

NSAIDs in the postoperative period

Use with caution in elderly people . . .

EDITOR,—Although non-steroidal anti-inflammatory drugs are a useful addition to the analgesic armamentarium, we disagree with Dermot F Murphy's view that "in most cases, the benefits of reducing an elderly patient's opioid requirement by a third will outweigh any short term reduction in renal function."¹ It is not uncommon to find pre-existing renal impairment in elderly people due to age, atherosclerosis, hypertensive renal disease, or other intrinsic renal disease. This may be compounded perioperatively by hypovolaemia and hypoalbuminaemia, and in this group of patients no non-steroidal anti-inflammatory drug can be prescribed with absolute safety with respect to renal dysfunction^{2,3} owing to inhibition of renal synthesis of prostaglandin.

As elderly people are the most likely to have multiple organ dysfunction there is great potential for interactions between non-steroidal anti-inflammatory drugs and other drugs. Non-steroidal anti-inflammatory drugs may interfere with the pharmacological control of hypertension and heart failure. The action of drugs such as frusemide depends on prostaglandin, and the unbound concentrations of some non-steroidal anti-inflammatory drugs (usually extensively protein bound (>95%)) are higher in elderly people.

Asthma induced by aspirin is a distinct clinical entity that affects about 10% of adult patients with asthma.⁴ Many explanations have been advanced, but they all operate within the framework of the cyclo-oxygenase inhibition theory. Some non-steroidal anti-inflammatory drugs have been withdrawn in the United States and elsewhere because of reports of anaphylaxis.

A quarter of all suspected adverse reactions reported to the Committee on Safety of Medicines in the United Kingdom some years ago were due to non-steroidal anti-inflammatory drugs⁵; the range of adverse reactions is wide. We urge that enthusiasm is tempered with caution when non-steroidal anti-inflammatory drugs are used for postoperative analgesia.

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- Murphy DF. NSAIDs and postoperative pain. *BMJ* 1993;306:1493-4. (5 June.)
- Brookes PM, Day RO. Nonsteroidal antiinflammatory drugs—differences and similarities. *N Engl J Med* 1991;324:1716-25.
- Harris K. The role of prostaglandins in the control of renal function. *Br J Anaesth* 1992;69:233-5.
- Szczeklik A. The cyclooxygenase theory of aspirin-induced asthma. *Eur Respir J* 1990;3:588-93.
- Committee on Safety of Medicines. Non-steroidal anti-inflammatory drugs and serious gastrointestinal adverse reactions. *BMJ* 1986;292:614.

. . . and after major surgery

EDITOR,—Dermot F Murphy is to be congratulated for encouraging the use of non-steroidal anti-inflammatory drugs for postoperative pain but underestimates the risk of renal failure when these drugs are used early after major surgery.¹ The maintenance of renal function during postoperative conditions such as hypovolaemia or sepsis depends

Advice to authors

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on vasodilator renal prostaglandins,² and, though every effort is made to ensure that patients are not hypovolaemic after major surgery, inevitably some are at risk. To advocate the widespread use of non-steroidal anti-inflammatory drugs in this context will compromise renal function in the few who, for example, suffer unexpected haemorrhage.

Recent experience in this hospital's intensive care unit illustrates the potential hazards of this practice. Of the last five patients who developed unexpected renal failure after major surgery, all required inotropic support and one died. All received non-steroidal anti-inflammatory drugs in the early postoperative period.

The balance of risk against benefit suggests that routine early use of non-steroidal anti-inflammatory drugs after major surgery is potentially hazardous. I agree with Murphy's advocacy of their early use after minor surgery when there is no risk of cardiovascular compromise. Perhaps, though, in major surgery it would be better to continue the accepted practice of introducing them later in the postoperative period, when they are more effective and the integrity of renal function is established.

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- Murphy DF. NSAIDs and postoperative pain. *BMJ* 1993;306:1493-4. (5 June.)
- Harris K. The role of prostaglandins in the control of renal function. *Br J Anaesth* 1992;69:233-5.

Many factors threaten renal function

EDITOR,—Dermot F Murphy's editorial encouraging postoperative use of non-steroidal anti-inflammatory drugs does not mention the recognised risk factors for renal complications in patients taking these agents.¹ The commonest complication is a fall in the glomerular filtration rate, which, though usually minor and rapidly reversible, may progress to acute renal failure. Other complications include sodium and water retention, hyperkalaemia, hypertension, papillary necrosis, and the nephrotic syndrome with or without interstitial nephritis. Acute renal failure from any causes carries appreciable morbidity and mortality, and avoiding use of non-steroidal anti-inflammatory drugs in patients at high risk should reduce the incidence of renal complications.

Risk factors highlighted in reports of cases are pre-existent renal disease, age, male sex, use of diuretics, renal or coronary vascular disease, hypertension, diabetes, congestive heart failure, the nephrotic syndrome, and cirrhosis of the liver.² Case-control studies suggest a fivefold increase in risk in men aged over 65.³ Acute salt or volume depletion renders even healthy volunteers at risk of renal impairment.⁴

In prospective trials only patients with renal

blood flow critically dependent on the production of prostaglandin developed renal impairment when taking non-steroidal anti-inflammatory drugs.⁴ Although normal renal blood flow depends to some extent on tonic renal vasodilatation induced by prostaglandin, only if this dependency is increased does the inhibition of prostaglandin synthesis by non-steroidal anti-inflammatory drugs reduce renal blood flow and the glomerular filtration rate.⁴ This increased dependency in at risk groups is probably multifactorial. Structural disease of small or large vessels may contribute, but, additionally, there is often an enhanced vasoconstrictive drive from angiotensin II, which, at least in animal studies, is opposed by prostaglandins I₂ and E₂.⁵ Production of angiotensin II is increased in salt or volume depletion; many intrinsic renal diseases; certain hypertensive states, especially renal artery stenosis; and the oedematous states of heart failure, cirrhosis, and the nephrotic syndrome.

Non-steroidal anti-inflammatory drugs are commonly given to patients with clear—and sometimes multiple—risk factors for renal disease. This applies particularly to postoperative patients, who may have a degree of salt and water depletion in addition to any comorbid conditions. Opiates are reversible and if used with care may, in patients at high risk of renal complications, be preferable to non-steroidal anti-inflammatory drugs. Appreciation of the risk factors might reduce the incidence of renal disease related to use of non-steroidal anti-inflammatory drugs, especially after surgery.

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- Murphy DF. NSAIDs and postoperative pain. *BMJ* 1993;306:1493-4. (5 June.)
- Blackshear JL, Davidman M, Stillman T. Identification of risk for renal insufficiency from nonsteroidal anti-inflammatory drugs. *Arch Intern Med* 1983;143:1130-4.
- Sandler DP, Burr R, Weinberg CR. Nonsteroidal anti-inflammatory drugs and the risk for chronic renal disease. *Ann Intern Med* 1991;115:165-72.
- Clive DM, Stoff JS. Renal syndromes associated with non-steroidal anti-inflammatory drugs. *N Engl J Med* 1984;310:563-72.
- Aiken JW, Vane JR. Intrarenal prostaglandin release attenuates the renal vasoconstrictor activity of angiotensin. *J Pharmacol Exp Ther* 1973;184:678-87.

Clinical experience confirms risk

EDITOR,—Dermot F Murphy comments on the need to balance the risks of giving non-steroidal anti-inflammatory drugs postoperatively against their benefits but does not detail these risks.¹ We do not dispute the valuable analgesic properties of non-steroidal anti-inflammatory drugs, but we think that their potential adverse effects merit additional emphasis.

We have reviewed data on all patients referred to our unit with acute renal impairment between December 1992 and May 1993. In 14 of the 131 patients (seven male, seven female; mean age 62 (range 25-85)) renal impairment was associated with use of non-steroidal anti-inflammatory drugs. Coexistent aetiological factors identified in 12 patients included systemic sepsis (six), ischaemic heart disease or hypertension (four), hypovolaemia (five), and chronic renal failure (one). Four patients