Clinical Effectiveness of ß-hydroxybutyrate Assays in a Clinical Decision Unit
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One of the major consequences of diabetes Mellitus is the development of hyperglycemia with associated ketoacidosis and diabetic coma. Ketoacidosis may also result from malnutrition or alcoholism. Of the three ketone bodies, ß-hydroxybutyrate (BOHB) is present in the greatest concentration. It accounts for 75-78% of the ketone bodies which also include acetoacetate and acetone.[1]

For years, ketoacidosis was diagnosed and monitored in urine and/or serum with nitroprusside-based tests more commonly known as Ketostix or Acetest. The nitroprusside-based tests measure only acetoacetate and to a lesser extent acetone but do not detect ß-hydroxybutyrate. During periods of ketosis BOHB increases even more than acetoacetate. Thus the nitroprusside test is insensitive for detecting the early stages of ketoacidosis.

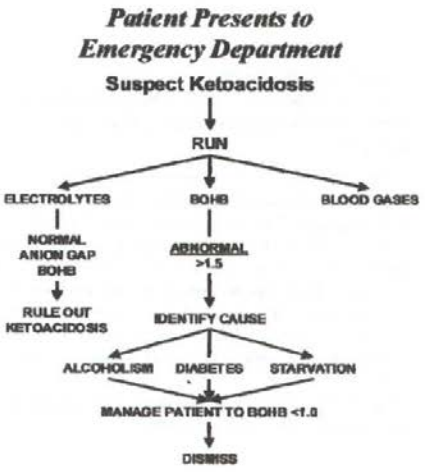
There are a number of other shortcomings related to the nitroprusside test. In cases of DKA with severe complications such as lactic acidosis, the equilibrium of BOHB-acetoacetate is strongly shifted towards BOHB away from acetoacetate. In such instances, the nitroprusside test may be negative or only weakly positive even though ketoacidosis is severe. As ketosis improves BOHB converts to acetoacetate causing a false indication by the nitroprusside tests that ketosis is increasing. Several reports conclude that the use of the Acetest may be misleading and should be avoided because the fall of acetoacetate lags behind the resolution of ketoacidosis. A study by Umpierrez et al points out that all patients with BOHB levels of 1.1 mM or less had resolved their ketosis. In contrast, 8 of 15 patients in whom ketosis had been resolved by acid-base parameters and BOHB levels still had positive serum Acetest results.[2] Studies in our Laboratory at Henry Ford Hospital demonstrated that at BOHB levels of 1.0-1.5mM with resolution of ketosis the Acetest procedure still gave positive results when diluted 1:8 and even 1:16 in several cases. In addition, Casko has pointed out that drugs containing sulfhydryl groups cause false positive results with the nitroprusside tests. [3,4]

Other recent publications state that the BOHB assay is a valuable parameter in the assessment of ketoacidosis.1 The American Diabetes Association, in their "Position Statement on Tests of Glycemia in Diabetes" states that "...healthcare professionals should be aware, however, that currently available urine ketone tests are not reliable for diagnosing or monitoring treatment of ketoacidosis.[1] Blood ketone methods that quantify BOHB, the predominant ketone body, are now available. These may offer a useful alternative to urine ketone testing because BOHB determinations are reliable for diagnosing and monitoring treatment of ketoacidosis."[5] Gibson et al suggest that KetoSite has the potential to provide early and accurate diagnosis of ketonemia and the ability to follow progress in clinical settings more effectively.[6] KetoSite provides quantitative results while Acetest provides semi-quantitative data that does not allow linear tracking of ketone levels over time.

We have been using KetoSite at Henry Ford Hospital for almost four years. We no longer perform the Acetest procedure for the diagnosis and treatment of ketoacidosis and have incorporated the KetoSite assay into our Clinical Decision Unit pathway for ketoacidosis.

This has resulted in several improvements in clinical outcomes:

- Improved turn around times for ketone testing was the first significant improvement noted. In cases of severe ketoacidosis, many dilutions had to be made with Acetest to obtain a reportable result. In some cases dilutions of 1:128 had to be made to get a negative result. In addition, with other important testing (electrolytes, enzymes, etc.) also being performed, it could sometimes take two hours to get ketone results to the emergency room physician. With KetoSite's ease of use and the elimination of dilutions, results are easily back to the physician within 45 minutes. Furthermore, the use of an instrument eliminates the subjectivity of results that is inherent with the visual interpretation of the Acetest



- The second significant improvement is a reduction in laboratory testing in patients with ketoacidosis (diabetes, alcoholism, or starvation). On average a patient presenting with suspected ketoacidosis would have blood drawn four to five times during an episode for a Chemistry 7 (electrolytes, BUN, Creatinine, and glucose) and blood gases. Since the introduction of KetoSite as a replacement for the Acetest only one or two complete sets of chemistry tests are preformed. Upon patient presentation, BOHB, Chemistry 7 (electrolytes), and blood gases are obtained. If the BOHB and anion gap are normal no further testing is required and the patient can be counseled and discharged. If the BOHB is abnormal, the patient will be monitored with serial KetoSite assays until resolution of ketosis is demonstrated by reduction of BOHB to levels below 1.5mM. Potassium may be monitored as necessary. When resolution of ketoacidosis is indicated, a final Chemistry 7 panel and/or blood gases may be requested.

  In the Henry Ford System approximately 150 patients with diagnosed ketoacidosis are seen each year. The use of KetoSite has resulted in a savings in laboratory cost of $90.00 per episode. On a yearly basis this represents over $13,000/year in savings. This alone more than justifies the modest increase in cost of KetoSite over Acetest. Physicians spend less time tracing laboratory data and patients are subjected to fewer venipunctures. Furthermore, when the possibility of ketoacidosis can be clearly ruled out in the very beginning, the total financial and patient benefits are enormous.

- The third, and most important, outcome improvement is a significant reduction in the time that the patients spend in the Clinical Decision Unit. Ketones have been the criteria by which ketoacidosis was considered to have resolved. As stated earlier in this paper, BOHB is more reliable and accurate for indicating resolution of ketoacidosis. Furthermore, it demonstrates resolution much sooner than Acetest. In our experience patients can be discharged from the CDU as much as three to six hours earlier than when Acetest was used for the assessment of ketoacidosis.

- In addition, KetoSite has been particularly useful in the assessment of alcoholic ketoacidosis, due to the equilibrium shift of ketones toward BOHB upon presentation to the Emergency Department. High BOHB levels without high levels of glucose indicate that the ketosis is due to intake of alcohol or starvation. [7]

In summary, we have found KetoSite to be far more efficient in the diagnosis and management of ketoacidosis than semiquantitative assessment of acetoacetate. It has resulted in quicker diagnosis and more efficient monitoring of patients with ketoacidosis. The bottom line has been improved utilization of hospital emergency room facilities and staff as well as improved outcomes for patient care.

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