Comment on the Letter by Meregalli et al., Nephron 1995; 69:98-99 Modified Urine Osmolal Gap: An Accurate Method for Estimating the Urinary Ammonium Concentration?

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Dear Sir,

I agree with Dr. Meregalli and coworkers that the rate of excretion of NH_4^+ is the critical component of net acid excretion because it is the major adaptable component of net acid excretion during metabolic acidosis. Furthermore, I agree that the hallmark for the diagnosis of distal renal tubular acidosis is a low rate of NH_4^+ excretion [1]. This only leaves me to define what is low and what is high for NH_4^+ excretion rates and the optimal tests for assessing NH_4^+ excretion at the bedside.

Quantitative analysis: Normal adults on a typical western diet excrete close to 30 mmol of NH_4^+ /day. In contrast, when metabolic acidosis is due to ingestion of NH_4Cl and if it is chronic, the expected rate of excretion of NH_4^+ is > 200 mmol/day [2, 3]. Accordingly, when faced with a patient who has chronic metabolic acidosis, a normal anion gap in plasma, and a normal glomerular filtration rates one should expect to find an NH_4^+ excretion rate close to 200 mmol/day, if the renal capacity to excrete NH_4^+ is normal; much lower values indicate a major defect in net acid excretion. Moreover, if the acidosis is strictly due to a renal defect in NH_4^+ excretion, the rate of excretion of NH_4^+ would have to be < 30 -40 mmol/day; otherwise the acidosis would resolve spontaneously. Hence the crucial initial information about the rate of NH_4^+ excretion is whether this rate is close to 200 mmol/day versus considerably less than 40 mmol/day. Bearing this in mind, let us

return to the accuracy needed from the indirect measures of NH_4^+ excretion. This will illustrate my disagreement with the interpretation of the data of Dr. Meregalli and colleagues.

Tests to measure the rate of excretion of NH_4^+ : The gold standard for assessing the concentration of NH_4^+ in the urine is a direct assay, as pointed out in the letter. Conversely, three indirect techniques are commonly used. First, some authors rely heavily on the urine pH which is, in my opinion, an unreliable way to assess the concentration of NH_4^+ [4]. The other two indirect techniques are the urine net charge [5] and the urine osmolal gap [6, 7]. Both require many individual measurements, and it goes without saying that if all of these measurements are not absolutely accurate, there could be considerable scatter in the data. More specifically, the urine net charge reflects the concentration of NH_4^+ only if the anion excreted with NH_4^+ is Cl^- . The urine osmolal gap has the advantage that it will detect NH_4^+ excreted with any anion. Pitfalls in the osmolal gap include excretion of unusual uncharged compounds such as alcohols, the excretion of polyvalent anions, or the excretion of cations such as Ca^{2+} , Mg^{2+} , or Li^+ . Since the excretion

of the above cations is trivial relative to the expected rates of excretion of NHJ (mEq/1), errors in this regard should be extremely rare.

Let us return to the crux of the argument raised by Dr. Meregalli and coworkers. Given the potential inaccuracies in any of the measurements in the urine osmolal gap, one should not try to use this technique to 'measure' small changes in the concentration of NHJ – it was not designed for and should not be used for that purpose. Rather, the test should be used as a bedside screen to detect 'gross' changes in the NHJ excretion rate (< 40 vs. close to 200 mmol/day); for that purpose it is still valuable as a screening test. In more practical terms, the order we would use these urine indices in a patient with chronic metabolic acidosis is as follows: If the urine [CF] exceeds the sum of [Na⁺] + [K⁺], we would presume that the [NHJ] is high; this can be confirmed by direct assay. We would then factor this for the excretion of creatinine [8] to estimate the rate of NHJ excretion. In contrast, if [Na⁺] + [K⁺] exceeds [CF] in the urine, we would measure the urine osmolal gap and again factor for creatinine as above, bearing in mind the ranges in excretion we are seeking. Once we know that the NHJ excretion is low, the urine pH is valuable to decide if the basis is primarily a low[H⁺] or NH₃[1].

In summary, we agree that the modified urine osmolal gap is not reliable for detecting small changes in NHJ excretion. Notwithstanding, it is a useful screen to imply that there are major changes in NHJ excretion rate at the bedside.

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