

Study on Diabetes Mellitus and the Balance of Electrolytes

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Abstract

The study was designed to investigate the relationship between some of extracellular and intracellular electrolytes with type2 diabetes mellitus. Sixty one patients suffering from type 2 diabetes mellitus (26 males, and 35 females) aged between (40) to (79) years with a mean age of $(55.96 \pm 10.72; 55.68 \pm 9.79)$ were included in this study respectively. All patients have a history of duration of disease and no one of them has another disease. The control group is comprised of (61) healthy individuals (30 males and 31 females) aged between (40) to (79) years with a mean age of $(55.5 \pm 9.08; 55.16 \pm 7.34)$ for male and female respectively. The control subjects were selected from the hospitals of Babylon city. They had no history of diabetes mellitus or any other disease. The results of this study showed that serum sodium was significantly decreased ($P < 0.05$) in patients (male and female) with diabetes type2 as compared to control (male and female) groups. Serum potassium was significantly elevated ($P < 0.05$) in patients (male and female) with diabetes type 2 as compared to control male group while the comparison to control female group was non-significant. Serum calcium indicated reduction in male patients and elevation in female patients with diabetes type 2 and compared to control male and female groups respectively but was non-significant.

Key words: Diabetes Mellitus , Calcium , Sodium , Potassium and Electrolytes.

الخلاصة

صممت هذه الدراسة للتقصي عن طبيعة العلاقة بين بعض الايونات الداخلة والخارج خلوية مثل (صوديوم، بوتاسيوم، كالسيوم) مع مرض السكري النوع الثاني. تضمنت الدراسة احدى وستون مريضاً يعاني من مرض السكري النوع الثاني منهم 26 مريض من الذكور و 35 من الاناث وقد تراوحت اعمارهم بين (40-79) سنة ومتوسط الاعمار والانحراف المعياري (10.72 ± 55.96) للذكور و (9.79 ± 55.68) للاناث. تم التحقق من تاريخهم بمرض السكري وليس لديهم مرض اخر . تمت المقارنة مع مجموعة السيطرة وقد بلغ عددهم 61 (30 من الذكور و 31 من الاناث) وتراوحت اعمارهم بين (40-79) سنة ومتوسط اعمارهم والانحراف المعياري (55.5 ± 9.08) ، (55.16 ± 7.34) للذكور والاناث على التوالي لقد تم اختيار عينات الدراسة من مرضى مشخصين في مستشفيات محافظة بابل قيد الدراسة وليس لديهم تاريخ بمرض السكري او أي مرض اخر. اظهرت النتائج انخفاض معنوي ($P < 0.05$) في مستوى ايونات الصوديوم لدى المرضى المصابين بالسكري النوع الثاني (الذكور والاناث) مقارنة بمجموعة السيطرة (للذكور والاناث). اظهرت النتائج ارتفاع معنوي ($P < 0.05$) في مستوى ايونات البوتاسيوم لدى المرضى المصابين بالسكري النوع الثاني عند مقارنتهم بمجموعة السيطرة للذكور في حين ان المقارنة مع مجموعة السيطرة للاناث كانت غير معنوية ($P > 0.05$). كما بينت نتائج مستوى ايونات الكالسيوم نقصان غير معنوي ($P > 0.05$) لدى المرضى الذكور المصابين بالسكري النوع الثاني وارتفاع غير معنوي ($P > 0.05$) لدى الاناث عند مقارنتها مع مجموعة السيطرة للذكور والاناث على التوالي.

الكلمات المفتاحية: داء السكري ، الكالسيوم ، الصوديوم ، البوتاسيوم والالكتروليات .

Introduction

Diabetes Mellitus is an endocrine disorder which affects over 100 million people worldwide. It is expected that more than one billion people will suffer from diabetes worldwide by the end of the 21st century (Amos *et al.*, 1997). The disease is characterized by inability of the pancreas to produce sufficient amounts of insulin, or failure of the body's cells to respond appropriately to insulin. In people with diabetes, glucose levels build up in the blood and urine, causing excessive urination, thirst, hunger, and problems with fat and protein metabolism (Cowie & Harris, 1995).

During diabetes, persistent hyperglycemia causes increased production of free radicals especially reactive oxygen species (ROS), for all tissues from glucose auto-

oxidation, lipid peroxidation and protein glycosylation((Moussa, 2008; Robertson, 2004). Several conditions were known to disturb the balance between ROS production and cellular defense mechanism and cause oxidative stress (Moussa, 2008; Robertson, 2004; West ,2000).

The electrolytes in serum include sodium (Na^+), potassium (K^+), calcium (Ca^{2+}) and magnesium (Mg^{2+}) (Hall & Guyton, 2006). Electrolytes play an important role in many body processes ,such as controlling fluid levels , acid- base balance (pH), nerve conduction, blood clotting and muscle contraction. Electrolyte imbalance resulting from kidney failure dehydration, fever ,vomiting has been suggested as one of the contributing factors toward complications observed in diabetes and other endocrine disorders (Rao ,1992).

The most common electrolyte imbalance is hyponatraemia, others are hypokalaemia, hypomagnesaemia and hyperkalaemia. Hyponatraemia, defined as a plasma sodium concentration $<130 \text{ mmol/L}$, usually reflect a hypotonic state. However, plasma osmolality may be normal or increased in some cases of hyponatraemia. Hypertonic hyponatraemia is usually due to hyperglycemia. Relative insulin deficiency causes myocyte to become impermeable to glucose. Therefore, during poorly controlled diabetes mellitus, glucose is an effective osmole and draws water from muscle cells resulting in hyponatraemia. Isotonic hyponatraemia may occur in conditions like hyperlipidemia and hyperproteinemia. In general, hypotonic hyponatraemia occurs due either to a primary Na^+ loss(secondary water gain) like sweating, burns, gastrointestinal loss: vomiting, diarrhea; renal loss: diuretics, hypoaldosteronism, salt wasting nephropathy; or due to a primary water gain (secondary Na^+ loss) like SIADH, hypothyroidism, primary polydipsia; or due to a primary Na^+ gain (exceeded by secondary water gain) like heart failure, hepatic cirrhosis, nephritic syndrome. It is important to note that diuretic-induced hyponatraemia is almost always due to thiazide diuretics and cerebral salt wasting after neurosurgery are also the cause of hyponatraemia (Gary ,2005)).

Potassium is the principal intracellular action and maintenance of the distribution of potassium between the intracellular and the extracellular compartments relies on several homeostatic mechanisms; when these mechanisms are perturbed, hypokalemia or hyperkalemia may occur (Kimberley & Arthur,2005), Hypokalemia, defined as a plasma K^+ concentration $<3.5 \text{ mmol/L}$, may result from one or more of the followings: decreased net intake like starvation; shift into cells like metabolic alkalosis, insulin, β_2 Adrenergic agonist, total parenteral nutrition; and increased net loss like diarrhea, sweating, renal loss: diuretics, primary and secondary hyperaldosteronism. Diminished intake is seldom the sole cause of K^+ depletion since urinary excretion can be effectively decreased to $<15 \text{ mmol/day}$ as a result of net K^+ reabsorption in the distal nephron. However, dietary K^+ restriction may exacerbate the hypokalemia secondary to increased gastrointestinal or renal loss (Gary, 2005).

Hyperkalemia defined as a plasma K^+ concentration $>5.3 \text{ mmol/L}$, occurs as a result of either K^+ release from cells or decreased renal loss. Increased K^+ intake is rarely the sole cause of hyperkalemia since the phenomenon of *potassium adaptation* ensures rapid K^+ excretion in response to increase in dietary consumption. Iatrogenic hyperkalemia may result from overzealous parenteral K^+ replacement or in patients with renal insufficiency. Metabolic acidosis, with the exception of those due to the accumulation of organic anions, can be associated with mild hyperkalemia resulting from intracellular buffering of H^+ . Insulin deficiency and hypertonicity (e.g., hyperglycemia) promote K^+ shift from the ICF to the ECF. The severity of exercise induced hyperkalemia is related to the degree of exertion. It is due to release of K^+ from

muscles and is usually rapidly reversible. Severe digitalis toxicity and treatment with beta blockers may contribute to the elevation in plasma K^+ concentration

Pseudohyperkalemia represents an artificially elevated plasma K^+ concentration due to K^+ movement out of cells immediately prior to or following venipuncture. Contributing factors include prolonged use of a tourniquet with or without repeated fist clenching, hemolysis, and marked leukocytosis or thrombocytosis. Intravascular hemolysis, tumor lysis syndrome, and rhabdomyolysis all lead to K^+ release from cells as a result of tissue breakdown (Gary, 2005).

Insulin secretion is a calcium-dependent biological process (Curry *et al.*, 1968), and an elevation in calcium is required for insulin secretion (Henquin *et al.*, 2003). In juvenile diabetic patients serum calcium is decreased with increased urinary excretion (Watts, 1999). It was reported that elevated cytosolic free calcium and reciprocally reduced extracellular ionized calcium levels were observed in type 2 diabetic patients (Barbagallo *et al.*, 1999).

Oxidative stress causes Ca^{2+} influx into the cytoplasm. Rising Ca^{2+} concentration in the cytoplasm causes Ca^{2+} influx into mitochondria and nuclei. In mitochondria Ca^{2+} accelerates and disrupts normal metabolism leading to cell death. In nuclei Ca^{2+} modulates gene transcription and nucleases that control cell apoptosis. Both in nuclei and cytoplasm Ca^{2+} can regulate phosphorylation/ dephosphorylation of proteins and can modulate signal transduction pathway as a result (Ermak & Davies, 2001). The aim of this study was conducted to investigate electrolyte imbalance in diabetic subjects in Babylon city in comparison with non-diabetic individuals.

Subjects and Methods

Sixty one subjects (males and females) patients suffering from diabetes mellitus type 2 and sixty one non-diabetics subjects (control) were used in this study. All subjects are adults aged between forty years (40) and seventy nine years (79). The study was done in different hospitals in Babylon city, in the period from November 2013 to March 2014.

Blood samples were obtained from each subject by venipuncture into clean sample bottle. The blood was allowed to clot and then centrifuged at 3000rpm for 10 minutes. The serum obtained was pipette into a clean bottle and analyzed for glucose immediately while the remaining portion was kept frozen for the rest of the analysis.

Fasting blood glucose was determined using the glucose oxidase method (Raabo & Terkildsen 1960). The fasting blood glucose was ≥ 10 mmol / L (more than 180 mg / dL). Serum Sodium and potassium ions were determined by Roche 9180 Electrolyte analyzer. Calcium ion was determined by Abbott Diagnostics (ARCHITECT c4000).

Statistical Methods

Summarized data are shown as mean $\pm$ standard deviation. One-way analysis of variance (one-way ANOVA) was used to compare the mean differences. SPSS for windows (version 17.0, SPSS, Chicago, IL, USA) was used to perform the statistical analyses. The significance level was P value < 0.05 .

Results

Total number of patients was 61, male were 26, female were 35, the male and female ratio was 1.0:1.35. The mean age was 55.96 years with SD ± 10.72 for male and 55.68 years with SD ± 9.79 years for female ranging from 40-79 years. Among them (18) 29.5% were of below 50 years, (22) 36.1% were of 50-59 years age group, 13 (21.31%) were of 60-69 years age group and 8 (13.11%) were of (70-79) years age group (Table 2).

The mean sodium level was 135.96 ± 5.22 for male and 137.45 ± 6.92 for female, this result showed that serum sodium was significantly decreased ($P < 0.05$) in patients (male and female) with diabetes mellitus type 2 as compared to control (male and female) group (Table 1).

The mean potassium level was (5.05 ± 1.06) for male and (4.59 ± 1.25) for female, this result was significantly elevated ($P < 0.05$) in patients (male female) with diabetes mellitus type 2 as compared to control male group, while the comparison to control female group was non – significant (Table 1).

The mean calcium level was (2.46 ± 1.14) for male and (2.84 ± 2.07) for female, this result was indicated reduction in patients male and elevated in patients female with diabetes mellitus type 2 as compared to control male and female groups respectively but were non- significant (Table 1).

Table 1: different between control and patients for male and female of serum Calcium, potassium and sodium also for age.

			Male	Female
Number of cases			30	31
Controls	Biochemical Parameters	Ages/Year	53.50±9.08	55.16±7.34
		S. Na ⁺ (mmol/L)	140.53±3.88*	139.67±3.82**
		S. K ⁺ (mmol/L)	4.35±0.65*	4.50±0.86
		S. Ca ²⁺ (mmol/L)	2.71±1.19	2.35±0.74
Number of cases			26	35
Patients	Biochemical Parameters	Ages/Year	55.96±10.72	55.68±9.79
		S. Na ⁺ (mmol/L)	135.96±5.22***	137.45±6.92
		S. K ⁺ (mmol/L)	5.05±1.06***	4.59±1.25
		S. Ca ²⁺ (mmol/L)	2.46±1.14	2.84±2.07

* To represent the signification relative between control male and patient female but,

** for appear significant value between control female and patient male. While

*** for significant value between control male and patient male at ($P < 0.05$).

Table 2: Number of male and female for ages from 40-79.

Age/Years	Patients		Control	
	No. of Cases		No. of Cases	
	Male	Female	Male	Female
40-49	9	9	10	7
50-59	7	15	10	14
60-69	5	8	7	9
70-79	5	3	3	1
Total number	26	35	30	31

Discussion

Derangement of water and electrolyte balances may occur in subjects with DM, resulting from insulin deficiency, hyperglycemia and hyperketonemia (Kitabchi *et al.*, 2006). The observed reduction in serum 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 (Rao ,1992). 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. Such rapid loss of sodium, if continued could soon bring about depletion of base in the body sufficient to cause dehydration of the tissues which may result in death (Leonard &, John, 1989). Significant reduction in serum Na^+ level an elevation in serum Ca^{2+} in subjects with DM were observed. These results were consistent with those reported by previous studies (Levy *et al.*, 1986; McNair *et al.*,1982; Haglin & Tornkvist, 2011).

Hyponatremia is increases mortality irrespective of age, sex, cause and co-existing hypokalaemia(Lee *et al.*, 2000).Hyperkalemia was present in our study, renal failure,drugs and hypercalcemia were precipitating factors (Christopher *et al.*,1998). It was also stated that hyperkalemia is associated with diabetes but the exact prevalence is lacking (Jarman *et al.*, 1995). Diabetes mellitus induces a decrease in sodium potassium–adenosine triphosphatase (Na/K-ATPase) activity in several tissues in the rat and red blood cells and nervous tissue in human patients. This decrease in Na/K-ATPase activity is thought to play a role in the development of long-term complications of the disease. Angiotensin converting enzyme (ACE) inhibitors and angiotensin II receptor antagonists reduce proteinuria and retard the progression of renal failure in patients with insulin-dependent diabetes mellitus (IDDM) and diabetic rats (Temel & Akyuz ,2007),).

The normal range of serum calcium concentration (2.2- 2.6 mmol/l). About 45% of serum calcium is bound to serum protein, 5% is complexed with anions (e.g., phosphate, bicarbonate, and citrate), and 50% is ionized. The ionized fraction affects cellular function(Mayne, 2002)). It was reported that, serum calcium is low in juvenile diabetic patients (Watts & Newsletter ,1999). and not affected in type 2 DM (Ugwuja & Eze 2007)), or non-significantly elevated in postmenopausal (Hadzibegovic *et al.*, 2008), and elderly type-2 diabetic women due to the release of calcium from bone tissues (Dobing *et al.*, 2006), which was in compatible with our results.

On the other side, it was reported that reduced extracellular ionized calcium ion levels are observed in males with type-2 diabetes mellitus compared to control group (Barbagallo *et al.*, 1999). This result is in agreement with our results.

A main limitation of our study was that we only measured the some of serum electrolytes levels, but not all extracellular and intracellular electrolytes or levels in other biological samples from the subjects. We also unmeasured factors, such as eating habits and other medications, may have indirect effects on the electrolyte regulation and interfere with the relationship between other disease and electrolyte disturbances. Our study also did not elucidate the causal relationship of serum electrolyte levels on the development of DM and diabetic macrovascular complications.

Conclusion

This study provided data to show that diabetics subjects in Babylon city have electrolytes imbalance characterized with depletion in sodium and elevation in potassium and calcium ions compared with their non-diabetic counterparts.

Hyponatremia and hypokalemia were common in electrolyte imbalance and is one of the contributing factors toward complications observed in diabetes. Prevalence of hyperkalemia was less common. Vomiting, diarrhea, various medications and renal impairment were the most common precipitating factors. The decreased levels of serum Ca^{2+} , that were shown in DM, may be due to changes in calcium homeostasis, which was represented by Ca^{2+} influx accompanied with this disease. This influx of Ca^{2+} in turn, increases ROS production and oxidative stress.

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