Relationship Between Body Composition and Physical Activity Level on Circulating IL-15 Concentrations in Individuals with Tetraplegic Spinal Cord Injury

Keywords: Spinal cord injury, physical activity level, interleukin-15, body composition.

Autores:

Pedro Godoi Scolfaro[1], Ana Paula Boito Ramkrapes[1], Henrique Monteiro Lapo[1], Bruno de Gioia Fernandes Lapa[1], Mara Patrícia Traina Chacon-Mikahil, Claudia Regina Cavaglieri[1]

1- Laboratório de Fisiologia do Exercício (FISEX), FEF/UNICAMP

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INTRODUCTION:

Spinal cord injury results in numerous functional and physiological changes in the body, promoting a sedentary lifestyle and modifications in body composition. These changes often lead to a reduction in muscle mass and an excessive increase in adipose tissue. A sedentary lifestyle, combined with autonomic alterations, contributes to the development of neurogenic obesity, which is associated with chronic low-grade inflammation. This inflammation is a significant risk factor for the development of cardiometabolic diseases, increasing morbidity and mortality in individuals with SCI. In the search for strategies to reduce the risks of cardiometabolic diseases, the literature has investigated IL-15 as an important biomarker of obesity and inflammation. IL-15 has anabolic and hypertrophic functions in muscle tissue, promotes lipolysis, and reduces fat deposition, contributing to the reduction of the inflammatory condition. However, there is a scarcity of literature on the impact of physical activity level and body composition on circulating IL-15 concentration in individuals with SCI and tetraplegia. Thus, the objective of this research project is to investigate the contribution of physical activity level to IL-15 concentration and its relationship with body composition in individuals with SCI and tetraplegia.

EXPERIMENTAL DESIGN

The sample consisted of a total of 30 individuals, including the control group (n=10), the physically active spinal cord injury group (n=11), and the physically inactive spinal cord injury group (n=9). Male subjects aged between 18 and 50 years, with spinal cord injury (SCI) of traumatic origin at a neurologically pre-diagnosed level of tetraplegia A, B, and C (complete and incomplete), according to the Abbreviated Injury Scale (AIS) (ASIA, 2011), participated in this study. This scale is evaluated according to the level and height of skin sensitivity, as well as individual characterization during anamnesis, of muscle tone below the level of injury (flaccid or spastic). As inclusion criteria, subjects were required to have had SCI with tetraplegia for more than one year. Individuals with cardiovascular diseases and type 2 Diabetes mellitus, and those using antihypertensive, anticoagulant, anti-inflammatory medications, and other drugs that could affect the study variables, such as beta-blockers, calcium channel blockers, and oral hypoglycemics, were excluded.

2.3. Assessments

2.3.1. Physical Activity Level

Participants will respond to the physical activity level questionnaire: Godin-Shephard Leisure-Time Physical Activity Questionnaire (GSLTPAQ) (GODIN, 2011). The protocol involves answering how many times the subject engages in physical activities during the week. Then, a formula will be used that multiplies the number of activities performed at different intensities: weekly leisure activity score = (9X strenuous) + (5X moderate) + (3X light). For the initial division of the groups, the score will be used: I) physically active: above 24 arbitrary units; II) moderately active: 14 to 23 arbitrary units; and III) insufficiently active: below 14 arbitrary units. Subjects will be allocated into one of three groups: non-LME irregularly active control; physically active spinal cord injury; and irregularly active spinal cord injury . Additionally, individuals who achieve the minimum score on the GSLTPAQ and also participate in moderate-intensity physical activities for ≥30 min • day-1 for 5 days a week, or ≥150 min • week-1, will be considered physically active, as this is the minimum recommendation for maintaining health indicators. Individuals who do not meet the minimum score on the GSLTPAQ and do not participate in activities according to the above criteria (GARBER et al., 2011) will be considered irregularly active.

2.3.2. Anthropometry and Body Composition

For the measurement of body composition, Dual-Energy X-ray Absorptiometry (DEXA) was used with the Horizon-Wi (Hologic) equipment, providing measurements of percentage, appendicular mass, total fat mass, and lean mass. Data will be collected for the whole body and body segments separately, with the subject in a supine position and absolute rest (adipose mass, lean mass, fat percentage, and relative lean mass index). All evaluations were conducted according to a standardized procedure, and T and Z scores was recorded. Body mass was measured using a digital scale with an electronic platform (LD 1050, Líder®). Circumference measurements (waist, chest, arm, leg, and neck) was taken using a standard tape measure (CAVEDON et al., 2021). The Body Mass Index (BMI) was calculated by the ratio of mass to height squared (BMI = mass/height^2), while the Waist-to-Height Ratio (WHtR) was calculated by dividing the waist circumference by the height measurement (WHtR = waist circumference/height).

2.3.3. Blood Collections and Analyses

Blood samples were collected from the antecubital vein using Vacutainer® (Becton Dickinson Ltd, Oxford/England) for serum samples. All collections will be performed at the same time (between 7:00 AM and 10:00 AM), after an exercise abstinence period of more than 72 hours and an overnight fast of 12 hours. Participants were instructed not to consume caffeine or alcohol 24 hours before the collection. The samples were collected, processed, divided into aliquots, and stored at -80°C for later analysis.

The analysis of circulating IL-15 concentration was obtained through ELISA (Enzyme-Linked Immunosorbent Assay) in duplicate, according to the manufacturer's specifications (Quantikine High Sensitivity Kit and DuoSet Kit, both from R&D Systems, Minneapolis, MN, USA). For sample preparation, the collected blood initially was centrifuged at 10,000 rpm, then homogenized, and specific antibodies for each cytokine will be added for subsequent reading by the equipment (RAMKRAPES et al., 2021).

2.4. Results Analysis

SPSS software was used for statistical analyses. The Shapiro-Wilk test was used to verify the normality distribution of the data. Then, the t-test was used to compare the groups for each evaluated variable. Pearson or Spearman correlation was also performed, depending on the normality of the data. Effect size analysis will be conducted using Cohen's d to determine the magnitude of the changes found. The effect size will be considered as follows: very small = d (0.1), small = d (0.2), medium = d (0.5), large = d (0.8), very large = d (1.2), and huge = d (2.0). The significance level adopted for the other analyses will be $p<0.05$.

RESULTS

The sample consisted of a total of 30 individuals, including the control group (n=10), the physically active spinal cord injury group (n=11), and the physically inactive spinal cord injury group (n=9). Significant differences were observed regarding the levels of spinal cord injury and physical activity levels (as reported in the GSLTPAQ) in both groups compared to the control group. However, BMI and weight were significantly different only when comparing the physically active LME group (LME-PA) and the control group, as shown in Table 1.

Caracterização dos indivíduos			
	Control (n=10)	**LME-FA (N=11)**	**LME-IA(N=9)**
Disability level (Asia)	0.00 ± 0.00	1.27 ± 0.46 *	1.13 ± 0.35 *
Age (Years)	30.70 ± 11.60	37.10 ± 6.59	40.50 ± 10.50
Weight (Kg)	97.00 ± 19.40	65.80 ± 10.20 *	77.90 ± 13.80
Height (Meters)	1.76 ± 0.05	1.72 ± 0.08	1.75 ± 0.04
IMC (Kg/m2)	31.30 ± 5.84	22.20 ± 2.32 *	25.20 ± 3.77
GSLLTPAQ(ua)	5.57 ± 8.02	37.10 ± 9.39 *	17.20 ± 6.63 *#

Table 1. Characterization table of the control group (CG), the physically active spinal cord injury group (LME-PA), and the physically inactive spinal cord injury group (LME-IA). GSLTPAQ: Godin-Shephard Leisure-Time Physical Activity Questionnaire; BMI: Body Mass Index; LME-FA: Spinal Cord Injury - Physically Active; LME-IA: Spinal Cord Injury - Irregularly Active. * p>0.05 compared to the Control group. # p>0.05 compared to the LME-FA group.

Regarding the concentrations of IL-15 levels, it is noted that the physically inactive spinal cord injury group and the control group showed significantly different values. The LME-IA group had lower circulating IL-15 values, as shown in figure 1. Additionally, the control and LME-FA groups, as well as the LME-FA and LME-IA groups, did not show significant differences between each other.

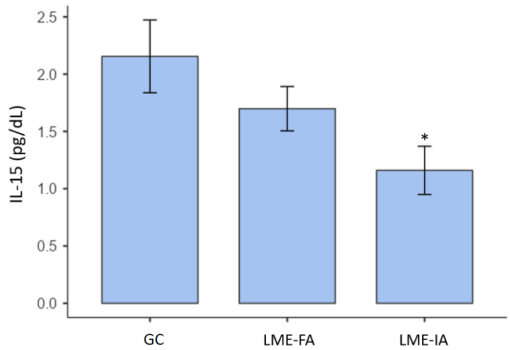


Figure 1. IL-15 concentrations among the groups.. LME-FA: Spinal Cord Injury - Physically Active; LME-IA: Spinal Cord Injury - Irregularly Active; GC: Control Group. * = p > 0.05 compared to the Control group.

When we look at the body composition of the volunteers, different values are observed between the groups. There is a significant difference when comparing the total % fat mass values of the control group with the LME-IA group (Figure 2). Furthermore, when observing body segments (figure 2, 3, and 4), we notice that the % fat of the left arm, right arm, and trunk shows significant differences when compared between the spinal cord injury groups, indicating that the LME-IA group has higher values compared to the LME-FA group. Additionally, significant differences are also observed between the control and LME-FA groups, with the spinal cord injury group now showing higher values in these segments.

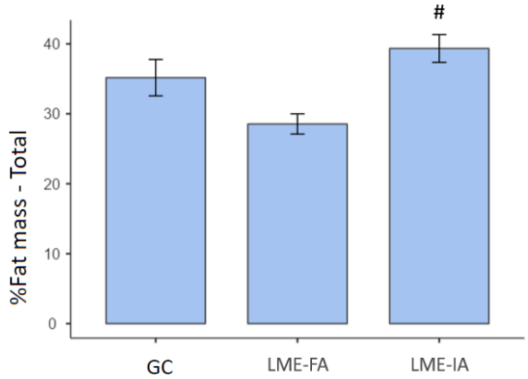
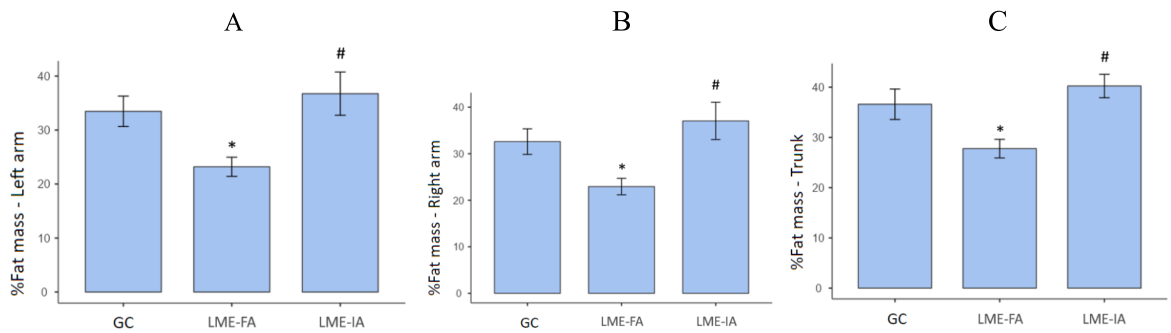


Figure 2. Demonstration of total fat values of the groups. LME-FA: Spinal Cord Injury - Physically Active; LME-IA: Spinal Cord Injury - Irregularly Active; GC: Control Group. # = p>0.05 compared to the LME-FA group..



Graphs 3, 4, and 5. Demonstration of % fat values in the upper limbs (figure A being the left arm and figure B being the right arm) and trunk (C). LME-FA: Spinal Cord Injury - Physically Active; LME-IA: Spinal Cord Injury - Irregularly Active; GC: Control Group. * = p>0.05 compared to the Control group. # = p>0.05 compared to the LME-FA group

When adjusting the physical activity levels verified in the GSLTPAQ and the serum concentrations of IL-15 in a linear regression, we obtain a p=0.01 and an adjusted R^2=0.29, allowing for a prediction of 29% trunk fat percentage.

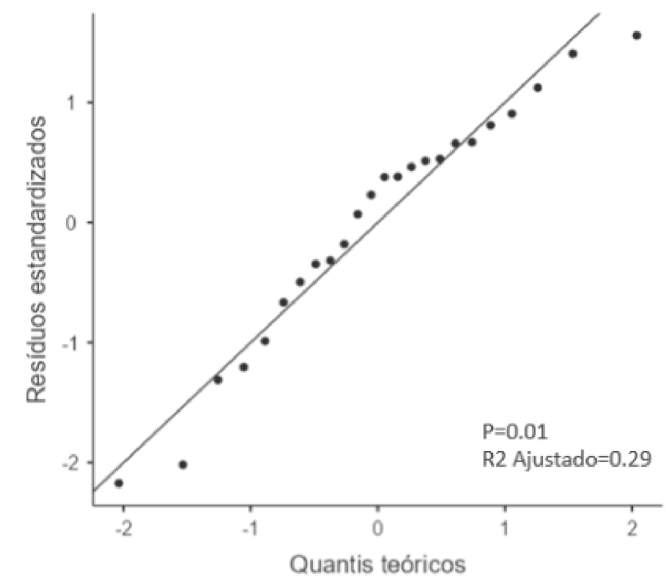


Figure 6. Linear regression between physical activity levels and serum IL-15 concentrations. Considering p > 0.05. R^2 = proportion of the variability in the dependent variable that is explained by the model

DISCUSSION

Our results show that although individuals with SCI present body limitations, a higher level of physical activity can be achieved. In Table 1, some important variables for the study design can be noted, especially the GSLTPAQ score and BMI, which guide us towards a direct relationship where the more active groups have lower BMI compared to the other groups. However, it can be observed through the %fat mass that only the LME-FA and LME-IA groups (Figure 2) show significantly different total %fat mass. Farther, when we compar fat mass separately in the upper limbs and trunk, it is noteworthy that the LME-FA group differed from the CG group, and, moreover, the LME-FA group presented lower fat percentages than the LME-IA group. These results corroborate studies that show a reduction in fat mass and fat percentage in individuals with SCI who practice regular physical activity (FARKAS & GATER, 2018).

On the other hand, our study is the first to show that individuals with SCI who present a higher level of physical activity have the same serum concentration of circulating IL-15 compared to the control group, while the LME-IA group showed a lower concentration in comparison to the control group. Recent studies have shown that a higher circulating concentration of IL-15, mainly in association with physical activity, has an important role in lipolysis and body fat deposition (HINGORJO ET AL., 2018; BRUNELLI ET AL., 2015).

In this sense, a linear regression was established between physical activity level and serum IL-15 concentrations. We observed a p-value=0.01 and an adjusted R^2 of 0.29, that show a capability of approximately 29% for physical activity level and serum IL-15 concentrations predict the trunk fat percentage, demonstrating a relationship between the obtained variables.

CONCLUSION

Based on the results, we conclude that SCI can contribute to an increase in the percentage of body fat and a reduction in the serum concentration of circulating IL-15, however, when these individuals present high levels of physical activity, these variables can be compared to results obtained by healthy control individuals, showing the importance of actions that motivate and offer practical physical activities for this population.

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