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SHORT REPORTS

Clearance of psoriasis with low dose cyclosporin

Previous studies have shown that T helper lymphocytes play an integral part in the pathogenesis of psoriasis.[1-3] Cyclosporin A is a selective immunosuppressive drug that specifically inhibits T helper cell function by impairing the production and effects of interleukin-2.[4] We therefore studied the efficacy of cyclosporin A in the treatment of psoriasis, using low doses because of its dose related nephrotoxic effects.

Patients, methods, and results

We studied 10 patients with severe psoriasis that was unresponsive to conventional treatment (including methotrexate and psoralens and ultraviolet A) (table). Informed consent was gained from each patient before entry to the study. Cyclosporin A was taken once daily in the evening for 12 weeks. In eight patients the initial daily dose was 1·66 μmol/kg (2 mg/kg); the other two, who had very severe active disease, were given 2·49 μmol/kg (3 mg/kg). The dose was increased by 0·83 μmol/kg (1 mg/kg) if there was no improvement after two weeks' treatment; the agreed maximum dose was 3·32 μmol/kg/day (4 mg/kg/day). Patients were assessed before treatment and at three days and one, two, three, four, six, eight, and 12 weeks. Before treatment and at each subsequent visit the following investigations were performed: blood pressure, urine analysis, urea and electrolyte concentrations, serum creatinine concentration, liver function, and full blood count. Blood cyclosporin concentrations were measured by radioimmunoassay as whole blood trough concentration about 12 hours after the last dose. The area of skin affected was determined at each visit and severity rated on a scale of 0-10.

Psoriasis cleared completely in five of the 10 patients and there was an appreciable improvement in the other five. Of the five in whom psoriasis cleared completely, clearance was achieved by six weeks in case 1 and by eight weeks in cases 2, 3, 4, and 5 (table). The therapeutic dose of cyclosporin A seemed to be 2·49 μmol/kg/day (3 mg/kg/day); increasing the dose to 3·32 μmol/kg/day (4 mg/kg/day) did not induce clearance in those in whom the disease had not cleared at the lower dose. There was no correlation between clinical response and whole blood cyclosporin concentrations, and in all but one patient concentrations were less than 0·62 μmol/l (750 ng/ml) on all occasions. Two patients experienced an increase in blood pressure, and in four serum creatinine concentration increased by more than 10% during the study, though the values were still within the normal range. Three of the six women developed hypertrichosis, consisting of fine lanugo hairs on the face and coarse terminal hairs on the legs. All three said that they were prepared to tolerate this side effect if their psoriasis cleared

Clinical data on patients with psoriasis participating in study

Case No	Age/sex	Previous systemic treatment	Body area affected*		Blood pressure (mm Hg)		Creatinine concentration (μmol/l)		Cyclosporin A dose (μmol/kg/day)	Mean (range) cyclosporin A blood concentrations (μmol/l)
			Start of study	End of study	Start of study	End of study	Start of study	End of study		
1	38/F	Methotrexate	5	0	100/80	120/85	68	85	1·66-2·49	0·23 (0·11-0·32)
2	32/F	PUVA	5	0	105/80	125/80	87	89	1·66-2·49	0·17 (0·11-0·25)
3	51/F	PUVA	5	0	140/80	120/75	85	75	2·49	0·31 (0·25-0·34)
4	40/M	PUVA	2	0	125/85	130/85	91	112	1·66-2·49	0·30 (0·16-0·39)
5	55/F	PUVA, Methotrexate	3	0	150/90	130/90	80	73	1·66-2·49	0·51 (0·31-0·60)
6	33/M	PUVA, Methotrexate	7	1	135/90	140/80	94	76	1·66-3·32	0·47 (0·26-0·61)
7	64/F	Methotrexate, PUVA	5	1	125/85	130/80	65	65	1·66-3·32	0·26 (0·16-0·30)
8	42/F	PUVA	2	1	140/90	160/105	85	98	1·66-3·32	0·34 (0·16-0·59)
9	62/M	PUVA, Methotrexate	5	2	120/85	140/100	84	94	2·49-3·32	0·63 (0·54-0·88)
10	38/M	Methotrexate, Razoxane	3	2	140/95	140/90	94	95	1·66-3·32	0·28 (0·18-0·34)

*0=<1%, 1=1-10%, 2=11-20%, 3=21-30%, 4=31-40%, 5=41-50%, 6=51-60%, 7=61-70%, 8=71-80%, 9=81-90%, 10=91-100%. PUVA=Psoralens and ultraviolet A treatment.
Conversion: SI to traditional units—Creatinine: 1 μmol/l≈0·01 mg/100 ml. Cyclosporin A: 1μmol≈1·2 mg.

up. Three other subjects suffered nausea for about one hour after taking cyclosporin A.

After 12 weeks' treatment cyclosporin A was withdrawn, and in all 10 patients the psoriasis relapsed, the time taken for relapse ranging from three days to two months. All side effects disappeared on withdrawal of the drug.

Comment

This study has shown low dose cyclosporin A to be effective in the treatment of severe psoriasis. Conventional treatment had failed to control the disease in the 10 patients studied, and this suggests that cyclosporin is more effective than other drugs that are currently available. Indeed, nine of the 10 patients said that cyclosporin was the most efficacious and tolerable treatment that they had received. Blood cyclosporin concentrations did not correlate with therapeutic response; psoriatic activity at the time of treatment is more likely to dictate individual response.

The effectiveness of cyclosporin in psoriasis supports the hypothesis that psoriasis is a T cell mediated disorder[3] and advances our understanding of this common and often intractable disorder.

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Haemorrhagic cystitis due to gentian violet

Gentian violet has been used extensively in children and adults to treat oral and vaginal candidiasis. Although many regard gentian violet as innocuous, there have been reports of mucosal ulceration after its use.[1] There is, however, no reported instance of damage to the bladder.

We describe a case of severe haemorrhagic cystitis due to accidental injection of gentian violet through the urethra.

Case report

A 32 year old woman presented to her local hospital with a two day history of gross haematuria, preceded by three days of severe pain in the lower abdomen, terminal dysuria, and half hourly urinary frequency both day and night.

An intravenous pyelogram suggested a mass lesion in the left side of the bladder. Cystoscopy showed gross inflammation and oedema of the left side of the bladder with acute ulceration of the overlying mucosa, and a large mass on the left side of the bladder was noted when the patient was examined under anaesthesia.

She was transferred to this department for further study with a provisional diagnosis of tumour of the bladder. On admission she told us that two weeks previously her general practitioner had advised her to inject gentian violet into her vagina (using a plastic syringe) to treat a severe pruritus. She admitted that by mistake she had injected some of the solution through the urethra and within a few seconds had developed burning pain in the lower abdomen, followed by urinary frequency and urgency and dysuria. Two days later she noticed haematuria, which frightened her and led to her admission to the local hospital.

Her condition gradually improved with a high intake of fluids, and a further cystogram showed a normal outline of the bladder with no evidence of the mass lesion seen in the original intravenous pyelogram. Cystoscopy and examination under anaesthesia at this stage showed only slight thickening of the left side of the bladder with fairly intense oedema and inflammation of the left base. Tissue was taken from this area for biopsy. Histological examination showed extensive ulceration and non-specific inflammatory changes with large numbers of eosinophils but no evidence of neoplasia; the urine was sterile.

Comment

The patient produced the gentian violet solution, which was analysed and found to be 1% gentian violet in 2% alcohol.

It is interesting that such violent symptoms developed within less than a minute of injecting the gentian violet into the bladder.

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Seasonal mortality among elderly people with unrestricted home heating

Mortality statistics for England and Wales show hypothermia as causing only about 300 out of the 40 000 excess deaths that occur every winter, with coronary and cerebral thrombosis and respiratory disease causing most of the rest.[1,2] The increase in thrombosis can be explained by haemoconcentration and hypertension after mild exposures to cold.[3] The role of cold houses and other factors in causing this is unknown; Alderson stated that mortality increases in winter among people in institutions in Great Britain, although indoor temperatures and the people's outdoor activities were not specified.[2] This paper describes seasonal mortality among people in well heated houses.

Methods and results

Anchor Housing Association provides centrally heated accommodation, with wardens, throughout England for generally able bodied elderly people, mainly widows. The charge does not vary according to how much heating a resident uses. Termination of a lease owing to death postdated death by up to 14 days; the number of such terminations was available for each three month period from July 1981 to June 1985. The number of housing units increased from 13 624 to 17 765 in this time, with a mean of 1·2 residents per unit. Mortality among the general population up to 1985 was provided by the Office of Population Censuses and Surveys, and minimum daily temperatures by the Meteorological Office. Thermistor probes (Digitron) were used to measure temperatures in 14 residents who volunteered to cooperate at two Anchor homes built in 1971 and 1981. Sublingual readings were taken, with the mouth closed for two minutes.

The figure shows that deaths among residents were 35·3% higher ($p<0·001$, group t test) during the four winter quarters (January-March) than the four summer quarters (July-September), when minimum daily air temperatures were 10·7°C higher. Among the general population aged over 65 mortality rose by 35·8% in the winter quarters before 1985, compared with 36·0% among residents. Mortality lagged behind air temperature[2]; a tendency to larger lags among residents than the general population was attributed to the delays of a few days in recording their deaths. Overall mortality was lower among residents, who were a selected population.

Between 0900 and 1600 on 17 January 1986, after overnight frost, the air temperature outside two homes was 2·3-4·4°C; the sublingual temperature of 14 residents, seven in each home, was (mean (SE)) 36·5 (0·1)°C, the skin temperature on the back of their hands 30·7 (0·4)°C, and the temperature indoors where these 14 readings were made 22·1 (0·3)°C. Each of the residents had a window open and had set all radiators at below maximum. All but one said that they switched off all heating, with windows open, at night. All of the seven who were fit enough made daily excursions outside, walking up to four miles and waiting for buses for up to 40 minutes. All of nine who had moved from accommodation without central heating said that they preferred the warmer accommodation, though some had had initial discomfort from "stuffy nose."

Comment

The continuous high daytime temperatures maintained in these homes did not prevent mortality among the residents from rising in winter by a percentage similar to that among the general population. Extensive outdoor excursions by able bodied residents, and perhaps the residents' preference for open windows and no heating at night, provided their only substantial