Lactate Levels in Diabetic Patients on Oral Hypoglycemic Drugs

Pranjalika Mishra, Rachna Ahuja, Rumana Ahmad, Tanvir Jafri, Aparna Misra

1MSC Student 2MD 3Assistant Professor 4Tutor 5Professor and Head, Department of Biochemistry, Era’s Lucknow Medical College and Hospital, Lucknow Uttar Pradesh 226003, India.

Abstract

L-lactate is the end product of anaerobic glycolysis. It is derived predominantly from white skeletal muscle, brain, skin, renal medulla and erythrocytes. Lactate dehydrogenase catalyses the reduction of pyruvate to lactate. There are two major clinical settings in which lactic acidosis occur: (1) Conditions associated with hypoxia e.g. shock, congestive heart failure, myocardial infarction, blood loss and pulmonary edema. (2) Metabolic or drug/toxin related disorders like diabetes mellitus, hepatic disease and neoplasia. Objective of study is to find out the variation of lactate level in diabetic patient taking hypoglycemic drugs and also the correlation between fasting blood glucose and lactate in diabetic patients. It is an observational study in which 50 control subjects (fasting blood sugar 110 mg/dl) considered as case, all diabetics irrespective of treatment (CHI/Insulin). Age group 35-70 yrs. Lactate level ±1.9 taken as normal. Lactate level among control group found to be 1.12±0.18 (mean±SD) with fasting blood sugar level found to be 92.99±5.64 (mean±SD). In control group lactate level among control group found to be 2.03±0.23 (mean±SD) with fasting blood sugar level found to be 115.28±2.83 (mean±SD). The two-tailed p-value is less than 0.0001. By conventional criteria, this difference is considered to be extremely statistically significant. In this, the lactate level found to be 2.03±0.23 among case group. This study also shows that after using metformin some individuals have fasting blood sugar more than 110 mg/dl 115.28±2.83. There is slight increase in lactate level among case group 2.03±0.23. These observations suggest that accumulation of metformin may not be as significant with respect to high arterial levels of lactate.

Keywords: Diabetes Mellitus; Blood Sugar Level; Metformin; Lactate Level; Lactic Acidosis.

Introduction

Diabetes mellitus (DM), a leading cause of death, world is one of the most challenging health problems in the 21st century [1]. The prevalence of diabetes mellitus in West is between 6-7.6%.

India has already become the diabetes capital of the world with over 3 Corers affected patients. Between 1995 and 2025, this is predicted to be a 35% increase in the world wide prevalence of diabetes. The rising number of people with diabetes will occur mainly in populations of developing countries, leading to more than 300 million people globally by 2025 [2].
Diabetes mellitus type 2 (also known as type 2 diabetes) is a long term metabolic disorder that is characterized by high blood sugar, insulin resistance, and relative lack of insulin [3]. Common symptoms include increased thirst, urination and unexplained weight loss. Symptoms may also include hunger, feeling tired and sores that do not heal [4], often symptoms come on slowly [5].

Diabetes complications are divided into micro-vascular and macro-vascular. Microvascular complications include damage to eyes (retinopathy) leading to blindness, to kidneys (nephropathy) leading to renal failure and to nerves (neuropathy) leading to impotence and diabetic foot disorders. Macro-vascular complications include cardiovascular diseases such as heart attacks, strokes and insufficiency in blood flow to legs. There is evidence from large randomized-controlled trials that good metabolic control in both type 1 and 2 diabetes can delay the onset and progression of these complications [6].

The sudden onset of hyperosmolar hyperglycemic state may occur; however, ketoacidosis is uncommon [7]. Metformin is the most commonly prescribed oral Hypoglycemic medication in the world and is considered first line therapy for newly diagnosed type 2 diabetes by many professional diabetes organizations [8]. Lactic acidosis is relatively rare complication in patient with diabetes. It has been associated with use of metformin [9]. Hypoglycemia is a major concern for using sulfonylureas. Magnitude and severity of sulfonylurea induced hypoglycemia range widely across studies [10].

Demographic and epidemiological evidence indicates that unless an effective treatment strategy is developed, there will be a sharp increase in the global prevalence of diabetes, as a consequence of increasing urbanization and associated lifestyle changes, this increase will be greatest in the developing world [11].

Several distinct type of DM exists and caused by complex interactions of genetics, environmental factors and lifestyle choices contributing to hyperglycemia, hyperlipidemia, reduced insulin secretions decreased glucose utilization, and increased glucose production.

L-lactate is the end product of anaerobic glycolysis. It is derived predominantly from white skeletal muscle, brain, skin, renal medulla and erythrocytes. Lactate dehydrogenase catalyzes the reduction of pyruvate to lactate.

There are two major clinical settings in which lactic acidosis occur:

1. Conditions associated with hypoxia e.g. shock, congestive heart failure, myocardial infarction, blood loss and pulmonary edema.

2. Metabolic or drug/toxin related disorders. Examples of metabolic disorders include diabetes mellitus, hepatic disease and neoplasia.

Congenital metabolic disorders include type I glycogen storage disease. Examples of drugs/toxins which give rise to elevated lactate are methanol, ethanol, epinephrine and acetaminophen.

L-lactate levels in CSF will generally mirror those in blood/plasma. However, increased lactate levels in CSF in the absence of increased blood/plasma lactate concentrations have been reported in cases of bacterial meningitis, cerebral hypoxia, ischemia and in certain inborn errors.

So the aim and objectives of study is to assess the lactate levels in diabetic patients on oral hypoglycemic drugs and also find out the correlation between fasting blood glucose and lactate in diabetic patients.

Materials and Methods

Subjects who have Fasting blood sugar less than 110mg/dl, considered as controls Estimation of Lactate Levels: Due to poor lactic acid, precautions started in pyruvic acid estimations are also required in lactic acid estimation.

The cases and controls enrolled in the study will be subjected for biochemistry investigations and blood sample will be collected under aseptic precautions.

Ethical clearance has been obtained from research and dissertation committee/ethical committee of the institution for this study. (Approval IEC/ELMC& R 2017)

The objectives and purposes of the study were clearly explained to eligible participants in a language suitable to them prior to inclusion into the study. Only patients who gave informed consent were enrolled. Patients were free to withdraw during the study period without discrimination. Information gathered from the study participants was kept confidential. Subject’s identity, name, age, gender and other detail, kept confidential and never shown to anyone. All experiments have been performed by me and never misuse the sample. Only blood samples intended for study were drawn and thereafter discarded after analysis. The study results were disseminated to health care providers to aid in patients care.
Selection Controls

- Subjects who have fasting blood sugar less than 110 mg/dl, considered as controls.

Inclusion Criteria

1. All controlled diabetic patients.
2. All diabetics irrespective of treatment (OHA/Insulin).
3. As consent form
4. Age group 35-70 yrs.

Exclusion Criteria

1. Patients having pancreatitis
2. Patients having steroid induced diabetes
3. Alcohol consumer
4. Critically ill diabetic patients
5. Newly diagnosed diabetic patients

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Sample Collection

Samples collected from all clinically diagnosed cases of lactate levels in DM irrespective of age and sex who attend patients OPD & Biochemistry laboratory of ELMC & R Hospital, Lucknow will be included in study. Age and sex matched healthy individuals will be taken as control group.

Standard operating procedures for specimen collection, preparation and storage were followed to minimize pre-analytical errors. Highly lipemic or hemolysed specimens were not used but replaced with others.

Peripheral venous blood is collected from antecubital vein by trained phlebotomist in appropriate vials under aseptic conditions.

2 ml venous blood will be collected from the subject of sample will be analyzed for FBS, and lactate levels.

Method of Collection of Data

Laboratory Investigation of Lactate Levels in DM

- A total of 2 ml venous blood from antecubital vein was collected after overnight fasting.
- Taken 1 ml of blood was collected in fluoride vial for estimation of fasting blood glucose.
- Taken 1 ml of blood was collected in plain vial for estimation of lactate levels.

Blood sample centrifuged at 4000 rpm for 15 min & separation of serum

Observation and Results

Table 1: Demographic representation of the subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Males (percentage)</th>
<th>Females (percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non diabetic</td>
<td>29 (58%)</td>
<td>21 (42%)</td>
</tr>
<tr>
<td>Diabetic</td>
<td>34 (68%)</td>
<td>16 (32%)</td>
</tr>
</tbody>
</table>

Demographical Representation

Chart 1:

In this study the study group were classified into two groups diabetic and non-diabetic both males and females. Non diabetic males (n=29) (58%), Non diabetic females (n=21) (42%), diabetic males (n=34) (68%) and diabetic females (n=16) (32%). (Chart 1).
In this study the mean of fasting blood sugar of non-diabetic males is 93.35±5.51 and their lactate level is 1.10±0.16, in diabetic males mean of fasting blood sugar is 114.72±3.03 and lactate level is 2.01±0.23. Similarly the mean of fasting blood sugar of non-diabetic females is 92.49±5.92 and their lactate level is 1.13±0.20, in diabetic males’ mean of fasting blood sugar is 116.45±1.94 and lactate level is 2.08±0.22.

**Discussion**

**Table 2:** This table shows the fasting blood sugar and lactate level among controls (non-diabetic) and case (diabetic) individuals

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Fasting Blood sugar (mean±SD)</th>
<th>Lactate Level (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Males (n=29)</td>
<td>93.35±5.51</td>
<td>1.10±0.16</td>
</tr>
<tr>
<td>Case male (n=34)</td>
<td>114.72±3.03</td>
<td>2.01±0.23</td>
</tr>
<tr>
<td>p value</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Control female (n=21)</td>
<td>92.49±5.92</td>
<td>1.13±0.20</td>
</tr>
<tr>
<td>Case female (n=16)</td>
<td>116.45±1.94</td>
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<tr>
<td>p value</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Chart 2:** This chart shows fasting blood sugar of diabetic and non-diabetic individuals

**Chart 3:** This chart shows Lactate Level of diabetic and non-diabetic individuals

The first lines of treatment are lifestyle modifications and metformin. If metformin alone cannot achieve a good glycemic control or it is not tolerated or is contraindicated. All tissues can produce lactic acid and pyruvic acid. The liver and kidneys play an important role in lactate homeostasis. Lactic acidosis may occur regardless of diabetes type and may develop both in patients with a long history of diabetes and those with newly diagnosed disease. Probably the first cases of lactic acidosis were described by Doughaday et al. 17 in 1962. In 1969, more cases were presented by Watkins et al.18 in the British Medical Journal. In our case reports, the most numerous group of patients admitted to the hospital with lactic acidosis consisted of patients with diabetes. Acidosis manifests itself most commonly with nausea, persistent vomiting, and abdominal pain. Philbrick et al. indicated that increased creatinine is a risk factor for lactic acidosis, but it is not an absolute contraindication to its use. Also in patients with heart failure, metformin therapy can provide therapeutic benefits unless other risk factors of lactic acidosis are present. Lactate levels strongly correlate with the severity of the disease and the risk of death in patients with sepsis. Metformin is generally considered as safe, when health risks that may lead to lactic acidosis occur during the treatment, particular precautions are necessary. In metformin-treated patients, especially in elderly ones, the possibility of a sudden deterioration of renal function has to be considered, which can increase the risk of lactic acidosis. In patients with type 1 diabetes, long term insufficient glycemic control and malnutrition may result in a considerable increase in lactic acid. In this study the blood glucose level of control (M) is 93.35±5.51 and their lactate levels is 1.10±0.16. In females blood glucose level of control (F) is 92.49±5.92 and lactate level is 1.13±0.20. In case of (F) blood glucose level is 116±5.92 and lactate level is 2.08±0.22. In case of (M) blood glucose level is 114.72±3.03 and lactate level is 2.01±0.23. In our findings the results are almost similar to the previous studies.

**Conclusion**

This study is done at Era’s Lucknow Medical College and Hospital, Era University in the Department of Physiology. The duration of the study was 6 months starting from January 2018.

Lactate level among control group found to be 1.12±0.18 (mean±SD) with fasting blood sugar level found to be 92.99±5.64 (mean±SD). In control group lactate level among control group found to be 2.03±0.23 (mean±SD) with fasting blood sugar level found to be 115.28±2.83 (mean±SD). In this, the lactate level found to be 2.03±0.23 among case group. This study also shows that after
using metformin some individuals have fasting blood sugar more than 110 mg/dl 115.28±2.83. There is slight increase in lactate level among case group 2.03±0.23 These observations suggest that accumulation of metformin may not be as significant with respect to high arterial levels of lactate.

Elevated lactate is encountered in a multitude of clinical presentations and disease states.

Despite the limitations and complexities discussed above, a lactate level is an easily measured lab parameter

References


