Incidence of hyperkalaemia induced by indomethacin in a hospital population

Non-steroidal anti-inflammatory drugs are among the most widely prescribed drugs. In addition to gastrointestinal toxicity several renal complications are associated with their use, including acute renal failure, the nephrotic syndrome, interstitial nephritis, and abnormalities of water and electrolyte homeostasis. Hyperkalaemia, usually associated with indomethacin, has only recently been recognised as a complication. The objective of the present study was to determine prospectively the incidence and severity of hyperkalaemia in a population of nta tients receiving indomethacin.

Patients, methods, and results

We studied all 50 patients admitted to the department of medicine at this medical centre between October 1983 and July 1984 in whom treatment with indomethacin was started. The increase in serum potassium and blood urea nitrogen concentrations after treatment was defined as the difference between the highest measurement before and after indomethacin was started.

The increase in serum potassium concentration was less than 0.5 mmol (mEq)/l in 20 patients (group 1). An increase of 0.5-0.9 mmol/l was observed in 17 patients (group 2) and >1.0 mmol/l in 13 patients (group 3). Absolute serum potassium concentrations exceeded 5.0 mmol/l in two (10%) patients in group 1 compared with eight (47%) patients in group 2 and all 13 patients in group 3. The mean (SD) daily dose of indomethacin was 168 (37) mg in group 1, 176 (22) mg in group 2, and 173 (35) mg in group 3.

The figure shows the variations in serum potassium concentrations in six patients in group 3 in whom peak values exceeded 6.0 mmol/l. In all potassium concentrations steadily increased until treatment with indomethacin was stopped. Peak values were observed on days 3-7 of treatment. Blood urea nitrogen concentration did not change or increased by less than 3.6 mmol/l (10 mg/100 ml) in 37 of the 50 patients. An increase of >3.6 mmol/l was found in four (20%) patients in group 1, two (12%) patients in group 2, and seven (54%) patients in group 3. These seven patients in group 3 had all had blood urea nitrogen concentrations before treatment exceeding 7.9 mmol/l (22 mg/100 ml).

The indications for treatment with indomethacin were musculoskeletal pain in 33 patients, pericarditis in 12, and fever associated with malignancy in three and autoimmune disease in two. The proportions of patients in these categories were the same for patients with and without a hyperkalaemic response to indomethacin. In contrast, the mean age of patients in group 1 (56±1 (18-9) years) was 10-12 years lower than that of patients in group 2 (66±9 (6-7) years) and patients in group 3 (68±11 (9-9) years) (p=0.025). An impressive difference was the threefold (61%) increase in the prevalence of mild to moderate (3-7-7-2 mmol/l (22-43 mg/100 ml)) pre-existent azotaemia in group 3 compared with groups 1 (25%) and 2 (18%) (p=0.01).

Effect of treatment with indomethacin on serum potassium concentration. Broken lines indicate measurements made after drug was stopped. Conversion: SI to traditional units—Serum potassium: 1 mmol/l=1 mEq/l.

Comment

We think that this study represents the first attempt to determine prospectively the incidence of hyperkalaemia in an inpatient population receiving indomethacin. Our findings indicate that hyperkalaemia is a common and potentially dangerous complication of treatment with indomethacin and that pre-existent mild to moderate azotaemia and old age are associated with an increased risk of the condition. Our findings together with previous reports lead us to make several recommendations for patients treated with indomethacin. Firstly, serum potassium concentrations should be measured in all patients before and repeatedly during the first week of treatment with indomethacin. Particular care should be exercised in patients with pre-existing renal disease, elderly subjects, and patients receiving potassium sparing diuretics, potassium supplements, angiotensin converting enzyme inhibitors, and β adrenergic blocking agents or digoxin. Finally, pre-existent uraemia and hyperkalaemia should be regarded as contraindications to treatment with indomethacin.
Chronic subdural haematoma: possible association with chronic granulocytic leukaemia in lymphoid transformation

Chronic subdural haematoma is a recognised complication of childhood acute lymphocytic leukaemia.1 We report on two adults with chronic granulocytic leukaemia who developed chronic subdural haematoma. Both were receiving maintenance treatment for acute lymphocytic leukaemia, having previously undergone lymphoid transformation.

Case reports

Case 1—A 58 year old man presented in February 1983 with a four week history of vomiting, headaches, and focal epilepsy affecting the right side. Chronic granulocytic leukaemia with presence of the Philadelphia chromosome had been diagnosed in 1973. Lymphoid transformation had been diagnosed in 1978 and successfully treated with standard treatment for acute lymphocytic leukaemia. In August 1982 he had developed a relapse in the central nervous system and was given treatment to induce remission of the acute lymphocytic leukaemia, intrathecal methotrexate, and radiotherapy to the cranium (24 Gy (2400 rad)) and spine (12 Gy (1200 rad)). Maintenance treatment for acute lymphocytic leukaemia had been restarted in November 1982. Computed tomography in February 1983 showed bilateral subdural haematomas, especially on the left side of both cerebral hemispheres, the larger being on the left side. The left sided haematoma was surgically drained. He recovered completely and continued to receive maintenance treatment for acute lymphocytic leukaemia.

Case 2—A 72 year old man presented in June 1984 with a six week history of headache and focal epilepsy affecting the left face and arm. Chronic granulocytic leukaemia with presence of the Philadelphia chromosome had been diagnosed in November 1981. He had developed lymphoid transformation in October 1983, and remission of acute lymphocytic leukaemia had been successfully induced. Maintenance treatment had been started in January 1984. Prophylactic cranial radiotherapy (24 Gy (2400 rad)) and intrathecal methotrexate had been given in March 1984. Computed tomography in June 1984 showed small bilateral subdural haematomas. Subsequent scans showed gradual resolution, and surgical intervention was not necessary. He remained well and continued with maintenance treatment for acute lymphocytic leukaemia.

Comment

Chronic subdural haematoma is a recognised complication of lymphoid transformation of chronic lymphoblastic leukaemia.1 A particular association with childhood acute lymphocytic leukaemia has been reported.1 Our experience suggests that adults with acute lymphocytic leukaemia or chronic granulocytic leukaemia in lymphoid transformation may also be at particular risk. The pathogenesis of this complication is probably multifactorial. Both of our patients had recently completed cranial or craniospinal radiotherapy with intrathecal methotrexate. Both had recently experienced prolonged periods of thrombocytopenia (two to four months) during the phase of treatment to induce remission of their acute lymphocytic leukaemia, though neither gave a history of head injury. Neither patient had abnormalities on computed tomography other than subdural haemorrhage, though a variety of abnormalities, some of which may predispose to chronic subdural haematoma, have been reported in children with acute lymphocytic leukaemia who have undergone prophylactic cranial irradiation.3

Neither patient had evidence of leukaemia of the central nervous system at the time of presentation with chronic subdural haematoma, though one had previously been treated for disease of the central nervous system.

Lymphoid transformation in chronic granulocytic leukaemia has a more favourable outcome than myeloid or mixed cell transformation.4 Our patients also recovered completely from chronic subdural haematoma. Lumbar puncture is a dangerous investigation in patients with chronic subdural haematoma but was undertaken in both our patients at presentation because of clinical suspicion of infection of the central nervous system or leukaemic infiltration. We recommend that computed tomography should precede lumbar puncture in the investigation of neurological symptoms in patients with leukaemia who have previously undergone cranial radiotherapy.

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Rejection of catheters

Although long term urinary catheterisation should be regarded as a last resort in the management of urinary incontinence, it is fairly common among elderly patients. Leakage, bypassing, and infection are common reasons for changing catheters.1 2 Rejection of the catheter, whereby it is apparently pulled out by the patient, has received little attention. We examined this problem.

Patients, methods, and results

We studied all long stay patients in seven wards of our geriatric unit who had had a catheter in place for more than three months. Each patient was assessed for degree of immobility, and mental function was tested using a 10 point memory questionnaire. Details about the catheter were recorded every two weeks for 16 weeks by interviewing ward staff and scrutinising nursing and medical records. Twenty five patients (21 women, four men; mean age 81±4 years) were studied. Twelve were chairbound, and 22 scored less than five out of 10 on the memory questionnaire, indicating appreciable cognitive impairment.

During the study 181 catheters were changed. The mean number of changes per patient was 74 (range 2-17), and the average life of a catheter was only 16-2 days (range 7-60 days). Of the catheters changed, 100 were removed by nursing staff and 81 were rejected by the patients. Only four patients did not reject their catheters at all.

The 81 episodes of rejection could be divided into three groups. In 29 cases the catheter was found in the patient’s hand or in an unusual place such as the bedside locker or under the pillow, suggesting that the patient had pulled it out. In 32 cases the catheter came out spontaneously, often while the patient was sitting on the commode, transposing position, or bathing. In some cases the catheter was observed by the patient, being expelled from the patient’s urogenital tract. In 20 cases the catheter was simply found in the patient’s bed and the cause of rejection was undetermined.

Though catheters with small and large retaining balloons (range 5-30 ml) were rejected, rejection was particularly common in those with 5-10 ml balloon volumes, according to 56% of changes of catheters with balloons of this size. Most catheters with big balloons (20-30 ml) were changed for reasons such as leakage or blockage (71% of changes of catheters with balloons of this size). No relation between the diameter of the catheter (median 16, range 12-30 French gauge) and rejection was observed.