is expected to influence symptoms of URTI. However, periods that consider volume reduction and intensity of physical training (Tapering) may not only contribute to reduction of URTI symptoms, but also to increase blood levels of IgA[30-32].

A series of studies by group of Professor Alexandre Moreira, studied effect of reduction of training volume on symptoms of URTI. Firstly, 15 elite basketball players were followed for 4 weeks in pre-competitive period. During each week athletes were monitored for training load, stress level and URTI-related symptoms. During second week of training, internal training load was greater than that identified during first and forth weeks. Concurrently, incidence of URTI symptoms and results of DALDA questionnaire (part A) (e.g. stress symptoms) showed similar kinetics to behavior of internal training load, thus being significantly higher for second week when compared to first and forth weeks. In addition, after four weeks of training, salivary cortisol concentrations were found to be increased, whereas salivary IgA was decreased in comparison to rest time[32]. Also, Moreira et al.[31] monitored internal load training, URTI symptoms and evaluated salivary IgA concentrations in a high-level futsal team for four weeks. Results for internal training load were higher in the first two weeks of training compared to third and fourth weeks. Also, in the last week, URTI symptoms were lower in athletes compared to other three weeks. In addition, symptoms of URTI at fourth week were correlated with training load of the same week; Overall URTI, in turn, was related to relative change in IgA over the 4-week experiment.

Recently in a study which published by a group, Moreira et al.[30] accompanied 21-week junior field soccer athletes for 21 weeks. Athletes were assessed for URTI symptoms, IgA salivary concentrations and internal training load. Periodization consisted of three stages: 12 weeks of preparatory period, 7 weeks of competitive period and 2 weeks of detraining (Tapering). During tapering concentrations of salivary IgA showed a significant increase in comparison to pre-moment. Similarly, symptoms of URTI were diminished after tapering. A summary of the articles cited above can be seen in Table 2.

Table 2. Primary and secondary results of chronic experiments that assessed the incidence of URTI

Authors	Samples	Experimental design	EF Protocol	URTI reports	Primary results	Secondary results	Immune system
Gleeson et al.,1999	22 Elite athletes 75 elite athletes	Prospective Observational	12 weeks training	Own questionnaire	45% ▲ URTI 55% ▲ non URTI	----------------------	↓ IgA, '↓ IgM, ↓NK
Fahlamn & Engels, 2004	25 EF practitioners	Prospective Observational	12 months	Own questionnaire / doctor	Highest% of URTI in ▲ compared to ▼	Changes in IgA concentrations influenced the appearance of URTI.	↓ IgA
Fricker et al.,2005	20 elite athletes	Prospective Observational	16 weeks training	Own questionnaire / doctor	75% ▲ URTI	URTI individuals presented lower mean distance traveled and higher mean intensity.	---------------------------
Neville et al., 2008	38 elite athletes	Prospective Observational	50 weeks training	Doctor	No differences between URTI in athletes with demands different physical	r = - concentrations of s-IgA and incidence of URTI	↓ IgA
Moreira et al.,2010	15 basketball players	Prospective Observational	4 weeks training	WURSS-21	↑ URTI in the week increase in IL	r = WURSS-21 with DALDA A and B.	↓ IgA secretion rate ↓ Lymphocyte count

Note: URTI = Upper Respiratory Tract Infections; ▲ = Group athletes; ▼ Control group; r = Pearson's correlation; f = Frequency; IgA = Immunoglobulin A; S-IgA = Salivary immunoglobulin A; IL = Internal training load

Table 2. Continued...

Authors	Samples	Experimental design	EF Protocol	URTI reports	Primary results	Secondary results	Immune system
Dias et al, 2011	12 young volleyball players	Prospective Observational	40 weeks training	Own questionnaire	↑ URTI in the periods competitive vs. pre competition	r = Incidence of URTI and training load.	↓ monocytes
Brunelli et al., 2012	12 young basketball players	Prospective Observational	9 weeks training	Own questionnaire	↑ URTI in the first weeks vs. the others	no relation between URTI and the rules of physical training.	Serum [IgA] compared to control during the 29 weeks
Ferrari et al., 2013	8 well-trained athletes 18 EF practitioners	Prospective Observational	29 weeks training	WURSS-44	↑ Total score and number of feel but in the WURSS-45 of the ▲ during the prepatulatory phase	r = WURSS-44 total score and 'tension' in the preparatory phase and 2nd phase competitive; No. of symptoms and strain in the preparatory phase.	↑ IL-10, ↑ IL-6, ↑ IL-8
Nieman et al., 2013	13 runners 22 cyclists	Experimental randomized	5 weeks training	WURSS-21	no differences between results of WURSS-21 between the two groups	---------------------- --------	↑ Counting and function of leukocytes
Moreira et al., 2013	12 futsal players	Prospective Observational	4 weeks intense training	WURSS-21	↓ URTI in week of IL decrease	r = Incidence of URTI and training load; URTI and relative changes in IgA	-------------------- -------
Moreira et al.,2013	34 teenager elite football players	Prospective Observational	21 weeks training	Own questionnaire	↓ URTI in week of IL decrease	------------------- -------	↑ IgA
Gleeson et al.,2013	90 EF Practitioners	Prospective Observational	4 months training	Own questionnaire	High and Med group showed higher URTI than Low	-------------------- -------	↑ IL-10
Brunelli et al., 2014	12 young basketball players	Prospective Observational	18 weeks training	Own questionnaire	↑ URTI in Competitive vs. Preparatory period	r = Incidence of URTI and 'stress' symptoms	↑ PC-r, ↑ IL-6, ↑ IL-10, ↑ TNF-α, ↑ Cortisol ↑ Counting and function of leukocytes

Note: URTI = Upper Respiratory Tract Infections; ▲ = Group athletes; ▼ Control group; r = Pearson's correlation; f = Frequency; IgA = Immunoglobulin A; S-IgA = Salivary immunoglobulin A; IL = Internal training load

ALTERNATIVE HYPOTHESIS: URTI INFECTIONS ARE REALLY?

Despite aforementioned outcomes, relationship between physical exercise and incidence of URTI symptoms, there are still no studies that have confirmed association of medical diagnosis or self-reported URTI symptoms, as well as laboratory tests, that evaluated presence of viral pathogens and/or bacterial[4,6]. Therefore, some authors suggest that symptoms associated with URTI after exercise is not product of an infectious but allergic or inflammatory picture[4,12].

In relation to allergy, it is possible that physical exercise triggers anaphylaxis (e.g. severe allergic reaction), and after an exercise session, athletes may present with allergic conditions, such as sinusitis and asthma[6]. Hypothesis is based on the premise that allergic states present clinical characteristics similar to those found in URTI, especially nasal congestion and coriza[4]. However, this relationship is still little studied, and the hypothesis has already been ruled out by some studies[4,12].

Given the lack of results confirming the hypothesis, two studies[5,12] observed relationship between incidence of URTI symptoms in athletes, evaluated through a questionnaire[5] and a medical examination[12], and correlated with clinical exams.

In the first study, Cox et al.[12] carried out a prospective study to verify association between diagnosis of URTI and results of laboratory tests to identify viral and bacteriological agents. Seventy athletes of various modalities (e.g. boxing, cycling and archery) had symptoms suggestive of URTI. Among 70 athletes who presented URTI with medical evaluation, 58 (83%) presented clinical symptoms unique to viral URTI and 4 (6%) had exclusive symptoms of bacterial infection. However, when diagnosis was confronted with laboratory tests, among 83% who presented viral symptoms, only 16 (76%) cases were evaluated for viral pathogens. On the other hand, from 4 cases of bacterial infection, only two bacterial pathogens were evaluated.

In turn, Spence et al.[5] studied elite athletes (n = 32), recreational athletes (n = 31), and sedentary individuals (n = 20) for 5 months, which included training and competitive period. Researchers observed that elite athletes had a higher incidence of URTI symptoms during high intensity and competitive training period compared to amateur and sedentary athletes. However, when relationship between symptoms and laboratory tests was evaluated, results were contradictory. Among 37 subjects who reported URTI symptoms, only 11 (30%) had confirmation by the exams. Thus, ¾ of the subjects who reported positive, did not present infectious agents in the exams.

Apart from negative relationship between URTI symptoms (reported by physicians or athletes) and laboratory tests, several biases may explain lack of correlation between variables observed in the aforementioned studies (e.g. different modalities, lack of follow-up in training, different environments attended by athletes, tests limited to some pathogens). Thus, a randomized experimental study is still needed to study and verify association of these factors. In any case, it is important to mention that Spence et al.[5] reported that condition characterized by increased symptoms or similar to URTI is modulated by physical exercise and should be avoided in order for athlete to maintain his or her health, well-being and performance.

CONCLUSIONS AND FUTURE DIRECTIONS

In point of view of reviewed articles, athletes with different levels of training and different categories in most diverse modalities, seem to suffer from symptoms of URTI in training and competitive periods. Increasing of URTI symptoms seems to be related to internal training load and evidence has pointed out that suppression of serum and salivary immunoglobulin concentrations appear to be a factor which influences appearance of these symptoms and may even be used as markers of immune status of athlete. However, studies that verify and provide "cutoff points" that indicate a higher risk for URTI onset is still needed.

AUTHOR'S CONTRIBUTION

SA and HJCJ conceived of the presented idea. HJCJ developed the theory and performed the computations. Barreto CB, RS, RCRP, RB, SSA and Asano RY verified the analytical methods. SA and HJCJ encouraged them to investigate upper respiratory tract infections and supervised the findings of this work. All authors discussed the results and contributed to the final manuscript. RB, SSA, Asano RY, HJCJ and SA analyzed the data and they wrote the paper with input from all authors. All authors contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript; finally, all authors read and approved the final manuscript.

CONFLICTS OF INTEREST

Nothing to declare.

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