Acute Response to One Bout of Dynamic Standing Exercise on Blood Glucose and Blood Lactate Among Children and Adolescents With Cerebral Palsy Who are Nonambulant

Petra Lundström and Katarina Lauruschkus
Lund University

Åsa Andersson
Halmstad University

Äsa B. Tornberg
Lund University

Purpose: To investigate the acute exercise effects of dynamic standing exercise on blood glucose and blood lactate among children and adolescents with cerebral palsy who are nonambulant. Methods: Twenty-four participants with cerebral palsy who are nonambulant performed 30 minutes of dynamic standing exercise using a motorized device enabling assisted passive movements in an upright weight-bearing position. Capillary blood samples were taken from the fingertip for measurement of blood glucose and blood lactate at rest and at the end of exercise. Results: At rest, the participants had hyperlactatemia that was unaffacted after exercise, presented as median and interquartile range at rest 1.8 (1.3:2.7) mmol/L, and after exercise 2.0 (1.1:2.5) mmol/L. Children and adolescents with Gross Motor Function Classification System, level V, had higher lactate levels at rest (2.5 [1.8:2.9] vs 1.4 [1.0:2.0]; P = .030) and after exercise (2.3 [2.0:2.6] vs 1.2 [0.9:2.2]; P = .032) compared with children and adolescents with Gross Motor Function Classification System, level IV, respectively. A statistically significant larger decrease in blood lactate levels after exercise was observed in children and adolescents with higher resting blood lactate levels (ρ = .56; P = .004). There were no statistically significant changes in blood glucose. Conclusions: Forty percentage of the participants had mild hyperlactatemia at rest and participants with the highest blood lactate levels at rest had the greatest decrease in blood lactate levels after one bout of exercise. Children and adolescents who were classified with the highest level of the Gross Motor Function Classification Scale had higher blood lactate levels. More studies are needed on how to prevent chronically high resting levels of lactate with exercise in children with cerebral palsy who are nonambulant.

Keywords: anaerobic metabolism, hyperlactatemia, physical activity, skeletal muscle, secondary muscle pathology

Excessive sedentary behavior, also defined as physical inactivity, may lead to deleterious alterations in glucose metabolism in children and adolescents (23), and may progress into metabolic and cardiovascular disease (7). The alterations are associated with an increase, in for example, body fat mass, a decrease in skeletal muscle mass, and low-grade inflammation (23). Endurance training elicits several physiological and metabolic adaptions in skeletal muscle (18), and in cardiorespiratory systems (6), which can be divided into long-term adaptations to many bouts of exercise, or acute responses to one bout (32). Cardiorespiratory and muscular fitness have positive metabolic effects in children and adolescents (10) in terms of increased utilization of blood glucose and muscle glycogen hence reducing the insulin requirement (4). Skeletal muscle is a key site for both insulin- and exercise-mediated glucose disposal and lactate metabolism, and a diminished/lack of muscle movement, could, over time, lead to an unbalanced metabolism of one or the other (20). Glucose uptake in skeletal muscle requires a normal viable muscle (12), but in some conditions, as in children and adolescents with cerebral palsy (CP), there may be an ongoing dynamic process of muscle hypertrophy and atrophy from birth, contributing to impaired glucose uptake (29).

Also, lactate metabolic pathways are essential to understand skeletal muscle physiology under resting conditions and in response to exercise (35). Anaerobic metabolism occurs when oxygen transport and tissue oxygenation are compromised leading to high levels of lactate (21). Mild hyperlactatemia is presented in underlying diseases, for example, sepsis associated with tissue hypoxia, although there are disorders in which tissue hypoxia is absent. Mild hyperlactatemia has been defined as persistent increase in blood lactate concentration (≥2.1–5 mmol/L) (8), whereas, lactic acidosis is defined as metabolic acidosis (≥5 mmol) (8).

CP is a permanent heterogeneous disorder caused by a lesion in the immature brain (30). The 5-level Gross Motor Function Classification System Expanded and Revised (GMFCS-E&R V) (24) refers to the ability of gross motor skills such as posture, sitting, and walking. Children and adolescents with CP who are ambulatory (level I–III) can either walk and/or stand independently or with support (24). Children and adolescents who are nonambulant (level IV–V) cannot stand or walk independently (24). The brain damage disrupts the brain’s power to command movement and posture (22), particularly in children and adolescents who are nonambulant, developing secondary muscle pathology and metabolic derangement from birth (26). During growth, CP increases the risk of an array of disorders such as muscular fibrosis and fat infiltration, chronic inflammation involved in insulin resistance, and an increased risk of cardiometabolic disease (3). The course of mild abnormalities in carbohydrate metabolism, including lactate metabolism to metabolic

Andersson is with the Rydberg Laboratory for Applied Sciences, Halmstad University, Halmstad, Sweden. Lundström, Lauruschus, and Tornberg are with the Department of Health Sciences, Lund University, Lund, Sweden. Lundström (petra.lundstrom@med.lu.se) is corresponding author.
disorders (1), is well investigated in adults, but has not been reported in nonambulatory children and adolescents with CP (3).

Independent of age and levels of motor function, young people with CP are less physically active than their peers and spend twice the recommended time in sedentary behavior (11). Few studies have investigated the effect of exercise in children and adolescents with CP. However, Verschuren et al (36) found that a 8-month standardized exercise program in children and adolescents with CP who are ambulant improved physical fitness. Robert et al (28) found that children with CP who are ambulant obtained the same exercise-related benefits while playing with an active video game console as children without CP. To our knowledge, no studies have reported the metabolic responses of one acute exercise bout of dynamic standing exercise (DyS) in children and adolescents with CP who are nonambulant. The aim was therefore to assess the effect of 30 minutes of DyS on blood glucose and blood lactate levels in children and adolescents with CP who are nonambulant.

Methods and Participants

The study was performed in the Southern part of Sweden and children and adolescents with CP who are nonambulant were recruited through the Child and Youth Habilitation Services, Skåne, Sweden, and by advertising on the website National Association for Disabled Children and Young People in Sweden.

Participants and Setting

In total, 45 children and adolescents with CP who are nonambulant (GMFCS-E&R level IV–V) were included. For participants who exercised at the Department of Health Sciences, Lund University, data were collected in 2016 (n = 8) and 2019/2020 (n = 13). For participants who exercised in their habitual environment (n = 24) at home or at school, data were collected in 2017. Data were analyzed from 16 participants who had exercised at the lab and from 8 participants who had exercised at home (Table 1). After merging the groups, the median age of the 24 participants was 12 years, with a range of 5 to 17 years. Reasons for dropout were either exercising shorter than 30 minutes or did not consent to a blood sample.

At all testing occasions, regardless of whether the test was performed at the lab or in the participant’s habitual environment, parents and/or personal assistants were present. The lab environment was quiet and there was no time pressure. Present at each test, both in the lab and at home, was a physiotherapist, specialized in children and adolescents with CP. All parents were informed orally and in writing of all study procedures and signed an informed consent form. The participants received child- and adolescent-appropriate information and the opportunity to give their assent. Permission to undertake the study was provided by the Swedish ethics review authority, (EPN-dnr 2016/375; 2017/ 67 and EPM-dnr 2019-00106), and the study was performed according to the World Medical Association Declaration of Helsinki (37).

Exercise Testing and Blood Sampling

A motorized medical device, Innowalk (Madeformovement, Skien, Norway), enables DyS with different training possibilities by assisted and repetitive movements of the lower extremities in an upright weight-bearing position.

Each participant was positioned in a personalized-adjusted Innowalk (Made for Movement), with a standing angle between 70° and 85°. Just before positioned in the Innowalk, a capillary blood sample was taken from the fingertip for measurement of blood glucose and blood lactate (Biosen C Line; EKF Diagnostic, Barleben, Germany). All participants started at the DyS at 30 to 70 cadence/minute, a pace adapted to each subject’s comfort. The cadence was chosen from safety and comfort among the participants. After 30 minutes of exercise, the final capillary blood sample was taken within a time frame of 2 to 4 minutes.

Blood Analysis

Glucose and lactate were analyzed by Biosen C Line, EKF Diagnostic, an enzymatic-amperometric method that uses a chip-sensor technology. The precision for plasma glucose has a difference greater than 10%, with an accuracy/bias, .998 coefficient of correlation. Plasma lactate has a .99 coefficient of correlation. Measuring range: glucose 0.5 to 50 mmol/L (9–900 mg/dL) and lactate 0.5 to 40 mmol/L (5–360 mg/dL) imprecision: coefficient of variation ≤ 1.5% (12 mmol/L).

Statistical Analyses

The data set was controlled for missing data and tested for normal distribution. The data were found to be nonnormally distributed and therefore are described by median and interquartile range (q25: q75). The confounding factors, sex, age, GMFCS-E&R level, spasticity, dyskinesia, and test location were analyzed for statistical significant effects on blood glucose and blood lactate with an independent Mann–Whitney U test. Whereafter, nonparametric effect size was calculated by $\eta^2 = Z^2/(N-1)$.

Differences between blood glucose and blood lactate levels at rest (before exercise) and after exercise were compared with a related-samples Wilcoxon signed-rank test. In addition, nonparametric effect size was calculated by $\eta^2 = Z^2/(N-1)$. For additional statistical analysis of the change in blood lactate levels from rest (before exercise) to after exercise, the relation between blood lactate levels at rest and change in blood lactate levels were analyzed with Spearman correlation factor ($\rho$).

Table 1 Participant Characteristics (N = 24)

| Age, y | 12 (8:14) |
| Height, cm | 135 (130:161) |
| Weight, kg | 33 (24:48) |
| Female, n | 9 |
| GMFCS-E&R (IV/V) | 13/11 |
| Spastic bilateral, n | 18 |
| Dyskinetic, n | 6 |
| Exercise test at home/in a lab, n | 8/16 |

Abbreviation: GMFCS-E&R, 5-level Gross Motor Function Classification System Expanded and Revised. Note: Data are described by median and interquartile range median (q25/q75).

Results

A statistical significance was found from GMFSC-E&R level on blood lactate levels, but not on blood glucose levels (Table 2). Sex, age, spasticity, dyskinesia, and test location did not have any statistically significant effect on blood lactate and blood glucose levels. On a group level, there was no significant difference in
Table 2 Glucose and Lactate Levels Before and After Exercise in the Groups of Children With GMFCS-E&R IV and V

<table>
<thead>
<tr>
<th>Glucose before, mmol/L</th>
<th>Glucose after, mmol/L</th>
<th>GMFCS-E&amp;R level IV</th>
<th>GMFCS-E&amp;R level V</th>
<th>P value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 13)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.9 (4.3:5.2)</td>
<td>4.9 (4.3:5.8)</td>
<td>0.63</td>
<td>0.007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.6 (4.0:5.3)</td>
<td>4.8 (4.6:5.2)</td>
<td>0.61</td>
<td>0.018</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4 (1.0:2.0)</td>
<td>2.5 (1.8:2.9)</td>
<td>0.30</td>
<td>0.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2 (0.9:2.3)</td>
<td>2.3 (2.0:2.6)</td>
<td>0.32</td>
<td>0.20</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Glucose and Lactate Levels Before and After Exercise in All Children (N = 24)

<table>
<thead>
<tr>
<th>Glucose, mmol/L</th>
<th>Lactate, mmol/L</th>
<th>P value</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Before)</td>
<td>(After)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.9 (4.3:5.3)</td>
<td>4.8 (4.1:5.2)</td>
<td>.60</td>
<td>0.01</td>
</tr>
<tr>
<td>1.8 (1.3:2.7)</td>
<td>2.0 (1.1:2.5)</td>
<td>.46</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Discussion

The main finding of this exercise study is that 42% (n = 10) had mild hyperlactatemia at rest, and one participant had blood lactate levels corresponding to metabolic acidosis (Figure 1). However, the most important finding was the children and adolescents with the highest levels of lactate at rest had the most positive effect of exercise on lowering the lactate levels after only one bout of DyS. Moreover, the higher GMFCS-E&R levels seem to elevate resting levels of blood lactate (Figure 1 and Table 2).

High levels of lactate can be the result of increased lactate production, decreased clearance, or both (2). Hyperlactatemia when mild to moderate (2.1–5 mmol/L) is divided into conditions linked to tissue hypoxia or disorders with no tissue hypoxia (21). In this study, the cause of the mild hyperlactatemia in the studied individuals is unknown. Theoretically inadequate tissue perfusion and oxygenation in inactive skeletal muscle could explain the observation. Metabolic acidosis occurs commonly in the presence of both inadequate tissue perfusion and abnormalities in carbohydrate metabolism (15). One participant had a lactate level of 8.9 mmol/L, which is classified as metabolic acidosis (≥5 mmol/L) (8). It is reasonable to assume that the decrease in lactate in the acidotic participant was a positive effect of DyS by increased blood flow, oxygenation, and perfusion of skeletal muscle (5). It is noteworthy that although the lactate level decreased considerably (5.4 mmol/L), it remained at the level of metabolic acidosis.

Notwithstanding the metabolic consequences, chronic high lactate could have several negative health consequences as it impedes bone formation and at the same time causes a loss of bone mass (9). It has been demonstrated that individuals with CP have lower bone mass with a risk of early onset of osteopenia and osteoporosis (33). Nevertheless, it is important to underline other possible explanations of low bone mass in this group such as the use of medications, lack of strain on bone mass due to excessive sedentary behavior, limited calcium intake, and low vitamin D, possibly due to a low exposure to sunlight due to indoor activities (19). In addition, lactate can modulate the immune-inflammatory response as demonstrated in rheumatoid arthritis synovitis (17). We did not investigate bone mass or markers of systemic inflammation, but it is important to underline that our findings demonstrate a positive lowering effect on blood lactate after only one bout of Dynamic Standing exercise (DyS). It is well accepted in adults, physical activity and exercise prevent the development of chronic low-grade systemic inflammation, partly by improving insulin resistance, and over time cardiometabolic disorders (25). Although less investigated in children and adolescents, a meta-analysis has found positive effects of aerobic exercise on insulin resistance markers in an adolescent population (13). Our findings indicate a positive effect after one bout of exercise that could be of importance for health in children and adolescents. More studies are needed to elucidate the mechanisms of the positive effects of both acute and long-term exercise in this nonambulant group with CP.

The population in this study had glucose levels that were within the normal range, except for slightly low levels in one participant, and slightly increased levels after exercise in another participant. This could be interpreted as the exercise was at too low absolute intensity and consequently had only a minor metabolic effect, despite the individual lowering of blood lactate. In contrast to our results, Short et al (34) found that upper body exercise had an impact on (whole-body) postprandial glucose
tolerance and insulin sensitivity in active children (spina bifida or CP) who are nonambulant or active ambulatory peers. They concluded that a single bout of handcycle exercise improved glucose tolerance with and without mobility limitations, and that could improve metabolic health. Enhanced glucose metabolism has been shown to help maintain or improve metabolic health in children with and without mobility limitations (34). There is evidence that people with spinal cord injuries adapt to acute and chronic exercise regarding cardiorespiratory, metabolic, and musculoskeletal systems to a similar extent as in people without disabilities (14). In children and adolescents with CP who are nonambulant, there is a paucity of knowledge of acute and chronic effects of exercise on metabolic and cardiovascular markers.

In this study, there was a difference in biological maturation in the group of study participants, and 40% were girls. Yet, these factors should not influence the results of blood glucose and lactate before and after exercise. Under normal conditions, both plasma glucose levels in infant to adult (fasting state 3.3–5.5 mmol/L) (16) and resting lactate concentration in children to adults (0.5–1.0 mmol/L) are preserved within a narrow range (21). Furthermore, although lactate concentration during exercise is age dependent, perhaps coincidentally with puberty, it does not influence the findings in this study because the high lactate concentration was revealed before exercise and therefore not affected by age (27). Ruby et al (31) found no differences in plasma glucose during exercise in adult men and women. For these reasons, we did not account for differences in biological maturation and sex. All exercise tests were standardized and supervised to ensure that the participants got the same exercise dose. A possible shortcoming was that the participants were unaccustomed to the motorized device, and they had no previous experience of regular and extended movement in their lower limbs. Although the level of effort was adjusted upon communication with the participants and/or our interpretation together with their parents, the intensity might have been too low to have any effect on blood glucose. Exercise at higher intensity could, in addition, have led to a better response on blood glucose levels after having performed DyS regularly. Moreover, the children were not in a fasted state, which could have influenced blood glucose at rest. Even so the DyS likely increased blood flow, oxygenation, and perfusion of skeletal muscle and by that exerted a positive effect on high blood lactate levels after exercise.

The findings demonstrate new knowledge concerning high lactate levels at rest and the response to acute exercise on high blood lactate levels among children and adolescents with CP who are nonambulant. Future studies are necessary to unravel the mechanisms behind chronically high levels of lactate and the long-term health effects in this group with CP who are nonambulant. The interplay of mild hyperlactatemia, secondary muscle pathology, low-grade inflammation, and excessive sedentary behavior needs further attention.

Acknowledgments

The authors especially want to thank all participating children and their parents for participating in the study. In addition, the authors like to thank RBU, the Swedish National Association for Disabled Children and Young People, for their support during the recruitment process. The authors also want to thank Madeformovement, Norway, for the provision of the Innowalks used at the lab, and Fredrik Rosengren, Rikke Damkjaer Moen, and Tomas Johansson from Madeformovement for their engagement in this study. This study was funded by the Swedish Research Council (2018–2433), the Swedish National Association for Disabled Children and Young People, the Linnea and Joseph Carlsson Foundation, the Promobila Foundation, and the Foundation of aid to disabled in Skåne. None of the authors reports personal or financial conflicts of interest.

References


