method as the glucose reference method.

We in the scientific community (authors, reviewers, associations) have a responsibility to readers of our journal to ensure accuracy in the reporting of scientific information. We certainly should exercise caution in referring to routine methods as reference methods when they have not been characterized and validated by the rigorous process endorsed by the Association's Standards Committee and other professional organizations.

References

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Increased Fractional Excretion of Sodium in Prerenal Azotemia: Need for Careful Interpretation

To the Editor:
The fractional excretion of sodium (FE\textsubscript{Na}) reportedly clearly differentiates prerenal azotemia from acute tubular necrosis (1, 2). The FE\textsubscript{Na}, calculated as (urinary sodium × serum creatinine)/(serum sodium × urinary creatinine), measures renal tubular reabsorption of sodium ion. It is <1 in prerenal azotemia and >1 in acute tubular necrosis (2). Its greatest value is its suggested use in distinguishing acute renal failure secondary to the above pathophysiological mechanisms. Here, I describe a case of prerenal azotemia in whom the FE\textsubscript{Na} was increased because of the increased urinary sodium excretion accompanying concomitant bicarbonate losses, a mechanism of sodium loss that differs totally from that seen in acute tubular necrosis.

A 45-year-old man with known alcohol-induced liver disease was brought into the Emergency Room because of persistent vomiting. His pulse rate was 90/min, his blood pressure 100/80 mmHg. His tongue was dry and skin turgor was decreased. When the patient stood up, his pulse increased to 120/min and his blood pressure decreased to 80/40 mmHg. His neck veins were not visible. Urine output was markedly subnormal. Physical examination showed no other abnormalities.

Clinical chemical values for serum at the time of admission were: sodium 122 mmol/L, potassium 2.7 mmol/L, chloride 55 mmol/L, total carbon dioxide 49 mmol/L, serum urea nitrogen 530 mg/dL, and creatinine 70 mg/L.

Arterial blood measurements showed a pH of 7.59, p\textsubscript{CO\textsubscript{2}} of 55 mmHg, p\textsubscript{O\textsubscript{2}} of 55 mmHg and bicarbonate of 82 mmol/L. Serum enzyme activities were: creatine kinase 2880 U/L (normal 20–165), lactate dehydrogenase 408 U/L (normal 90–210), and aspartate aminotransferase 99 U/L (normal 5–35).

Serum protein electrophoresis showed an albumin concentration of 26 g/L (normal 35–50) and a polyclonal increase in gamma-globulin of 19 g/L (normal 7–16), a pattern consistent with liver disease.

Measurements on urine included: pH 7.90, sodium 50 mmol/L, and creatinine 1.21 g/L. Chloride was not detectable.

The calculated FE\textsubscript{Na} was 2.4. The "renal-failure index" (urinary sodium × serum creatinine/urinary creatinine) was 2.9.

The patient’s renal function markedly improved after treatment with isotonic saline. Figure 1 shows the changes in serum urea nitrogen and creatinine.

The above case demonstrates the need for especially careful interpretation, in certain circumstances, of the FE\textsubscript{Na} and other derived indices of renal function such as the renal failure index. A urinary sodium concentration of 50 mmol/L is atypical for prerenal azotemia. In the case of a dehydrated individual, the urine sodium would be expected to be <10 mmol/L (3). Under certain circumstances, especially when vomiting is severe, the concentration of serum bicarbonate exceeds the bicarbonate reabsorption capacity of the renal tubule. Thus the sodium ion that is not reabsorbed will be excreted into the urine with the bicarbonate, resulting in an alkaline urine (4). The capacity to reabsorb chloride ion is maintained, which explains the absence of chloride from the urine of this patient.

Therefore, when considering current laboratory criteria for the diagnosis of acute renal failure, it is conceivable that prerenal azotemia associated with severe metabolic alkalosis, as occurs with vomiting, laxative abuse, and chloride-losing diarrhea, may be confused with acute tubular necrosis. Although the factors responsible for the transition of prerenal azotemia to acute tubular necrosis are not well understood, therapeutic intervention clearly is effective in preventing the progression of prerenal azotemia to oliguric renal failure, but is ineffective once the latter is established (5). The patient discussed above most likely had uncomplicated prerenal azotemia, judging from the response of his serum urea nitrogen and creatinine to fluid replacement. Part of the contribution to the markedly elevated creatinine could be due to muscle damage (6). However, others have shown that muscle breakdown does not contribute to an increase in serum creatinine (7). The relatively low serum urea nitrogen/creatinine ratio of 7.6 (normal = 10–20) seen at admission may have been due to a combination of liver disease and a poor nutritional state (6).

In conclusion, in severe metabolic alkalosis the FE\textsubscript{Na} may not clearly distinguish prerenal azotemia from acute tubular necrosis.

References

Fig. 1. Chronological changes in serum urea nitrogen and serum creatinine
Interference by Fluorescein with the Single End-Point Determination of Creatinine by Use of the Jaffé Reaction

To the Editor:

We describe an example of fluorescein interference with determination of creatinine on an SMA-II continuous-flow analyzer. No other analyte measured on the SMA-II was affected. Measurement of creatinine by a Beckman Creatinine Analyzer 2 was unaffected by the presence of fluorescein.

Fluorescein, a xanthene dye, is one of the most strongly fluorescent compounds yet synthesized. Its disodium salt is known as uranium and is water soluble (1).

Fluorescein is used both topically and parenterally in ophthalmology (2). In the latter context, fluorescein is used as an agent in retinal angiography to detect and assess vascular changes encountered in various diseases (3, 4). For this, a bolus dose of fluorescein solution is injected into an arm vein, with subsequent dispersal throughout the body. Serial photographs are taken of the fluorescence occurring in the fundus of the eye (3, 4).

Although fluorescein is retained in various degrees by different tissues, most of the dye is excreted hepatorenally within 12 h (5) or 24 to 36 h (6).

Case history. D.M., a 22-year-old female diabetic, underwent retinal angiography to determine the presence and severity of diabetic retinopathy. The dose given was 5 mL of a 250 g/L solution of disodium fluorescein. The physician then requested an SMA-II profile, which was performed according to the supplier’s protocol.

In the context of the other results, we believed the creatinine result (291 μmol/L; reference interval 70-120 μmol/L) was spuriously high, and had the plasma creatinine re-assayed in a form of binding or interference with the dialysis of fluorescein, which can probably be attributed to differences in protein concentrations.

Fluorescein did not interfere with creatinine analysis by the Beckman Creatinine Analyzer 2 for any of the matrices. In the case of the de-ionized water matrix the pattern shown by this instrument was a very rapid increment in rate of absorbance increase, followed by an equally rapid decrease in rate, finally stabilizing at zero absorbance increase after about 9-10 s. This is consistent with the addition and mixing that occurs in the Beckman cuvette and is the rate of fluorescein addition and dispersal that is being monitored initially. Because the rate measurements are made at 28 s, any constant chromophore would not be expected to interfere with this method.

Figure 2 shows the spectrum of fluorescein at pH 6.1. Fluorescein is likely to interfere with any single-point assay read at wavelengths between 440 and 510 nm. The chloride method on the SMA-II involves measurements at 480 nm, but fluorescein did not show any interference. This is because the pH of the chloride recipient solution is about 1.8. At a pH less than 5 one of the phenolic oxygen atoms is protonated, thus inhibiting electron delocalization across the xanthene nucleus with consequent disappearance of the absorption maximum at 492 nm (Figure 2).

We recommend that, in those rare cases where a plasma creatinine assay is required after fluorescein angiography, it be assayed by kinetic analysis or by a method involving a sample blank.

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Interference by Fluorescein with the Single End-Point Determination of Creatinine by Use of the Jaffé Reaction

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Fig. 1. Effect of fluorescein on creatinine results with SMA-II

Beckman Creatinine Analyzer 2, according to the supplier’s protocol, the result being 77 μmol/L. We noticed that the color of the plasma was yellow-brown, with a green, filmy opalescence. Viewed under ultraviolet light, the specimen was strongly fluorescent, and spectrophotometric scanning showed maxima at 460 and 492 nm, identical to those for fluorescein (1). The patient’s recent clinical history confirmed that the abnormal specimen color was due to the presence of fluorescein.

A 20 g/L stock solution of disodium fluorescein (BDH Chemicals, Melbourne) was made up in de-ionized water, and 0.1 mL of this stock was added to 10.0-mL aliquots of de-ionized water, “Ortho normal,” and “Ortho abnormal” quality-control sera. These mixtures were diluted with the corresponding media to give fluorescein concentrations up to 526 μmol/L.

The presence of fluorescein affected only the creatinine analysis on the SMA-II (Figure 1). As shown, the magnitude of this interference is affected by the type of matrix used. These differences for the three matrices imply some