

# Review: NSAIDs after surgery in patients with normal renal function decrease renal function on day 1 but not day 2

Lee A, Cooper MG, Craig JC, Knight JF, Keneally JP. Effects of nonsteroidal anti-inflammatory drugs on post-operative renal function in adults. *Cochrane Database Syst Rev.* 2001;(2):CD002765 (latest version 6 Feb 2001).

## QUESTION

In patients with normal renal function who have had recent surgery, are nonsteroidal anti-inflammatory drugs (NSAIDs) associated with adverse renal effects?

## DATA SOURCES

Studies were identified by searching MEDLINE and EMBASE/Excerpta Medica from their inception to June 1999; the Cochrane Library; bibliographies of relevant studies, review articles, and clinical practice guidelines; and conference proceedings from 7 journals. Pharmaceutical company representatives were also contacted.

## STUDY SELECTION

Randomized and quasirandomized (e.g., by day of week or odd vs even chart numbers) controlled trials were selected if NSAIDs were compared with each other or with placebo for pain management; patients were adults with normal renal function before surgery who had had surgery in the previous 24 to 48 hours; and outcome data were provided for creatinine clearance rate (primary outcome), serum creatinine level, urine volume, urinary sodium and potassium levels, fractional

excretion of sodium or potassium, need for dialysis, or need for diuretic or dopamine treatment for renal insufficiency.

## DATA EXTRACTION

Data were extracted or obtained from the authors on study quality, duration of treatment, type and dose of NSAIDs (ketorolac, ibuprofen, diclofenac, indomethacin, tenoxicam, and ketoprofen), patient characteristics, type of surgery, anesthetic procedure, and outcomes at days 1 and 2.

## MAIN RESULTS

14 randomized controlled trials met the inclusion criteria. 6 trials had insufficient data for meta-analysis. 6 NSAIDs were included, and administration routes varied across studies. No cases of renal failure needing dialysis were reported. When creatinine clearance data were pooled, NSAIDs were associated with a 21% decrease from baseline in creatinine clearance rate (18 mL/min, 95% CI 6 to 31) on the first day after surgery in 111 patients, but this difference was no longer significant by day 2. On the first day after surgery, the groups did not differ for serum creatinine levels;

on day 2, patients in the NSAID groups had a mean 15  $\mu$ mol/L (CI 2 to 28) increase in levels. The groups did not differ for proportion of patients who became oliguric, urinary volume on day 1 or 2, reduction in fractional sodium and potassium excretion measures on day 1, or urinary sodium levels on day 1 or 2. Urinary potassium levels were lower in the NSAID group on day 1 (decrease of 38 mmol/d, CI 19 to 56) but not day 2. Data were insufficient to determine differences between different NSAIDs or doses.

## CONCLUSION

Nonsteroidal anti-inflammatory drugs in patients with normal renal function are associated with reduced renal function the first day after surgery, but renal function resolves by day 2.

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## COMMENTARY

Once again, a Cochrane systematic review skewers a specific clinical question, holds it under the direct light of close scrutiny of the evidence, and yields clinically useful information. The review by Lee and colleagues uses rigorous methods typical of Cochrane reviews: broad, sensitive searches for all relevant evidence (big net, small holes), independent assessment of trial eligibility and quality, and quantitative pooling if the data allow.

Thus, we learn that NSAIDs in the first 24 to 48 hours after surgery in adults with normal preoperative renal function are associated with mild, transient decreases in renal function. All patients had general anesthesia for mostly major procedures (aortic, other abdominal, thoracotomy, or hip or knee replacement). These results corroborate data in other clinical settings that NSAID-induced renal impairment in most patients with normal baseline function is mild, is short-lived, and resolves promptly after therapy. Clinically, we can use these results to maximize early postoperative pain control in normal patients, with more caution used in patients at renal risk: those with hypertension, congestive heart failure, and liver disease.

But caveats exist. The relevant trials were very short and small, and even after pooling, the meta-analytic stewpot was relatively small—

111 patients maximum. Resolution of renal impairment was inferred mostly because of confidence intervals crossing the line of no effect rather than because of a clear shift of effect estimate from harm to no harm. Most patients having major surgery need pain management for more than 2 days, so further follow-up is needed. Finally, recent bench data have unhinged the original concept of independent roles for cyclooxygenase (COX)-1 in physiologic homeostasis and COX-2 in pathologic inflammation. Their actions appear much more complex and intertwined (1). Both affect renal function through both shared and unique mechanisms. Therefore, we can look to future systematic reviews to tell us more about both types of COX inhibition for pain management.

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## Reference

1. Lipsky PF, Brooks P, Crofford LJ, et al. Unresolved issues in the role of cyclooxygenase-2 in normal physiologic processes and disease. *Arch Intern Med.* 2000;160:912-20.