CHAPTER 1

INTRODUCTION

At present, exercise is being promoted to improve general health in both women and men. The benefits of exercise recognized so far include reduction in the risk of cardiovascular diseases, cancer, osteoporosis and diabetes mellitus (1, 2), but many studies show some adverse effects from aggressive exercise such as increasing oxidative stress in the body (3, 4). The main mechanism of free radical production is an ischemic-reperfusion theory, with rapid depletion of oxygen after exercise starts, and then recruitment after deep breathing, thus yielding many free radicals. A free radical is an unstable molecule with unpaired electrons, and is thus able to directly capture any electrons on various biological molecules within cells such as protein, lipid, or DNA. Change in structure occurs via results of oxidation from organ dysfunction (3, 5).

Numerous free radicals are produced within the mitochondria during muscle contraction from exhaustive exercise. Oxidation of the catecholamine hormone while exercising (auto-oxidation) relates to micro-injury (delayed onset of muscle soreness) around the tissue at the sarcolemma on the cell membrane, and induces the inflammation process (5). Short and heavy intensity exercise does not only generate free radicals, but also induces inflammatory processes in the body. Lactate dehydrogenase (LDH), and creatinine phosphokinase (CPK) are markers of muscle

damage that can be detected in the blood (6). Moreover, Tumor necrotic factor-alpha (TNF- α) and interleukin-6 (IL-6), refer to the inflammatory markers, which can be evaluated after exhaustive exercise (7, 8).

A regular control system of free radicals comprising superoxide radical ($O_2^{\bullet-}$), hydroxyl radical ($OH^{\bullet}$), hydrogen peroxide (H_2O_2) and nitric oxide (NO) is processed by two antioxidant groups; enzyme (catalase, superoxide dismutase, glutathione reductase) and non-enzyme (glutathione, vitamin C, vitamin E) (9). Intracellular glutathione (GSH) is the main antioxidant and potential protector within the cell, when either low or high intensity exercise is carried out in a short period of time (10-15 min) (10, 11). Heavy exercise stimulates production of more free radicals within the cell than intracelluar antioxidants can destroy (12). Thus, over oxidative stress affects physical performance in both ability of muscle contraction and aerobic capacity (13).

Prevention the free radicals or muscle injury from exercise at the heavy intensity level has been studied. Demirbag and co-workers showed the benefit of L-ascorbic acid (vitamin C) against free radicals from acute exercise on a mechanical treadmill in 113 healthy individuals (9). Mastaloudis et al., (14) reported that supplementation of vitamin E reduced free radical production in running athletes, who exercised regularly and non-regular**.** Using a nutrient supplement is very popular among athletes or individuals, who are concerned about oxidative stress and inflammation. Many commercial nutrients contain vitamin C (ascorbic acid) or vitamin E (alpha-tocopherol), but these are not stable and excrete from the body quickly (15). Pure glutathione (GSH), which is composed of three amino acids;

glutamic acid, cysteine, and glycine, is a strong antioxidant against free radicals, due to its thiol group on cysteine, but its absorption and effectiveness are very low in the blood (15). Thus, the precursor of GSH, N-acetylcystine (NAC), is a great challenge regarding its potential use. Commercial NAC is one of many medical drugs composed of the thiol group of cysteine, and is stabilized with an aceytyl group (16). It is also used in patients with chronic obstructive pulmonary disease (COPD) or acute respiratory distress syndrome (ARDS) (16). A previous short-period study (5 days) in COPD patients showed that phagocytosis decreased, and a significantly improved level of GSH in the blood was noted. Moreover, a low concentration of NAC supplementation at 600 mg per day for only 14 weeks, reduced superoxide radicals and improved glutathione peroxidase in healthy subjects, whereas a high dose of NAC supplementation at 1,200 mg per day reduced hydrogen peroxide (H_2O_2) (17). Interestingly, Ferreira's study evidenced the capacity of NAC on scavenging free radicals and inhibition of muscle fatigue (18).

From the above, the aim of this study was to evaluate the effects of N-acetylcysteine at 1,200 mg daily for a short period (7 days) on oxidative stress; nitrite, malondialdehyde (MDA), glutathione (GSH), total antioxidant capacity (TAC), physical endurance; maximal running time, and anti-inflammation; interleukin-2 (IL-2), from short heavy exercise in healthy volunteers.

Research Questions and Hypotheses

Research questions

1. Does short period NAC supplementation at 1,200 mg per day for 7 days reduce oxidative stress and inflammation?

2. Does short period NAC supplementation at 1,200 mg per day for 7 days increase physical performance?

Hypotheses

1. NAC supplementation at 1,200 mg per day can significantly reduce the depletion of total antioxidant and glutathione, and increase of malondialdehyde and nitrite from short heavy exercise, when compared with a non-supplement group (control group).

2. NAC supplementation at 1,200 mg per day can significantly increase the level of interleukin 2 (IL-2) after short heavy exercise, when compared with a non-supplement group (control group).

3. NAC supplementation at 1,200 mg per day can significantly increase running time, when compared with a non-supplement group (control group).

Dependent variables

1. Oxidative stress markers (MDA, Nitrite, GSH, and TAC)

2. Inflammation marker (IL-2)

3. Maximal running time until heart rate reading of 85% MHR

Purposes of the study

1. To compare between the changing levels in nitrite, malondialdehyde, glutathione, and total antioxidant from short heavy exercise before and after NAC supplementation for 7 days.

2. To compare between the changing levels in Interleukin-2 from short heavy exercise before and after NAC supplementation for 7 days.

3. To compare between the maximal time of running before and after NAC supplementation for 7 days.

Advantages of the study

The results of this study show scientific evidence that NAC supplementation affects oxidative stress, inflammation, and physical endurance in healthy subjects at 1,200 mg daily.

It is recommended that supplementation of NAC from Fluimucil A600 will promote good health status.

Operational definition

Heavy exercise test: Exercise until heart rate reaching to 85% of maximal heart rate that calculated from a 220-age (y), for 20 minutes on a treadmill following the Bruce protocol**.**

Maximal running time: Time of running on a treadmill, following the Bruce protocol, unitl heart rate reaching to 85% of maximal heart rate.

Oxidative stress: Condition of imbalance between excess free radicals and low antioxidant.

Free radical: An unpaired electron molecule; superoxide radical (O_2^-), hydroxyl radical (HO^-), peroxyl radical (ROO^-) or non-unpaired electron molecules, hydrogen peroxide (H_2O_2) and nitric oxide (NO) or plasma nitrate.

Antioxidant: A chemical substance that can damage or reduce free radicals within the body, such as glutathione, uric acid, L-ascorbic acid, tocopherol and albumin.

NAC: N-acetylcysteine is a synthesized chemical that composed of cysteine and acetyl group to a stable form.