An Evaluation of Basal Lactate in Athletes and Patients with Type 2 Diabetes Mellitus

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Abstract:

Metabolic Dysfunction (MetD) is the co-occurrence of conditions including insulin resistance, obesity, hypertension and dyslipidemia. Decreased physical activities influence numerous pathological and clinical conditions such as MetD and type 2 diabetes mellitus. In some cases, type 2 diabetes mellitus follows or coexists with MetD, though not always. Lactate level indicates oxidative capacity which is reduced in MetD and type 2 diabetes mellitus as such it is hypothesized that lactate can be a useful diagnostic tool in the detection of these conditions. In this study 88 persons which include athletes in training, and persons who did not exercise regularly were selected and screened for MetD and diabetes mellitus using the NCEP ATP iii for MetD and HbA1c and fasting glucose for diabetes mellitus. They were then categorized into groups: male athlete (MA), female athlete (FA), male diabetes patients (MD), female diabetes patients (FD), Female control (FC), male control (MC) and participants with metabolic syndrome (MetD). Basal
lactate was assessed for all categories. Basal lactate was significantly higher (P<0.05) in persons with MetD and diabetes mellitus for both males and females. Lactate levels changed significantly as glucose levels exceeded 6 mmol/L. Fasting blood glucose concentration below 6 mmol/L was not associated with any significant change in lactate concentration. Changes in mean blood lactate are consistent with changes in mean HbA1c across the groups. Lactate can be used as a parameter in diagnosing MetD and as a tool to monitor type 2 diabetes.

**Key words:** Metabolic Dysfunction, Type 2 diabetes mellitus, Lactate, HbA1c, Glucose

**Introduction:**

Published work has shown that limited physical activity is integral in the development of chronic diseases such as type 2 diabetes (1). Physical inactivity is implicated in the initiation of 35 different pathological and clinical conditions (1). Thus, physical activity is integral in preventing some of the diseases that plague modern society (2). It has been proposed that evolved genes in human support a physically active lifestyle while modern technology facilitates a more sedentary lifestyle (3). Researchers also support the evidence that sedentary lifestyle leads to the development of numerous chronic diseases (3). Where it relates to efficacy, exercise can compete with drugs in the treatment and prevention of type 2 diabetes and can even be more effective (4). This study assessed the metabolic profiles of physically active males and females and compared these profiles to the metabolic profiles of sedentary and type 2 diabetes patients. The metabolic profile of participants with MetD was assessed.
Type 2 diabetes mellitus often co-occurs with metabolic dysfunction (5). Metabolic dysfunction or metabolic syndrome (MetD) is the co-occurrence of several known cardiovascular risk factors (5). These risk factors are interrelated and share mechanisms and pathways. These risk factors include insulin resistance, obesity, hypertension and dyslipidemia. There are four common definitions of MetD (5). The first was established by the World Health Organization in 1998. In this case insulin resistance was an absolute requirement in the diagnosis of MetD (6). Three more definitions were later established: the European Group for the Study of Insulin Resistance in 1999, the International Diabetes Foundation in 2005 and the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III). In the current study, we employed the definition of the NCEP ATP III (5).

Lactate concentration is associated with MetD and diabetes because it is positively associated with glycated hemoglobin and fasting glucose levels (7). Research has shown that obese individuals with type 2 diabetes have very elevated lactate concentration, non-diabetes patients who were obese have a lower lactate concentration and normal (without diabetes, lean) individuals have lower lactate concentration (7).

Lactate levels are elevated in type two diabetes mellitus (8) and is also elevated during physical activities (9). It was found that independent of the quantity of physical activity one engages in, the basal lactate increases with body fat percentage (9). Increased body fat percentage is also associated with an increased risk of developing type two diabetes mellitus (5).

The study looked at basal lactate in healthy male and female athletes, male and female diabetes patients, participants diagnosed with MetD and male and female controls without diabetes who did not take part in regular exercise programs. It was hypothesized that basal lactate should be higher in persons with MetD and diabetes mellitus because of the correlation between lactate and
metabolic dysfunction. Lactate is proposed to be an important marker in the development is type 2 diabetes mellitus and MetD.

Method:

Ethical approval was granted by the University Hospital/ University of the West Indies Ethics Committee for conduct of the research. Athletes were selected from the University of the West Indies, Jamaica Track and Field team as well as a track club whose members train on the University of the West Indies Campus. Patients diagnosed with type 2 diabetes were selected from the University Hospital of the West Indies after they had recorded HbA1c and fasting glucose levels that were diagnostic for diabetes mellitus. Signed informed consent was obtained from each participant.

Six defined groups were categorized and selected for this study. The groups included male athletes, female athletes, males with diabetes mellitus, females with diabetes mellitus, male controls and female controls. All participants were between the ages 18 and 50 years old. Alcoholics and smokers were excluded from this study as these activities affect lipid profile (10, 11). Although some of the participants were diagnosed with diabetes, HbA1c and fasting glucose tests were performed on all participants. The participants were asked to fast and rest overnight before the start of the assessment. All samples were collected in the mornings. Two consecutive resting pulse rate and blood pressure measurements while participant was seated were recorded using an electronic sphygmomanometer (12). Anthropometric measurements inclusive of waist circumference, hip circumference, height and weight were taken. A modified American Council on Exercise physical fitness questionnaire (13) was used as a tool to distinguish groups. The questionnaire was modified to include past and present medical history. Each athlete trained 5 days
each week with a certified coach while the non-athletes and patients with diabetes mellitus exercised for 0-20 minutes per week at the time of the assessment.

Body fat percentages were measured using the BodyMetrix Analyzer. This method utilized the three site technique which employed a modified version of the Jackson-Pollock three site skinfold equation for males and the Pollock three site equation for the females (14). The Machine measures the thickness of the fat at the specific site by use of ultrasound technology (15). Three points on the right side of the body were used. For males, the ultrasound machine was placed at the chest mid-way between the nipple and the shoulder joint. A read out was displayed on a computer which recorded the thickness of each tissue that is fat, muscle and the interfaces in millimeters. This was done 2 to 3 times and an average for improved accuracy was determined. This was repeated at the two other areas; one, an inch right of the umbilicus and the other on the thigh mid-way between the knee and hip joints. For females, the sites used are; mid right triceps, the right hip an inch above the pelvic bone and an inch right of the umbilicus. From the readings obtained the percentage body fat was calculated.

A glucometer was used to measure the fasting glucose levels and a Lactate Plus Analyser used to measure the resting lactate levels. Both cases involved a small prick of the index finger to produce the sample needed. Venipuncture was used to collect two samples of blood. One was collected for serum and the second sample with anticoagulant was collected for HbA1c. Serum samples were obtained after centrifugation and fasting blood total cholesterol (TC), high density lipid cholesterol (HDL-C) and triglyceride (TG) were measured and low density lipid calculated (LDL-C). The
Cobas 6000 autoanalyzer was used for analysis of the lipid using spectrophotometry with reagents supplied by Roche Diagnostics (Roche Diagnostics, Indianapolis, USA). The LDL-C concentration was calculated using the Friedewald equation (LDL-C = non-HDL-C – (triglycerides / 5) in mg/dL.) (16). Glycated hemoglobin (HbA1c) were assessed.

The remaining serum samples were immediately frozen and kept at -23 degrees Celsius for further analysis. The samples were thawed once and tested for leptin adiponectin and troponin T. These assessments were done using kits supplied by Thermo Fisher Scientific Inc.

Data Analysis

Anova analysis was done using the SPSS 17 software to compare the means across the groups. Anova analysis was combined with Turkey’s post hoc procedure to determine significant differences across the groups. Pearson’s bivariate correlation was used to assess the relationships between fasting glucose and HbA1c.

The level of significance was noted at the P≤0.05 level. Data was reported as mean ±SD.

Results:

Based on the criteria of NCEP ATP III, no male in the study was diagnosed with MetD. Four females had MetD. There was a proportional increase in fasting glucose with HbA1c. Fasting glucose and HbA1c were significantly higher in the male and female patients with diabetes, compared to the control and athletic groups (P<0.05). Similarly, basal lactate was elevated in the patients with diabetes and MetD groups. Lactate levels are relatively constant across the groups, where the corresponding fasting glucose concentration is below 6 mmol/L. lactate was elevated when glucose concentrations exceed 6 mmol/L, however the increase was not directly proportional. Changes in mean blood lactate concurs with change in HbA1c across the groups.
The groups varied based on anthropometric data. The athletes in general (males and females) had significantly lower fat when compared to patients with diabetes and the controls.

Table 1: Comparisons of anthropometrical characteristics among the groups.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MA</th>
<th>MC</th>
<th>MD</th>
<th>FA</th>
<th>FC</th>
<th>FD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
<td>N 23</td>
<td>19</td>
<td>9</td>
<td>10</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>88</td>
<td>177.3±6.5</td>
<td>176.9±6.8</td>
<td>179.3±2.4</td>
<td>162.8±4.3</td>
<td>164.4±6.4</td>
</tr>
<tr>
<td>Weight (lbs)</td>
<td>88</td>
<td>163.4±29.1</td>
<td>157.4±20.4</td>
<td>178.1±10.6</td>
<td>130.3±4.9</td>
<td>137.4±26.1</td>
</tr>
<tr>
<td>BMI (kg/M²)</td>
<td>88</td>
<td>23.5±3.3</td>
<td>22.8±2.4</td>
<td>25.1±0.9</td>
<td>22.3±1.0</td>
<td>23.0±3.8</td>
</tr>
<tr>
<td>WHR</td>
<td>88</td>
<td>0.8±0.0</td>
<td>0.8±0.0</td>
<td>0.9±0.0</td>
<td>0.8±0.0</td>
<td>0.8±0.1</td>
</tr>
<tr>
<td>SYSTOLIC PRESSURE</td>
<td>88</td>
<td>117.7±12.6</td>
<td>120.4±8.9</td>
<td>123.3±10.9</td>
<td>110.3±8.2</td>
<td>114.9±10.0</td>
</tr>
<tr>
<td>DIASTOLIC PRESSURE</td>
<td>88</td>
<td>67.0±8.5</td>
<td>73.3±8.5</td>
<td>74.3±12.4</td>
<td>72.8±6.7</td>
<td>67.8±8.8</td>
</tr>
<tr>
<td>PULSE (BPM)</td>
<td>88</td>
<td>60.8±12.2</td>
<td>69.7±8.2</td>
<td>86.7±12.2</td>
<td>66.6±9.0</td>
<td>77.8±9.4</td>
</tr>
<tr>
<td>BODY FAT PERCENTAGE</td>
<td>88</td>
<td>8.7±5.2</td>
<td>12.0±3.6</td>
<td>21.0±5.1</td>
<td>20.9±4.0</td>
<td>28.1±4.5</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD.
Table 2: Significant differences in anthropometrical characteristics among the groups. \( P \leq 0.05 \) is significant.

<table>
<thead>
<tr>
<th>Group</th>
<th>Height</th>
<th>Weight</th>
<th>BMI</th>
<th>W HR</th>
<th>SYSTOLIC PRESSURE</th>
<th>DIASTOLIC PRESSURE</th>
<th>PULSE</th>
<th>BODY FAT PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MA</strong></td>
<td>FA, FC</td>
<td>FA, FC, FD</td>
<td>FD</td>
<td>FC, MD</td>
<td>0</td>
<td>FD</td>
<td>FC, MD, FD</td>
<td>FA, FC, MD, FD</td>
</tr>
<tr>
<td><strong>MC</strong></td>
<td>FA, FC</td>
<td>FD</td>
<td>FD</td>
<td>FC, MD</td>
<td>0</td>
<td>0</td>
<td>MD, FD</td>
<td>FA, FC, MD, FD</td>
</tr>
<tr>
<td><strong>MD</strong></td>
<td>FA, FC</td>
<td>FA, FC</td>
<td>FD</td>
<td>MA, FA, MC, FC</td>
<td>0</td>
<td>0</td>
<td>MA, FA, MC</td>
<td>MA, MC, FC, FD</td>
</tr>
<tr>
<td><strong>FA</strong></td>
<td>MA, MC, MD, FD</td>
<td>MA, MD, FD</td>
<td>FD</td>
<td>MD, FD</td>
<td>0</td>
<td>MD, FD</td>
<td>MA, MC, FC, FD</td>
<td></td>
</tr>
<tr>
<td><strong>FC</strong></td>
<td>MA, MC, MD, FD</td>
<td>MA, MD, FD</td>
<td>FD</td>
<td>MA, MC, MD, FD</td>
<td>0</td>
<td>FD</td>
<td>MA</td>
<td>MA, FA, MC, MD</td>
</tr>
</tbody>
</table>
The table shows the various arthrometric characteristics and the groups with which there are significant (P≤0.05) differences. The MD had significantly higher waist hip ratio compared to the other non-diabetes groups while FD had significantly higher body mass index when compared to all other groups.

Table 3: The mean of the parameters assessed in females diagnosed with metabolic dysfunction based on the requirements of the National Cholesterol Education Program ATP III.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>MetD (Male)</th>
<th>MetD (Female)</th>
<th>Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosed Females (4)</td>
<td>Diagnosed Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>&gt;101.6</td>
<td>&gt;88.9</td>
<td>106.8</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>≥5.55</td>
<td>≥5.55</td>
<td>14.45</td>
</tr>
<tr>
<td>TG Dyslipidemia</td>
<td>≥1.7</td>
<td>≥1.7</td>
<td>2.63</td>
</tr>
<tr>
<td>HDL-C Dyslipidemia</td>
<td>&gt;1</td>
<td>&gt;1.3</td>
<td>0.85</td>
</tr>
</tbody>
</table>
Systolic  >130  >130  132.5  

Diastolic  >85  >85  87.5  ___  --

At least three of the parameters detailed in the list defined for MetD males or females must be satisfied before diagnosis is confirmed. Four females in the population studied satisfied the requirements for MetD diagnosis. No male had MetD.

Figure 1: The association between HbA1c and fasting glucose.

A significant positive correlation was found (P<0.05) with a Pearson’s correlation of R=0.823.
Figure 2: A comparison of the mean fasting glucose concentration among the groups.

There was a significantly higher concentration of fasting glucose in the patients with diabetes for both males and females when compared with corresponding athletic groups and controls (p<0.05). Individuals with MetD had highest fasting glucose while the MA had the lowest fasting glucose.
Figure 3: A comparison of the mean basal lactate concentration among the groups.

Basal lactate in the MD and FD were significantly higher when compared with corresponding athletes and controls (p<0.05).
Figure 4: A comparison of the mean HbA1c % concentration among the groups.

There was a significantly higher concentration of HbA1c in the diabetes population of both males and females when compared with corresponding athletes and controls (p<0.05).
Figure 5: A comparison of the changes in fasting glucose and HbA1c concentration with basal lactate.

Fasting blood glucose concentration below 6 mmol/L is not associated with any significant change in lactate concentration. Lactate levels increase when glucose levels exceed 6 mmol/L, however the increase is not positively correlated with glucose concentration. The mean basal lactate across the groups concurred with changes in mean HbA1c concentration.
Discussion:

The groups studied differed based on level of physical activity. As expected, individuals who were involved in less physical activities, had higher body fat percentages and BMIs. HbA1c is an excellent method of assessing glucose control as it defines glucose attached to red blood cells over an extended period (17). It was observed that fasting glucose significantly and positively correlated with HbA1c. This provides credibility to the fasting glucose assessment and reinforces confidence that the participants with diabetes studied have impaired glucose control.

If the metabolic pathway involved in lactate production is affected by impaired glucose tolerance, then it is expected to differ when diabetes patients are compared to athletic and control groups (18). Lactate was elevated in the diabetes patients and MetD groups independent of sex (Figure 3). Female athletes have significantly lower body fat percentage than the female non-athletes and diabetes patients (Table 1). It is known that body fat percentage is positively correlated with lactate concentration. Despite the differences in body fat, there were no significant differences between the lactate concentrations in both groups of females. This proves that independent of fat, type 2 diabetes mellitus has an impact on blood lactate concentration.

A study done on insulin resistant offspring of type 2 diabetes mellitus patients suggested that insulin resistance in the skeletal muscles is associated with dysregulation of intramyocellular fatty acid metabolism (19). The researchers suggested that this may be caused by inherited defects in mitochondrial oxidative phosphorylation (19). Studies suggest that insufficient oxidative capacity results in the development of type 2 diabetes mellitus T2DM (8). Oxidative stress is also a common feature in diabetes mellitus (20). Oxidative stress stimulates the production of lactate in adipocytes (21). These findings provide a possible explanation for the elevation in lactate observed in the diabetes patients.
Figure 5 suggests that there can be changes in glucose concentration with no corresponding increase in lactate concentration. This means that while lactate is elevated in diabetes, it is not sensitive enough to have a diagnostic significance. Its elevation in MetD however, may have a more significant relevance in clinical biochemistry as it can be used as a marker in the diagnosis of MetD. This may lead to earlier detection of MetD as the population only conveyed MetD concurrently with type 2 diabetes.
Conclusion:

Lactate concentration is elevated in both male and female diabetes patients. The elevation in lactate concentration in type 2 diabetes patients is likely due to oxidative stress. Its relationship with mean fasting glucose is not consistent making lactate ineffective in diagnosing diabetes mellitus, when compared to fasting glucose. Mean lactate concentration is however proportional to mean glycated hemoglobin. Given its critical involvement in the glycolytic pathway during oxidative stress, it can be helpful in the long-term monitoring of the disease. Basal lactate is elevated in MetD, however the MetD in the population studies concurs with type 2 diabetes. The inclusion of lactate as a parameter for MetD may result in earlier detection.
Compliance with Ethical Standards

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Conflict of Interest: Mr. Aldeam Facey declares that he has no conflicts of interest. Dr. Rachael Irving declares that she has no conflicts of interest. Dr. Lowell Dilworth declares that he has no conflicts of interest. Prof. Rosemarie Wright-Pascoe declares that she has no conflicts of interest. Ms. Melissa Walker declares that she has no conflicts of interest.

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References:


