Recurrent oral ulceration treated with Mysteclin: a controlled study

A M DENMAN, A A SCHIFF

British Medical Journal, 1979, **1**, 1248-1249

Summary and conclusions

Twenty patients with recurrent oral ulceration participated in a placebo-controlled, double-blind trial of Mysteclin syrup (tetracycline hydrochloride and amphotericin) used as a mouthwash. Though a small, consistent improvement occurred with placebo, there was a significant reduction in mean pair scores and numbers of new ulcers recorded daily during the active-treatment periods, the effect lasting for at least four weeks after treatment was stopped.

In contrast to topical steroid preparations, Mysteclin syrup is efficacious when begun at any stage of the disorder and is not associated with adverse systemic effects.

Introduction

Numerous aetiological factors have been implicated in recurrent aphthous ulceration of the mouth, including infective agents such as *Streptococcus sanguis*. There is thus some rationale for the widely recommended use[1] of the broad-spectrum antibiotic-antifungal syrup Mysteclin (tetracycline hydrochloride 125 mg and amphotericin 25 mg per 5 ml). We, however, report what we believe to be the first controlled trial of Mysteclin in aphthous ulcers.

Northwick Park Hospital, Harrow, Middlesex HA1 3UJ
A M DENMAN, FRCP, consultant physician

E R Squibb and Sons Ltd, Twickenham TW1 3QT
A A SCHIFF, MRCS, LRCP, deputy head of medical division

Method

Patients attending the outpatient clinic of the division of immunological medicine at this hospital were seen by AMD; those with mouth ulcers of the aphthous type[2] were asked to record for four months on forms provided daily pain scores (severity scale 0-3) and the number of new ulcers appearing daily. No medication was prescribed during the period. Patients returning at the end of the four months with adequate records who were still troubled by ulcers were asked to participate in a comparative trial of two mouthwashes. Fully informed consent was obtained from each patient and the trial was approved by the hospital's ethical committee.

Patients were allocated at random on a double-blind basis to a sequence of four weeks with treatment, four weeks without treatment, a further four weeks with treatment, and a final four weeks without treatment. Treatment was either 5 ml Mysteclin syrup or 5 ml matching placebo syrup used three times daily, the order being randomised. The medicine was swilled around the mouth for a few minutes and then spat out. Patients continued to keep daily records of pain and new ulcers throughout the 16 weeks of the trial.

Results

The first 20 patients who kept satisfactory pretrial records participated in and completed the trial. There were 10 women and 10 men, and their age range was 16-75 (mean 25) years. Seven patients were suffering from Behçet's syndrome, defined as mucocutaneous lesions associated with at least one major system disease—for example, arthritis, skin manifestations, or colitis. The remaining patients included one with coeliac disease receiving a gluten-free diet, one with rheumatoid arthritis taking salicylates, one with discoid lupus erythematosus, and one with rheumatic heart disease. Tables I and II give the results.

The mean pain scores were significantly ($P < 0.01$) lower during the active-treatment than placebo periods, and significantly fewer new ulcers ($P < 0.05$) were recorded. During the course of the study pain scores significantly decreased ($P < 0.01$) in patients taking the active treatment but not in those taking placebo. Significantly fewer ulcers

TABLE I—*Mean and standard error (SE) of pain scores and numbers of new ulcers recorded by patients (n = 20) completing trial*

	Pretrial period		Treatment periods				Post-treatment periods			
	Mean	SE	Mysteclin (mean)	Placebo (mean)	SE of difference	P*	Mysteclin (mean)	Placebo (mean)	SE of difference	P*
Pain scores	0·93	0·10	0·31	0·68	0·13	<0·01	0·40	0·63	0·17	NS
No of new ulcers	15·25	2·06	2·70	9·35	2·39	<0·05	3·35	7·55	1·60	<0·05

*Significance of difference between treatments assessed by analysis of variance.
NS = Not significant.

TABLE II—*Mean changes in pain scores and numbers of new ulcers recorded (arithmetical differences) during consecutive periods of trial. Results expressed with standard error*

		All patients (n = 20)		Patients with Behçet's syndrome (n = 7)		Patients with other diseases (n = 13)	
		Mean	SE	Mean	SE	Mean	SE
Period before Mysteclin minus period on Mysteclin	Pain	0·43**	0·12	0·47	0·23	0·41*	0·14
	Ulcers	7·90***	1·96	7·42	3·70	8·15**	2·24
Period before placebo minus period on placebo	Pain	0·12	0·14	0·10	0·32	0·13	0·14
	Ulcers	1·00	2·58	0·57	3·56	1·23	3·57
Period on Mysteclin minus period after Mysteclin	Pain	−0·09	0·13	−0·44	0·35	0·10	0·09
	Ulcers	−0·65	1·22	−1·71	3·38	−0·08	0·67
Period on placebo minus period after placebo	Pain	0·05	0·07	0·12	0·07	0·01	0·09
	Ulcers	1·80	1·41	0·57	2·43	3·08	1·70

Significance of difference from zero: *P < 0·05; **P < 0·01; ***P < 0·001.

also occurred in the four weeks after active treatment was stopped than in the four weeks after placebo treatment ($P < 0.05$).

None of the order effects was found to be significant.

Comment

The therapeutic effect of Mysteclin syrup clearly exceeded the consistent, small improvement seen with placebo. Topical steroid preparations are the other main form of treatment for aphthous ulcers, but these need to be started at the prodromal stage, before frank ulceration develops, and dosage must be carefully restricted to avoid systemic effects. Our findings show that Mysteclin is efficacious irrespective of the phase of the disorder and suggest that the improvement is maintained for at least four weeks after treatment is stopped. Further work will determine whether complete remission can be produced by prolonging treatment enough to eliminate the bacteria responsible for putative antigenic cross-reactions.

We are grateful to Dr John Anderson, of the department of statistics, University of Newcastle upon Tyne, for the statistical analyses.

References

1 *British Medical Journal*, 1974, **3**, 757.
2 Scully, C, and Lehner, T, *Dental Update*, 1978, **5**, 379.

(*Accepted 20 March 1979*)

SHORT REPORTS

High-density-lipoprotein cholesterol in the Maasai of East Africa: a cautionary note

The Maasai are a Nilo-Hamitic tribe well known for their low incidence of cardiovascular disease.[1] Many reports have shown high serum cholesterol concentrations to be related to an increased risk of coronary artery disease, and the Maasai were found to have a significantly lower mean serum cholesterol concentration than an age-matched group of Europeans.[2] It has recently been suggested that high-density lipoproteins (HDLs) have an inverse relation to the risk of coronary artery disease.[3] We have compared the concentrations of HDL cholesterol in the Maasai with those in a group of healthy men attending a screening centre in London.

Subjects, methods, and results

Blood samples were taken from 37 tribal and 20 non-tribal Maasai men living in Southern Kenya in August 1977, and from 317 European men attending for routine health screening in London in August 1978. The total serum cholesterol (TC) concentrations of the Maasai were estimated by Searle Laboratories using a Lieberman-Burchard method without extraction, whereas those of the Europeans were measured at the Radcliffe Infirmary, Oxford, using the same method but with extraction. All HDL samples were measured in Oxford with a heparin-manganese precipitation method. The Maasai HDL samples were stored at −20°C for six months before analysis. To allow for the non-comparability of cholesterol measurements between Maasai and Europeans, a correction factor based on the correlation between measurements made at the two laboratories was applied to the cholesterol value of each of the Maasai. There were no significant differences between tribal and non-tribal Maasai in mean HDL concentration, total cholesterol concentration, or HDL:TC ratio. The results were therefore combined to form a single Maasai sample.

The mean serum HDL concentration in the Maasai was significantly lower than in the Europeans (table). As the mean serum cholesterol concentration was also significantly lower, however, the HDL:TC ratio did not differ significantly between the two groups.

Comment

In view of the reported inverse association between HDL and coronary heart disease we were surprised to find such low HDL values in the Maasai. Even when the low total serum cholesterol concentrations of the Maasai were taken into account by considering the ratio of HDL to total cholesterol, there was no significant difference between the Maasai and Europeans. The values reported here are much lower than those found in Nigerian men[4] and rural black South Africans,[5] whose mean HDL:TC ratios are about twice that found in the Maasai. Further work on populations with differing incidences of heart disease is thus required, but at present it seems that the relation between coronary heart disease and indices such as HDL or the HDL:TC ratio is far from straightforward.

Mean (± SD) serum high-density lipoprotein (HDL) and total cholesterol (TC) concentrations and HDL:TC ratios in populations studied

	HDL (mmol/l)	TC (mmol/l)	HDL:TC ratio (%)
Maasai (n = 57)	1·05 ± 0·31	4·77 ± 0·81	22·63 ± 7·71
Europeans (n = 317)	1·40 ± 0·29*	6·21 ± 1·14*	23·34 ± 6·77 (NS)

*Significance of difference between means (*t* test): $P < 0.001$.
NS = Not significant.
Conversion: SI to traditional units—HDL and TC: 1 mmol/l ≈ 38·6 mg/100 ml.

We thank Dr R A Moore, department of clinical biochemistry, Radcliffe Infirmary, Oxford, and Dr Alan Craig, Searle Laboratories, High Wycombe, and their staff for the biochemical assays. This work was supported by grants from the British Heart Foundation and the Boise Fund, Oxford.

1 Mann, G V, *et al*, *Journal of Atherosclerosis Research*, 1964, **4**, 289.
2 Day, J, *et al*, *Atherosclerosis*, 1976, **23**, 357.
3 Miller, G J, and Miller, N E, *Lancet*, 1975, **1**, 16.
4 Onitiri, A C, Sander, M, and Boyo, A E, *Clinica Chimica Acta*, 1977, **81**, 57.
5 Walker, A R P, and Walker, B F, *British Medical Journal*, 1978, **2**, 1336.

(*Accepted 26 February 1979*)

BUPA Medical Research, London WC1
DAVID ROBINSON, MSC, ARCS, research statistician
PETER WILLIAMS, BM, BCH, assistant to research director

London NW3
JOSÉ DAY, MB, MRCGP, general practitioner

Unprocessed bran causing intestinal obstruction

Unprocessed bran has been widely advocated by the medical profession and the lay press for the management of constipation, the irritable colon syndrome, and diverticular disease. We report a patient who developed intestinal obstruction due to excessive intake of bran.

Case report

A 53-year-old housewife was admitted to hospital complaining of nausea, cramping abdominal pains, distension, and incontinence of faeces for three days. She had a 20-year history of chronic anxiety requiring treatment with imipramine in doses of up to 150 mg/day. Over this period she had had chronic constipation for which she took two Coloxyl with Danthron tablets (dioctyl sodium sulphosuccinate 50 mg with 1,8-dihydroxy anthraquinone 50 mg) nightly.

A year before admission she began taking about 20 g/day of unprocessed bran. Subsequent improvement in her bowel actions encouraged her to increase her intake progressively, culminating in consumption of 160-200 g/