Asian Journal of Pharmaceutical Technology & Innovation
ISSN: 2347-8810

Research Article

Received on: 25-01-2017
Accepted on: 01-02-2017
Published on: 15-02-2017

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Evaluation of Plasma Lactate and Electrolytes In Type II Diabetes Mellitus

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ABSTRACT

Aim: To estimate sodium (Na^+), potassium (K^+) , bicarbonate (HCO_3^-) and lactate levels in arterial blood of diabetes mellitus type II patients.
Material and Method: 90 non-alcoholic, non-smoker subjects above the age of 40 years were participated in the present study, subdivided in 3 groups. *Group 1*: 30 diabetic subjects above the age of 40 years suffering from diabetes mellitus type II as diagnosed by the physician and having random plasma glucose < 400 mg/dl. *Group 2* : 30 diabetic subjects above the age of 40 years suffering from diabetes mellitus type II as diagnosed by the physician and having random plasma glucose ≥ 400 mg/dl. *Control group* : 30 non-diabetic age and sex matched subjects. Arterial blood samples were collected from radial artery in a heparinised syringe & processed immediately on blood gas analyzer GEM PREMIER 3000, using GEM PREMIER 3000 pak cartridge.
Results: There was significant decrease in plasma sodium levels in diabetic patients compared to controls. Plasma potassium levels were significantly increased in diabetic patients than controls.
Conclusion: Uncontrolled hyperglycemia (group 2 diabetics) is significantly associated with electrolyte imbalance and lactic acidosis in type II diabetes mellitus patients.
It was concluded that electrolyte imbalance found in diabetics may have great potential as a diagnostic tool in clinical practice and have a significant effect upon controlling the risk of many diseases & complications.

Key-words: electrolytes; diabetic; Na^+; K^+; lactate, bicarbonate

Cite this article as:
Narwade N B, Kolpe D V, Udaykiran Bhalge, Evaluation of Plasma Lactate and Electrolytes In Type II Diabetes Mellitus, Asian Journal of Pharmaceutical Technology & Innovation, 05 (22);54-58, 2017. www.asianpharmtech.com

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Introduction:

The worldwide prevalence of diabetes mellitus [DM] has risen dramatically over the past two decades. Based on current trends, >360 million individuals will have diabetes by the year 2030. India is first among top 10 countries with highest prevalence of diabetes. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.[1]

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. A random plasma glucose concentration ≥ 200 mg/dl accompanied by classic symptoms of Diabetes mellitus (polyuria, polydipsia, weight loss) is sufficient for the diagnosis of Diabetes mellitus.[2]

Diabetes mellitus is a heterogenous group of metabolic disorders characterized by hyperglycemia with alteration in carbohydrate, lipid, and protein metabolism due to defects in insulin secretion and/or action.[3]

Type II DM is characterized by insulin resistance, impaired insulin secretion, excessive hepatic glucose production, and abnormal lipid metabolism. In diabetes, lipid catabolism increases and is diverted to ketone body formation. Reduced insulin levels in combination with elevations in catecholamines and growth hormone, increase lipolysis and the release of free fatty acids. Normally, these free fatty acids are converted to triglycerides or VLDL in the liver. However, in diabetic ketoacidosis, hyperglucagonemia alters hepatic metabolism to favor ketone body formation, through activation of the enzyme carnitine-palmitoyl-transferase 1. This enzyme is crucial for regulating fatty acid transport into the mitochondria, where β oxidation and conversion to ketone bodies occur. Accumulation of ketone bodies i.e. β-hydroxyl-butyrate and acetoacetate, results in high anion gap metabolic acidosis. Increased lactic acid production also contributes to the acidosis.[1-4]

Hyperglycemia in diabetes leads to glycosuria and excretion of these osmotically active glucose molecules entails the loss of large amounts of water (osmotic diuresis) and an appreciable urinary loss of Na^+ and K^+ as well. Osmotic effect of glucose results in decreased circulating blood volume and fluid shift from the intracellular spaces causing cellular dehydration.[3] In acidosis, total body Na^+ is markedly depleted, and when Na^+ loss exceeds water loss, plasma Na^+ also decreases. Also insulin resistance affects Na^+-K^+-ATPase pump changing intracellular and extracellular concentrations of Na^+ and K^+. Hyperglycemia, osmotic diuresis, serum hyperosmolarity and metabolic acidosis result in severe electrolyte disturbances. The most characteristic disturbance is total body potassium loss. This loss is not mirrored in serum potassium levels, which may be low, within the reference range, or even high. Potassium loss is caused by a shift of potassium from the intracellular to the extracellular space in an exchange with hydrogen ions that accumulate extracellularly in acidosis. Another factor tending to maintain the plasma K^+ is the lack of insulin-induced entry of K^+ into cells.[1-4]

Lactic acidosis, an acute complication of DM, occurs due to increased rate of anaerobic glycolysis and/or impairment of citric acid cycle.[5] Increased cellular oxidative stress due to diabetes also leads to increased cellular lactate production. Adipose tissue is responsible for a large portion of the lactate produced in obesity. Among obese subjects, decreased blood flow to adipose tissue leads to local hypoxia and increased lactate production. Furthermore, adipocyte production of lactate increases as adipocyte size increases. There is also evidence that hypoxia drives adipocytokine dysregulation and decreased insulin signaling in adipocytes from obese individuals.[6]

Oxidative capacity may also be decreased in insulin-resistant skeletal muscle as evidenced with increased glycolysis in muscle, decreased mitochondrial size & density, decreased oxidative gene expression, decreased oxidative phosphorylation and decreased aerobic capacity. The decrease in oxidative capacity may account for the markedly altered lactate metabolism in insulin-resistant muscle, where lactate concentration is increased and the lactate - pyruvate interconversion rates are enhanced as much as 3 to 4 fold.[6-7]

Material and Methods:

This study was carried out in the department of Biochemistry in collaboration with Department of Medicine. The study protocol was approved by the institutional Ethics Committee of the institute. A total number of 90 subjects above the age of 40 years were participated in the present study. Detailed medical history and relevant clinical examination data and written consent were obtained from all subjects by explaining the study procedure. A total number of 90 subjects above the age of 40 years were participated in the present study which were further subdivided in to 3 groups; *Group 1*: 30 diabetic subjects above the age of 40 years suffering from diabetes mellitus type II as diagnosed by the physician and having random plasma glucose < 400 mg/dl. *Group 2*: 30 diabetic subjects above the age of 40 years suffering from diabetes mellitus type II as diagnosed by the physician and having random plasma glucose ≥ 400 mg/dl. *Control group*: 30 non-diabetic age and sex matched subjects.

Arterial blood samples were collected from radial artery in a heparinised syringe. Samples were carried to the laboratory on ice pack and processed immediately on blood gas analyzer GEM PREMIER 3000, using GEM PREMIER 3000 pak cartridge for estimation of sodium (Na^+), potassium (K^+) , bicarbonate (HCO_3^-) and lactate levels in arterial blood.

All the calculations were done using Microsoft Office Excel 2010 and statistical analysis was done using the Graph Pad Prism software, Version 5.04. All statistical data was analysed by ANOVA (one way analysis of variance) test. P-value less than 0.05 ($P < 0.05$) was considered to be statistically significant (S). P-value less than 0.001 ($P < 0.001$) was considered to be statistically highly significant (HS). P-value more than 0.05 ($P > 0.05$) was considered to be statistically non-significant (NS).

The present study showed no significant difference in demographic characters as age and sex in control and study groups.

Results:

Table 1. Comparison of sodium (Na^+), potassium (K^+) , bicarbonate (HCO_3^-) and lactate levels in arterial blood in all groups.

Parameter	Control group (mean ± SD)	Group 1 diabetics (mean ± SD)	Group 2 diabetics (mean ± SD)
Plasma Na^+ mmol/L	138.83 ± 5.40	133.83 ± 7.95	128.03 ± 10.14
Plasma K^+ mmol/L	3.81 ± 0.41	3.96 ± 0.51	4.22 ± 0.60
Plasma Lactate mmol/L	1.14 ± 0.38	1.99 ± 1.21	2.68 ± 2.56
Arterial pH	7.405 ± 0.044	7.38 ± 0.09	7.31 ± 0.11
Plasma HCO_3^-mmol/L	22.65 ± 1.58	20.99 ± 6.72	16.95 ± 5.69

Table-2: Significance of sodium (Na^+), potassium (K^+), bicarbonate (HCO_3^-) and lactate in all groups:

Parameter	Group 1 vs Control	Group 2 vs Control	Group 2 vs Group 1
Plasma Na^+ mmol/L	> 0.05 (NS)	< 0.001 (HS)	< 0.05 (S)
Plasma K^+ mmol/L	> 0.05 (NS)	< 0.05 (S)	> 0.05 (NS)
Plasma Lactate mmol/L	> 0.05 (NS)	< 0.05 (S)	> 0.05 (NS)
Arterial pH	> 0.05 (NS)	< 0.05 (S)	< 0.05 (S)
Plasma HCO_3^-mmol/L	> 0.05 (NS)	< 0.05 (S)	< 0.05 (S)

NS-Not significant, S-Significant, HS-Highly Significant

In present study, the plasma Na^+ levels were found decreased in all diabetic patients. But significant decrease was found in group 2 diabetics (128.03 ± 10.14) when compared with group 1 diabetics (133.83 ± 7.95) and controls (138.83 ± 5.4). [Table 1, 2]

The plasma K^+ levels were increased in all diabetics (group1= 3.96 ± 0.51, group2 = 4.22 ± 0.60). But significantly increased levels were found only in group 2 diabetics compared with controls (3.81 ± 0.41). [Table1, 2]

In the present study, it was also found that the plasma lactate levels were significantly increased in group 2 diabetics (2.68 ± 2.56) compared with controls (1.14 ± 0.38). Though, the increase in plasma lactate levels was more in group 2 compared with group 1 diabetics (1.99 ± 1.21), but was non-significant. [Table 1, 2]

Arterial pH was not significantly decreased (> 0.05) when group 1 diabetics (7.38 ± 0.09) compared with controls (7.405 ± 0.044) but significantly decreased (< 0.05) when group 2 (7.31 ± 0.11) compared with group 1 diabetics (7.38 ± 0.09) and controls (7.405 ± 0.044). [Table 1, 2]

Plasma (HCO_3^-) levels were not significantly decreased (>0.05) when group 1 diabetics (20.99 ± 6.72) compared with controls (22.65 ± 1.58). But significantly decreased (< 0.05) when group 2 (16.95± 5.69) compared with group 1 diabetics (20.99 ± 6.72) and controls (22.65 ± 1.58). [Table 1, 2]

Discussion:

Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Classic symptoms of DM are polyuria, polydipsia and weight loss. Diabetes is caused by a complex interaction of genetics, environmental, immunologic and lifestyle factors. Approximately 80% to 90% of diabetic patients have type II diabetes. Type II diabetes is polygenic and multi-factorial. Insulin resistance and impaired insulin secretion are central to the development of type II DM. Most studies support that insulin resistance precedes an insulin secretory defect but that diabetes develops when insulin secretion becomes inadequate.[1]

The association between blood glucose and serum electrolytes is multi factorial. Increased urination leads to loss of electrolytes and water and results in the imbalance which disturbs sodium and potassium levels in the body. Studies suggest that uncontrolled DM can also induce hypovolemic hyponatremia due to osmotic diuresis.[8]

The observed reduction in plasma Na^+ in diabetic subjects might be a result of electrolyte loss which arises due to dehydration or a result of kidney dysfunction caused by diabetes. As the body tries to flush out excess glucose due to hyperglycemia, water is also flushed out continuously through the kidney tubules. This water loss is accompanied by Na^+ loss.[9]

Increased rate of anaerobic glycolysis in muscles, impairment of citric acid cycle, decreased mitochondrial size and density, decreased oxidative gene expression, decreased oxidative phosphorylation, decreased aerobic capacity, decreased oxidative capacity all account for the markedly increased lactate concentration.[5-7]

Diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS) are acute complications of diabetes. Accumulation of ketone bodies, β-hydroxy-butyrate and acetoacetate results in high anion gap metabolic acidosis. Metabolic changes in diabetes, DKA, HHS are associated with absolute or relative insulin deficiency, hyper-osmolarity, volume depletion, acid-base, lactate and electrolyte abnormalities.[10]

Hyperglycemia, osmotic diuresis, serum hyper-osmolarity and metabolic acidosis result in severe electrolyte disturbances. At physiologic pH, ketone bodies exist as ketoacids, which are neutralized by bicarbonate resulting in depletion of bicarbonate stores. As body tries to compensate for acidosis, compensatory increase or decrease in pCO_2 and bicarbonate (HCO_3^-) levels is observed.[4-5]

Conclusion:

Diabetes mellitus type II patients with uncontrolled hyperglycemia (group 2) have shown hyper-lactetemia and hypo-natremia.

The present study shows significant hyperkalemia in group 2 diabetic patients only (uncontrolled hyperglycemic). This may be due to acidosis induced extracellular shifting of K^+ or lack of insulin-induced entry of K^+ into cells.[1] In support of above conclusion, many studies shows significant hyperkalemia in diabetics[8-9], though some studies suggest total body potassium loss.[3]

Uncontrolled hyperglycemia is significantly associated with acid base and electrolyte imbalance in type II diabetes mellitus patients.

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