Diagnostic Accuracy of Point-of-Care Testing for Diabetic Ketoacidosis at Emergency-Department Triage

β-Hydroxybutyrate versus the urine dipstick

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OBJECTIVE—In the emergency department, hyperglycemic patients are screened for diabetic ketoacidosis (DKA) via a urine dipstick. In this prospective study, we compared the test characteristics of point-of-care β-hydroxybutyrate (β-OHB) analysis with the urine dipstick.

RESEARCH DESIGN AND METHODS—Emergency-department patients with blood glucose ≥250 mg/dL had urine dipstick, chemistry panel, venous blood gas, and capillary β-OHB measurements. DKA was diagnosed according to American Diabetes Association criteria.

RESULTS—Of 516 hyperglycemic subjects, 54 had DKA. The urine dipstick had a sensitivity of 98.1% (95% CI 90.1–100), a specificity of 35.1% (30.7–39.6), a positive predictive value of 15% (11.5–19.2), and a negative predictive value of 99.4% (96.6–100) for DKA. Using the manufacturer-suggested cutoff of >1.5 mmol/L, β-OHB had a sensitivity of 98.1% (90.1–100), a specificity of 78.6% (74.5–82.2), a positive predictive value of 34.9% (27.3–43), and a negative predictive value of 99.7% (98.5–100) for DKA.

CONCLUSIONS—Point-of-care β-OHB and the urine dipstick are equally sensitive for detecting DKA (98.1%). However, β-OHB is more specific (78.6 vs. 35.1%), offering the potential to significantly reduce unnecessary DKA work-ups among hyperglycemic patients in the emergency department.

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Rapid and accurate identification of patients with diabetic ketoacidosis (DKA) is critical but is complicated by the fact that DKA only affects a small percentage of the total number of patients with hyperglycemia (1,2). Current clinical practice in the emergency department is to screen hyperglycemic patients with a urine dipstick for ketones and conduct a laboratory evaluation for DKA on patients whose results screen positive (3). Although the urine dipstick is easily accessible, inexpensive, rapid, and has excellent sensitivity for DKA, its poor specificity (estimated at <50%) results in a large number of false-positive tests and unnecessary work-ups (4). This has led the American Diabetes Association (ADA) to discourage using the urine dipstick and encourage using serum ketones for DKA screening (5). The development of point-of-care β-hydroxybutyrate (β-OHB) devices has made following these ADA recommendations feasible in the emergency department (6). The goal of this prospective study was to compare the test characteristics of a point-of-care β-OHB meter with the urine dipstick for screening for DKA at emergency-department triage.

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RESEARCH DESIGN AND METHODS

Setting

This prospective, observational study was conducted at a large, urban emergency department. Institutional review board approval was obtained, and study participants provided written informed consent. The cohort studied represents a convenience sample of emergency-department patients with triage capillary blood glucose ≥250 mg/dL enrolled on 320 individual days over a 2-year period based on research-assistant availability. Subjects were excluded if they were *1*) critically ill, *2*) in police custody, *3*) suffering from acute psychosis, or *4*) unable to give informed consent.

Study procedures and data collection

Included patients had a urine dipstick (Siemens Multistix 10SG) for ketones (recorded as positive or negative), a serum chemistry panel, a venous blood gas to determine serum pH, and a point-of-care capillary β-OHB measurement (Precision Xtra meter; Medisense/Abbott Laboratories). DKA was defined according to the following ADA criteria: serum glucose ≥250 mg/dL; anion gap >10 mmol/L; carbon dioxide ≤18 mmol/L; and pH ≤7.30 (7). Subjects' race, ethnicity, age, sex, previous history of diabetes, and insulin use were recorded.

Sample size considerations

On the basis of previous literature, we assumed that the true sensitivity of β-OHB for detecting DKA was between 98 and 100% and determined that a sample including 54 cases of DKA would confirm this point estimate with a confidence limit no lower than 90% (8–12). The study was stopped after the 54th DKA patient was enrolled.

Statistical analysis

Data were analyzed using Stata version 10.0 (StataCorp, College Station, TX). Diagnostic test characteristics with 95%

CIs were calculated. According to the manufacturer's guidelines, point-of-care β-OHB ≤1.5 mmol/L was considered negative and >1.5 mmol/L was considered positive. The difference in specificity for β-OHB and urine dipstick ketones was assessed using the McNemar test with a Yates correction (13). We explored the optimal capillary β-OHB cutoff by creating a receiver-operator curve and analyzing diagnostic test characteristics at various cutoffs.

RESULTS

Participants

A total of 859 patients were screened, 616 provided informed consent, and 516 (83.7%) had all data elements necessary for data analysis (excluded patients: 49 with no urine dipstick, 30 with no serum pH via venous blood gas, and 21 with no serum chemistry panel). In our final sample, 54 of 516 subjects (10.5%) met the ADA criteria for DKA. See Table 1 for sample characteristics.

Table 1—*Demographic and laboratory characteristics of the study sample*

	DKA	No DKA
n (%)	54 (10.5)	462 (89.5)
Age (years)	41 (30–48)	48 (40–57)
Female (%)	27.8	35.3
Race/ethnicity (%)		
Non-Hispanic white	0	3.1
African American	16.7	13.6
Hispanic	79.2	80.2
Asian	4.2	2.6
Other	0.5	0
Admitted (%)	95.2	35.9
Newly diagnosed diabetes (%)	25.9	14.6
Insulin treated (%)	56.6	44.5
Venous pH	7.19 (7.10–7.25)	7.39 (7.36–7.41)
β-OHB (mmol/L)	0.3 (0.2–1.2)	4.9 (3.7–5.6)
HCO_3 (mmol/L)	8 (6–11)	23 (21–26)
Glucose (mg/dL)	678 (448–955)	409 (328–409)
Anion gap (mmol/L)	29 (26–34)	13 (11–17)
Positive urine dipstick ketones (%)	98.1	64.9

Data are median (interquartile range), unless otherwise indicated.

Diagnostic accuracy

At the manufacturer-suggested cutoff of >1.5 mmol/L, the sensitivity of capillary β-OHB and the urine dipstick for DKA were identical at 98.1% (95% CI 90.1–100). However, the specificity of β-OHB was significantly higher than that of the urine dipstick (78.6 [74.5–82.2] vs. 35.1% [30.7–39.6]; $P < 0.01$). Positive and negative predictive values of capillary β-OHB were 34.9 (27.3–43) and 99.7% (98.5–100), respectively. Positive and negative predictive values of the urine dipstick were 15 (11.5–19.2) and 99.4% (96.6–100), respectively. Test characteristics of β-OHB were stable across a wide range of potential cutoffs (Table 1). The receiver-operator curve suggested that the optimal β-OHB cutoff is >2 mmol/L, where sensitivity remains at 98.1% but specificity improves to 82.3% (Supplementary Data).

CONCLUSIONS—Approximately one-fourth of emergency-department patients have diabetes, and almost half have poor glycemic control (2). Common clinical emergency-department practice is to consider the diagnosis of DKA in all patients presenting with blood glucose ≥250 mg/dL regardless of the reason for the visit. Because emergency-department overcrowding has stretched resources to the breaking point, there is increasing emphasis on developing, testing, and using the most rapid, accurate, and easy-to-use DKA screening tool available. The results of this study show that the specificity of capillary point-of-care β-OHB is superior to the urine dipstick.

Two retrospective emergency-department studies have shown that capillary point-of-care β-OHB is 100% sensitive for DKA (8,9). Charles et al. (10) likewise found that β-OHB was 100% sensitive in a prospective study of seven DKA patients. Naunheim et al. (11) reported a β-OHB sensitivity for DKA of 98% in a prospective sample of 160 patients (57 with DKA). Our study is the first to prospectively compare the test characteristics of point-of-care β-OHB against the urine dipstick in a cohort of emergency-department patients. Using β-OHB in lieu of the urine dipstick to screen our sample could have reduced full laboratory work-ups for DKA by 56.9%.

Our study has several limitations. First, we did not provide specific training to the nurses who interpreted the urine dipsticks. We felt this was unnecessary because they *1*) are Clinical Laboratory Improvement Amendment certified, *2*) are familiar and comfortable with this process, and *3*) do so regularly in routine clinical practice. Second, the urine dipstick was considered only negative or positive, and consideration of trace/small ketones versus moderate/large ketones may impact the findings. Third, we did not send blood samples to the laboratory for an enzymatic analysis to correlate the values measured by the point-of-care β-OHB meter because, despite early concerns, current-generation β-OHB meters have been shown to be highly accurate compared with laboratory enzymatic analysis (6,14). Fourth, although there are many ways to define DKA, we chose to use the ADA definition because this is commonly used in DKA literature, allowing for direct comparison between our results and previous reports.

In conclusion, point-of-care capillary β-OHB testing at a cutoff of >1.5 mmol/L was equally sensitive (98.1%) but markedly more specific (78.6 vs. 35.1%) than the urine dipstick for the detection of DKA in our prospective sample of emergency-department patients with hyperglycemia. Utilizing point-of-care β-OHB testing has the potential to substantially reduce comprehensive laboratory evaluations for DKA among hyperglycemic emergency-department patients.

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The authors alone had sole control of study design, data collection and analysis, and dissemination of findings. S.A. conceived of the project, helped design the study, and contributed to the writing and revising of the manuscript. S.O.H. helped design the study and assisted with collection of data. T.L. collected

and organized data and participated in the writing of the manuscript. M.M. helped design the study, performed all statistical analyses, and helped write and revise the manuscript.

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