Varenicline-Associated Acute Renal Failure: Case Report

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Introduction:
• Varenicline is a novel medication that is effective for smoking cessation.
• Adverse effects are generally mild and self-limiting, with GI side effects most commonly reported.
• To the best of our knowledge, this is the first case report of varenicline induced RF in a patient with a completely normal renal function.

Case Description:
• A 70 year old female with PMH of HTN, GERD, dyslipidemia, and nicotine dependence presented to the hospital with watery diarrhea, abdominal pain and decreased appetite.
• Pt was started on varenicline 2 weeks prior to admission when she started to have these symptoms.
• Medications prior to admission:
  - Amlodpine 5 mg
  - Lisinopril 2.5 mg
  - HCTZ 12.5 mg
  - Omeprazole
  - Simvastatin
  - Varenicline
  - No recent use of over the counter medications or herbal products, also denied any exposure to toxins or contrast dye.
• Physical examination:
  - VS: BP 86/54 mmHg; P 72 beat/min; RR 20/min; T 95.2 F; Pulse oximetry 95% on room air.
  - General: NAD, well developed Caucasian female.
  - HEENT: Dry oral mucosa.
  - Pulmonary: Clear to auscultation bilaterally.
  - CVS: RRR, no murmurs.
  - Extremities: No rash or LE edema.
  - Rest of physical exam was unremarkable.
• Laboratory data:
  - Na: 129 mmol/L
  - K: 7.8 mmol/L
  - Cl: 100 mmol/L
  - HCO3: 13 mmol/L
  - BUN: 128 mg/dl
  - Cr: 12.21 mg/dl (previous creatinine was 0.9 mg/dl)
  - Ca: 9.9 mg/dl
  - UA:
    - Glucose: 100 mg/dl
    - Phosphorus: 6.6 mg/dl
    - Hb: 13.3 g/dl
    - Platelets: 416 K/mcl
    - Hct: 0.41
    - Albumin: 3.3 g/dl, other LFTs normal
    - CK: 90 ng/ml
    - Myoglobin: 232 ng/ml
    - Ph: 6
    - Hyaline cast: 1-5, no ATN casts
    - Esinophil: 1
  - Urea chemistry:
    - Urine creatinine: 22.6 mg/dl
    - Urine protein: 29 mg/dl
    - Urine sodium: 95 mmol/L
    - Urine protein/creatinine ratio: 1.283 mgPR/mCR
    - Urine urea nitrogen: 126 mg/dl
    - FeNa: 38.95%
  - Imaging:
    - Retroperitoneal US: Normal sized kidneys without hydronephrosis.

Clinical Course:
• Patient was started on aggressive IVF resuscitation.
• She remained oliguric even after 10L of IVF.
• She was started on CVVH for 2 days.
• Her serum creatinine level decreased from 12.2 to 5.8 mg/dL.
• No further dialysis needed.
• The only offending agent suspicious for her proteinuric AKI was varenicline.
• Post discharge follow up at 2 years; pt has a creatinine of 1.28 with a GFR of 44 (stage III CKD). Proteinuria resolved.

Discussion:
• Varenicline is a novel medication that is effective for smoking cessation.
• Renal elimination of varenicline is primarily through glomerular filtration along with active tubular secretion.
• According to the package insert, varenicline does not change creatinine clearance to any appreciable extent, but it should be used with caution in patients with renal impairment.
• No adjustment is needed for mild-to-moderate renal dysfunction.
• For patients with severe renal impairment (estimated creatinine clearance <30 mL/min), and for patients with ESRD undergoing hemodialysis, dosage adjustment is needed. The incidence of ARF is less than 1%.
• Varenicline is thought to be the cause of proteinuric AKI in our patient because of the temporal relationship.
• This is suggested by the worsening and improvement of renal function with the initiation and withdrawal of the drug.
• Other causes such as obstruction, and intrinsic renal disease were ruled out from the differential diagnosis during the hospital workup.
• One case reporting the association of ARF with varenicline has been described in the literature, however that patient had a preexisting moderate renal insufficiency and required no hemodialysis or diuresis.
• To the best of our knowledge, this is the first case report of varenicline induced RF in a patient with a completely normal renal function.

Conclusion:
• Clinicians should be aware of this potential adverse effect and should monitor renal function with initiation of varenicline therapy, not only in patients with chronic kidney disease but also in patients with completely normal renal function.

References:
• http://www.ncbi.nlm.nih.gov/pubmed/18984856