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Clinical Decision Tool Reviews

Fractional Excretion of Urea (FEUrea)

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Abstract

In patients with acute kidney injury (AKI), it is important to differentiate between states that are considered, "prerenal", i.e., experience improvement in AKI with increase in effective circulating volume, and intrinsic kidney diseases such as acute tubular injury. Many tools are used to make this distinction including scores that calculate fractional excretion of solutes such as sodium and urea. In patients on diuretic therapy, sodium excretion and thus fractional excretion of sodium (FENa) can be high even in "prerenal" states where this is expected to be low. To overcome this limitation, fractional excretion of urea (FEUrea) is often measured to differentiate prerenal causes of AKI from intrinsic kidney diseases. The evidence for better accuracy of FEUrea is mixed and higher quality studies show low accuracy of this test for the indication of identifying "prerenal" states. Both FENa and FEUrea are considered adjunct tools for identifying a "pre-renal" state and overall clinical picture must be considered rather than relying on single test results. Since cardiorenal and hepatorenal syndromes also have low effective circulating volume, these states have very similar FENa and FEUrea as a "prerenal" state from true volume depletion. Urinary tract obstruction must be excluded using imaging studies when appropriate.

I. HOW TO USE

When to Use

FEUrea may be used in patients with acute kidney injury (AKI) while on diuretic therapy as an adjunct tool to differentiate between pre-renal azotemia and acute tubular necrosis.

Pearls / Pitfalls

- FEUrea can theoretically be used in patients on diuretics, since urea excretion is not significantly affected by diuretics. However, in both patients with or without diuretic use, the diagnostic accuracy of FEUrea is poor (AUC 0.57 and 0.56, respectively) and lower than FENa (0.75 and 0.83, respectively).
- Note that both FENa and FEUrea are adjunct tools. Overall clinical picture must be considered when applying these tools. Other tests helpful in differential diagnosis of AKI such as urine microscopy and novel urine kidney injury biomarkers are not discussed here.
- States of low effective circulating volume such as cardiorenal syndrome and hepatorenal syndrome will have similar FEUrea findings as true volume depletion despite having total body volume overload. Management of these conditions differs from that of true volume depletion.
- Rule out urinary tract obstruction using imaging studies when clinically appropriate.

Why to Use

FEUrea is theoretically unaffected by loop and thiazide diuretic use unlike FENa, and thus might retain the ability to differentiate between pre-renal azotemia and acute tubular necrosis although current data do not show its superiority over FENa in differentiating pre-renal azotemia from acute tubular necrosis.

II. NEXT STEPS

Advice

This test is considered an adjunct in management of AKI. Full clinical picture must be evaluated and no single test used for clinical decision making.

Management

In patients with low FEUrea, the diagnosis is thought to be pre-renal azotemia and an increase in effective circulating volume is considered as a treatment for AKI. In patients with high FEUrea, the diagnosis is thought to be acute tubular necrosis (ATN) or other forms of intrinsic kidney disease and management focuses on treating these causes.

Critical Actions

If FEUrea is <35%, diagnosis is more likely to be pre-renal azotemia. Consider increasing effective circulating volume based on the clinical situation (e.g., IV fluid administration, vasopressors)

FEUrea>50%, diagnosis is more likely to be intrinsic renal disease (e.g., acute tubular necrosis). Consider withdrawing nephrotoxic medications or other diagnosis specific management.

Urinary tract obstruction must be ruled out when clinically appropriate before applying this test.

III. EVIDENCE

Evidence Appraisal

Studies evaluating accuracy of FEUrea have shown conflicting results. Larger and higher quality studies tend to show modest FEUrea accuracy for identifying a "prerenal" state which is lower than that of FENa but equivalent accuracy to FENa in those on diuretics. In a retrospective study (n=87), Kaplan et al identified a group of participants with low FEUrea but high FENa, who tended to have diuretic use prior to obtaining the sample. This discordant relationship often "normalized" over time particularly with discontinuation of diuretic therapy. In a prospective, single center study largely from the ICU (n=102), Carvounis et al showed that FEUrea had sensitivity and specificity of 90 and 96%, respectively, with an AUC of 0.97 for identifying a prerenal state. In a prospective observational study (n=99) at a single center enrolling consecutive patients classifying AKI into transient or persistent, Pepin et al showed that FEUrea had an AUC of 0.56 (0.11) without prior diuretic use and 0.57 (0.08) with prior diuretic use. FENa had better performance than FEUrea regardless of diuretic use. Finally, in a prospective, multicenter observational study (n=203), Darmon et al showed that FEUrea was not associated with AKI type with an AUC of 0.59 (0.49, 0.70), and sensitivity and specificity of 63% and 54% at 35% FEUrea cut-off. AUC in those on diuretics was 0.58 (CI, 0.41-0.75). Overall, FEUrea is considered an adjunct with modest accuracy for differentiating pre-renal azotemia from acute tubular necrosis as the etiology of acute kidney injury (AKI) in patients on diuretic therapy where FENa might have lower accuracy.

Formula

Fractional Excretion of Urea (FEUrea) = $(Serum_{Cr} * U_{Urea}) / (Serum_{Urea} * U_{Cr})$ %

Facts & Figures

This test can provide similar information to the FENa equation, but can still be used in patients on diuretic therapy (diuretics alter the sodium concentration, making the FENa equation unusable).

	Prerenal	Intrinsic renal	Postrenal
FENa	<1%	>1%	>4%
FEUrea	≤ 35%	>50%	N/A

Literature

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