

Azotemia Associated with Tetracycline Use

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BACKGROUND

- Tetracycline can cause gastrointestinal side effects, teeth discoloration, photosensitivity, azotemia, and bone growth inhibition in children (10)
- Hepatotoxicity, intracranial hypertension, and esophageal ulcerations have been reported in some cases, but nephrotoxicity is less common (2,10)
- Only a few cases of nephrotoxicity associated with tetracycline have been reported including acute tubular necrosis (1) and acute interstitial nephritis (2)
- The rise in BUN has been found to be due to impaired protein synthesis from tetracycline action on various enzyme mechanisms, especially in patients with impaired renal function (8)

CASE PRESENTATION

- Age 77 female with CKD stage IIIb, history of recurrent UTIs (Klebsiella), hypertension, bipolar disorder
- Presented with intractable nausea and vomiting for 4 days with decreased appetite and PO intake
- Recently hospitalized for a complicated UTI and discharged home to complete her antibiotic course with Tetracycline 500 mg TID for 7 days
- Labs:
 - Creatinine 3.7
 - BUN 149
 - Alkaline phosphatase 207
- CT abdomen/pelvis without contrast showed bilateral renal atrophy, post-cholecystectomy without evidence of biliary dilation
- With her elevated BUN:Cr of 42, there was concern of upper gastrointestinal bleeding. However, her hemoglobin remained stable without signs or symptoms of bleeding.
- Supportive care with intermittent maintenance fluids with LR at 125 cc/hr, compazine, and ondansetron for nausea. Diet was slowly advanced with improvement of her nausea.
- Upon discharge, her acute kidney injury resolved, and renal function returned to normal.

QUICK REVIEW OF AKI

- KDIGO guidelines for Acute Kidney Injury:
 - Increase in serum creatinine by 0.3 mg/dL or more (26.5 micromoles/L or more) within 48 hours
 - Increase in serum creatinine to 1.5 times or more baseline within the prior seven days
 - Urine volume less than 0.5 mL/kg/h for at least 6 hours (5)
- Fractional excretion of sodium or FeNa can be used to determine what type of kidney injury
- $FENa = [(UNa \times PCr) / (PNa \times UCr)] \times 100$,
 - $FeNa < 1$, then likely prerenal
 - > 2 , then likely intrarenal;
 - > 4 , then likely postrenal
- If the patient is on diuretics, use FEurea instead of FENa.
 - Can be calculated with Complete blood count, BUN, creatinine (Cr), arterial blood gases (ABGs). $FeUrea > 65\%$ in AKI and below 35 in prerenal

DISCUSSION

- Mechanisms of drug-induced nephrotoxicity include changes to glomerular hemodynamics, tubular cell toxicity, inflammation, crystal nephropathy, rhabdomyolysis, and thrombotic microangiopathy (7)
- Treatment of AKI involves treating the underlying cause or removing the offending agent, as well as fluid resuscitation for intravascular depletion.
- Diuretics can be used in AKI, specifically loop diuretics. Although literature review shows no evidence that it reduces mortality, the need for dialysis, the number of dialysis sessions, or length of Intensive Care Unit/hospital stay or that it increases the recovery of renal function (11)
- RRT is indicated in anuria, refractory hyperkalemia, volume overload, and uremia.
- When BUN is elevated in the setting of AKI, it is important to rule out GI bleed, high dose steroids, and medications (tetracyclines)
- Having an AKI increases risk for developing chronic kidney disease. One study showed that even complete recovery from AKI (return of serum creatinine to less than 1.1) was significantly associated with development of incident stage 3 CKD. (9).

CONCLUSIONS

- Acute cystitis among women is extremely common in both outpatient and inpatient settings. With growing rates of antibiotic resistance, individualized management of acute cystitis presents new challenges regarding antibiotic selection.
- Tetracycline group of antibiotics can produce a rise in the level of BUN in the presence of renal impairment.
- As tetracycline is renally excreted and not dialyzable, dosage adjustment and frequency must be considered.
- Awareness of the existence of this tetracycline toxicity can be beneficial to patient care.

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