with Hb A_{1C}. Patients with very high Hb A_{1C} values possibly represent a subgroup of the diabetic population, outside the normal criterion of long-term control, during a phase of metabolic decompensation; and they may show features more typical of the lipid disturbances of ketosis than of long-term diabetic control.

Thus our main finding is related not to diabetic control but to the type of diabetes, in that patients with maturity-onset diabetes have abnormally low HDL cholesterol concentrations irrespective of vascular disease and, possibly, of mode of treatment, whereas patients with juvenile-onset diabetes have essentially normal concentrations of HDL cholesterol.

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SIDE EFFECTS OF DRUGS

Ritodrine-induced acidosis in pregnancy

Beta-sympathomimetic agents such as salbutamol, terbutaline, and ritodrine[1] are commonly used to prevent premature delivery but may have metabolic side effects,[2 3] particularly in the case of salbutamol.[4] Enhanced lipolysis and glycolysis result in raised blood glucose, fatty acid, and lactate concentrations and a fall in serum bicarbonate.[5] Severe metabolic acidosis, however, has been described only in pregnancy complicated by diabetes.[6] We report a case of decompensated acidosis that occurred during an infusion of ritodrine.

Case report

An 18-year-old woman in the 32nd week of pregnancy was admitted to the department of obstetrics having been in labour for about two hours. The cervix admitted one finger and the membranes were intact. Ritodrine, diluted in 5% dextrose in water, was infused by a pump at 100 μg/min to delay delivery. Hydrocortisone succinate 1 g four times daily was given intravenously to prevent neonatal lung prematurity. Twelve hours after admission abdominal tenderness unrelated to uterine contractions was noted. Fetal heart rate monitoring showed a permanent tachycardia of 170/min and some late decelerations. The mother also had tachycardia but was otherwise physically normal. Attention was drawn to a serum bicarbonate concentration of 8 mmol(mEq)/l with a 10 mmol/l anion gap. Qualitative test for ketonuria was negative. Blood glucose concentration was 8·8 mmol/l (159 mg/100 ml) and pH 7·25. Ritodrine infusion was slowed to 30 μg/min and sodium bicarbonate (40 mmol/hour) given. Three hours later the serum lactate concentration was 7 mmol/l (63 mg/100 ml) and the anion gap 8 mmol/l. Ritodrine was stopped, and within three hours the lactate and bicarbonate concentrations were 2·7 mmol/l (24·3 mg/100 ml) and 20 mmol/l respectively. Delivery occurred 24 hours after admission; mother and child did well.

Comment

Although we cannot exclude the possibility of mild gestational daibetes in this case, normal fasting and postprandial blood glucose concentrations the day after delivery strongly suggest that the patient had a normal glucose tolerance. We therefore conclude that ritodrine, associated with corticosteroids, induced transient severe acidosis with predominant hyperlactacidaemia.

Blood electrolyte and glucose concentrations should be carefully monitored in non-diabetic patients given ritodrine for premature labour to detect potentially harmful metabolic acidosis.

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Departments of Medicine and Gynaecology, Hôpital Universitaire Saint-Pierre, Rue Haute 322, 1000 Brussels, Belgium
D DESIR, MD, assistant in medicine
A VAN COEVORDEN, MD, assistant in medicine
C KIRKPATRICK, MD, fellow of the Lekime-Ropsy Foundation
A CAUFRIEZ, MD, assistant in gynaecology

Reversible oliguric renal failure associated with ibuprofen treatment

Nephrotoxicity has been associated with non-steroidal anti-inflammatory agents such as phenylbutazone, oxyphenbutazone, and aspirin.[1] It has not been reported after use of ibuprofen, although similar propionic-acid derivatives—namely, fenoprofen and naproxen—have been associated with renal papillary necrosis.[2] We report here a case of reversible oliguric renal failure, which occurred in a patient with osteoarthritis treated with normal doses of ibuprofen.

Case report

A 65-year-old man was admitted to this hospital with acute left-sided weakness. His medical history included atherosclerotic and hypertensive cardiovascular diseases treated with frusemide, spironolactone, and digoxin;

osteoarthritis treated intermittently with aspirin; a 10-year history of adult-onset diabetes mellitus treated with diet; and mild renal insufficiency. Abnormal physical findings were limited to the central nervous system, with left-sided deficits. Laboratory investigation showed that creatinine concentration was 159 μmol/l (1·8 mg/100 ml), blood urea nitrogen 12·8 mmol/l (36 mg/100 ml), and creatinine clearance 64 ml/min. Computerised tomography (CTT) of the skull with dye contrast using 120 ml of sodium iothalamate injection was performed on the day of admission and showed a right parietal-occipital infarction. Physiotherapy, digoxin, frusemide, spironolactone, and a 2-g sodium diet were begun, and the patient's condition improved until seven days after admission, when he complained of arthralgia in his lower back. Lumbarsacral films were consistent with osteoarthritis, and he was given ibuprofen 400 mg four times daily. After six days' ibuprofen treatment (13 days after CTT) his urinary output decreased from an average of 1440 ml/24 h to 300 ml/24 h. At this time his blood urea nitrogen concentration was 27·8 mmol/l (78 mg/100 ml), and creatinine 318 μmol/l (3·6 μg/100 ml). Acute renal failure was suspected, and spironolactone and ibuprofen were discontinued. Renal function improved over the next eight days (serum creatinine concentration 186 μmol/l (2·1 mg/100 ml); blood urea nitrogen 14·3 mmol/l (40 mg/100 ml)). He was discharged, taking frusemide, spironolactone, and digoxin, with minimal neurological residual signs and stable renal function. Six months after discharge his condition remains stable.

Comment

Ibuprofen is a non-steroidal analgesic, antipyretic, and anti-inflammatory agent used in treating rheumatoid arthritis and osteoarthritis. Adverse effects are primarily gastrointestinal; dermatological, central nervous system, otic (tinnitus), and ophthalmological side effects occur less frequently.[3]

The two possible causes of the sudden onset of renal failure were the intravenous dye contrast material and the ibuprofen. The patient received intravenous dye contrast material 13 days before renal function was clinically decreased. Two cases of acute renal failure after injection of contrast media for CTT have been recently reported.[4] In both, however, renal failure occurred within 24 hours and these times of onset were consistent with other reported episodes of acute renal failure induced by contrast media (usually occurring within 12 to 24 hours). Possibly this patient had undetected renal insufficiency after CTT, since laboratory data were not collected immediately after this procedure. As oliguria usually occurs concurrently with dye-induced acute renal failure and is of short duration, we think that this patient's renal insufficiency was not related to the dye. Oliguria developed on the sixth day of ibuprofen treatment with no other changes in treatment, thus strongly implicating this drug. He had not taken ibuprofen before. He had been receiving frusemide, digoxin, and spironolactone in therapeutic doses for at least nine months without clinical evidence of adverse reactions, and did not react adversely when this treatment was reinstituted at discharge.

Ibuprofen is a potent inhibitor of prostaglandin synthesis and may thus be capable of decreasing renal function,[5] since prostaglandin E_2 affects renal blood flow and is a factor in the regulation of the glomerular filtration rate. We believe that ibuprofen was the precipitating factor in this patient's acute oliguric renal failure and suggest that fluid input and output as well as renal function should be carefully monitored in such cases. The acute renal failure appears to be reversible, as renal function improved when the drug was discontinued.

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New York Hospital—Cornell Medical Centre, New York, New York 10021

ROBERT D BRANDSTETTER, MD, resident physician, department of medicine
DEXTER D MAR, PHARM D, clinical co-ordinator, department of pharmacy

(We suggest to readers that any suspected adverse reaction to a new drug should be reported to the Committee on Safety of Medicines, preferably on a yellow card. Serious or unusual reactions to all drugs should also be reported.)

SHORT REPORTS

Heparin and infusion phlebitis

The problem of infusion phlebitis has produced a variety of explanations and advice on avoidance. The cause is not known—particularly, infection,[1] reaction to the canula[2] and to infusion fluids,[3] or simple trauma are all possible but unproved causes. In some hospitals the policy is to change the site of drips every day.[1] In a busy surgical unit there is not the time available for this and many patients do not have suitable veins. In practice, most drips are left in situ until early phlebitis occurs, they stop spontaneously, or are no longer required. Anecdotally, heparin is said to prolong the life of drips but the advice on this is conflicting.[4 5] The present study was designed to test the hypothesis that small doses of heparin, either subcutaneously or added to the infusion, both prolong drip life and reduce infusion-related phlebitis.

Methods and results

A total of 60 consecutive patients entering a general surgical unit under the care of one particular consultant, having intravenous infusions expected to continue for more than two days, were entered for this trial. They included patients admitted for routine and emergency procedures but excluded those actively bleeding from any site. No other groups were excluded. Patients admitted for routine procedures at high risk from pulmonary embolus received as routine practice 5000 units of subcutaneous (sc) heparin three times a day. Patients were alternately allocated to a control group receiving no intravenous (iv) heparin or to a group receiving a total of 2000 units of heparin per day via the infusion. This was divided into four doses of 500 units given six hourly into the infusion bags and did not affect the partial thromboplastin time.

When a drip was discontinued the length of time it had been running and the reason for its discontinuation were recorded. Three reasons for discontinuing were recognised; (1) local pain, redness, and swelling (phlebitis); (2) spontaneous stoppage, cause unknown (often called tissuing); and (3) elective removal. Within both the control and added iv heparin groups there were some patients who had routinely received sc heparin; initially

Drip life and reasons for discontinuation in control patients and those receiving subcutaneous (sc) or intravenous (iv) heparin

		Controls	sc heparin	iv heparin
Mean (±SD) drip life in days (n)		2·1±1·0 (23)	3·4±1·6 (15)	5·2±3·2 (21)
P values			0·005	0·025
			0·001	
Reasons for discontinuation	Phlebitis	6	4	5
	Spontaneous stoppage	8	4	1
	Elective removal	9	7	15
P values for spontaneous stoppage versus elective removal			NS	
			0·025	