

BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

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NSAIDs

Many patients don't realize that NSAIDs can harm the kidneys.

It can happen because NSAIDs decrease blood flow to the kidneys. Rarely, the kidney damage is irreversible. And adding other meds known to cause kidney problems can compound the issue.

For example, adding an NSAID to an ACEI or ARB can be a "double whammy" to the kidneys...or a "triple whammy" if patients are also on a diuretic or SGLT2 inhibitor.

And the risk of acute kidney injury jumps if patients become dehydrated due to heat, viral illness, etc.

This can trigger a domino effect with meds cleared by the kidneys...such as a sulfonyleurea buildup that causes hypoglycemia.

Think about a patient's risk before suggesting an NSAID.

Keep in mind, NSAIDs are generally okay for patients with normal kidney function when needed...even chronic use.

And an occasional dose of an OTC NSAID should be safe even for most patients with mild to moderate chronic kidney disease.

But try to avoid NSAIDs in patients with severe kidney disease... or multiple conditions that raise kidney injury risk (heart failure, diabetes, etc). NSAIDs can tip the balance, especially chronic use.

In these cases, continue to recommend acetaminophen first.

Or consider a topical NSAID for mild osteoarthritis pain in smaller joints (hand, knee, etc)...systemic absorption is low.

Point out that no oral NSAID seems safest for the kidneys.

You might've heard that short-acting NSAIDs (ibuprofen, etc) are least kidney toxic. But this isn't supported by evidence.

Advise using the lowest NSAID dose for the shortest duration.

If a higher-risk patient needs a chronic NSAID, regularly assess if it's still necessary. Also suggest checking kidney function and electrolytes within about 2 weeks...and periodically thereafter.

Counsel patients to stay hydrated, especially during an acute illness...and to seek immediate care for signs of kidney problems (swelling, low urine output, confusion, etc).

Assess CV and GI concerns in our *Managing NSAID Risks* resource.

(For more on this topic, see Clinical Resource #381005 at [PharmacistsLetter.com](https://www.pharmacistsletter.com).)

Kunitsu Y, Hira D, Morikochi A, et al. Time until onset of acute kidney injury by combination therapy with "Triple Whammy" drugs obtained from Japanese Adverse Drug Event Report database. *PLoS One*. 2022 Feb 9;17(2):e0263682.

See LEADER NOTES for answers to discussion questions.

6. What were the strengths and weaknesses of this study?

7. Were the results expressed in terms we care about and can use?

HOW SHOULD THE NEW FINDINGS CHANGE CURRENT THERAPY?

8. Do the results change your practice? How?

APPLY THE NEW FINDINGS TO THE FOLLOWING CASE

SN is a 61-year-old male who started an SGLT2 inhibitor for type 2 diabetes a month ago. He has a history of hypertension, hyperlipidemia, and diabetes. His medications include lisinopril 40 mg daily, chlorthalidone 25 mg daily, atorvastatin 80 mg daily, metformin 1,000 mg twice daily, and empagliflozin 25 mg daily. You note that his BP is well-controlled today at 117/62. He states that his blood sugars have been better controlled since starting the empagliflozin, with fasting blood sugars ranging from 140-170 mg/dL. He does state that he's noticed more frequent urination since starting the SGLT2 inhibitor and has developed progressively worsening dizziness, especially in the morning.

9. What are some potential adverse effects of SGLT2 inhibitors?

See LEADER NOTES for answers to discussion questions.

SN also complains of bilateral knee pain that has worsened recently after joining a rec league pickleball team. He has been told he has mild osteoarthritis and occasionally takes acetaminophen or ibuprofen for the pain. He notes that the ibuprofen does help but he is unsure how often he should take it.

10. What should you recommend to treat SN's knee pain?

You discuss limiting the use of ibuprofen due to kidney risks, especially in combination with SN's ACEI and SGLT2 inhibitor.

Approximately 2 weeks later, SN returns complaining of a 2-day history of profuse watery diarrhea, intermittent vomiting, and inability to keep down food. He reports he's lost almost 5 pounds.

Lab work reveals a current serum creatinine of 4.6 mg/dL, up from 1.2 mg/dL at baseline. SN is hospitalized due to acute kidney injury, likely due to dehydration from the GI illness in combination with overdiuresis from the diuretic and SGLT2 inhibitor.

11. Which of SN's medications should be held upon admission to the hospital?

SN remains hospitalized for 3 days and his renal function improves with aggressive IV hydration. His creatinine decreases to 2.4 mg/dL on the day of discharge. His blood pressure was elevated during his hospitalization so he was started on amlodipine 10 mg daily. He was discharged on only amlodipine 10 mg daily and atorvastatin 80 mg daily with instructions to follow up with his outpatient prescriber for further management of his blood pressure and diabetes.

He is now 2 weeks out from his hospitalization. His blood pressure is slightly elevated at 152/88 mmHg, but he is otherwise feeling well and without any complaints. He has been checking his blood sugar since he arrived home from the hospital and notes that his fasting blood sugars are now typically in the low 200s. Assuming his creatinine level is back to baseline, he asks about resuming his original medication regimen.

12. What should you recommend about restarting SN's prior medication regimen?

[e LEADER NOTES for answers to discussion questions.](#)

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Hareźlak T, Religioni U, Szymański FM, et al. Drug Interactions Affecting Kidney Function: Beware of Health Threats from Triple Whammy. *Adv Ther.* 2022 Jan;39(1):140-147.

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Additional Pharmacist's Letter Resources available at [PharmacistsLetter.com](https://www.pharmacistsletter.com)

[Managing NSAID risks.](#) *Pharmacist's Letter/Prescriber's Letter.* September 2022.

[Analgesics for Osteoarthritis.](#) *Pharmacist's Letter/Prescriber's Letter.* July 2022.

[Monitoring ACEIs and ARBs.](#) *Pharmacist's Letter/Prescriber's Letter.* May 2021.

[Using an ACEI or ARB After Acute Kidney Injury.](#) *Pharmacist's Letter/Prescriber's Letter.* February 2019.

[Comparison of Commonly Used Diuretics.](#) *Pharmacist's Letter/Prescriber's Letter.* May 2021.

[Slowing Progression of Kidney Disease in Patients With Diabetes.](#) *Pharmacist's Letter/Prescriber's Letter.* October 2021.

[Management of Albuminuria: Focus on Pharmacotherapy.](#) *Pharmacist's Letter/Prescriber's Letter.* September 2018.

[Drugs for Type 2 Diabetes \(United States\).](#) *Pharmacist's Letter/Prescriber's Letter.* July 2022.

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