Lesson of the Week

Antagonistic effect of non-steroidal anti-inflammatory drugs on frusemide-induced diuresis in cardiac failure

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Non-steroidal anti-inflammatory drugs (NSAID) with prostaglandin synthetase inhibitory activity are widely used to treat patients with arthritis. The diuretic effect of frusemide is thought to be mediated at least in part by renal prostaglandins.¹ The antagonistic effect of NSAID to frusemide is well documented in short-term studies of human volunteers and in animal experiments,^{2,3} yet there are no reports of NSAID interfering with the treatment of patients in cardiac failure. We report on such an interaction of NSAID with frusemide in three patients in cardiac failure.

Case reports

A 79-year-old man with ischaemic heart disease had been treated for cardiac failure for 18 months. He had no oedema, and his condition was stable on treatment with frusemide 80 mg/day, digoxin, and isosorbide dinitrate. The serum urea concentration was 21.6 mmol/l (129.8 mg/100 ml) and serum creatinine concentration 175 μ mol/l (2.0 mg/100 ml). He was started on treatment with ibuprofen 400 mg three times a day for backache owing to osteoarthritis of the lumbar spine. He then redeveloped congestive cardiac failure with ascites for no apparent reason. The dose of frusemide was increased to 160 mg/day without a satisfactory response. After admission to hospital bed rest and a further increase in his diuretic treatment—even by slow intravenous infusion—failed to start a diuresis. The serum urea concentration increased to 35.1 mmol/l (189.3 mg/100 ml) and the creatinine concentration to 230

Non-steroidal anti-inflammatory drugs have an antagonistic effect on frusemide in patients being treated for cardiac failure

μ mol/l (2.6 mg/100 ml). Ibuprofen was stopped and the patient's medication maintained as before. Two days later he responded with a brisk diuresis, reaching 3 litres of urine per 24 hours (figure). Thereafter his condition improved steadily, and his renal function returned to normal.

Two women in their seventies in congestive heart failure, with high concentrations of serum urea and creatinine, did not respond to treatment with frusemide and digoxin until they stopped taking naproxen for their arthritis.

Discussion

Arthritis and cardiac failure commonly occur in elderly patients, thus treatment with both NSAID and diuretics is not uncommon. The antagonistic effect of NSAID to frusemide is probably seen more frequently in clinical practice than is reported. Since NSAID reduce the dose response to frusemide² this adverse drug interaction is likely to be overcome in most cases only by increasing the dose of diuretic. Our patients, however, failed to respond to this. It has been suggested that renal prostaglandins assume clinical importance only when renal function is compromised—either structurally, as in systemic lupus erythematosus,⁴ or physiologically, as in the response to decompensated chronic liver disease⁵—and do not affect patients with adequate renal reserve. Our patients were elderly and had pre-existing renal impairment abetted by severe cardiac failure.

We suggest that NSAID are avoided in combination with frusemide in treating patients with cardiac failure, especially if there is also renal impairment.

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Diuretic and weight response to cessation of ibuprofen therapy in case 1.

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