quantities may be absorbed through the skin during one episode of hair dyeing. Although individual sensitivity is extremely rare, these substances used in hair dyeing must continue to be the subject of close scrutiny.

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Successful treatment of myeloma kidney by diuresis and plasmaphoresis

We report a patient with myeloma kidney and severe renal failure treated by forced diuresis and plasmaphoresis. Excellent recovery of renal function has been maintained for nine months, a survival far longer than expected in such a case.

Case history

A 29-year-old Englishman developed a lump on his head in September 1974. Three months later he presented with nocturia and tiredness. He looked ill, with a fluctuant swelling 3 cm by 3 cm over the right parietal bone; tenderness over the left ribs and lower thoracic spine; and some anterior angulation at D8. Haemoglobin was 6·0 g/dl, white blood count $4·1 \times 10^9$/l (4100/mm^3), erythrocyte sedimentation rate 69 mm in 1 hour. Immunoelectrophoresis showed a monoclonal excess of IgG (44 g/l) with low IgA and IgM. Bence Jones protein was present in the urine (1·2 g/24 h). Skeletal survey showed widespread lytic deposits. The diagnosis of multiple myeloma was confirmed by narrow aspirate, showing 20% primitive plasma cells. His blood urea was 44·8 mmol/l (270 mg/100 ml); creatinine 1220 μmol/l (13·8 mg/100 ml); plasma calcium 2·2 mmol/l (8·9 mg/100 ml); urine specific gravity 1031, urate 0·50 mmol/l (8·4 mg/100 ml). Urine osmolality was 310 mmol/kg (310 mosmol/kg), 24-hour urine calcium and urate were not elevated. There was no amino-aciduria.

He was treated initially with melphalan 5 mg daily for one week. Renal biopsy showed myeloma kidney with tubular casts, tubular dilatation, and atrophy with surrounding inflammation. The glomeruli were normal, and there was no amyloid or vascular change.

Over the next two weeks the renal function deteriorated (blood urea rising to 78 mmol/l (470 mg/100 ml)) despite saline repletion, and he developed pleural and pericardial effusions, drowsiness, and confusion. He was treated with peritoneal dialysis from 31 December 1974 to 7 January 1975; simultaneously a diuresis was induced with 5 litres daily of intravenous saline, and frusemide, 500 mg daily. Urine pH was above 6.

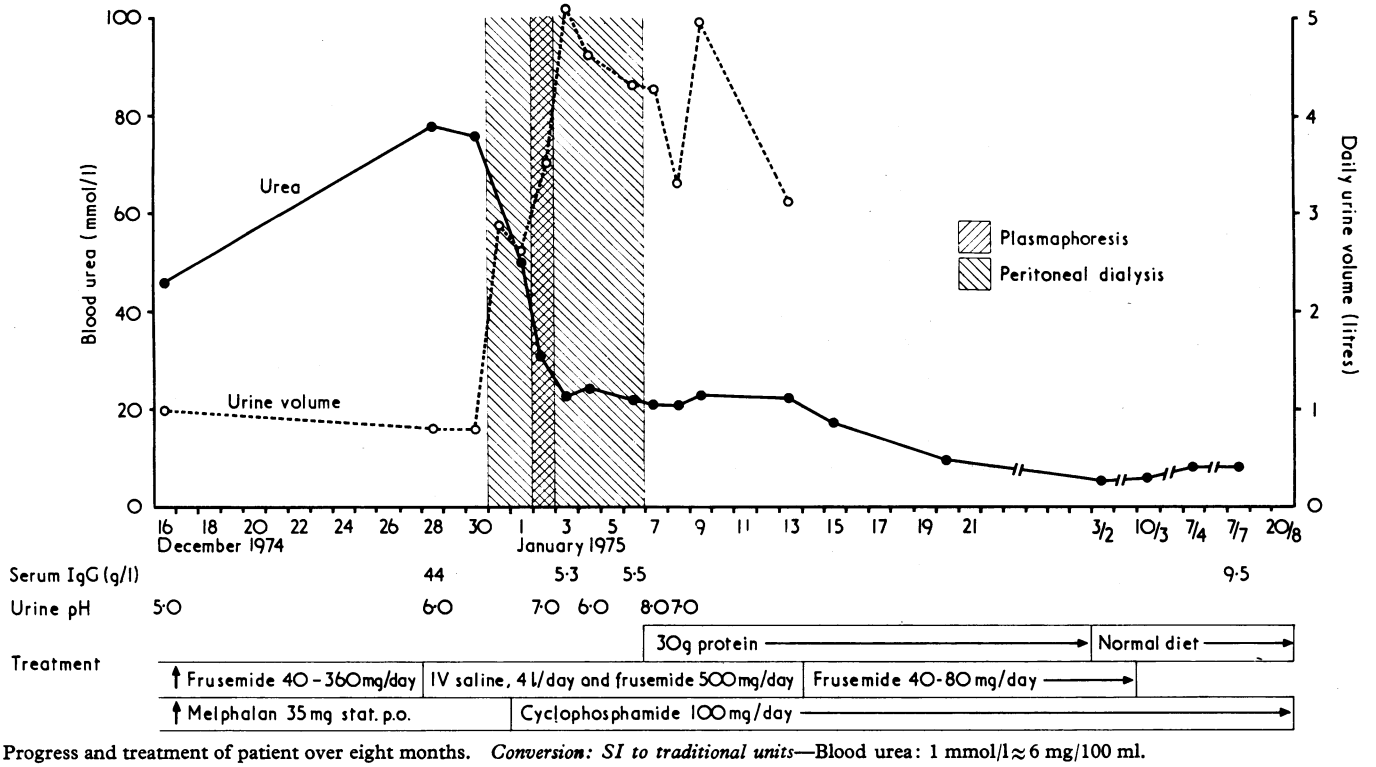
On 2 January 1975 plasmaphoresis was performed, exchanging 1180 ml plasma for plasma protein fractions, at which his IgG fell from 44 g/l to 5·5 g/l, and Bence Jones proteinuria ceased. He improved greatly, the blood urea and creatinine continuing to fall after dialysis was stopped. Nine months later he is well and working normally; the haemoglobin 12 g/dl, blood urea 10·0 mmol/l (60 mg/100 ml), creatinine 160 μmol/l (1·8 mg/100 ml), creatinine clearance 66 ml/min, IgG 9·3 g/l, 24-hour urine protein 300 mg. He is maintained on intermittent courses of melphalan.

Discussion

When acute renal failure occurs in myelomatosis the prognosis is poor: in one series 13 of 14 patients died within two months[1]. There is a strong correlation between the occurence of Bence Jones proteinuria and renal failure in myeloma.[1 2] The precise role of these proteins in the pathogenesis of renal failure is uncertain, but direct toxicity of light chains to the renal tubule,[3] and tubular obstruction by casts[4] have both been postulated.

It seems reasonable to treat myeloma kidney by attempting to remove Bence Jones proteins from the kidney, and to prevent reaccumulation by removing them from the serum. Bence Jones protein precipitates most readily if the urine is concentrated, the pH is below 6, and solutes and albumin are present.[5] An alkaline diuresis should thus help to prevent cast formation, and possibly remove existing casts. Such treatment has been shown to protect mice with Bence Jones proteinuria from renal damage, reducing cast formation, and has prevented progression of renal failure in a patient with myelomatosis.[4]

Our patient deteriorated on conventional treatment. Treatment with a sustained alkaline diuresis and plasmaphoresis to remove



Progress and treatment of patient over eight months. *Conversion: SI to traditional units*—Blood urea: 1 mmol/l ≈ 6 mg/100 ml.

the Bence Jones proteins resulted in excellent recovery of renal function with survival much longer than expected on conventional treatment alone.

We would like to thank Professor J S Cameron of Guys Hospital for his encouragement and advice.

Reprint requests should be sent to SLC.

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Comparison of effects of metoprolol and propranolol on asthmatic airway obstruction

Propranolol, which acts unselectively on cardiac (β_1) and bronchial (β_2) adrenoceptors, may cause bronchoconstriction in asthmatic subjects. This risk is less with the cardioselective beta-adrenoceptor blocking drugs practolol or acebutolol.[1] Practolol has been in use the longer of the two and until recently was thought not to cause adverse reactions, but as more patients have been treated with it in the long-term some have developed serious side effects.[2]

Metoprolol is a recently introduced beta-blocking drug which is cardioselective in animals.[3] We report here the effect of intravenous metoprolol and propranolol on airways obstruction in asthmatic subjects.

Patients, methods, and results

Twelve asthmatic outpatients were studied. They understood that their asthma might temporarily worsen, and the study was approved by the local ethical committee. The mean age of the patients was 35·3 years (range 20-46) and their mean weight was 61·4 kg (range 52-70). Only patients with mild airways obstruction were selected, because this was unlikely seriously to worsen as a result of the experiment. They visited the laboratory on three different days at about the same time, to exclude the effect of diurnal variation in ventilatory function. They took no bronchodilator drugs for 12 hours beforehand. At each visit baseline measurements of the forced expiratory volume in one second (FEV_1), forced vital capacity (FVC), specific airways conductance (SGaw), and resting pulse rate were made, and the mean values were closely similar on each occasion. The FEV_1 and the FVC were recorded in litres (ambient temperature and pressure saturated with water vapour (ATPS)) from the best of three forced expiratory spirograms obtained with a dry wedge spirometer. Specific airways conductance (SGaw) was measured in a constant volume body plethysmograph and each reading was the mean of three determinations (normal range 1140-4140 ml s^{-1} kPa^{-1} l^{-1}). The logarithms of SGaw were used for statistical analysis since the distribution of this measurement is log normal. After the baseline measurements intravenous metoprolol 8 mg, propranolol 5 mg, or placebo (saline) was given over 60 seconds in a double-blind randomised sequence. These doses were chosen because, when given intravenously, they had been found to cause a similar decrease in resting heart rate.[4] Measurements of FEV_1, FVC, and pulse rate were repeated at 5, 10, 15, 30, and 45 minutes after the injection and measurement of SGaw was repeated at 15 minutes after the injection. Salbutamol was given by pressurised aerosol at 45 minutes.

The table shows the mean differences between the average of all the readings at 5, 10, 15, 30, and 45 minutes from baseline for FEV_1, FVC, and pulse rate and for log SGaw from baseline and at 15 minutes.

Mean changes (±SE) in 12 asthmatics in FEV_1, FVC, pulse rate, and log SGaw between averages of 5, 10, 15, 30, and 45 minutes after placebo, metoprolol, and propranolol

	FEV_1 (l ATPS)	FVC (l ATPS)	Pulse rate	Log SGaw ($ml\ s^{-1}\ kPa^{-1}\ l^{-1}$)
Placebo	−0·06±0·04	−0·09±0·04	−4·13±2·10	+1·03±1·06
Metroprolol	−0·28±0·08	−0·37±0·14	−12·0±1·74	−1·35±1·27
Propranolol	−0·44±0·07	−0·55±0·13	−12·0±1·98	−6·21±1·74

FEV_1
Placebo *v* metoprolol $P<0·05$.
Placebo *v* propranolol $P<0·001$.
Metoprolol *v* propranolol $P<0·01$.

FVC
Placebo *v* metoprolol $P<0·05$.
Placebo *v* propranolol $P<0·01$.
Metoprolol *v* propranolol $P<0·05$.

Pulse rate
Placebo *v* metoprolol $P<0·01$.
Placebo *v* propranolol $P<0·05$.
Metoprolol *v* propranolol NS.*

Log SGaw
Placebo *v* metoprolol P NS*.
Placebo *v* propranolol $P<0·01$.
Metoprolol *v* propranolol $P<0·05$.

*Not significant.

Comment

When given intravenously to asthmatic subjects metoprolol caused less bronchoconstriction than propranolol in doses that lowered the resting pulse rate to the same extent, but although the mean effect of metoprolol on bronchial calibre was slight the FEV_1 fell over 500 ml in two patients, which could well be clinically significant. This was also seen with propranolol, and the response to each of the two drugs tended to be similar in any one patient. Thus, cardioselective beta-adrenoceptor blocking drugs must be used with caution in patients with airways obstruction because their response to β_2-blocking is unpredictable. The bronchoconstriction resulting from both drugs was readily reversed by salbutamol. Therefore in asthmatics in whom metoprolol causes bronconstriction it may be combined with a selective β_2-receptor-stimulating drug such as salbutamol, which will not diminish the desired β_1-blocking action of metoprolol.

We thank Mr D McKenzie for technical help.

Requests for reprints should be sent to Dr K N V Palmer.

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