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The Untold NSAID Story

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Patients need to be cautious about what they are taking, and aware that combinations of various NSAIDs should be avoided. This is especially true of a patient who may be taking an over-the-counter NSAID and a prescription NSAID at the same time.

I remember it like no other night. I admitted a patient to the hospital who was taking over-the-counter ibuprofen, meloxicam prescribed by her primary care physician, and Celebrex prescribed by her orthopedic physician. Her kidney function was severely decreased and, as a result, her legs and thighs were severely swollen. Her potassium level (usually excreted by the kidney) was 7.6, which at that level is enough to cause cardiac arrest. I gave her calcium, insulin and sodium polystyrene to try to lower this life-threatening potassium level, but to no avail. Dialysis then was initiated.

My patient never knew that all three medications were nonsteroidal anti-inflammatory drugs (NSAIDs) that, in combination or sometimes alone, may decrease kidney function. I spent a great deal of time thinking about how I could try to prevent this from happening again to any of our patients, which is why I have written this article for you.

Aspirin, produced in 1897 by Felix Hoffman of the Bayer company, was the first NSAID. Later, phenylbutazone and indomethacin were introduced. At that time, the mechanism of the action of these medications was unknown. Dr. John Vane eventually discovered that these medications work by inhibiting the production of prostaglandins, which promote inflammation and pain. After that discovery, the pharmaceutical industry was able to produce similar agents such as ibuprofen and naproxen, which we now know inhibit the enzyme cyclooxygenase (COX).

After recognizing that COX was the target enzyme, numerous NSAIDs have been introduced since the early 1970s. In response to side effects from steroids (prednisone and cortisone), the pharmaceutical industry coined the term "nonsteroidal" because these NSAIDs were not prednisone or cortisone. These medications, however, which were formulated to have a lower side effect potential than steroids, actually had their own potential severe adverse effects. One of the first NSAIDs, phenylbutazone, eventually was removed from the market when a number of cases reported that it caused aplastic anemia.

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List of NSAIDs

Aspirin *(may be taken at low dose (81 mg) with other NSAIDs)*
Celebrex
Diclofenac *(Common brand name: Voltaren)*
Diflunisal
Etodolac *(Common brand name: Lodine)*
Flurbiprofen *(Common brand name: Ocufen)*
Ibuprofen *(Common brand names: Advil, Motrin)*
Indomethacin *(Common brand name: Indocin)*
Ketoprofen *(Common brand name: Orudis)*
Ketorolac *(Common brand names: Toradol, Sprix, Acuvail, Acular)*
Meclofenamate
Mefenamic acid *(Common brand name: Ponstel)*
Meloxicam *(Common brand name: Mobic)*
Nabumetone *(Common brand name: Relafen)*
Naproxen sodium *(Common brand names: Aleve)*
Oxaprozin *(Common brand name: Daypro)*
Piroxicam *(Common brand name: Feldene)*
Salsalate *(Common brand name: Disalcid)*
Sulindac *(Common brand name: Clinoril)*
Trisalicylate

NSAIDs increase the risk of stomach ulcerations and bleeding, which prompted the development of specific medications that selectively target the COX-2 enzyme. Theoretically, this would reduce the risk of stomach ulcers and bleeding. Celebrex, among other COX-2 inhibitors, received FDA approval in 1998. These drugs did show less gastrointestinal bleeding but were noted to cause an increased risk of clotting, leading to a slight increase of heart attacks and strokes in at-risk patients.

All NSAIDs, however, cause a decrease in kidney function by limiting blood flow to the kidney. It is important to note that when normal, healthy individuals take an NSAID, their kidney function mildly decreases transiently and most of those patients are able to recover. In the setting of dehydration, certain blood pressure medications, older age, lower blood pressure states (i.e., heart failure or cirrhosis) or baseline low kidney function, the addition of an NSAID may reduce kidney function by almost 100%. Certainly baseline blood work to estimate kidney function (as measured by BUN and creatinine) should be done before NSAIDs are started, and regular monitoring should occur after they are started if taken on a consistent basis.

As noted in my story, patients need to be cautious about what they are taking, and aware that combinations of various NSAIDs should be avoided. This is especially true of a patient who may be taking an over-the-counter NSAID and a prescription NSAID at the same time! Always be sure to review all your medications carefully with your doctor. This problem is not uncommon with NSAIDs accounting for 70 million prescriptions and 30 billion over-the-counter doses sold annually in the United States. ■