The Effect of Incentive Spirometry on Level of Fatigue and Creatine Kinase in Chronic Spinal Cord Injury Patients

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Abstract: The reduced ability of the respiratory muscles in Spinal Cord Injury (SCI) patients is associated with the physical fatigue. Incentive Spirometry (IS) breathing exercise can be used as a strategy to minimize the fatigue through its effect improving bloodstream and oxygenation on the diaphragm and periphery muscles. Creatine Kinase (CK) can be used to monitor muscle damage due to exercise or overtraining status. The study was aimed to investigate the effect of IS on the level of fatigue and CK in blood. A quasi interventional design with a pre- and posttest approach was done to eleven patients with chronic SCI patients. It was measured the fatigue level using the Fatigue Severity Scale (FSS) before and after the treatment. It was also measured the value of CK before treatment and after treatment in 2 and 4 weeks. There was a significant decline in the FSS value, 35.45±9.699 to 25.36±11.918(p=0.007) after 4 weeks intervention. On the other hand, there was a significant increase in CK value, from 111. 63±77.628 U/l to 146.36±81.185 U/l (p=0.033), after 2 weeks intervention. However, it was not significant CK value was to be 127.45±82.117 U/l (p=0.168) after 2 weeks intervention. These findings showed IS breathing exercise after 4 weeks can improve fatigue level and no muscle damage due to IS exercise in chronic SCI patients.

1 INTRODUCTION

Fatigue becomes one of the concerns in chronic SCI patients (Lidal, 2013). There are two types of fatigue following SCI, namely physical fatigue and chronic fatigue. Physical fatigue is defined as intrinsic muscular fatigue that occurs in muscles partially or total paralyzed at the level of or below the spinal cord lesion. Chronic fatigue is defined as a debilitating condition involving multiple factors including physical, psychological and aging components (Craig, 2012). The incidence of fatigue in SCI patients varied between 18–57% (Nooijen, 2015; Hammel, 2009).

After SCI, paralyzed skeletal muscle generally becomes atrophic including respiratory muscle, possesses lower tension generating capacity and is less fatigue resistant. Muscle histochemical and metabolic profile shifts toward type II (fast glycolytic) fibers have been well documented following SCI and may explain the problem of rapid muscle fatigability in SCI survivor (Pola, 2014; Kim, 2017). This may lead to more rapid fatigue of the respiratory pump in patients with SCI during physical activity.

The cause of fatigue is probably multifactorial, but a central role for changes in high-energy phosphates (i.e., ATP and ADP) or accumulation of by-products of rapid energy metabolism has been postulated. A key enzyme for maintaining a constant ATP/ADP ratio during rapid energy turnover is CK, which catalyzes phosphate exchange between the high free energy phosphates ATP and phosphocreatine (PCr) via the reaction:

$$\text{PCr} + \text{ADP} + \text{H} \longleftrightarrow \text{creatine (Cr)} + \text{ATP} \quad (1)$$

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CK is employed to mark muscle injury that occurs after an exercise. CK value is primarily used to know whether there is an overload limit achieved or instead, muscle adaptation has occurred. Muscle damage regarding an exercise can occur due to unaccustomed exercise or heavy exercise intensity. The increase of CK value is related to the number of type II muscle fiber in the muscle. As we know that following SCI, become predominantly composed of type II muscle fiber. The increase of CK value in serum significantly occurs in the initial exercise indicates that the exercise intensity exceeds muscle capability. Exercise will affect the decrease elevation of CK when it is done regularly in a certain period. Such an effect is called a repeated bout effect, indicating that there is muscle adaptation towards the exercise. (Soon-Gi, 2015; Margaritelis, 2015).

The effects of respiratory training in SCI patients are related to increased strength and endurance of respiratory muscle fitness, as well as reduced ventilation efforts required during training by the process of adaptation. Respiratory training also increases neural adaptation which is required to coordinate muscle contractions synergistically, thereby maximizing the respiratory muscle activation. Increased respiratory muscle strength directly correlates with reduced muscle fatigue due to increased training capacity and tolerance, so inspiratory muscle training (IMT) can be used as a strategy to minimize respiratory fatigue (Sisto, 2014; Hartz, 2018).

Incentive Spirometry is one of the assistive devices of respiratory training which can be used to maintain maximum inspiration by providing feedback of predetermined air volume. A study found that the use of IS in respiratory training with additional abdominal drawing-in maneuver resulted in improvement in pulmonary function of a patient with SCI (Kim, 2017).

Several studies had investigated the effects of IMT on fatigue. Bosnak-Guclu et al. conducted a study of IMT using Inspiratory Muscle Trainer in NYHA II-III congestive heart failure patients and Turner et al conducted a study on asthma patients. Both of these studies show positive effect in reducing the fatigue (Bosnak-Guclu, 2011; Turner, 2011).

In this study, we provide IS breathing exercise to investigate its effects on the level of fatigue and CK value on chronic SCI patients in Sasana Bina Daksa Budi Bhakti, Pondok Bambu, East Jakarta. The severity of fatigue is assessed by the Fatigue Severity Scale (FSS) questionnaire. It assesses a person's perception of fatigue and its use has been validated in patients with neuromuscular disease. We hypothesized that IS breathing exercise can improve fatique level and no more muscle damage caused by IS breathing exercise after 4 weeks intervention.

2 METHODS

This study used a quasi-interventional research design with a pre- and posttest approach. The samples were recruited from subjects who met the inclusion criteria in population of chronic SCI patients who occupied in the Social Care Center of Sasana Bina Daksa Pondok Bambu, East Jakarta, Indonesia.

The inclusion criteria are chronic SCI, aged 18 – 59 years old, paraplegic, no acute infection, stable spinal structure, able to perform breathing muscle training inspiration procedure for 30 minutes, Hamilton Depression Score (HDS) less than 20, Mini Mental State Examination (MMSE) score between 22–30. Exclusion criteria unable to take a deep breath due to pain, taking statin drug and patients with vital capacity <10 mL/kg. The subjects signed an informed consent to be included in the study. After each set, a one-minute rest was allowed.

The subjects signed informed consent in order to be included in the study. All the subjects were given respiratory muscle training with IS intensity from residual capacity to total lung capacity. The IS breathing exercise prescriptions are 5 days a week, once a day, with total of five sets, with 10 repetitions making up one set. After each set, a one-minute rest was allowed.

The IS training program was conducted after the subjects were given explanations of the exercise device, watched a video about the use of the exercise and familiarizing the device for 2 consecutive days. To do the exercise, the subjects sat in reclining chairs with their torso upright. The pulse oxymeter was pinned to the subject's fingers as a tool to monitor the general condition during training. The IS was held with one hand in an upright sitting position, mouthpiece was placed into the mouth between the teeth with the lips clamped tightly around the mouthpiece The subjects maintained a maximal inspiration position for 3 to 5 seconds, and then performed maximal expiration. This exercise was performed for a total of five sets, with 10 repetitions making up one set. After each set, a one-minute rest was allowed.

The primary endpoint measurements included fatigue evaluated with the FSS and CK level in blood. FSS were assessed before and after intervention, while the CK levels were examined before intervention, after 2 weeks and 4 weeks intervention (in 24 hours after exercising).

Numerical data including age were presented with mean and standard deviations, maximum values, and minimum values. The subjects' characteristic data were presented in frequency distribution tables. Categorical variables were presented in percentage (%) and continuous variables were presented in mean ± standard deviation (SD). Statistical analysis was carried out by performing normality test to determine that the data were normally distributed or not normally distributed.

Data distribution were discovered using the Shapiro Wilks test since the samples were less than 50. Paired t test was used to compare FSS variables between before and after the intervention since the data were normally distributed. Wilcoxon test was used to compare CK before and after 2 weeks and to compare before and after 4 weeks intervention since the data were not distributed normally. Significance of the statistical test results was determined based on p value (<0.05). All procedures were performed using the SPSS for Windows version.

The study was approved by the Ethics Committee of Padjadjaran University, Bandung, Indonesia with ethical numbers of 0318050767. All data and information of the subjects will be kept confidentially.

3 RESULTS

The study enrolled 11 chronic SCI patients. Mean age of the subjects was 44 years old. Number of male subjects (90.9 %) were higher than female subjects. The subjects had SCI approximately 260 months due to trauma (90. 9%) (Table 1). Most of the subjects had complete SCI (81.8 %). Based on body mass index (BMI), the subjects was mostly underweight (63.6 %) with an average of 18.72 kg/m2 without any other complications of chronic SCI. Occupation of the subjects was mostly craftspeople. Eighty one percents of the subjects had smoking history. In addition, there was no subject has pressures sore and did not consume medicines which could influence CK levels. The mean of pre- and post-training FSS scores were respectively 35.45 ± 9.699 and 25.36 ± 11.918. There was a significant improvement in the FSS after the intervention (table 2, p = 0.007). For The CK value, there was a significant increase after 2 weeks intervention (table 3, p=0.033), but there was no significant increase after the 4 weeks intervention (table 4, p =0.168).

4 DISCUSSIONS

From baseline data in table 1, the mean age of the patient is 44 y.o. with 10 male patients and 1 female patient. Based on international data, male accounts for eighty-one percent of new SCI cases and the average age at injury is 42 years old. In developing countries, SCI is more frequent in male than female, with a male: female ratio of 10: 1 to 6.69: 1. The high incidence of SCI in male is associated with the higher activity of men in the community, moreover, men do dangerous activities more frequently than women (WHO, 2013).

The lower FSS score in our study after four weeks intervention with IS (Table 2) demonstrated that the level of fatigue was reduced significantly.

Several studies had investigated the effects of IMT on fatigue but never been done in individuals with SCI. Bosnak-Guclu et al. conducted a study of IMT using Inspiratory Muscle Trainer in NYHA II-III congestive heart failure patients, dividing the study subjects into two groups: the treatment group (receiving 40% dose of MIP) and the control group (receiving 15% dose of MIP). A statistically significant (p≤0.0001) reduction in FSS score was demonstrated in both treatment and control group (p=0.008). However, the difference in FSS reduction between these groups was not statistically significant, indicating that low-dose Inspiratory Muscle Trainer gives the same effect in reducing fatigue perceptions. Bosnak-Guclu et al. concluded that the IMT using Inspiratory Muscle Trainer may increase peripheral blood flow, peripheral muscle strength and exercise capacity, thereby reducing the severity of fatigue in daily activities and training (Bosnak-Guclu, 2011).

Table 1: Characteristics of subjects.

Variables	n=11
Age (year-old)	44.27±7.695
Gender (male/female)	10 (90.9%) / 1(9.1%)
Bodyweight (kilogram)	51.09±6.64
BMI	18.72±2.17
Underweight	7(63.6%)
Normal	3(27.3%)
Overweight	1(9.1%)
Vocational	
Craftsman	10(90.9%)
Mechanics	1(9.1%)
Smoking status	9(81.8%)
Medication	
Mecobalamin	1(9.1%)
No	10(90.9%)
Pressure sores history	
Yes	11(100%)
No	0(0%)
AIS classification (complete/incomplete)	10 (90.9%) / 1(9.1%)
MMSE>24	11(100%)
HDS<20	11(100%)

Categoric data are expressed as number/frequency and percentage, numeral data as mean±standar deviation. BMI, body mass index; AIS, American Spinal Injury Association Impairment Scale.

Table 2: Fatigue Severity Scale (FSS) before and after the intervention.

	Before Intervention	After Intervention	P value
Mean±SD	35.45±9.699	25.36±11.918	0.007**

**p value<0,05: statistically significant different. SD = Standard Deviation.

Table 3: CK value before and after 2 weeks intervention.

Variable	Before Intervention	2 Weeks after Intervention	P value
CK Value (U/l)			0.033**
Mean±SD	111.63±77,628	146.36±81.185	
Median	84.00	145.00	
Range (Min- Max)	53.00-335.00	64.00-321.00	

**p value<0,05: statistically significant different. SD = Standard Deviation.

Table 4: CK value before and after 4 weeks intervention.

Variable	Before Intervention	2 Weeks after Intervention	P value
CK Value (U/l)			0.168
Mean±SD	111.63±77.628	127.45±82.117	
Median	84.00	119.00	
Range (Min- Max)	53.00-335.00	56.00-338.00	

SD = Standard Deviation.

Duruturk et al. conducted a study on asthma patients. The study subjects were divided into two groups: the treatment group (receiving a 50% dose of IMT) for 6 weeks and the control group (receiving respiratory training only). A significant reduction in the FSS score was only demonstrated in the treatment group (p = 0.028). Positive impacts were also seen in respiratory muscle strength, exercise capacity and quality of life in asthma patients. Increased respiratory muscle strength is believed to have a dyspnea-reducing-effect during training due to the reduced need for required oxygen. The reduction of required respiratory effort leads to the reduction of required energy thereby reducing the severity of fatigue in a person (Durutur, 2018). The results of our study demonstrated that respiratory training using IS significantly reduced the severity of fatigue in individuals with SCI after four weeks of intervention. Respiratory muscles are vital and play an important role in performing training. Having strong, long-lasting respiratory muscles may increase exercise capacity because they improve lung function, delay fatigue in respiratory muscles, and increase blood flow to respiratory muscle tissues as well as other peripheral muscles. The association between respiratory muscle function and fatigue had been investigated by Ray et al. They investigated the association between respiratory muscle function and fatigue in 37 multiple sclerosis patients with mild to moderate disability (still able to ambulate). There was a negative correlation between respiratory muscle strength (MIP and MEP) and fatigue perception using Modified Fatigue Impact Scale (MFIS) questionnaire (Ray, 2015).

Following the CK value in this study, a significant statistical increase occurred in this study after 2 weeks intervention (table 3) and became not significant statistical increase of CK value after 4 weeks intervention (table 4). This is following the literature stating that increased CK value usually happens in the initial weeks of exercise indicating that the initial exercise intensity is given exceeds muscle capability. This is based on the exercise principle that in order to give a strengthening effect, overload exercise intensity should be given. After 4 weeks intervention, CK value increase occurred insignificantly. This indicates that there has been muscle adaptation towards the exercise. Several works of literature mentioned that muscle adaptation can occur in the third week of the exercise, depends on the exercise intensity and muscle condition (Ray, 2015; Magal, 2010).

Research on the effect of exercise on CK value in blood of SCI patient has been done by Robergs et al., in 1993. They conducted research on CK and endothelin level of SCI patient (level C7-L1) through bicycle exercise added by Functional Electrical Stimulation (FES). The exercise was done three a week by comparing the CK enzyme and endothelin level before the exercise, the first week, the third week, the sixth week and the twelfth week of the exercise. There was a significant increase of CK level each week, however, since the third week on, the increase of CK was not as much as the first week. This indicated that muscle adaptation started in the third week of exercise.

Barroso et al performed research on the effect of regular elbow flexor eccentric exercise. One of the markers used was the CK examination. The result of the research indicated that there was a significant increase in CK value in the first week, while in the fourth and sixth week, the increase was less. This is called a repeated-bout effect mechanism which is the effect of muscle adaptation towards the exercise. The repeated-bout effect has a protective effect on the muscle, thus during such condition, muscle damage will not happen, or even it happened, the effect will be minimal. Repeated-bout effect involved a combination of neural, mechanical and adaptation of cellular. Barroso et al concluded that there was protection effect towards the effect of myofibril structure so that it will prevent the occurrence of muscle damage in the fourth week (Barroso, 2010). Research conducted by Chen et al indicated that there was significant muscle damage for the first two weeks of elbow eccentric exercise, and it started to decrease in the third week. After the fourth week of the exercise, the effect of muscle damage became insignificant. This can be explained by the occurrence of neural adaptation in the form of motor unit recruitment efficiency, firing synchronization increase from the motor unit and the increase of low type muscle fiber ratio (Chen, 2009).

The limitation of this study did not assess several factors that may influence the level of fatigue such as pain, sleep problem, nutrition, the effort of coping, activity level and spasticity severity.

5 CONCLUSIONS

Four-week respiratory training with IS was effective at reducing the severity of fatigue in individuals with SCI. This study also obtained results that there was no significant increase in the value of CK after 4 week intervention which indicates that the muscles have adapted to exercise so that there is no longer any effect of muscle damage due to exercise. Thus, respiratory training with IS was one of the safety and effective strategies to reduce fatigue in individuals with SCI.

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