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FACTORS CONTRIBUTING TO ALTERATIONS IN THE LEVEL OF CONSCIOUSNESS IN PATIENTS WITH DIABETIC KETOACIDOSIS: ANALYSIS OF 189 CASES

GHOLAMREZA PISHDAD* AND AHMAD ALAVIAN GHAVANINI**

From the Department of Internal Medicine, Shiraz University of Medical Sciences, Shiraz, I.R. Iran.

ABSTRACT

The relation between serum osmolality, glucose, sodium, bicarbonate, arterial pH, BUN and level of consciousness was studied in 189 patients with diabetic ketoacidosis (DKA). There was much overlap between all laboratory values among various groups, even when there was a statistically significant difference. To find a better predictor, we defined a new factor as serum osmolality/arterial pH. This factor was significantly higher in drowsy and stuporous compared with alert and drowsy patients (p= 0.007 and p= 0.03 respectively), but not different between stuporous and comatose patients (p= 0.46). Again much overlap could be seen between groups. There was at least one other problem, either as a coexisting or a precipitating factor, in 18 (23.3%) of the alert, 24 (29.2%) of the drowsy, 11 (43.4%) of the stuporous and 4 (57.1%) of the comatose group. We conclude that none of these clinico-biochemical parameters can be a reliable predictor of the level of consciousness in patients with DKA, and consideration and exclusion of other conditions associated with altered consciousness that may occur in diabetics should be routine.

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Keywords: Diabetic ketoacidosis, Serum osmolality, Arterial pH, Level of consciousness.

INTRODUCTION

Level of consciousness is frequently altered, more or less, in patients with diabetic ketoacidosis (DKA). This frequency differs among various observations from 26 to 62 percent.[7,12,15] While only about 5% present with coma,[3,7,12,15] subclinical brain dysfunction is reported to occur commonly in patients with DKA and no obvious clinical manifestation.[6]

Correspondence: A.A. Ghavanini, Nemazee Hospital, Shiraz, 71935, Iran.
Tel: +98 71 662728,
E-mail: alavianm@sums.ac. ir.

*Associate Professor, Endocrinology Group, Department of Internal Medicine, Shiraz University of Medical Sciences, Shiraz, I.R. Iran.
**Intern, School of Medicine, Shiraz University of Medical Sciences, Shiraz, I.R. Iran.

Cerebral swelling, often fatal if symptomatic, is usually present before treatment.[10]

Many factors, especially the serum osmolality,[7, 12] are considered to influence the level of consciousness in these patients, but there is no exact predictor for this neurologic manifestation of DKA. The need for such a predictor is emphasized considering the fact that many other conditions associated with altered consciousness may occur in diabetics and should be excluded in patients with DKA. In these regards, we studied the relationship between serum osmolality, glucose, sodium, bicarbonate, arterial pH, BUN and level of consciousness in patients with DKA.

MATERIALS AND METHODS

205 of the patients who were admitted with an impression of DKA in Shiraz Nemazee and Faghihi Hospitals from 1986 till 1996 were randomly selected. Considering serum glucose>250 mg/dL, arterial blood pH<7.30, HCO_3^-<15 and positive acetoacetest at 1:2 serum dilution as the criteria for DKA, 16 patients were excluded.

Level of consciousness on admission for each patient was extracted and classified as alert, drowsy, stuporous, and comatose. Alertness was defined as being awake and fully responsive to stimuli. Patients reported to have a Glasgow Coma Score (GCS) of 15 were considered alert. Drowsiness was defined as light sleep from which the patient can be easily aroused by touch or noise and can maintain alertness for some time. Patients reported to be confused or have a GCS of 12-14 were also considered drowsy. Stupor was defined as a state in which the patient can be awakened only by vigorous stimuli. Patients reported to be obtunded or have a GCS of 9-11 were classified as stuporous. Coma was defined as a state from which the patient can not be aroused by stimulation. A GCS of 8 or less was considered equivalent to coma.[14, 16]

Serum osmolality on admission was calculated as:

$2 \times (Na^+ + K^+)(mEq/L) + glucose\ (mg/dL)/18 + BUN\ (mg/dL)/2.8$

ANOVA was used to evaluate the association between level of consciousness and each factor. A two-tailed *t*-test (homoscedastic or heteroscedastic, based on the result of *F*-test) was used to statistically evaluate the significance of differences between mean values of each factor for each group. Kendall tau-b correlation coefficient was calculated as a measure of association between level of consciousness and other factors.

RESULTS

The distribution of level of consciousness was 77 (40.7%) alert, 82 (43.4%) drowsy, 23 (12.2%) stuporous, and 7 (3.7%) comatose. The mean, standard deviation (SD), maximum and minimum values for each factor are summarized in Table I.

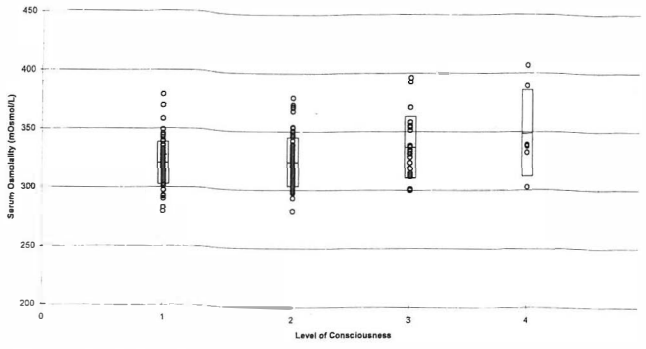

Fig. 1. Relation between level of consciousness and serum osmolality in 189 patients with DKA [1=A
3=

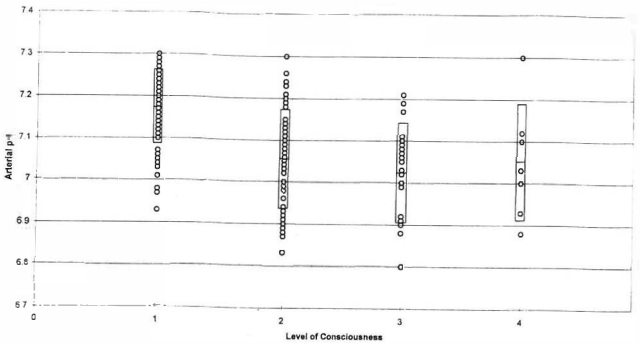

Fig. 2. Relation between level of consciousness and arterial pH in 189 patients with DKA [1=Alert, 2=
4=Comatose].

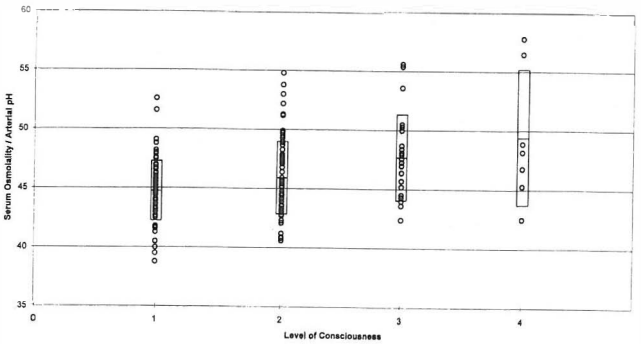

Fig. 3. Relation between level of consciousness and serum osmolality/arterial pH in 189 patients with DKA [1=Alert, 2=

Level of consciousness was significantly associated with serum osmolality (p<0.001 using ANOVA). The correlation coefficient was -0.15 (p= 0.006). However, the difference between serum osmolalities of alert and drowsy patients was not significant (p= 0.24). This was significant when comparing drowsy with stuporous patients (p= 0.03), but not for stuporous and comatose patients (p=0.44). There

Table I. Average, standard deviations, minimum and maximum values of some laboratory findings in 189 patients with DKA.

Level of Consciousness	Osmolality (mosm/kg) Mean ±SD Min.-Max.	Glucose (mg/dL) Mean ±SD Min.-Max.	Na^+ (mEq/L) Mean ±SD Min.-Max.	pH Mean ±SD Min.-Max.	HCO_3^- (mEq/L) Mean ±SD Min.-Max.
Alert	321±17 280-379	576±211 250-1430	135±5 120-148	7.17±0.08 6.93-7.30	7.87±3.6 1.9-15
Drowsy	324±20 282-379	648±281 263-1800	134±6 119-148	7.05±0.11* 6.83-7.30	4.99±3.5+ 1.4-15
Stuporous	337±26++ 300-396	715±266 400-1400	138±7§ 121-148	7.02±0.11 6.80-7.21	4.40±3.4 1.1-14.2
Comatose	349±36 303-407	742±283 400-1170	141±10 127-160	7.05±0.13 6.88-7.30	4.51±4.4 1.5-14.5
Total	325±21 280-407	630±256 250-1800	135±6 119-160	7.10±0.12 6.80-7.30	6.08±3.9 1.1-15

* Significantly lower than alert group ($p<0.001$).
\+ Significantly lower than alert group ($p<0.001$).
++ Significantly higher than drowsy group ($p<0.003$).
§ Significantly higher than drowsy group ($p<0.003$).

was much overlap between serum osmolalities of different groups as shown in Fig. 1.

The association between level of consciousness and arterial pH was also significant ($p<0.001$ using ANOVA). The correlation coefficient was 0.39 ($p<0.001$). The difference between arterial pH of alert and drowsy patients was significant ($p<0.001$). This was not significant when comparing drowsy with stuporous and stuporous with comatose groups ($p=0.26$ and $p=0.60$, respectively). Again, much overlap could be seen between groups (Fig. 2).

Serum Na^+ was significantly higher in stuporous patients than in drowsy patients ($p=0.03$), but didn't differ among alert and drowsy ($p=0.19$), and stuporous and comatose patients ($p=0.48$). Serum bicarbonate level in the drowsy group was significantly different from the alert group ($p<0.001$), but not from the stuporous group ($p=0.47$). This difference was also not significant between stuporous and comatose patients ($p=0.95$), in fact being statistically equal.

Other laboratory values were not significantly different between groups. There was much overlap between all laboratory values of various groups, even when there was a statistically significant difference.

To find a better predictor, we defined a new factor as serum osmolality/arterial pH. Level of consciousness was significantly associated with this factor ($p<0.001$ using ANOVA). The correlation coefficient was -0.23 ($p<0.001$). This factor was significantly higher in drowsy and stuporous comparing with alert and drowsy patients ($p=0.007$ and $p=0.03$, respectively), but not different between stuporous and comatose patients ($p=0.46$). Although to a lesser degree than the other factors, much overlap could be seen between groups here too. The relation between level of consciousness and serum osmolality/arterial pH is shown in Fig. 3.

There was at least one other problem, either as a coexisting or a precipitating factor, in 57(30.1%) of our patients. Renal failure 24 (42.1%), urinary tract infections 13 (22.8%), pneumonia 7 (12.2%), and septicemia 4 (7%) were the more common problems. Other findings were sinusitis, pharyngitis, diabetic foot, meningitis, mediastinitis, neck abscess, septic arthritis, shigellosis, hydatid cyst of the lung, post-infarction heart failure, pericardial effusion, thalassemia major, and hemolysis due to G6PD deficiency. These problems were present in 18 (23.3%) of the alert, 24 (29.2%) of the drowsy, 11 (43.4%) of the stuporous, and 4 (57.1%) of the comatose group. Exclusion of these patients didn't influence the significance of differences between laboratory findings of various groups.

DISCUSSION

While some authors believe that the degree of consciousness does not always correlate with the degree of clinico-biochemical manifestations of DKA,[3] others have found a relation between level of consciousness and many other factors. Serum osmolality,[7,11,12] serum concentration

of glucose,[7] ketone bodies,[5] bicarbonate,[11] sodium,[1,8] blood hydrogen ion concentration,[15] CSF pH,[13] and CSF concentration of ketone bodies,[2] are some of these factors. Phosphate replacement during treatment of DKA has been associated with improved mental status,[4] but no relation between level of consciousness and serum phosphate concentration has been shown.

There are studies that show blood glucose concentration is not significantly different in unconscious and conscious DKA patients,[11] along with studies that find a correlation between plasma glucose and the state of consciousness.[7] Moreover, hyperglycemia is more severe if the oxidation of fuels is compromised in the brain by coma.[11] In our study, no significant association between level of consciousness and serum glucose was found.

Serum osmolality has been found to be significantly higher in unconscious rather than conscious patients with DKA or nonketotic hyperglycemia.[1,8,11] It has been shown that hyperosmolality impairs function of both central and peripheral nervous system structures.[17,19] Fulop et al. found that altered sensorium correlates best with the magnitude of hyperosmolality, and serious alterations in sensorium with serum osmolality<340 mosm/kg should suggest etiologies other than DKA.[7] In a study by Kitabchi et al., calculated total osmolality correlated inversely with mental status, with stupor and coma typically seen with osmolalities of greater than 340 mosm/kg.[12] They suggested that when a patient with a plasma osmolality of 340 mosm/kg or less is severely obtunded or comatose, another catastrophic event rather than DKA must be present. Tachibana et al. believe that plasma osmolality between 320 and 350 mosm/kg primarily causes suppression of the pyramidal pathway, plasma osmolality exceeding 380 mosm/kg suppresses the extrapyramidal pathway, and values above 440 mosm/kg cause severe suppression of both efferent pathways.[17,18,19] In this study, although stuporous patients had a significantly higher serum osmolality than drowsy patients (p=0.03), this was not true for the other groups and the correlation was not strong (correlation coefficient= -0.15). All of our comatose patients and all except one of the stuporous patients had a serum osmolality greater than 300 mosm/kg, but only 2 (28.5%) of the comatose and 7 (30.4%) of the stuporous patients had a serum osmolality of greater than 340 mosm/kg. No other cause was found in two of the comatose and nine of the stuporous patients with serum osmolality less than 340 mosm/kg. In contrast, another cause was found in one of the comatose and 3 of the stuporous patients with serum osmolality greater than 340 mosm/kg. Sixteen of the drowsy and 9 of the alert patients had a serum osmolality of greater than 340 mosm/kg.

Posner and colleagues found that mental confusion and coma occur when the pH of CSF falls below 7.15.[13] However, despite Rosival's observation that the level of consciousness in patients with DKA correlates well with blood hydrogen ion concentration,[15] Assal et al. showed that neurological impairment in diabetic ketoacidosis is associated with normal CSF pH and with bicarbonate replacement, a progressive CSF acidosis develops despite definite neurological improvement.[2] Other workers have found no correlation between blood pH and level of consciousness in DKA patients.[7,11] Acidosis per se probably is not an important cause of coma since acidosis produced by infusion of hydrochloric acid does not cause coma at an arterial pH similar to that which produces coma when acetoacetic acid is infused.[9] Although the strongest, the relation was very weak in our patients. In fact, we had a comatose patient with a pH of 7.30.

Level of consciousness was significantly associated with the osmolality/pH ratio, and there was less overlap between groups than the other factors. However, with a weak correlation coefficient and much overlap between the groups, the osmolality/pH ratio was also not a good predictor for level of consciousness.

We conclude that none of these clinico-biochemical parameters can be a reliable predictor for level of consciousness in patients with DKA, and consideration and exclusion of other conditions associated with altered consciousness that may occur in diabetics should be routine.

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