

CHAPTER V

DISCUSSION AND CONCLUSION

In the present study, the experiments were conducted to investigate the effects of acute exercise and exercise training combined with vitamin C supplementation on physiological changes and symptoms in allergic rhinitis patients. The results of study I showed that both acute exhaustive and moderate-intensity exercise resulted in a significant improvement in symptoms of allergic rhinitis. However, a significantly enhanced IL-2/IL-4 ratio was found following only acute moderate exercise intensity. In study II, the results demonstrated that resting heart rate in both EX and EX + Vit. C were significantly decreased ($p < .05$) but Vo_2max were significantly increased and higher than the CON ($p < .05$). Plasma Vit C of the EX + Vit. C group was significantly higher than both the CON and Ex groups ($p < 0.05$). Additionally, malondialdehyde (MDA) levels of the both EX and EX + Vit. C were significantly lower than pre-test and the CON ($p < 0.05$). In part of cytokines levels, EX and EX + Vit. C had significantly decreased interleukin (IL)-4 levels. Moreover, the percent difference of IL-2 was significantly higher than the CON ($p < 0.05$) and the percent difference of IL-4 was significantly lower than the CON ($p < 0.05$). After nasal challenge by house dust mite (*D.pteronyssinus*), the percent difference of IL-4 and IL-13 in the both EX and EX + Vit. C were significantly lower than the CON ($p < 0.05$), but the percent difference of IL-2 in the both EX and EX + Vit. C was significantly higher than the CON ($p < 0.05$). For objective rhinitis symptoms, the percent difference of peak nasal inspiratory flow (PNIF) were significantly higher while those of nasal blood flow were significantly lower in the EX and EX + Vit. C when compared to the CON ($p < 0.05$). Moreover, the EX and EX + Vit. C had a significantly higher PNIF after nasal challenge 60 minutes when compared to pre-test ($p < 0.05$). For subjective rhinitis symptoms, the total rhinitis symptoms score of congestion, itching, sneezing and rhinorrhea at baseline and following nasal challenge were significantly decreased in both EX and EX + Vit. C ($p < .05$). Discussion is expressed in relation to the results as mentioned earlier are as followed:

Study I: The effect of acute exhaustive and moderate intensity exercise on physiological changes and symptoms in allergic rhinitis patients.

Our results demonstrate that baseline cytokines in nasal secretion of patient with allergic rhinitis were higher than those of healthy controls. Acute moderate-intensity exercise had beneficial effects on cytokine response in nasal secretion by showed increasing the ratio of IL-2 and IL-4 in both C and AR groups.

Allergic rhinitis is a significant cause of widespread morbidity, high medical treatment costs, reduced work productivity, and can affect a patient's quality of life and can be associated with conditions such as fatigue, headache, cognitive impairment, and sleep disturbance (Wallace DV. et al., 2008). In the present study, the AR group had lower in body composition and lipid profile than the healthy subjects. The data from the present study are in contrast to other studies, which found that body mass index in allergic rhinitis patients was higher than control subjects (Ciprandi G. et al., 2009). Moreover, Erel et al. (2007) investigated the serum levels of leptin and lipid profiles on allergic rhinitis and found that they were not different than those in controls.

In our study, the level of total immunoglobulin E (IgE) in the AR group (416.50 ± 352.69 IU/ml) was significantly higher than the C group (77 ± 52.06 IU/ml), which agrees with previous studies that have also reported that the IgE in patients with rhinitis was higher than in healthy controls (Rondon C. et al., 2007; Aldred S. et al., 2010; Chan IH. et al., 2010). Patients with allergic rhinitis present an inflammatory IgE-mediated response characterized by a Th2 immunologic pattern, with mast cell and eosinophil activation and release of inflammatory mediators in response to an allergen (Rondon C. et al., 2007). IgE levels greater than 140 IU/ml are suggestive of an atopic etiology for patients with signs and symptoms of rhinitis (Demirjian M. et al., 2011).

Using flow cytometry, we found that cytokines in nasal secretion contained significantly higher concentrations than serum in both the C and AR groups. This indicates that cytokine determination should be determined in local area (nasal secretion) rather than in the systematic system (serum). In the present study, the IL-2, IL-4 and IL-13 in nasal secretion of allergic rhinitis patients were significantly higher than

the healthy subjects, which is in agreement with previous studies (Bachert C. et al., 1995; Scavuzzo MC et al., 2003).

In terms of the cytokines response following acute exercise, the data showed that there was no significant difference between exhaustive and moderate-intensity exercise in both the C and AR groups. However, we found that IL-2/IL-4 ratio after moderate-intensity exercise was significantly higher than exhaustive exercise in both the C and AR groups ($p < .05$). IL-2 is critical for supporting T cell activation, and the dominant physiological function of IL-2 signals in vivo is to restrain T cell activation and prevent autoimmunity (Ma A. et al., 2006). IL-2 induces macrophage activation, which are very effective in controlling infection along with intracellular pathogens (Biedermann T. et al., 2004). Alternatively, IL-4 may play a central role in the IgE synthesis system, the development of Th-2-like cells, and act as co-ordinator of airway inflammatory process in allergic disorders (Ohashi Y. et al., 1996). A number of recent studies have shown an increase of IL-4 level in allergic rhinitis patients (Benson M. et al., 2000; Rapp J. et al., 2000; Scavuzzo MC et al., 2003). Our studies indicated that moderate intensity exercise induced the increase of anti-inflammatory cytokines but decrease the pro-inflammatory cytokine. Moreover, Pedersen BK. et al. (1998) found that strenuous exercise is accompanied by an increase in circulating pro-inflammatory cytokines (Pedersen BK. et al., 1998). We suggest that moderate-intensity exercise appears to have beneficial effects for allergic rhinitis patients. Consistently with previous study, Jeurissen A. et al. (2003) reported that moderate-intensity exercise could protect against upper respiratory tract infections. The mechanisms for this cytokine response to acute exercise is not known, and requires further investigation.

In summary of study I, our data demonstrate that moderate-intensity exercise has positive response to pro-inflammatory cytokines levels. We conclude that moderate-intensity exercise is beneficial for allergic rhinitis patients. Therefore, we use moderate-intensity exercise as the intervention for study II in order to prove that whether moderate exercise training combined with vitamin C supplementation have beneficial effects to allergic rhinitis patients.

Study II: The effects of moderate exercise training combined with vitamin C supplementation on physiological changes and symptoms in allergic rhinitis patients.

The primary findings of the study II were that after 8 weeks, the results demonstrated that resting heart rate in both EX and EX + Vit. C were significantly decreased ($p < 0.05$) but Vo_2 max were significantly increased and higher than the CON ($p < 0.05$). Malondialdehyde (MDA) levels of the both EX and EX + Vit. C were significantly lower than pre-test and the CON ($p < 0.05$). In part of cytokines levels, EX and EX + Vit. C had significantly decreased interleukin (IL)-4 levels. Moreover, the percent difference of IL-2 was significantly higher than the CON ($p < 0.05$) and the percent difference of IL-4 was significantly lower than the CON ($p < 0.05$). After nasal challenge by house dust mite (*D. pteronyssinus*), the percent difference of IL-4 and IL-13 in the both EX and EX + Vit. C were significantly lower than the CON ($p < 0.05$), but the percent difference of IL-2 in the both EX and EX + Vit. C was significantly higher than the CON ($p < 0.05$). For objective rhinitis symptoms, the percent difference of peak nasal inspiratory flow (PNIF) were significantly higher while those of nasal blood flow were significantly lower in the EX and EX + Vit. C when compared to the CON ($p < 0.05$). Moreover, the EX and EX + Vit. C had a significantly higher PNIF after nasal challenge 60 minutes when compared to pre-test ($p < 0.05$). For subjective rhinitis symptoms, the total rhinitis symptoms score of congestion, itching, sneezing and rhinorrhea at baseline and following nasal challenge were significantly decreased in both EX and EX + Vit. C ($p < 0.05$).

Physiological characteristics

The principal findings of physiological characteristics showed that the both EX and EX + Vit. C groups had decreased in resting heart rate and increased in Vo_2 max after 8 weeks. In addition, the both EX and EX + Vit. C groups had significantly lower percent difference in resting heart rate but had significantly higher percent difference in Vo_2 max while no significant difference in those parameters were observed in the CON groups.

The moderate exercise training has been proposed due to the health benefits, including an increase of physical fitness and decreased risk of obesity, cardiovascular disease and the metabolic syndrome (Fogelholm et al., 2000; Sato et al., 2007). Many studies have reported that allergic rhinitis drugs are stimulants and may cause increased heart rate in patients with allergic rhinitis (Salerno et al., 2005; Blaiss, 2007; Scow et al., 2007). In the present study, exercise training protocol consisted of walking-running on a treadmill (65-75% of HRR) 30 minutes, three times per week for 8 weeks. These training program is the minimum recommended quantity and quality of exercise for developing and maintaining cardiorespiratory fitness (Pollock et al., 1998). It is adequate to induce physical adaptations as with decrease in resting heart rate and increase maximum oxygen consumption ($VO_2\text{max}$). In agreement with our study, several studies showed that moderate aerobic exercise training improved resting heart rate and $VO_2\text{max}$ in healthy people and disease (Jurca et al., 2004, Mitranun et al., 2010, Phanpheng et al., 2010). Zanesco and Antunes (2007) reported that exercise training decrease in heart rate at rest and at submaximal work load is the hallmark of cardiovascular adaptation in response. The mechanisms underlying reduced HR include increased parasympathetic and sympathetic stimulation of the sinoatrial node, and altered intrinsic firing rate of the sinoatrial node (Moore, 2006). The greater improvement in $VO_2\text{max}$ observed in our study may have been due to an increased stroke volume include a training induced enlargement of left ventricular chamber size, cardiac muscle hypertrophy with enhance contractility during systole and (a-v) O_2 difference improvement (Trilk et al., 2011). $VO_2\text{max}$ is a value expressed quantitatively of a person's capacity for aerobic resynthesis of ATP. It provides important information on the capacity of long term energy system (Heyward, 1997). It is an indication of the ability of the body that can carry oxygen to the muscle of the body parts effectively and increasing the transport of oxygen to the muscle in higher volume (Hepple et al., 1997). Those development of cardiovascular and respiratory endurance resulted in an increase of the performance to bring oxygen and nutrients to the organs for longer working (Smarty, 2009).

Blood chemical data

In the present study, the results showed that after 8 weeks the total immunoglobulin E level in the moderate exercise training combined with vitamin C supplementation group (EX + Vit. C) was significantly lower than pre-test and significantly lower when compared with both control (CON) and moderate exercise training (EX) groups ($p < 0.05$). However, there were no significant difference in specific IgE (*D.pteronysinus*) between pre and post test in all groups of subjects. Additionally, malondialdehyde (MDA) levels of the both exercise training groups were significantly lower than pre-test and when compared with the control group.

Immunoglobulin E (IgE) was synthesized by plasma cells in the nasal mucosa in allergic rhinitis, providing a local source for the sensitization of tissue mast cells against common inhaled aeroallergens (Takhar et al., 2005). This condition is an IgE-mediated inflammatory disease of the nasal mucosa, characterized by obstruction, rhinorrhea, sneezing, itching, and/or postnasal drip; ocular symptoms are also frequent (Rondon et al., 2007). Our results showed that after 8 weeks total IgE of the EX + Vit. C group had a significantly lower than pre-test ($p < 0.05$), but there were no significant difference in the both CON and EX groups. Moreover, the percent difference of total IgE in the EX + Vit. C group was significantly lower than the both CON and EX groups ($p < 0.05$). Vitamin C (ascorbic acid) is an essential water-soluble nutrient (Hartel et al., 2004) which acts as an electron donor for many kinds of human enzymes, facilitates iron transport, and is regarded as one of the most important physiological antioxidants. In addition, Vitamin C exerts several diverse effects on the immune system. It increases neutrophil motility and phagocytic function in human (Noh et al., 2005). Our results showed that dietary vitamin C supplementation 2,000 mg/day for 8 weeks reduced total serum immunoglobulin E in allergic rhinitis patients. In support this study, recent reports showed that vitamin C presents some anti-inflammatory effects, which are helpful in the treatment of asthma (Hatch, 1995), a common symptom that occurs in hypersensitivity. Furthermore, consumption of vitamin C can lower blood levels of histamine (Clemeston, 1980) and reduce the natural inflammatory response in nasal passages (Fortner et al., 1982), which exhibit some anti-allergic activity. Noh et al. (2005) reported that in vivo administration of mega-dose vitamin C decreased IL-4 secretion from their T cells and

reduced serum ovalbumin-specific IgE. In contrast to Sausenthaler (2009), reported that vitamin C intake not effect on allergic sensitization and total IgE concentration. However, it was not speculate that moderate exercise combined vitamin C supplement had better beneficial effect on improve function in allergic rhinitis due to there were no significant difference in specific IgE (*D.pteronysinus*) in EX + Vit. C group.

Oxygen free radicals, such as superoxide anion radical, singlet oxygen, hydroxyl radical, and perhydroxyl radical are together referred to as reactive oxygen species (ROS) and play an important role in the pathogenesis of several diseases (Ahsan et al., 2003), including some skin diseases (Utas et al., 2002; Okayama, 2005). MDA is the end product of lipid peroxidation, is a good marker of free radical-mediated damage and oxidative stress (Del Rio et al., 2005). The role of free oxygen radicals (FOR), occurring in the inflammation area, on tissue damage and ethiopathogenesis of various diseases is gradually drawing more attention in medicine. Inflammatory cells become active in patients with asthma and allergic rhinitis and produce too much FOR (Jarjour and Calhoun, 1994). This way, it was revealed that FOR, more accurately oxidative stress, can take part in the pathogenesis of allergic diseases like asthma and allergic rhinitis, chronic idiopathic rhinitis, and several studies have been and are still being conducted to enlighten this topic (Tekin et al., 2000; Macnee and Rahman, 2001). The present study indicated that moderate aerobic exercise training 8 weeks declined plasma MDA in patients with allergic rhinitis. Oxidative stress can be defined as exposure to increased oxidant or decreased antioxidant capacity (Mc Cormick et al., 1999). Oxidative stress plays an important role in allergic disorders and increased levels of oxidants are considered as markers of the inflammatory process. There are superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GSH-Px), GSH redox rings, there are also some non-enzymatic antioxidants like ceruloplasmin and vitamin C and vitamin E act as for scarençer (Ünlü et al., 1999). Overproduction of oxygen free radicals, while the natural scavenging mechanisms are weakened, is a process that is implicated in cell damage and multiorgan failure (Li et al., 2011). It has important implications on the pathogenesis of chronic obstructive airway diseases (Nounou et al., 2010). As a result, we speculate that moderate intensity exercise training effects conferred beneficial effect to ameliorate the harmfulness of oxidative stress in

rhinitis patients. Many studies have reported that 5 days/week for 12 weeks exercise training improved tissue perfusion and attenuated increasing oxidative stress (Metin et al., 2003; Viboolvorakul et al., 2009). Asghar et al. (2007) found that 6 weeks treadmill exercise training decrease MDA levels and increases total superoxide dismutase (SOD) in mice. This study demonstrated that exercise training decrease oxidative stress, reduce inflammation and induce anti-oxidant defense. The mechanism of attenuating oxidative stress by exercise training due in part to an increase in antioxidant activity, therefore, facilitating the removal of reactive oxygen substances (Suksom et al., 2011).

Cytokine levels in nasal secretion

In this study, the cytokine level in nasal secretion was determined before and after 8 weeks. The results showed that the both EX and EX + Vit. C groups had significantly decreased interleukin (IL)-4 levels. Moreover, the percent difference of IL-2 was significantly higher than the CON group ($p < 0.05$) and the percent difference of IL-4 was significantly lower than the CON group ($p < 0.05$). After nasal challenge by house dust mite (*D.pteronyssinus*), the percent difference of IL-4 and IL-13 in the both EX and EX + Vit. C groups were significantly lower than the CON group ($p < 0.05$), but the percent difference of IL-2 in the both EX and EX + Vit. C groups was significantly higher than the CON group ($p < 0.05$).

Cytokines are soluble glycoproteins that are produced by and mediate communication between and within immune and nonimmune cells, organs and organ systems throughout the body (Turnbull and River, 1999). Allergic rhinitis is characterized by the development of nasal mucosal inflammation in response to natural allergen exposure which induce by the production of numerous cytokines. Allergic inflammation is associated with a shift in the balance between cytokines produced by Th1 and Th2 cells toward a Th2 predominance. Activated Th2 lymphocytes produce IL-4, IL-13, and IL-5, which are responsible for IgE production by B cells, eosinophil activation and recruitment and mucus production. In contrast, Th1 cells differentiate from naïve CD4⁺ cells in response to micrabria activation of antigen-presenting cells under the influence of IL-12. Differentiated Th1 cells secrete interferon- γ and IL-2, which is important in

intracellular destruction of phagocytosed microbes. Furthermore, IL-2 produced by Th1 cells and IL-4 produced by Th2 counter-regulate each other (Ngoc et al., 2005). Nasal secretions contain minute amounts of cytokines and other inflammatory mediators expressed by various epithelial and nonepithelial cells. In this study, we use a filter paper method technique for the collection of nasal epithelial lining fluid. It involves the use of a sampler with absorptive properties which is placed within the nasal cavity. This technique was considered suitable for cytokine determination (Bensch et al., 2002). Cytokine in nasal secretion are found in concentrations considerably higher than in blood plasma (Riechelmann, et al., 2003).

IL-4 promotes the production of IgE antibodies by B-cells, it is one of the key cytokines in the development of allergic inflammation (Cameron et al., 1998; Draheim et al., 2004; Sausenthaler et al., 2009). IL-4 plays a key role not only in inducing and increasing the generation of primary polyclonal and secondary specific IgE responses by B lymphocytes (Finkelman et al., 1990; Prete et al., 1993) but also in developing Th2-like cells (Abehsira-Amar et al., 1992). In addition, IL-4 has been shown to up-regulate the expression of adhesion molecules such as VCAM-1 on endothelial cells, which are involved in the selective infiltration of eosinophils in allergic inflammation (Schleimer et al., 1992). IL-4 mediates important proinflammatory functions in asthma in induction of the IgE isotype switch, promotion of eosinophil transmigration across endothelium, mucus secretion, and differentiation of T-helper type 2 lymphocytes leading to cytokine release (Steinke and Borish, 2001). Thus, IL-4 may be the most important cytokine involved in allergic pathogenesis. Several studies have documented a significant elevation of serum IL-4 levels in atopic individuals compared with nonatopic controls (Matsumoto et al., 1991; Reddy et al., 1992; Ohashi et al., 1996). A recent study reported the higher levels of IL-4 in the nasal fluid of allergic rhinitis patients compared to controls (Scavuzzo et al., 2003). In the present study, the levels of IL-4 after 8 weeks moderate exercise training in allergic rhinitis patients were significantly lower than pre-training in both at baseline and after nasal challenge with house dust mite (*D.pteronyssinus*). In agreement with our studies, many studies showed that aerobic exercise training could be attributed to decrease levels of IL-4 (Pastva et al., 2004; Pastva et al., 2005; Vieira et al., 2007; Vieira et al., 2008). Nevertheless, Shimizu et al.

(2008) found that moderate exercise training 5-days a week for 6 months did not change in IL-4 cytokine.

Th1 cells produce, IL-2, TNF- α , IFN- γ and other cytokines for control of cell-mediated immunity (McGhee, 2005) and promote both macrophage activation resulting in delayed-type hypersensitivity (DTH), and production of complement-fixing and -opsonizing antibodies (Viillard et al., 1999). IL-2 is a growth promoting cytokine that has received a great deal of attention over the past decade with respect to aging and cancer. It is produced primarily by helper T cells and regulates the growth and function of various cells that are involved in cellular and humoral immunity. The expression of IL-2 has been found to decrease with age in humans and rodent. The decline in IL-2 production has been shown to parallel the age-related decrease in immunologic function (Pahlavani and Richardson, 1996). Our results demonstrated that moderate exercise training increase IL-2 when compared to control group. In agreement with our study, Arai et al. (2006) reported that long-term endurance training can increase the production of IL-2 to comparable levels found in young male subjects. This finding suggested that chronic exercise could delay immunosenescence by IL-2 association with higher T cell proliferation.

In the present study, we demonstrated that the improvement in aerobic capacity by exercise training in allergic rhinitis patients were associated with inhibiting the production of IL-4 but increasing IL-2. In agreement with previous study, they reported that the anti-inflammatory effects of aerobic exercise training could be attributed to decrease levels of IL-4, IL-5, IgE and also increase in the anti inflammatory cytokine (Pastva et al., 2004; Pastva et al., 2005; Vieira et al., 2007; Vieira et al., 2008). Potential mechanism relating moderate exercise training and cytokine levels have not been clearly elucidated. The one possible mechanism is that exercise training improved physical capacity and sweating function so that body temperature was more easily regulated during and after exercise. This may due to improved production of specific cytokine and chemokine in sweating during exercise (Lee et al., 2010). Another mechanism may be due to VO_2 max improvement from exercise training may be linked to attenuate levels of oxidative stress which in turn may alternate inflammatory cytokine expression (Smart et al., 2011). Exercise training-induced improvement in inflammatory

status may also result from the modulation of intracellular signaling pathways and cellular function that are mediated by ROS. While ROS are generated at low rates under resting conditions, the production of these molecules increases transiently during exercise and plays a role in inducing anti-inflammatory defense mechanism (Scheele et al., 2009). ROS have acute effects on contractile regulation and exert chronic effects on muscle gene expression. In particular, the adaptive process involves the up-regulation of genes encoding antioxidant enzymes and heat shock proteins. Given that ROS mediates some of the catabolic effects of cytokines, reductions in ROS generation may lead to attenuation of the inflammatory response (Beavers et al., 2010).

Rhinitis symptoms analysis

In this study, the results showed that after 8 weeks, the both EX and EX + Vit. C groups had increased in peak nasal inspiratory flow (PNIF) and decreased in rhinitis symptoms such as; nasal congestion, itching, sneezing, rhinorrhea and total rhinitis symptoms were reduced after examine by level (mild, moderate and severe) technique. We found that PNIF of both exercise groups were significantly higher than the control group (CON) and after nasal challenge 60 minutes, the EX and EX + Vit. C groups had a significantly higher PNIF when compared with pre-test ($p < 0.05$). Furthermore, nasal blood flow and rhinitis symptoms scores in the both exercise groups (EX and EX + Vit. C) were significantly lower than the control group (CON).

PNIF proved to be a reliable method to detect change to nasal patency due to obstructive or inflammatory causes. It indicated a pattern of definitive values, with one acceptable statistical significance, for individuals with and without rhinitis (Teixeira et al., 2011). We found that PNIF was increased after exercise training. In agreement with Marioni et al. (2010), they reported that the mean PNIF after physical exercise was significantly higher than the mean PNIF value found before physical exercise. Moreover, the present study demonstrated that the percent difference of nasal blood flow in both EX and EX + Vit. C groups were significantly lower than CON group. Nasal blood flow is increase with nasal inflammation due to infective rhinitis (Busse and Holgate, 2000). This

is attributed to decreased blood flow to the nasal passages following exercise, which results in less swelling and congestion (Mendenhall, 2011).

Furthermore, the present study showed the effects of exercise training and exercise training combined with vitamin C supplementation decrease rhinitis symptom. Allergic rhinitis associated nasal congestion results from dilation of venous capacitance vessels in the nasal submucosa and increase vascular permeability, mucosa oedema with influx of inflammatory cells, and excess secretions (Rappai et al., 2003). Sneezing, generally occurs as multiple events and for extended periods, itching, in and around the nose and nasal mucosa and rhinorrhea, a copious water secretion from the nose (Al Suleimani and Walker, 2007). Vitamin C was found to decrease symptoms of perennial allergic rhinitis patient, parallelly there was a decrease of the pH of nasal secretion to normal limits (Podoshin et al., 1991). However, it was negatively associated with and decreased risk of AR symptoms in same study. In this study, we speculate that effects of exercise training combined with vitamin C supplementation on rhinitis symptoms did not shown different from exercise training alone. Inconsistency, with previous studies, they reported that vitamin C is antioxidant and effects to reduce allergic inflammatory due to decrease allergic rhinitis symptoms in patients with allergic rhinitis (Podoshin et al., 1991; Kompauer et al., 2006). Therefore, we suggested that moderate exercise training seems to have a beneficial effect for reducing clinical symptoms in rhinitis patients. Exercise causes a fall in nasal resistance that may be due to sympathetic vasoconstriction in the nasal mucosa (Olson and Strohl, 1987). The fall in nasal resistance is caused at least partly by reducing blood flow (Clarke, 1996). The nasal mucosa is composed of both resistance and capacitance blood vessels (Howarth, 2005). This leads to reduced nasal congestion by decreasing blood flow and increasing sinus emptying in the capacitance vessels (Ramey et al., 2006). A decrease in nasal resistance with exercise which lead to the assumption that nasal symptoms improve rather than worsen with exercise (Silvers and Poole, 2005).

Although, in this study our hypothesis were moderate exercise training combined with vitamin C supplementation had more beneficial effects than moderate exercise training for decreasing cytokine response and rhinitis symptoms in patients with allergic rhinitis. But the results of the present study showed no significant difference

between the moderate exercise combined with vitamin C supplementation and moderate exercise training group. On the other hand, other researches has demonstrated that vitamin C has been shown to stimulate the immune system by enhancing T-lymphocyte proliferation in response to infection leading to an increased cytokine production and synthesis of immunoglobulins (Hartel et al., 2004; Noh et al., 2005) and to decrease in allergic symptoms (Podoshin et al., 1991). However, some studies found that vitamin C supplementation had no effects on immune function (Nounou et al., 2010) and allergic sensitization (Sausenthaler et al., 2009). In this study, the EX + Vit. C group was supplemented vitamin C daily with an oral dose of 2,000 mg 2 times/day (1,000 mg in the morning and evening) for 2 months. The Ex group was supplemented placebo daily with an oral dose of 2,000 mg 2 times/day (1,000 mg in the morning and evening) for 2 months too. We also determined plasma vitamin C but it had error in blood chemical analysis, therefore, we did not present the result of plasma vitamin C. There were no significant difference between the EX and the Ex + Vit. C group may be due to the sample size in our study was small as mentioned above and the ability to detect effect of vitamin C supplementation may have a limitation and the duration of vitamin C supplementation. In this study the subjects were vitamin C supplemented daily for 2 months. Sasazuki et al. (2006) found that vitamin C was supplemented for 5 years will be able to reduced the frequency of the common cold. Besides, Nounou et al. (2010) showed that vitamin C was supplemented for 12 week decrease of serum IL-4 levels in asthma patients. Accordingly, this point was interested in further study.

Conclusion

Our data present evidence supporting exercise training can modulate immune response in allergic rhinitis patients. The extensive benefits of moderate

intensity exercise training were to increase IL-2 cytokine and decrease IL-4 cytokine. The cardiorespiratory improvement by exercise training can alternated oxidative stress result in improve immune function lead to the reduction of rhinitis symptoms in patient with allergic rhinitis. However, no synergistic effect between exercise training and vitamin C supplementation was found in the present study. Therefore, we suggest that without vitamin C supplementation, moderate exercise training had beneficial effects in allergic rhinitis by attenuating inflammatory response and reducing rhinitis symptoms (Figure 5.1). Future studied should aim to delineate the mechanism of immune modulation in allergic rhinitis by exercise training.

Limitations of the study

The dietary intakes of participants were not recorded in the present study. Therefore, further study needs to assess daily food intake of the subjects in order to monitor food quantities and nutrient intake.

Suggestions for further research

1. In depth mechanisms in exercise and immunology systems of allergic rhinitis study would be included.
2. The increasing in duration of vitamin C supplementation and sample size would be done.
3. There were needed to study in the effect of other exercise on allergic rhinitis patients.

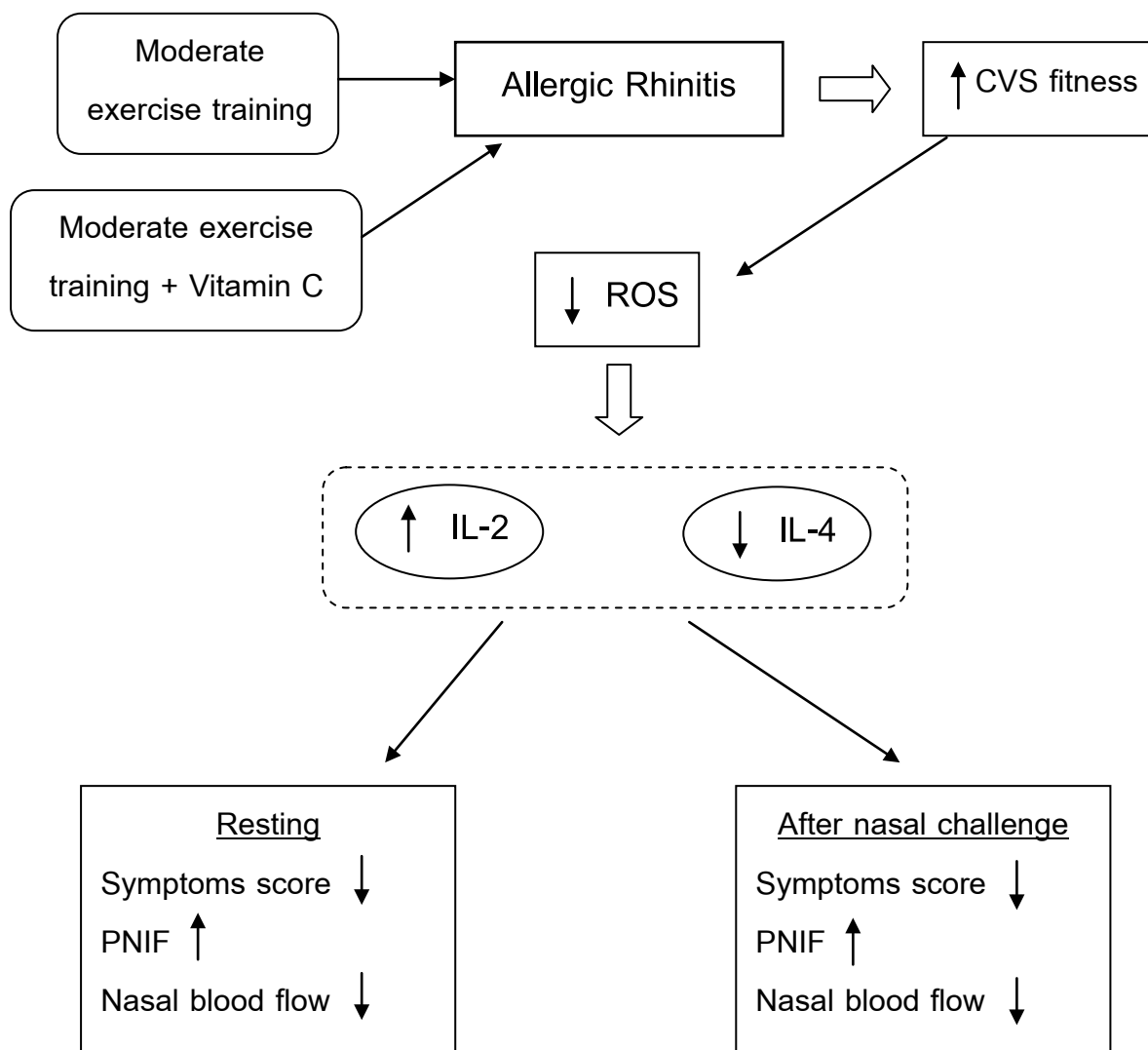


Figure 5.1 The conclusion of study.