Is the Urine Anion Gap a Reliable Index of Urine Ammonium Excretion in Most Situations?

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Dear Sir,

The recent review by Halperin et al. [1] and their previous paper [2] showed that the urine anion gap (AG; urine net charge) is a rough estimate of urine ammonium (NH_4^+) and that this index is very helpful in the differential diagnosis of hyperchloremic metabolic acidosis. A paper by Battle et al. [3] supported this. The urine is calculated using urine Na^+ , K^+ and Cl^- concentrations as follows: $\text{AG} = \text{Na}^+ + \text{K}^+ - \text{Cl}^-$. Although it seems true that a negative value of AG means urine $\text{NH}_4^+ > 80 \text{ mEq/l}$, it is not clear how accurately this index estimates the urine NH_4^+ in the situation where urine AG is positive (urine AG is usually positive in normal subjects). The readers of the article [1] might have the impression that the urine AG can be used to estimate urine NH_4^+ in the situation where urine NH_4^+ excretion is in normal range as well as when $\text{NH}_4^+ < 11$ excretion is stimulated such as in metabolic acidosis.

We studied 20 normal subjects comparing the urine AG and the urine NH_4^+ . The 24-hour urine was collected, and the urine volume, pH, Na^+ , K^+ , Cl^- and NH_4^+ were determined. In each subject, the urine pH was less than 6.3, the arterial blood pH was in the range of 7.35–7.45 and the endogenous creatinine clearance was more than 40 ml/min. They were not ingesting drugs that might influence the urine AG. Figure 1 shows the relationship between the urine NH_4^+ (y) and the urine AG (x) in the

70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
Urine AG (mEq/day)

Fig 1. Relationship between the urine ammonium (NH_4^+) and the urine AG in normal subjects (n = 30).

Urine Anion Gap

70
60
50
40
30
20

Fig 2. Relationship between the urine ammonium (NH_4^+) and the urine AG minus urine bicarbonate (HCO_3^-) in stable chronic respiratory acidosis (n = 11).

10
-10
30 50
Urine AG- HCO_3^-
70
(mEq/day)
90
110

24-hour urine samples. No significant correlation between the two values was demonstrated in normal subjects whose daily urine NH_4^+ excretions were in the range of 10–70 mEq (R = 0.421). Bicarbonaturia is one of the pitfalls in the use of urine AG as an index of urine NH_4^+ . Halperin et al. [1] claimed that if the urine pH is less than 7, bicarbonate would not significantly contribute to urine AG. We also studied 11 patients with stable chronic respiratory acidosis with bicarbonaturia whose urine pH was 6.5–7.0. Urine bicarbonate was measured by total CO_2 analyzer (Corning 965). Because arterial PCO_2 , (thus, urine PCO_2) was high in these patients, a substantial amount of urine bicarbonate was present in relatively acidic urine (pH 6.5–7.0). Urine bicarbonate excretion measured as total CO_2 was in the range of 1.2–9.8 (mean 4.7 ± 2.8 mEq/day, SD). Again, as shown in figure 2, no significant correlation between the urine NH_4^+ and the urine AG was observed, even if the urine AG was corrected for urine bicarbonate (r = 0.406).

We concluded that the urine AG does not reflect urine NH_4^+ excretion in most clinical situations (i.e. when urine NH_4^+ excretion is not stimulated) although it can be useful when urinary NH_4^+ excretion is highly stimulated.

References

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