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ACUTE KIDNEY INJURY

There's Nothing Cute About It ..... Level II

Scott Bolesta, PharmD, BCPS, FCCM, FCCP

CASE SUMMARY

A 72-year-old man with a history of hypertension (HTN), CAD, heart failure (HF), and RA is admitted to the hospital with an acute UGI bleed resulting in prerenal acute kidney injury (AKI) from hypovolemia and hypotension. After an unsuccessful attempt to stop the bleeding during an EGD, the patient is taken for emergent surgery where hypotension continues requiring the start of norepinephrine. Postoperatively, the patient remains hypotensive and experiences oliguric acute tubular necrosis (ATN) that fails to respond to IV hydration and furosemide. Subsequently, he experiences acute pulmonary edema from volume overload and worsening HF and is started on dobutamine and continuous venovenous hemodiafiltration (CVVH-DF).

QUESTIONS

Collect Information

1.a. What subjective and objective information indicates the presence of AKI?

- Decrease in urinary frequency prior to admission and during his hospital course.
- Elevated BUN and serum creatinine.
- The potassium is elevated even though the patient is on a loop diuretic.

1.b. What additional information is needed to fully assess this patient's AKI postoperatively?

- Accurate quantification of urine output (ideally hourly output) along with daily assessment of his serum creatinine to look for any continued changes.
- A urinalysis will also be helpful in determining the pathophysiology of his AKI.
- A FENA would not be accurate since this patient was taking a loop diuretic as an outpatient.

Assess the Information

2.a. Assess the severity of AKI based on the subjective and objective information available.

- Based on the patient's change in serum creatinine since admission and production of more than 400 mL of urine postoperatively, he can be said to have nonoliguric AKI. The severity of his AKI, however, can best be described by the decrease in urine output. His AKI would be classified as Stage 2 since his urine output has been less than 0.5 mL/kg/h for at least 12 hours.[1]

2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

- *Problem #1:* AKI requiring nonpharmacologic and pharmacologic management and modification of drug therapy that may contribute to AKI.
- *Problem #2:* Acute UGI bleed likely caused by the combination of NSAID and dual antiplatelet therapy (DAPT) use.
- *Problem #3:* Continued utilization of drug therapy for HTN, HF, and CAD that may worsen AKI.

Develop a Care Plan

3.a. What are the goals of pharmacotherapy for AKI in this case?

- *Stop the acute bleeding:* This is the root cause of the patient's symptoms and complications.
- *Restore and maintain hemodynamics and organ perfusion:* The patient's intravascular volume needs to be restored to prevent further complications from his UGI bleed, like his AKI.
- *Correct anemia:* The patient has a history of CAD and HF and may benefit from transfusions that will increase his hemoglobin level above 10 mg/dL. However, caution should be observed because aggressive transfusion, along with volume repletion, may put the patient at risk for acute decompensated HF.
- *Avoid or withhold medications that have the potential to worsen this patient's AKI:* Once the patient's kidney function improves, medications for the treatment of chronic disease states could be restarted except for those that confer a direct cause of AKI (ie, naproxen).

3.b. What nondrug therapies might be useful for this patient's AKI?

- *IV hydration:* Repletion of intravascular volume for patients with prerenal azotemia is the most effective therapy for rapid resolution of this cause of AKI.[1] 0.9% sodium chloride or balanced crystalloids are considered the primary therapy for rapid repletion of intravascular volume, but some evidence shows balanced crystalloids have more favorable outcomes related to kidney function.[1,2] In patients with a history of HF, such as the one in this case, hydration should be applied conservatively to reduce the risk of an acute HF exacerbation.[3]
- *Renal replacement therapy (RRT):* This may be necessary if aggressive volume resuscitation and transfusions for the patient lead to an exacerbation of HF with resultant pulmonary edema.[1,4]
- *Nutritional support:* Patients with AKI have a high rate of protein catabolism secondary to several metabolic factors, but mainly due to increased hepatic gluconeogenesis from amino acids released during protein catabolism.[2] It is recommended that patients with noncatabolic AKI receive 0.8–1 g/kg per day of protein.[1] Patients who require RRT have even greater protein requirements due to substrate loss, breakdown from proteases, and release of cytokines. It is recommended that patients requiring RRT receive 1–1.5 g/kg per day of protein, and those on CRRT receive up to 1.7 g/kg per day.[1]

3.c. What feasible pharmacotherapeutic alternatives are available for treating the disease or drug therapy problem?

- *Furosemide:* Loop diuretics may have a role in the therapy of intrinsic AKI because they can convert a patient from an oliguric to a nonoliguric state and may decrease the metabolic workload in the tubule.[5] They may be used clinically to remove excess intravascular volume in order to avoid the need for RRT due to hypervolemia.[1] However, loop diuretics should be used with caution, because they could further worsen kidney function in patients with prerenal azotemia due to hypovolemia.

- *Low-dose dopamine (≤3 mcg/kg/min):* Although widely used in the past for prevention and treatment of AKI, the use of low-dose (so-called "renal-dose") dopamine is no longer recommended due to a lack of impact on clinical outcomes.[1]
- *Natriuretic peptides:* Atrial natriuretic peptide (ANP) increases urine output by inhibiting sodium and water resorption in the collecting duct.[5,6] It also increases GFR by dilating afferent arterioles and constricting efferent arterioles. Nesiritide, or brain natriuretic peptide, works similarly to ANP. However, none of these agents have been shown to improve patient outcomes and are therefore not recommended for the treatment of AKI.[1]
- *Mannitol:* Due to its diuretic effect, mannitol was initially thought to have potential benefits in patients with AKI. However, clinical trials have failed to show a benefit in the prevention or treatment of AKI and it is not recommended.[1]

3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's AKI and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Problem #1: AKI requiring nonpharmacologic and pharmacologic management and modification of drugs that may contribute to AKI

- *Provide IV hydration:* Resuscitation with IV fluids is recommended for patients with prerenal azotemia. Most trials have shown a benefit of crystalloids over colloids, but more recent evidence shows that balanced crystalloids may have better outcomes compared to 0.9% sodium chloride.[2] Most trials recommend providing at least 1 mL/kg/h of fluids IV over the first several hours with a target mean arterial pressure of greater than 65 mm Hg and urine output greater than 0.5 mL/kg/h.[1]
- *Initiate loop diuretic therapy:* Therapy for patients with intrinsic AKI is mainly supportive, such as initiating a loop diuretic to improve urine output.[5,6]
- Continue to *hold* metoprolol, furosemide, enalapril, and amlodipine while the patient is experiencing hypotension and AKI. These agents could be gradually reintroduced one at a time as the patient's hemodynamics begins to recover, along with their kidney function.

Problem #2: Acute UGI bleed likely caused by the combination of NSAID and DAPT use

- Provide IV resuscitation and transfusion (as discussed previously under Problem #1).
- Discontinue naproxen. This patient should permanently discontinue the use of NSAIDs due to history of AKI and UGI bleed.
- DAPT should not be discontinued since his most recent ACS was 2 months ago and a drug-eluting stent was placed; however, a hold may be necessary in the setting of the acute bleed.
- Vasopressor therapy (norepinephrine) and pantoprazole should be continued to manage hypotension and the UGI bleed.

Problem #3: Continued utilization of drug therapy for HTN, HF, and CAD that may worsen AKI

- *Hold* medications for these conditions that could worsen the patient's acute hypotension and unstable hemodynamics. This would include amlodipine, furosemide, metoprolol, and lisinopril.
- *Reintroduce* these medications individually and at low doses once vasopressor therapy is discontinued and the patient's hemodynamics improve and stabilize.

Implement the Care Plan

4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

- You should avoid the use of naproxen or related medications known as NSAIDs. Another common example of these medications includes ibuprofen. The use of medications such as these could lead to another stomach bleed or worsen your kidney function.
- Call your doctor immediately or go to the emergency room if you develop dark black stools or blood in your stool, if you are vomiting blood, or if you observe any change in urinary frequency or urine quantity or color.
- It is important that you take your medications as prescribed by your physician. If you miss a dose of one of your medications, take it as soon as you realize you missed the dose. However, if it is halfway to the time of your next dose, wait until the next scheduled dose. Never double-up a dose of your medications to make up for a missed dose.
- It is very important that you see your doctor as scheduled and go for all your scheduled laboratory work so the effectiveness and safety of your medications can be monitored.

4.b. Describe how care should be coordinated with other healthcare providers.

- Treatment of AKI is complex, especially in critically ill patients. The involvement of a nephrologist is critical for managing therapeutic interventions such as hydration, diuretic therapy, and RRT. A nephrologist will often be the provider who initiates and adjusts these therapies, but close communication with other team members through team huddles, the medical record, and discussions is essential.
- Pharmacists are also beneficial in addressing IV hydration therapy selection and dosing, in addition to monitoring the response to diuretic therapy. They may recommend titration of diuretic dosing and when to increase or decrease IV hydration therapy volume. They are also key to adjustment of drug dosing in patients with AKI, especially in those requiring RRT. Pharmacists will assess kidney function based on several objective assessments, including estimates of creatinine clearance and renal function, and make subsequent recommendations for medication dose adjustments. They also have the knowledge and skills necessary to make specific dosing recommendations for patients receiving RRT depending on the mode of RRT and other patient parameters. In consultation with nephrologists, dialysis nurses, and other team members, they can determine the best dose and timing of medication administration for patients requiring RRT.
- Nurses are integral to the care of patients with AKI as they can monitor and record changes in urine output and other indicators of volume status. They can quantify hourly urine output at the bedside and alert other providers, such as the nephrologist and pharmacist, of acute changes in kidney function based on this objective parameter. They can also perform necessary physical assessments, such as with the pulmonary and cardiovascular systems, to determine the efficacy and safety of IV hydration therapy. They are a key member of the healthcare team as they can convey up-to-date information on the patient's status and organ function, such as any acute changes in urine output or vital signs.

Follow-Up: Monitor and Evaluate

5. Explain how to monitor and evaluate the care plan for medication appropriateness, effectiveness, safety, and patient adherence

by using clinical and laboratory data, patient feedback, and other information.

Medication appropriateness and effectiveness

- Monitor the patient's intravascular volume during his initial IV hydration and blood transfusions to assure adequate volume status and avoid hypervolemia in the setting of oliguria. This should be done frequently (at least every hour) during the initial hours of his resuscitation, at least the first 6 hours. Dynamic assessments of intravascular volume status, such as passive leg raise and capillary refill, should be used to assess the patient's volume status as opposed to more invasive static assessments, such as central venous pressure. The patient's hourly intake and output should also be carefully recorded and totaled every 8 hours. His weight should also be recorded daily.
- Monitor the patient's BP, mean arterial pressure, and heart rate at least every hour along with his temperature. This is especially true while the patient is receiving RRT.
- Assess the patient's medication therapy daily for any medications that require dose adjustment based on the current known or estimate of the patient's kidney function (eg, creatinine clearance). Also assess the patient's medication therapies for appropriate timing of administration relative to their RRT. Finally, assess medication therapy daily for medications that require therapeutic drug monitoring as necessary based on degree of estimated kidney function (eg, creatinine clearance) or current requirements for RRT.
- Monitor Chem-7, calcium, magnesium, phosphate, complete blood cell count with differential, and arterial blood gases daily (especially while on mechanical ventilation and RRT). The goal is to have these parameters in the normal range.
- Assess the patient's hepatic panel (aspartate aminotransferase, alanine aminotransferase, direct and total bilirubin), albumin, and prealbumin weekly. The goal is to have these parameters in the normal range.
- Each provider involved in the care of this patient should perform an assessment of the patient at least once daily. More frequent assessment may be necessary during the patient's initial IV hydration and during the postoperative period. This is especially true of the assessments conducted by the patient's nurse(s) to assure adequate hydration and resuscitation along with close monitoring of input and output (especially urine output).

Medication safety

- The patient should be assessed for wound and skin breakdown daily.
- Monitor the patient's coagulation studies as necessary depending on the type of anticoagulant used for CVVH-DF (ie, activated partial thromboplastin time if using heparin). Such parameters should be assessed at least daily, or any time CRRT is restarted or a change is made to the dialysis prescription.

Patient adherence

- Upon follow up as an outpatient, the patient should be assessed for avoidance of NSAID use. The patient should also be assessed for any signs or symptoms of UGI bleeding.

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