The Effect of Additional Inspiratory Muscle Strengtening on Aerobic Exercise in Systemic Lupus Erythematosus: A Preliminary Study

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Abstract: Background: Aerobic exercise, an effective and safe nonpharmacological treatment for systemic lupus erythematosus (SLE), does not prevent muscle strength decline that has been proven to be predictor of decreased functional capacity. A decrease of inspiratory muscle strength had been demonstrated in SLE. This study aimed to explore the effect of adding inspiratory muscle strengtening (IMS) to aerobic exercise in SLE patients. Method: A quasi experimental study with pre-post test was conducted. Study sample was 11 patients low lupus activity disease state (LLDAS), age 20-50 years, normal body mass index. Interventions were aerobic exercise (3 times/week, moderate intensity, 20 minutes, using treadmill) and IMS (3 times/week, low intensity, using respironic tresshold). The outcomes were inspiratory and handgrip muscle strength, cardiopulmonal and handgrip muscle endurance. Results: The median of inspiratory muscle strength (49.66 vs 65.00 cmH_2O) and handgrip (11.00 vs 14.67 kilograms) increased ($P<0.005$) significantly prior compared to after exercise. The median of cardiopulmonary endurance (432.00 vs 480.00 meters) also increased ($P<0.005$) significantly but not handgrip muscle endurance (1.50 vs 2.36 minutes). Conclusion: The addition of inspiratory muscle strengtening to aerobic exercise did not only increase cardiopulmonary function but also handgrip muscle strength which is usefull in daily activities.

1 INTRODUCTION

The decrease in physical fitness is common in systemic lupus erythematosus (SLE). Balsamo et al. showed that SLE patients walked shorter distances on the six minute walking test (6MWT) and were significantly associated with lower quality of life (Balsamo, 2013). Another study, conducted by Spinelli et al showed decreased in aerobic capacity correlated with decreased cardiopulmonary endurance of SLE patients (Spinelli et al, 2017). Decreased skeletal muscle strength had also been shown in SLE patients. Balsamo et al found that premenopausal SLE patients with low disease activity showed lower muscle strength and functional capacity, and fatigue (Balsamo et al, 2013).

Many studies have been carried out related to pharmacological and non-pharmacological management strategies for SLE patients with (Shaharir and Gordon, 2016). A systematic review proved that aerobic exercise was an effective and safe therapy in patients with mild to moderate activity of SLE (Wu et al, 2017). Other study showed that aerobic exercise was better than muscle strengthening exercises in improving the quality of life of SLE patients, although they still suggest the addition of muscle strengthening exercises (Abrahão et al, 2016). Soriano et al pointed out the importance of muscle strengthening exercises, because lower muscle strength has been shown to be a predictor of decreased functional capacity over time in SLE patients. (Soriano-Maldonado et al, 2016).

Related to the respiratory muscles, Amra et al. mentioned a decrease in maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) in SLE patients (Amra et al, 2006). Currently, there are no study related to IMS exercises in SLE patients. While IMS exercises has been shown to be safe and positive effect in health and also other chronic disease populations such as multiple sclerosis (Ray et al, 2013), sarcoidosis (Karadall et

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al, 2016) and chronic kidney disease (de Medeiros et al, 2017).

This preliminary study aims to determine the effect of additional IMS on aerobic exercise in SLE patients.

2 METHOD

This study design was a quasi experimental with pre-post test. The study was conducted September 2018-February 2019 at Departement of Physical Medicine & Rehabilitation, Dr. Hasan Sadikin General Hospital, Bandung. This study has obtained ethical approval number LB.04.01/A05/EC/314/XI/2018 from hospital ethics committee.

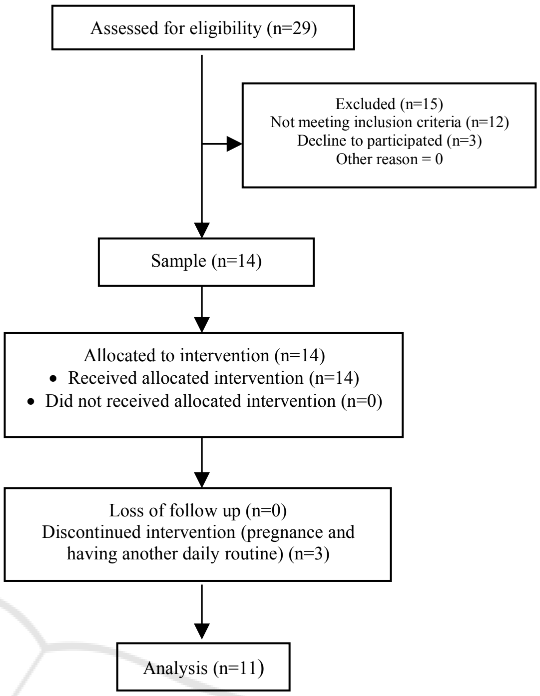
Target population was SLE patients who had routine medical treatment at Rheumatology Clinic, Departement of Internal Medicine, Dr. Hasan Sadikin General Hospital, Bandung. Sampling was done consecutively. The sample size was obtained by a 95% confidence level and 90% power of the test.

Inclusion criteria were female, aged 20-50 years, low lupus activity disease state (LLDAS) (Franklyn et al., 2016), normal body mass index, and able to walk independently. Exclusion criteria were history of heart and lung disease, surgery on the thoracal and or abdominal site, involved in aerobic exercise and/or muscle strengthening in the last 6 months. Elimination criteria were the subjects did not do exercise 3 times consecutively for 1 week.

Interventions were aerobic exercise and inspiratory muscle strengthening 3 times a week in, 12 weeks period. Aerobic exercise was given at moderate intensity (40% of heart rate reserve/HRR), 20 minutes duration, using treadmill. IMS with a mild intensity (30% of MIP), 5 sets, 10 repetitions per set, using respironic tresshold.

Outcomes of this study were inspiratory and other peripheral muscle (handgrip) strength which represents strength output, cardiopulmonary and peripheral muscle (handgrip) endurance which represents endurance output. Handgrip muscle was selected because while not directly involved in both exercises. In addition, handgrip muscles could represent overall body muscle performance. Measurement of IMS was performed using a micro respiratory pressure meter (RPM) and cardiopulmonary endurance using a 6 minute walk test (6MWT) while the strength and endurance of handgrip using a jamar hand dynamometer.

Figure 1: Research Pathway.



3 RESULT

3.1 Subject Characteristics

Table 1: Subject characteristics prior to exercise.

Characteristic	n=11
Age (years) †	33.00 (22.00-49.00)
Body mass index °	21.36±2.440
Physical activity (MET/week) †	1040 (693-1400)
Duration of illness (years) †	5.50 (1.33-18.33)
Corticosteroid dose use (miligram/day)°	2.55 ± 0.93
Inspiratory muscle sterngth (cmH_2O) †	49.66 (23.33-87.00)
Handgrip muscle strength (kilograms) †	11.00 (9.00-23.00)
Cardiopulmonal endurance (meter) †	432.00 (201.00-492.00)
Handgrip muscle endurance (minute) †	1.50 (1.09-3.18)

Note: n=number of samples; °=normal data distribution using mean±deviation standard; †=abnormal data distribution using median (range).

Table 1 showed the characteristics of the research subjects were age 33.0 years with a fairly wide range (22.00-49.00 years) and 5.50 years of duration disease with also wide range (1.33-18.33 years). Range of age and duration of disease were left wide because this study was the first study including strengthening exercise in our hospital. At the end of this study, these data and results will provide a basis for future studies. In addition, based on International Physical Activity Questionairre (IPAQ), the average of physical activity of research subject was minimal active.

Table 1 also showed the research subjects were have good cardiopulmonal endurance but low strength of the inspiratory and handgrip muscles. These results indicate that SLE patients, although they have good cardiopulmonary endurance, still have low peripheral muscle strength including the inspiratory and handgrip muscles. Good cardiopulmonary endurance can be explained by the fact that this group consisted of patients in LLDAS category and minimaly active according to IPAQ. Meanwhile, results showed low muscle strength. Therefore, muscle strengthening is still needed in SLE patients as an addition to aerobic exercise to prevent decreased functional capacity.

In this study, IMS were chosen because it has additional effect in improving oxygen supply to peripheral muscles and also decrease the effects of metaboreflexes on other peripheral muscles.

3.2 Effects of Additional Inspiratory Muscles Strengthening in Aerobic Exercise to Inspiratory and Other Peripheral Muscle (Handgrip) Strength

Table 2: Comparative characteristics of inspiratory and handgrip muscle strength before and after exercise.

	Before exercise n=11	After exercise n=11	*P*
Inspiratory muscle strength (cmH_2O)†	49.66 (23.33-87.00)	65.00 (44.30-115.00)	0.0001*
Handgrip muscle strength (kilogram)†	11.00 (9.00-23.00)	14.67 (9.33-27.00)	0.016*

Note: n=number of samples; °=normal data distribution using mean±deviation standard; †=abnormal data distribution using median (range); *Wilcoxon test.

Table 2 showed the increase of inspiratory muscle strength after administration of combination exercise was significant (p <0.05). Not only inspiratory muscle, but also other peripheral muscle such as handgrip muscle strength increase significantly (p <0.05) after adminsitration those combination exercise.

3.3 Effects of Additional Inspiratory Muscles Strengthening in Aerobic Exercise to Cardiopulmonal and Peripheral Muscle (Handgrip) Endurance

Table 3: Comparison characteristics of cardiopulmonal and handgrip muscle endurance before and after exercise.

	Before exercise n=11	After exercise n=11	*P*
Cardio-pulmonary endurance (meter) †	432.00 (201.00-492.00)	480.00 (384.00-528.00)	0.003*
Handgrip muscle endurance (minute) ††	1.50 (1.09-3.18)	2.36 (1.37-2.56)	0.075*

Note: n=number of samples; °=normal data distribution using mean±deviation standard; †=abnormal data distribution using median (range); *Wilcoxon test.

Table 3 showed the increase of cardiopulmonal endurance was significantly (p<0.05) after administration of combination exercise but not significantly (p>0.05) on handgrip muscle endurance.

4 DISCUSSION

4.1 Effects of Additional Inspiratory Muscles Strengthening in Aerobic Exercise to Inspiratory and Other Peripheral Muscle (Handgrip) Strength

Muscle strength in SLE patients is generally lower than normal. In this study, the inspiratory and handgrip muscle strength was still low. The low inspiratory muscle strength in our study was same with study by Amra et al which showed low MIP and MEP in 76 women with SLE who were followed for 12 months (Amra et al, 2006). Another autoimmune disease study by Weber et al, rheumatoid atrhitis (RA), concluded that there was a significant difference in respiratory muscle strength, MIP (46.25 ± 17.67 vs 81.00 ± 19.69 cmH_2O) and MEP (58.75 ± 17.26 vs 78.00 ± 6.32 cmH_2O) between RA patients and healthy controls (Weber et al, 2014).

The low strength of handgrip muscle in our study was same with study by Balsamo et al which showed low muscle strength in 25 premenopausal SLE women with low disease activity compared to healthy in both handgrip (24.2 ± 4.9 kg) and quadriceps (47.4 ± 8.1 kg) (Balsamo et al, 2013). Andrew et al also conducted studies related to muscle strength in 146 SLE patients showed low handgrip (22.7 ± 6.0 kg) and extensors (44.5 ± 15.7 kg) and knee flexors (29.9 ± 11.2 kg) muscle strength (Andrews et al, 2015).

The low muscle strength can be caused by inactivity and corticosteroids resulting changes in muscle pathology. Muscle pathological changes in SLE patients include myositis, vasculitis, type 2 muscle atrophy, thickening of blood vessel walls, and vacuolar myopathy (Jakati et al, 2015). Vascular changes interfere oxygen (O_2) transport from arteries to muscles or from muscle capillaries to mitochondria (Silva AG, 2015).

This study result showed significantly increasing of the inspiratory muscle strength after administration combination exercises. This results can be explained by the specifics of the strengtening exercise itself that increase muscle properties, namely recruitment of motor units and proportion of muscle fibers (Bausek et al, 2013; McConnell, 2013).

This study result showed significant in increasing of the strength of handgrip muscle although no specific exercise was given specifically. This effect can be explained by crossover training from exercise combination. How strengthening of certain muscles can cause increased strength of other muscles. Zhang et al obtained significant handgrip muscle strength in a combination intervention of aerobic exercise and muscle strengthening for 8 weeks compared to aerobic exercise alone in middle-aged and elderly women (Zhang T et al, 2015).

Another effect of additional inspiratory muscle strengthening is improvement in pulmonary mechanical ventilation so it enable increased lung volume and capacity which have impact on increasing oxygen supply in peripheral muscles. So, the increasing of handgrip muscle strength can also be explained as a result of increased lung function and respiratory muscle strength. Smith and Son study found that handgrip strength has a strong correlation with lung function as measured by spirometry (Smith et al, 2018; Son et al, 2018).

The mechanism which underlying the correlation of respiratory and other peripheral muscles is the effect of metaboreflex. This metaboreflex increased sympathetic activity in peripheral muscles including the handgrip muscles to be more earlier fatigue. Decrease of this metoboreflex can prevent early fatigue in peripheral muscles so it increase peripheral muscle performance (Bausek et al, 2013).

4.2 Effects of Additional Inspiratory Muscles Strengthening in Aerobic Exercise to Cardiopulmonal and Peripheral Muscle (Handgrip) Endurance

Cardiopulmonary endurance in SLE patients is generally low compared to normal, but this study showed these patient has good cardiopulmonary endurance prior to exercise. This study is different from previous study by Pinto et al which showed lower cardiopulmonary endurance values with VO_2max (12.8±3.6 ml/kg/ min) compared to healthy controls (14.6±4.6 ml/kg/min) (Pinto et al, 2016). The difference probably because our research subjects were categorized as LLDAS, who have low disease activity and low dose of corticosteroid. The other factor is that according to the IPAQ, subjects in this study are categorized as minimally active, not inactive, which could explain the state of cardiopulmonary endurance in this study.

Low cardiopulmonary endurance depends on multiorgan involving heart, lungs and peripheral muscles. Disturbances in O_2 transport to muscle or O_2 diffusion transport from muscle capillaries to the mitochondria are determinants of cardiopulmonary endurance in SLE patients. Deconditioning of peripheral muscles is also believed to cause a decrease in aerobic capacity in SLE patients. Other factors such as the use of corticosteroids can negatively impact the capillary number and myofibril mass thereby contributing to the decrease in aerobic capacity (Pinto et al., 2016; Silva AG, 2015).

This research showed significant result in increase of cardiopulmonary endurance after administration combination exercises. This study is in line with the Miossi et al conducted study in 24 inactive SLE patients showed cardiac effect after 12 weeks of aerobic exercise with a treadmill for 30 minutes and resistance in the form of bench press, leg press, leg extension, seated row, squat, and crunches for 30-45 minutes (Miossi et al., 2012). In our study, the strengthening exercise targeted only the inspiratory muscle. Result of this study shows that adding one exercise can benefit SLE patients.

The physiological mechanism responsible for increasing of aerobic capacity are due to changes in the central component (cardio-pulmonary) and peripheral components (muscle). Cardiac output increases after exercise through increased stroke volume as a result of increased myocardial contractility. Exercise can reduce the sympathetic effect so that peripheral resistance decreases. Exercise can also increase diffusion capacity of O_2 as a result of larger lung volume and alveolar-capillary surface area that develops. The capacity of muscle blood flow also increases with exercise due to vascular remodeling in the form of capillary angiogenesis and or changes in vascular resistance (Kisner and Colby, 2012; Kraemer et al, 2012).

This study shows the increase of handgrip muscle endurance after exercise combination. Handgrip endurance was also assessed because the function of the handgrip is not only measured by handgrip strength. Handgrip function is needed for SLE patients in daily activities besides cardiopulmonary endurance for mobilization. The increase of hangdrip endurance can be explained by crossover training effect of these combination exercise. The crossover effect showed that pasien not only able to get results that are consistent to the specificity of training, but also improve performance in one type of exercise by training using another type (Kraemer et al, 2012).

Although there is increasing of handgrip muscle endurance, but not significantly different. This result might be due to insufficient cross training effects of exercise combination, because the inspiratory and handgrip muscle strength in this study were still low compared to normal. Another factor is sarcopenia, which can occur in chronic inflammatory diseases such as in SLE patients that were not measured in this study. The diagnosis of sarcopenia should be based on decreased muscle mass and strength and/or lower physical performance. Therefore, nutritional evaluation is also needed because it affects the muscle mass itself.

Further research is needed to assess the sarcopenia and nutritional on this new exercise protocol in SLE patients. Another research is also needed to define how much role of inspiratory muscle strengthening compared to aerobic exercise in providing a positive effect on this results.

5 CONCLUSION

The addition of inspiratory muscle strenghtening on aerobic exercise not only increases the cardiopulmonary function but also impacts on the other functional performance, including handgrip which is usefull for daily activities. Further research is needed to explore other functional effects of this additional inspiratory muscle strengtening to aerobic exercise in SLE patients.

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