Clin Schizophr Relat Psychoses
Volume 16:2, 2022
Doi: 10.3371/CSRP.SMVC.081922

Clinical Schizophrenia & Related Psychoses

Research Article

Hybrid Open Access

Inflammatory Markers and Reduced Response to Physical Intervention in Schizophrenia: A Controlled Study with Chronic Outpatients

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Abstract

Introduction: Schizophrenia is a complex chronic mental health disorder; this disease also shows signs of systemic inflammatory injury and possible muscle damage. This study aimed to evaluate the effects of a 3-month aerobic physical intervention program on functional capacity, systemic inflammatory response, and muscle damage in patients diagnosed with schizophrenia in comparison with healthy controls.

Method: This is a paired clinical trial of physical intervention with patients diagnosed with schizophrenia. Functional capacity was explored with a 6-Minute Walk Test (6MWT), the systemic inflammatory response was assessed High-Sensitivity C-Reactive Protein (hs-CRP), and muscle damage Creatine Kinase (CK) and lactate.

Results: Forty-eight patients concluded the intervention (24 cases with mean age of 39.3 ± 2.55 and 24 controls with mean age of 40.1 ± 2.51); patients with schizophrenia had a worse physical performance compared to controls. On the other hand, patients with schizophrenia showed significant clinical improvement in body mass index, blood pressure, whereas the lactate increased after physical intervention.

Conclusion: The physical activity improved cardiometabolic variables, but did not improve functional capacity in people with schizophrenia, so there is a need for physical interventions for this group of patients.

Keywords: C-reactive protein • Nuscular damage • Inflammatory disease • Functional capacity • Schizophrenia

Introduction

Schizophrenia affects approximately 24 million people or 1 in 300 people worldwide [1]. The pathogenesis of schizophrenia is influenced by many risk factors, both environmental and genetic [2]. Characteristics of schizophrenia typically include positive symptoms, such as hallucinations or delusions; disorganized speech; negative symptoms, such as a flat affect or poverty of speech; and impairments in cognition, including attention, memory, and executive functions [3].

The disease is commonly associated with impairments in social and occupational functioning. Patients diagnosed with schizophrenia have a life expectancy shortened by 10 years to 20 years compared to the general population [4]. The reduced life expectancy is associated with an increased risk of cardiovascular disease, type 2 diabetes mellitus, and obesity [5,6].

There is evidence suggesting that the higher risk of metabolic syndrome observed in patients with schizophrenia may be associated with inflammatory and immune processes [7,8]. Although the etiology of this disease is still unclear and may include different causes, it is known that the immune/inflammatory system plays a role in this process and infections during pregnancy and early childhood, as well as several autoimmune diseases, increase the risk of schizophrenia [9,10]. Inflammation has been associated with schizophrenia and other neuropsychiatric disorders: cytokines may influence multiple neurological processes, including neurotransmitter metabolism, neuroendocrine function, and neural plasticity [11].

The C-Reactive Protein (CRP) is the primary inflammation biomarker in clinical practice, a meta-analysis reported moderately increased CRP levels in patients with schizophrenia irrespective of antipsychotic use and the CRP levels were also reported to increase with the severity of positive symptoms but not with negative symptoms [12]. The elevated C-reactive protein may be associated with disease severity, which is, in turn associated with psychomotor deficits retardation [13].

Nevertheless, the literature does not show studies evaluating muscle damage in patients with schizophrenia, only mentioning that the use of antipsychotics can cause rhabdomyolysis [14,15]. Muscular damage occurs with the disorganization of myofibrils and Z-line loss. Further mitochondrial swelling and sarcolemmal disruption indicate skeletal muscle necrosis, releasing intracellular myoglobin, Creatine Phosphokinase (CK), and some other sarcoplasmic proteins into the bloodstream. Tissue damage triggers a response that promotes pathogen exclusion, tissue restoration, and tissue damage arrest, in a sequential activation of pro- and anti-inflammatory processes [16].

Patients with schizophrenia have limited access to medical care and fewer opportunities to receive adequate prevention and treatment for their physical problems, presenting increased morbidity and mortality [17]. A consequent reduction in physical activity levels may hamper further benefits for the brain, mood, cognition, and overall mental health [18]. Many studies have reported that acute and chronic exercise display immune-modulating

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Received: 18-Jul-2022, Manuscript No. CSRP-22-69424; **Editor assigned:** 20-Jul-2022, PreQC No. CSRP-22-69424 (PQ); **Reviewed:** 05-Aug-2022, QC No CSRP-22-69424; **Revised:** 11-Aug-2022, Manuscript No. CSRP-22-69424(R); **Published:** 19-Aug-2022, DOI: 10.3371/CSRP.SMVC.081922.

properties, as well as effects in the cardiovascular, muscular, and endocrine systems [19-23]. Until the present moment, the effects of aerobic physical exercise are promising in improving the patient's symptoms, but no study has evaluated whether it is possible to modify biomarkers through physical exercise in patients with schizophrenia.

The primary aims of the present study were the following: evaluate the effects of physical exercise on biomarkers of inflammation (hs-CRP), and muscular damage (lactate and CK) peripheral levels. The secondary were to compare the physical and mental (body mass index, blood pressure, flexibility, functional capacity and disease symptomatology) effects of an aerobic exercise intervention those with a schizophrenia diagnosis and matched healthy controls.

Materials and Methods

Trial design

This is a paired clinical trial of physical intervention Aerobic Physical Intervention Program (APIP) in a group of stable outpatients with diagnosis of schizophrenia and healthy controls. All patients received regular care at a public health facility Psychosocial Attention Center (CAPS) in a mid-sized town of southern Brazil (Camaquã).

Participants

Stable outpatients under regular treatment at the CAPS, in Camaquã, state of Rio Grande do Sul, Brazil, received a psychiatric diagnosis after a three-step procedure consisting of: (1) Clinical observation with at least 3 evaluations; (2) A family interview; and (3) A review of their medical records performed by a trained psychiatrist. The selected patients met the following inclusion criteria: Diagnostic and Statistical Manual of Mental Disorders (DSM-5) [24] and International Classification of Diseases (ICD)-10 diagnoses of schizophrenia [25]; were aged between 18 and 65 years; were under stable drug treatment adjusted to their clinical state for at least 3 months; and were not involved in other physical activity programs during the intervention. Exclusion criteria were: alcohol or other drug abuse in the last month; major systemic or neurological diseases; physical disability contraindicating physical activity; risk of suicide confirmed by direct contact with the patient and family; pregnancy or women of reproductive age that did not use a contraception method; and not agreeing to participate in the study after full explanation of the program.

Paired healthy controls were recruited through researchers social networks (Facebook) with the following inclusion criteria: same sex as the patient in question; similar age (3 years older or younger); same social class (occurred through the social classification by salary range by IBGE (Brazilian Institute of Geography and Statistics); absence of any major mental illness defined by enrollment interview using direct questioning of lifetime experiences of memory loss, psychosis (delusions and or hallucinations), depression, mania, generalized anxiety disorder, or obsessive-compulsive disorder. Exclusion criteria were the same as those applied for patients with schizophrenia.

Ethics

The study was registered in the Brazilian Research Registry under No. 43408615.7.0000.5327, registered in the Brazilian Registry of Clinical Trials (ReBEC) under No. RBR-2h2hjy and approved (150066) by the Research Ethics Committee of Hospital De Clínicas De Porto Alegre (HCPA). Patients and their legal guardians provided written informed consent after reading and understanding the intervention program and their rights.

Clinical assessment

After patient recruitment, previously trained professionals performed standardized clinical and physical assessment of the study participants before physical intervention and after 3 months of treatment.

Blood collection

The Clinical Pathology Service of HCPA analyzed blood samples according to routine laboratory practice. High-sensitivity C-Reactive Protein (hs-CRP) was measured through the serum by a turbidimetric immunoassay (reference range:<3.0 mg/L=low/moderate risk; ≥ 3.0 mg/L=high risk), lactate was assayed through plasma by an enzymatic colorimetric method (reference range: 0.5 mmol/L to 2.2 mmol/L); and Creatine Kinase (CK) was measured through the serum by a UV enzymatic test (reference range: 0 U/L to 170 U/L).

All participants had blood samples (hs-CRP, lactate, and CK) collected at rest, not needing the overnight fasting, at least 24 hours after their last physical exercise. Before any clinical assessments and tests, we collected blood samples without any active muscle recovery technique to reduce changes in blood tests and reflect the most accurate basal levels.

Disease severity-the Brief Psychiatric Rating Scale (BPRS)

The BPRS is one of the most widely used instruments to evaluate the presence and severity of various psychiatric symptoms; it is currently used by the Brazilian Unified Health System (SUS) for patient monitoring. This tool assesses 18 domains of symptoms: somatic concern, anxiety, emotional withdrawal, conceptual disorganization, guilt feelings, tension, mannerisms and posturing, grandiosity, depressive mood, hostility, suspiciousness, hallucinatory behavior, motor retardation, uncooperativeness, unusual thought content, blunted affect, excitement, and disorientation. The assessment takes approximately 5 min to 10 min, following an interview with the patient, and the clinician rates each item on a scale ranging from 0 (not present) to 6 (extremely severe) through observation and questioning depending on the assessed item.

Physical performance-the 6-Minute Walk Test (6MWT)

The 6MWT was applied by two trained and certified physical therapists according to the American Thoracic Society Guidelines [26]. The test was performed in a corridor containing minimal external stimuli and demarcated turnaround points. The participants received careful instructions to walk as briskly as possible, without running, during 6 minutes; they should do their best during this time, but could stop if needed. The technicians used standard encouragement words and attitudes throughout the test. Blood pressure, heart rate, respiratory rate, peripheral blood oxygen saturation, and dyspnea (measured by Borg's perceived exertion scale) were measured at the beginning, in the third minute, and at the end of the test. Algorithms by Enright and Sherrill predicted ranges for 6-Min Walk Distances (6MWD) using sex, height, age, and weight parameters [27].

Stretching-Wells' bench

The Wells' sit and reach flexibility test was used for measuring the flexibility of the posterior muscles of the lower limbs and the mobility of the hip joint. The participant sat on the floor or exercise mat with fully extended legs and soles of the feet against the bench and slowly bent over and projected forward as far as possible, with the fingers sliding along a scale, the scale is measured in centimeters (cm). The total distance reached after 3 attempts provided the final score [28].

Physical intervention-Aerobic Physical Intervention Program (APIP)

The patients continued receiving regular clinical treatment in addition to the standardized APIP. This 12-week program included 1-hour sessions of aerobic exercise twice a week. Participants were monitored during the exercises by a digital rate monitor (POLAR FT1®, USA) and their results were adjusted by age, sex, weight, and height. Most of the patients had never performed any type of physical exercise. In the first sessions, the patients were taught how to use the equipments, after the patient's adaptation, the intensity was increased reaching up to 70% to 80% of maximum heart rate calculated by the Karvonen formula respecting the tolerance of patients [29]. The session began with a 5-minute warm-up of comfortable intensity and continued with an aerobic exercise of increasing intensity using any of the 3 modalities: a stationary bicycle (Embreex 367C, Brazil), a treadmill (Embreex 566BX, Brazil), or an elliptical trainer (Embreex 219, Brazil).

This strategy was consistent with public health recommendations that suggest an adaptation of the program to individual preferences, and has demonstrated feasibility in patients with diagnosis of schizophrenia [30,31]. A trained professional from the research staff coordinated the intervention sessions with guidance, adjustments of the equipment, and encouragement of the participant's exercise performance as best as possible for each patient. After completing aerobic exercise, participants performed global stretching of large muscle groups. Heart monitors recorded initial heart rates, maximum heart rates, and calories expended during a session.

Statistical analyses

Statistical analyses were performed using SPSS version 20.0. Categorical variables were described by frequencies and percentages, and a Kolmogorov-Smirnov test assessed data symmetry. Quantitative variables with symmetrical distribution were expressed by means and standard error or means and standard deviation, and those with asymmetric distribution, by medians and Interquartile (IQR) ranges. A McNemar's test compared categorical variables, while a paired Student's t-test was used for quantitative variables with symmetrical distribution and a Wilcoxon test for those with asymmetric distribution. A Generalized Estimating Equations (GEE) model was performed to analyze the variation over time of the variables and the between group interaction over time. This method analyzes the data using an intention to treat approach. Pearson or Spearman correlation coefficients assessed the correlation between quantitative variables with a significance level of 5%.

Results

Out of the 103 patients with schizophrenia that were initially invited to participate, 26 agreed to participate and met the inclusion criteria. Of these, 24 patients (92%) completed the physical exercise intervention. Dropouts consisted of two patients (8%) that did not achieve minimum attendance. Regarding the paired healthy controls, 24 of the original 30 participants (80%) completed the APIP and six controls (20%) were excluded due to insufficient attendance.

The group of patients with schizophrenia, Table 1 included mostly male participants (83.3%), with a mean age of 39.3 years (SE=2.55), single, with overall low education levels; 29.2% of them were smokers. The mean height in this group was 1.68 m (SE=0.01). There was a significant difference between the groups: in age (p=0.041), in single marital status (p<0.005) and in the height (p=0.039).

The mean weight of patients with schizophrenia, Table 2 reduced from 89.4 kg (SE=5.00) to 87.4 kg (SE=4.88) after APIP (p=0.005); the same decreasing effect was observed in Body Mass Index (BMI) (p<0.001), systolic blood pressure decreased from 125 mmHg (SE=2.17) to 121.3 mmHg (SE=2.27) and diastolic blood pressure decreased from 82.9 mmHg (SE=2.21) to 77.9 mmHg (SE=2.40), (p=0.008 and p=0.001, respectively). The patients' flexibility did not show improvement (p=0.277). The healthy controls improved in weight decreased from 92.2 kg (SE=3.3) to 91.2 kg (SE=3.2) (p=0.037) and flexibility improved from 15 cm (SE=1.7) to 17.9 cm (SE=1.6) (p<0.001).

Table 1. Demographic and clinical characteristics of patients with schizophrenia and healthy controls (n=48).

Characteristics	Cases (n=24)	Controls (n=24)	p
Age, mean ± SE	39.3 ± 2.55	40.1 ± 2.51	0.041
Gender Male, n (%)	20 (83.3)	20 (83.3)	1.000
Basic education, n (%)	24 (100.0)	20 (83.3)	-
Single marital status, n (%)	23 (95.8)	6 (25.0)	<0.005
Smoker, n (%)	7 (29.2)	-	-
Height, mean ± SE	1.68 ± 0.01	1.71 ± 0.01	0.039
Equivalence of haloperidol >4,5, n (%)	18 (75.0)	-	-
Chronicity >7 years, n (%)	20 (83.3)	-	-

Note: *It was not possible to calculate due to the lack of a category. Data is presented as mean ± standard error; McNemar's test compared categorical variables; Paired Student's t-test was used for quantitative variables; p<0.05.

Table 2. Demographic and clinical characteristics of patients with schizophrenia and healthy controls (n=48).

	Cases (n=24)		Controls (n=24)		p*	p*	p*
					Cases	Controls	Interaction
Physical	**Pre**	**Post**	**Pre**	**Post**			
Weight, mean ± SE	89.4 ± 5.00	87.4 ± 4.88	92.2 ± 3.3	91.2 ± 3.2	0.005	0.037	0.254
BMI, mean ± SE	31.6 ± 1.72	30.8 ± 1.66	31.1 ± 1.1	30.8 ± 1.1	<0.001	0.069	0.102
Systolic BP, mean ± SE	125.0 ± 2.17	121.3 ± 2.27	125.4 ± 2.88	121.6 ± 2.6	0.008	0.075	0.999
Diastolic BP, mean ± SE	82.9 ± 2.21	77.9 ± 2.40	82.9 ± 2.5	82.9 ± 2.9	0.001	0.999	0.052
Flexibility, mean ± SE	16.4 ± 1.71	17.4 ± 1.76	15 ± 1.7	17.9 ± 1.6	0.277	<0.001	0.083
Functional capacity-6MWT, mean ± SD	406 ± 128	393 ± 90	461 ± 71	516 ± 106	0.516	0.007	0.016
Disease severity							
BPRS, median (IQR)	17 (8.5-23.7)	18.5 (8.25-27)	-	-	0.553**	-	-
Blood markers							
hs-CRP, median (IQR)	2.5 (1.2-5.8)	3.5 (2.7-6.9)	2.7 (1.3-5.9)	2.9 (1.5-4.9)	0.114	0.999	0.235
Lactate, median (IQR)	1.7 (1.3-2.4)	2.2 (1.7-2.6)	1.3 (1.1-1.7)	1.4 (1.2-1.9)	<0.001	0.024	0.294
CK, median (IQR)	140.5 (103.0-206.3)	150.5 (102.0-239.5)	136.5 (105.7-262.0)	158.0 (108.0-258.2)	0.437	0.814	0.833

Note: Data is presented as mean ± standard error or mean ± standard deviation; *p-value: Analyzed by GEE (Generalized Estimating Equation Models); **p-value: Wilcoxon test; p<0.05. BMI: Body Mass Index; BP: Blood Pressure; BPRS: Brief Psychiatric Rating Scale; hs-CRP: High-sensitivity C-Reactive Protein; CK: Creatine Kinase; 6MWT: 6-Minute Walk Test; IQR: Interquartile Range; p-interaction: Change between groups.

Mean hs-CRP levels did not change neither among patients with schizophrenia (p=0.114) nor in healthy controls (p=0.999). Mean lactate levels in patients with schizophrenia changed from 1.7 mmol/L (IQR, 1.3-2.4) to 2.2 mmol/L (IQR, 1.7-2.6), with p<0.001. Lactate levels among healthy controls changed from 1.3 mmol/L (IQR, 1.1-1.7) to 1.4 mmol/L (IQR, 1.2-1.9) mmol/L (p= .024). Mean CK levels in patients with schizophrenia and controls increased after APIP, but not significantly. No change was observed in analyzes between the groups. A positive correlation was observed between increases in CK and hs-CRP (r=0.47 and p=0.021) in patients with schizophrenia. Data is shown in Table 2.

Disease severity, quantified as the total BPRS score, reached medians of 17 points (IQR, 8.5-23.7) and 18.5 points (IQR, 8.25-27.0) pre-and post-intervention, respectively (p=0.553). There was no association between antipsychotic dosage and changes in BPRS results (p=0.923) (Table 2).

Regarding physical performance Table 2, patients with schizophrenia were initially able to walk 406 m (SD=128) in the 6MWT, while healthy controls walked 461 m (SD=71). Participants with schizophrenia failed to improve their performance on the 6MWT (p=0.516) whereas healthy controls had a significant improvement (p=0.007). Additionally, the mean change in the performance of patients was significantly different from that of healthy controls (p=0.016). When considering the chronicity of schizophrenia, patients who traveled the shortest distances tended to be in the early years of the disease (p=0.093); when correlating BMI with the 6MWT results, patients with a lower BMI walked longer distances (r=-0.424 and p=0.039). The use of antipsychotics by patients with schizophrenia did not appear to interfere with the 6MWT results (p=0.617).

Discussion

The major finding of the study was that the aerobic physical intervention program reduced weight; body mass index and blood pressure in patients with schizophrenia, whereas the lactate increased after APIP, we also had this effect in hs-CRP and CK increased after APIP but not significantly. No effects were seen in functional capacity in patients with schizophrenia, but an improvement was found in healthy controls.

Physical inactivity is a risk factor for mortality [32]. The concept of physical activity includes any movement of skeletal muscles that uses energy, whereas physical exercise is a planned, structured, and repeatedly performed physical activity that improves or maintains physical fitness [33]. The literature shows that regular exercise has a positive effect on the body and mind [34,35]. Although our results did not reflect all of the benefits of exercise on the functional capacity, we have found a significant clinical improvement in weight; body mass index and blood pressure in patients with schizophrenia, while healthy controls showed significant improvements in weight, in flexibility and functional capacity.

Weight loss is known to be a major challenge for patients with schizophrenia; nevertheless, patients in our study had a decrease in BMI (p=0.002). The meta-analysis by Vancampfort, et al. reported that exercise improved cardiorespiratory fitness but did not reduce BMI [35]. The improvement in blood pressure observed in the patients participating in this study corroborates other studies that reported aerobic exercise as beneficial [36,37].

On the other hand, we did not observe an improvement in physical performance in the patients with schizophrenia, which contrasts with other studies that showed increases in the 6MWT scale after physical intervention. The patients' initial performances were 13% below the minimum predicted level, and remained so after intervention (15% below the expected level). The increases on healthy controls corroborated with the literature. Although no scale was applied to observe motivation, they adhered well to the treatment shown by the low dropout. A possible explanation for a weaker effect of the APIP in patients with schizophrenia when compared to healthy controls could consider that this study failed to provide adequate incentive for patients to perform the exercises at higher intensities that are more likely to yield in significant change in aerobic capacity [38]. Firth et al., reviewed studies on the impact of motivation and lifestyle in patients with schizophrenia; their analyses evidenced that low motivation was associated with lower cognitive performance, poor functionality, low treatment adherence, and low activity learning [21]. The second hypothesis may have occurred due to the functional impairment that the disease causes, to preclude the patients with schizophrenia to evolve in their functional capacity.

Although we have not evaluated the muscular strength of the included patients, it is an important measure that may have interfered with physical performance results. For example, Nygard et al. concluded that the force-generating capacity and functional performance of skeletal muscles were reduced in patients with schizophrenia, and correlated rapid force development with 6MWT results (r=0.54 and p<0.01) [39]. Goldsmith et al. showed that inflammatory markers were elevated in patients with schizophrenia and were associated with psychomotor deficits [13]. As expected, aerobic exercise did not improve the patients' flexibility and the stretches performed after APIP were mainly an exercise deceleration technique. While patients with schizophrenia did not present significant improvement, healthy controls had improved results in the Wells' test (p<0.001).

Abnormalities of the immune system have been reported in patients with schizophrenia [40]. Previous studies have shown increases in inflammatory and immunological reactions in patients with schizophrenia, suggesting a critical role of these markers in the pathogenesis of this disease [10,41]. Although the full mechanism involving inflammation and elevated CRP levels in schizophrenia is not clearly understood, these levels are known to be correlated with metabolic syndrome [42-44]. Moreover, studies suggest that vascular structural abnormalities in the brain may contribute to the etiology of aspects of schizophrenia, such as psychosis. In this study, patients with schizophrenia and healthy individuals had elevated baseline hs-CRP that remained elevated after APIP. Of these, 33% were considered abnormal at the beginning of the intervention and 58.3%, at the end in patients with schizophrenia. Hammonds, et al. conducted a meta-analysis that evidenced an association between exercise and hs-CRP reduction both in healthy adults and in those with cardiovascular disease [45]. Fragala, et al. showed that aerobic or strength exercises were associated with a decrease in hs-CRP both in men and women. Our results differ from these studies, since in our cases and controls the hs-CRP levels have not changed [46]. Zhu, et al. reported increased serum hs-CRP levels in patients with first-episode schizophrenia; this suggested that hs-CRP could be used as a biological marker to roughly evaluate cognitive function in patients with schizophrenia [47]. However, it is still not clear whether the elevated CRP level is a by-product of the pathophysiology of schizophrenia or directly contributes to the clinical characteristics of the disorder [48].

Lactate levels can indicate muscle damage of varying etiologies [49]. Patients with schizophrenia had higher lactate increases after APIP. Our first hypothesis is that lactate had an important role in muscle damage, especially when associated to CK. A lactate curve presented a smaller increase over time when compared to CK; however, it is important to note that lactate can be transported in and out of cells that have dedicated transporters, and its role could be much more complex than just that of a muscle injury marker. Sullivan, et al. showed increased lactate levels in the dorsolateral pre-frontal cortex in patients with schizophrenia and suggested that lactate changes could be a key feature of this mental disorder [50]. Proia, et al. suggested that the lactate produced during physical exercise could have an important neuroprotective role [51]. According to this hypothesis, intercellular lactate circulating between glial cells (especially astrocytes and neurons) could be considered one of the major aspects of the neuron-glia metabolic coupling. Since lactate is necessary to neurons during their recovery from hypoxic conditions, it could represent the substrate produced in astrocytes and used by neurons [52]. Elmorsy, et al. showed that chlorpromazine and haloperidol caused significant increases in lactate levels within the first ten days of therapy; after 90 days, typical and atypical antipsychotics resulted in significant increases in blood lactate levels when compared to initial measurements [53].

CK is a predominantly muscle-specific enzyme of great importance in the assessment of muscle function. In our study we obtained an elevation after APIP, but it was not significant in both groups. Some studies reported that CK can play other roles or signal other changes in addition to muscle damage. Meng, et al. showed that aggressive behavior was positively correlated with serum CK levels (r=0.262 and p=0.000) [54]. Laoutidis and Kioulos performed a systematic review on antipsychotic-induced CK elevation showing that this increase ranged between 2% and 7% [55].

Our study is a pioneer in evaluating muscle damage biomarkers in patients with schizophrenia, but it also has limitations. First, other muscle damage biomarkers such as Aspartate Aminotransferase (AST), CK-MM, myoglobin, calcium, magnesium, selenium, and potassium should be also measured; the measurement of these biomarkers will show us greater visibility of muscle damage. We have compared muscle damage in moderate-intensity aerobic exercise, so our inferences should be limited to this exercise type and within this intensity. Considering our controls, perhaps we should have included a third group of controls with the same pathology without performing physical intervention. Due to our sample size, we do not divide patients by types of antipsychotic (typical or atypical), however in future studies this classification is important, as well as the evaluation of extrapyramidal symptoms that the medicines result. The worsening of some aspects such as the total BPRS scores or the unexpected results of the 6MWT represents a great challenge for our group. Nevertheless, we need to encourage, prescribe, and guide patients with schizophrenia to associate physical activity as an adjunct treatment of this disease.

Conclusion

In conclusion, an aerobic exercise intervention improved physical health outcomes such as weight, BMI and blood pressure in patients with schizophrenia. In addition lactate levels increased in both groups, while functional capacity improved only in the control group. Through illustrating that patients with schizophrenia do not respond to a physical intervention in the same way as healthy controls, we highlight the need for specialized treatments that require a multidisciplinary team trained for the needs of this population; this could contribute to improving the understanding and management of mental and physical health in patients diagnosed with schizophrenia.

Acknowledgment

This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior-Brasil (CAPES)-Finance Code 001, and data collection and processing was supported by the Fund for Research Incentive (FIPE)-HCPA, Brazilian Research Registry (Plataforma Brasil) under number 43408615.7.0000.5327.

Conflicts of Interest

The authors declare that this research was conducted in the absence of any commercial or financial relationships that could be construed as potential conflicts of interest.

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How to cite this article: Szortyka, Michele Fonseca, Viviane Batista Cristiano, Felipe Schuch and Paulo Belmonte-De-Abreu. "Inflammatory Markers and Reduced Response to Physical Intervention in Schizophrenia: A Controlled Study with Chronic Outpatients." *Clin Schizophr Relat Psychoses* 16 (2022). Doi: 10.3371/CSRP.SMVC.081922.