Diabetic ketoacidosis: difference between potassium determined by blood gas analysis *versus* plasma measurement

Cetoacidose diabética: diferença entre as concentrações do potássio na gasometria sanguínea versus *potássio plasmático*

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ABSTRACT

Objective: To evaluate the accuracy of potassium concentrations measured by blood gas analysis (PBG) compared with laboratory serum potassium (LSP), in the initial care of patients with diabetic ketoacidosis (DKA). **Subjects and methods:** Fifty three patients with *diabetes mellitus* were evaluated in a retrospective analysis. PBG was carried out using the Radiometer ABL 700 (Radiometer Copenhagen®), and results were compared with LSP ADVIA 1650 Chemistry system (Siemens®), the gold standard method. Both methods are based on potentiometry. **Results:** Mean PBG was 3.66 mmol/L and mean LSP was 4.79 mmol/L. Mean difference between PBG and LSP was -1.13 mmol/L ($p < 0.0005$, 95% CI, -1.39 to -0,86). Lin concordance correlation coefficient was rc = 0.28 (95% CIb, 0.10 to 0.45), demonstrating low concordance between the methods. **Conclusion:** Although PBG measurement is faster and easier, it should not be used as a surrogate for LSP in the clinical treatment of DKA. Arq Bras Endocrinol Metab. 2011;55(4):256-9

Keywords
Diabetic ketoacidosis; serum potassium concentration; blood gas analysis of potassium

RESUMO

Objetivo: Avaliar a acurácia da mensuração da concentração de potássio realizado nos analisadores de gasometria sanguínea (PGS) em relação ao potássio plasmático laboratorial (PPL) no atendimento inicial dos pacientes com cetoacidose diabética (CAD). **Sujeitos e métodos:** Foram avaliados, retrospectivamente, 53 pacientes com diabetes melito e CAD. A análise do PGS foi realizada pelo equipamento ABL 700 (Radiometer Copenhagen®), sendo este comparado ao método padrão-ouro de PPL ADVIA 1650 (Siemens®), ambos por potenciometria. **Resultados:** A média do PGS foi de 3,66 mmol/L e do PPL, de 4,79 mmol/L. A diferença das médias do PGS em relação ao PPL foi de -1,13 mmol/L ($p < 0,0005$, IC = 95%; -1,39 a -0,86). O coeficiente de concordância de Lin foi de rc = 0,28 (ICb = 95%; 0,10 a 0,45), demonstrando, assim, uma baixa concordância entre os métodos. **Conclusão:** Apesar de a realização do PGS ser tecnicamente mais rápida e fácil, não deve ser usada como parâmetro substituto ao PPL para o tratamento clínico da CAD. Arq Bras Endocrinol Metab. 2011;55(4):256-9

Descritores
Cetoacidose diabética; potássio plasmático laboratorial; potássio no analisador de gasometria sanguínea

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Received on Jul/13/2010
Accepted on Apr/26/2011

INTRODUCTION

Diabetic ketoacidosis (DKA) is the most common hyperglycemic emergency in patients suffering from *diabetes mellitus* (DM), with mortality rates lower than 5% in centers of excellence, and high mortality rates in patients with concomitant serious diseases (1). Worldwide mortality for each DKA episode varies from 0.15% – 0.31% (2-5). Two-thirds of the deaths are caused by

cerebral edema, and one-third by other causes, including hydroelectrolytic disorders such as hypokalemia (6). A study from India, with 68 patients, showed that the most common complications during DKA treatment were hypokalemia in 41% of the cases, hypoglycemia in 15% of the cases, and cerebral edema in 13.2% of the cases (7). In another recent study, Ogbera and cols., evaluated 111 patients with hyperglycemic emergencies, and showed that hypokalemia occurred in 37% of the cases, being considered a predictor of death (8).

In DKA treatment, serum potassium concentration is essential information, considering that after the initial improvement in blood flow, it is a limiting factor for insulinization. If the patient shows significant hypokalemia (serum potassium concentration lower than 3.3 mmol/L), the risk of arrhythmia risk, cardiac arrest and respiratory muscle weakness is increased (1,9).

Laboratory measurement of serum potassium is technically more troublesome and lengthy (10). Thus, in emergency centers of tertiary hospitals that receive a large number of serious patients, serum potassium measurement is carried out by blood gas analysis when DKA patients are cared for, because it is easier and faster.

The aim of this study was to evaluate accuracy of potassium concentration measured using blood gas analysis compared with laboratory measurement of serum potassium, both based on potenciometry and collection of venous blood, in initial care of DKA patients.

SUBJECTS AND METHODS

Records of DM patients over 12 years of age were evaluated retrospectively, one DKA event per patient. Patients were admitted in our emergency department from January 2005 to January 2009. Diagnosis and level of seriousness of DKA were evaluated according to the guidelines of the American Diabetes Association 2004 (1).

The following parameters were evaluated when patients were admitted in the emergency department: blood glucose, laboratory serum potassium concentration (LSP), pH, and bicarbonate and potassium concentration evaluated by blood gas analysis (PBG).

PBG analysis was carried out by the Radiometer ABL 700 (Radiometer Copenhagen®, Denmark) in undiluted samples and with heparin sodium as the anticoagulant agent. Results were compared with the gold standard method, LSP-ADVIA 1650 Chemistry system (Siemens®) in undiluted samples. Both methods are based on potenciometry with one ion-selective electrode. Analysis of pH was carried out by venous blood gas analysis, as recommended by the Diabetes Ketoacidosis Consensus of the American Diabetes Association, 2006 (9). The method presents excellent correlation with arterial gas analysis, which is only indicated in critical patients. Average difference between arterial and venous blood gas analysis is about 0.03 lower in venous blood pH, as observed in several studies, without relevant interferences in clinical interpretation (11).

Statistical analysis was carried out by description, paired *t* test and the Lin (rc) concordance correlation coefficient (12). This study was evaluated and approved by the Research Ethics Committee of our institution on May 11th, 2009 in report #110/2009 and protocol #3140/2009.

RESULTS

From the 53 patients evaluated, 58.5% (n = 31) were female and 41.5% (n = 22) were male. Mean age was of 31.3 ± 33.7 years old (ranging from 13 to 78 years old).

Mean pH was 7.11 ± 0.15 (6.77 to 7.30), with 20.8%, 51% and 28.2% of DKA cases classified as mild, moderate and severe, respectively. Mean serum glucose was 25.7 (or 463 mg/dL) ± 10.9 mmol/L (11.0 to 69.6 mmol/L), mean PBG was 3.66 ± 1.03 mmol/L (1.6 to 6.0 mmol/L), and mean LSP was 4.79 ± 0.87 mmol/L (3.0 to 7.1 mmol/L).

Mean difference between PBG and LSP was 1.13 ± 0.96 mmol/L ($p < 0.0005$, 95% CI, -1.39 to -0.86) in paired *t* test (Table 1). In 66% of patients, difference between LSP and PBG was greater than 0.5 mmol/L.

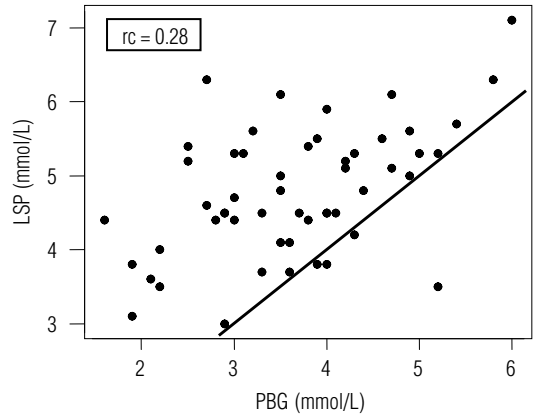
There was no statistically significant correlation between the difference of PBG and LSP means and pH quartile ($p = 0.213$) or serum glucose ($p = 0.475$).

Table 1. Means and difference in concentration between laboratory serum potassium and potassium assessed by blood gas analysis

	N	Mean (mmol/L)	SD	95% CI mean (mmol/L)	mean difference (mmol/L)	Difference 95%CI	P Value
LSP	53	4.79	0.87	3.0 to 7.1	-	-	-
PBG	53	3.66	1.03	1.6 to 6.0	-1.13	-1.39 to -0.86	P < 0.0005

LSP: laboratory serum potassium; PBG: potassium concentration determined by blood gas analysis; SD: standard deviation. 95% CI, 95% confidence interval.

Lin concordance correlation coefficient was rc = 0.28 (95% CIb, 0.10 to 0.45), demonstrating low concordance between methods (very mild to mild) (Figure 1).



LSP: laboratory serum potassium concentration; PBG: potassium concentration determined by blood gas analysis.

Figure 1. Lin's concordance correlation coefficient between laboratory serum potassium concentration and potassium evaluated by blood gas analysis.

DISCUSSION

Analysis of potassium concentration in initial care of patients with DKA is extremely important for the correct approach and treatment, to prevent hypokalemia and delay in the use of insulin in the beginning of therapy. In our study, 66% of the patients assessed presented differences between PBG and LSP greater than 0.5 mmol/L. From 53 patients studied, 17 (32% of the cases) had potassium in blood gas lower than 3.3 mmol/L. This represents a considerable number of patients that would not start insulin treatment immediately before intravenous potassium replacement.

In a pilot study published in 2003, Kelly and Middleton evaluated the difference between PBG and LSP samples of 43 patients, and found that the difference was greater than 0.5 mmol/L in 23% of them (13). In an important Australian study, Fu and cols., evaluated this difference in patients with DKA and asked 15 intensivists to mark on a form the clinically acceptable difference between potassium concentrations in different samples, in relation to a "true" potassium level. Answers ranged from 0.25 to 1.0 mmol/L, with an average of 0.5 mmol/L. They also carried out a retrospective analysis of records of DKA patients whose potassium concentration was determined both by blood gas analysis and serum measurement, and found out that 80% of samples had a difference within the maximum clinically acceptable difference predefined by them (14). In another recent study, José and Preller asked 64 physicians to evaluate the results of 529 pairs of samples of arterial blood gas analysis and serum potassium of 121 critical patients with any condition, and concluded that 51.6% of these physicians would wait for laboratorial serum potassium results to make any clinical decision, while 48.4% would accept potassium measurement determined by blood gas analysis (10).

The reasons for these disparities in the samples analyzed by PBG and LSP are still unknown and raise doubts on the actual validity of PBG measurement in the initial care of DKA patients. However, it is known that the potenciometric (or ion-selective electrode) LSP evaluation widely used in the world also has some limitations. In a Canadian study, Haag and cols. evaluated the accuracy of 9,279 serum potassium measurements in 503 laboratories, having flame atomic emission spectrophotometry as the reference method for potassium measurement. They found out that 45.9% of these laboratories presented statistically significant variations in their results (15).

The International Consensus on the standardization of sodium and potassium measurements by ion-selective electrodes in undiluted samples, recommends that methodologies used should be evaluated in comparison with flame atomic emission spectrophotometry when the sample has normal concentrations of protein, lipids and other macromolecules, so that the electrodes have a normal coefficient of activity (16).

Errors observed in the potentiometric methods fall in one of two categories. One includes obvious errors caused by lack of selectivity, proteins, lining, ion-sensitive membrane, or contamination of the membrane by ions that compete or react with the selected ion, changing the response to this effect (mass effect). The second category, the solvent exclusion effect, is mainly applied to indirect methods. The errors in this category are mainly due to extreme lipid and protein concentrations in the sample. Except in cases of extreme hypoproteinemia or hyperproteinemia and hyperlipidemia, electrolyte concentrations in whole plasma are reliably parallel to plasmatic water, where electrolytes play their special physiological roles. The magnitude of the error is less than 5% when triglyceride concentration is lower than 28.3 mmol/L (2,500 mg/dL) (17).

Patients with DM have increased incidence of hypertriglyceridemia (18), especially in DKA (19), what may contribute to mass effect and increase disparity between samples analyzed by PBG and LSP. However, lack of data prevented the evaluation of this parameter in our study.

In the study of Fu and cols., there was positive correlation between serum glucose and the difference between PBG and LSP (p = 0.0033) (14), a fact that was not observed in our study, maybe because of the lower mean blood glucose (25.7 mmol/L against 29.5 mmol/L). Besides, we included a patient who differed from the studied population for presenting blood glucose of 69.6 mmol/L (1,253 mg/dL), increasing our mean blood glucose. Only 34% of our samples had blood glucose greater than 27.8 mmol/L (500 mg/dL) at the admission of the DKA patient.

Other factors that may interfere in serum potassium concentration are: type of sample, between whole blood or serum that underwent hemolysis (potassium released from ruptured platelets in the clotting process); muscular activity before venous pucture (potassium may increase from 10% to 20% if the patient opens and closes his/her hands before blood collection (17); extreme thrombocytosis and leukocytosis (20); and lower temperature of whole blood sample before separation, increasing potassium concentration in the serum (17,21,22).

This study is the first in the literature to evaluate difference in potassium concentration between PBG and LSP exclusively in venous blood collected upon admission of DKA patients. New, prospective studies are necessary, with appropriate design to compare results and clarify possible factors influencing the disparity between potentiometric methods. It is clear that these results require further evaluation in other services in order to contribute for the improvement of DKA treatment, from the moment blood is collected to the final result of the treatment.

In conclusion, a weak concordance correlation coefficient was demonstrated between potassium concentrations measured by blood gas analysis (PBG) and laboratory serum potassium (LSP), in the initial assessment of DKA. Although it is technically faster and easier, PBG should not be used as surrogate for LPS in the management of these patients.

Disclosure: no potential conflict of interest relevant to this article was reported.

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