Method-specific Reference Intervals for Serum Anion Gap and Osmolality

To the Editor:

We wish to comment on reference intervals for the serum anion gap and osmolality. The serum anion gap, which is most commonly defined as \( AG = Na-Cl-\text{TCO}_2 \), traditionally has had a reference interval of 8–16 mmol/L with a mean value (i.e., mean of values used to determine its reference interval) of 12 mmol/L (1, 2). In a recent report (3), the stated reference interval for the anion gap was 12–16 mmol/L with potassium included in the calculation, approximately equivalent to 8–12 mmol/L without inclusion of potassium. This range of only 4 mmol/L appears to be too narrow for a healthy human population. Moreover, recent studies have shown that mean values for current analyzers often differ from the traditional value and may vary from 5.9 mmol/L for the Beckman Synchrom to 12.4 mmol/L for the Nova 5.9 mmol/L for the Beckman Synchrom (Advanced Instruments Model 3MO osmometer) in 59 healthy volunteers of ages 20–60 years. Kolmogorov-Smirnov analysis indicated that we could not reject the hypothesis that the results were normally distributed \( (P = 0.64) \). The mean serum osmolality was 288 mOsm/kg, with a SD of 4.1 mOsm/kg, yielding a parametric reference interval of 280–298 mOsm/kg. The lowest and highest values measured were 280 and 298 mOsm/kg, respectively. Other published serum osmolality reference intervals based on freezing point depression measurements are 275–290 or 275–295 mOsm/kg in children and adults and 280–301 mOsm/kg in adults >60 years of age (7, 8). Both analytical methodology and characteristics of the reference population, such as age, can contribute to differences in serum osmolality reference intervals. Again, the clinical laboratory must establish or at least verify the serum osmolality reference interval to aid in accurate interpretation.

References


Capillary Electrophoresis in the Analysis of the Deletion/Insertion Polymorphism of the Angiotensin I-Converting Enzyme Gene

Capillary gel electrophoresis (CGE) in molecular pathology and genetics is an ideal instrument for fast, fully automated analysis. The number of reports dealing with the analysis of, e.g., PCR products, is continuously increasing. In this context, we noticed with interest the description of a CGE analysis of the angiotensin I-converting enzyme polymorphism by X.H. Huang et al. (1). The CGE procedure is very similar to our communication published in 1996 (2), but with our method, running times are substantially shorter: we have separation times of <10 min (2). In general, modern CGE analysis of PCR products can easily be achieved in <10 min when there are such big differences in basepairs (100–300 bp) (3, 4).

If Huang et al. (1) plan to screen a large number of samples for the angiotensin I-converting enzyme polymorphism by CGE, the use of a polyacrylamide-coated capillary and 0.6% hydroxyethylcellulose will increase their sample throughput by nearly 300%.

References

Acute Effects of Fracture on Bone Markers and Vitamin K

To the Editor:

New biochemical markers provide useful information in the diagnosis and monitoring of metabolic bone disease and in the prediction of fracture risk. Vitamin K has become increasingly of interest in this field because of its role as a cofactor in the carboxylation of osteocalcin (1). Because hip fractures generally occur in severely osteoporotic patients, biochemical markers of bone metabolism and vitamin K have been studied extensively in patients with hip fractures. However, it is not clear whether a fracture itself affects the concentrations of biochemical markers of bone metabolism or, if so, how soon after or for how long after the fractures. The ideal way to study this is to obtain samples before a fracture. This is not feasible, however, because it requires a huge amount of sampling and a long follow-up. A secondary way is to do successive sampling immediately after a fracture to observe whether values change.

We studied 28 women with hip fracture, ages 64–94 years (mean age, 80.3 years). Their fractures were caused by low-energy trauma, such as a fall. They were immediately taken to an emergency room at a hospital. Serum and urine were collected from them on 3 successive days immediately after admission to the hospital (termed day 0). Most patients had surgery on day 2 after the sampling of that day. All had been ambulatory before the fracture. Exclusion criteria were: hip fractures resulting from severe trauma, admission to the hospital >24 h after the onset of fracture, blood transfusions or surgical procedures during the period of sample collection, past and present illnesses related to bone metabolism, and increased concentrations of serum creatinine. No subjects had been treated for osteoporosis, and none received medications before or during the study that might have affected calcium metabolism. Informed consent was obtained from all participants. The procedures followed were in accordance with the principles of the Declaration of Helsinki in 1975, as revised in 1983.

Serum osteocalcin was measured by RIA with a Yamasa osteocalcin kit with the use of polyclonal antibodies. Intra- and interassay CVs were <15%. Pyridinoline and deoxypyridinoline in urine were measured by HPLC after hydrolysis according to an automated analysis described by Pratt et al. (2). Before hydrolysis, urinary creatinine content was measured. The values of urinary Pyr and Dpyr were expressed per mol of urinary creatinine. The intra- and interassay CVs were <10%. Vitamin K_2, menaquinone 4 (MK4), and menaquinone 7 (MK7) were measured by HPLC. The method is based on a hydrogen gas-saturated mobile phase with fluorescent detection after postcol-

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