

tions after the consumption of different carbohydrate foods has been emphasised as the insulin responses can vary considerably even when glucose responses are similar and might be of more clinical significance in the non-diabetic population.¹⁹ In our study the sustained high insulin concentration after salted bread was probably responsible for the steep drop in plasma glucose concentration after 30 minutes (fig 2). Our findings of the small rise in plasma glucose concentration after the consumption of lentils and the fall below fasting concentrations (fig 1) have been seen after the consumption of other test meals of lentils and soya beans.²⁰

The findings of this preliminary study, if confirmed by others, including those of diabetics, would support the recommendation that diabetics,^{21,23} as well as the general population,^{24,26} should reduce their intake of salt. The differences seen after the consumption of unsalted and salted foods justify a controlled trial of the use of salt restriction in a group of stable diabetic patients as an additional way to lower postprandial plasma glucose concentrations.

This work was supported by the Sydney University Nutrition Research Foundation. We thank Professor G Berry, School of Public Health and Tropical Medicine, University of Sydney, for statistical advice.

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(Accepted 10 April 1986)

Assessment of oral candidiasis in patients with respiratory disease and efficacy of a new nystatin formulation

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Abstract

Fifty consecutive patients with respiratory diseases who developed oropharyngeal candidiasis were assessed clinically and microbiologically before and after seven days' treatment with nystatin suspension or pastilles (a new formulation). In 45 patients in whom microbiology yielded positive results there was frequent associated use of oral corticosteroids, antibiotics, sedatives, and inhaled corticosteroid, while in a few patients atropine analogues may have predisposed to infection. Dentures were worn by 32 of the infected patients. Concomitant treatment of dentures in chronically infected patients appeared to improve

the therapeutic response. Pastilles and suspension were equally efficacious both clinically and microbiologically.

The potential for enhanced drug delivery to the oropharynx suggests that nystatin pastilles may be useful in patients in whom poor compliance seems likely.

Introduction

Oral candidiasis is common in patients with respiratory disease and predisposing states have been described.¹ Despite repeated treatment chronic infection occurs, and nystatin pessaries have therefore been prescribed to achieve greater contact time between drug and oropharynx.^{2,3} Pessaries have an unpleasant taste, however, so that compliance with treatment may be poor. To overcome these problems a pastille of nystatin has been formulated. We have assessed its clinical efficacy and carried out a clinical audit of 50 patients with respiratory diseases who developed oral candidiasis.

Patients and methods

After removing antifungal agents from the wards we investigated 50 consecutive patients who had been prescribed this treatment. All were questioned about symptoms, primary chest disease, and current drug treatment. Other predisposing factors such as diabetes, malignancy, recent infection, and dentures were recorded.¹ Chronic infection was defined as four or more infections in the past 12 months. Six clinical signs of oral

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candidiasis¹ were scored 0 to 3 and summed. Mouth swabs were taken at predetermined sites and cultured on Sabouraud glucose peptone agar. Direct microscopy and a colony forming unit count (after three days' incubation at 37°C) were performed.

Patients were allocated at random to receive pastilles or suspension (nystatin 100 000 units) four times a day for seven days; no food or drink was taken for one hour after dosing. Dentures were soaked in 0.5% chlorhexidine and alcohol each night.

Patients kept a diary card comparing symptoms with the previous day (scoring -3 to +3) and a weekly score quantifying degree and rate of improvement was derived: daily scores were multiplied by the reciprocal of the day of scoring and summed. At end of treatment patients were reassessed clinically and microbiologically with the assessor blind to treatment. Patients provided scores (0 to 3) for palatability and acceptability.

Brompton Hospital's ethics committee approved the study and all patients gave informed consent. Statistical comparison between treatments was assessed by Student's paired and unpaired *t* tests.

Results

Twenty four men and 21 women aged 18-80 (mean age 59) had positive cultures. Table I lists their primary diagnoses and frequency of predisposing conditions. A large proportion wore dentures or had been prescribed oral corticosteroids, antibiotics, and sedatives. Five used atropine analogues or had Sjögren's syndrome.

Forty of the 45 patients had symptoms. Thirty eight complained of a painful mouth, 13 a husky voice, seven pain on swallowing, and two a painful tongue. All 45 had abnormal physical findings, including 40 with white plaques, 36 with glossitis, and four raw oral mucosa alone.

Of the 45, 22 patients were given the pastilles and 23 the suspension. Nine died or defaulted, however, leaving 18 in each treatment group. For mean diary card scores and improvement in clinical signs and microbiological accounts (table II) there was no significant difference between formulations. The score for mean clinical signs improved by 87% ($p < 0.001$) for pastilles and 80% ($p < 0.001$) for suspension. A statistically significant ($p < 0.001$) reduction in mean colony forming counts for pastilles (123 colonies; SEM 22) and for suspension (124; SEM 22) occurred. The treatments were equally palatable and acceptable (table II).

All eight patients with chronic infection has significant improvement after treatment (five given pastilles, three suspension). Five had failed with all other treatments, this being their best response.

The five patients with negative initial cultures all had clinical signs with mean scores of 6.1 (SEM 1.4) before treatment and 1.7 (SEM 0.4) after treatment. The mean score for improvement in symptoms was 1.3 (SEM 0.5).

TABLE I—Primary diagnosis and possible predisposing conditions to candidal infection in 45 sequential patients with microbiologically confirmed oropharyngeal candidiasis

Primary diagnosis	No of patients	Predisposing condition	No of patients
Carcinoma	18	Dentures	32
Chronic airways obstruction (including asthma)	13	Oral corticosteroids	27
Pneumonias and lung infections	4	Antibiotics	25
Fibrosing alveolitis	3	Tranquillisers/narcotics	25
Cystic fibrosis	2	Inhaled corticosteroids	17
Others	5	Recent chest infections	7
		Atropine/Sjögren's syndrome	5
		Radiotherapy	5
		Diabetes	5
		Cancer chemotherapy	4

Discussion

Nystatin, a polyene antifungal agent, is reasonably effective in candidiasis.⁴ Maintaining adequate concentrations in the oropharynx cannot be ensured, however, which may influence success in individual patients. Oral nystatin salivary concentrations are considerably greater for pessaries and pastilles than for suspension (data available on request). In this study, though pastilles and suspension were similarly efficacious, restricting food and drink after dosing may have enhanced the contact time for suspension, reducing detectable differences. Nystatin's bitter taste needs masking to be acceptable but three patients disliked the aniseed flavouring and stopped the treatment. Taste and compliance must be superior to pessary, however, which has no masking at all.

TABLE II—Mean (SE) scores for diary card symptom score, clinical signs score, microbiology colony counts, palatability score, and acceptability score for pastilles and suspension (includes, where relevant, data from patients with negative cultures)

	Pastilles (n=16-23)	Suspension (n=18 or 19)
Improvement in symptoms (diary card)	1.5 (0.2)	1.5 (0.3)
Signs before treatment	7.9 (0.9)	8.1 (0.9)
Signs after treatment	1.0 (0.3)*	1.6 (0.7)*
Colony forming unit count before treatment	151.0 (19.0)	162.0 (17.0)
Colony forming unit count after treatment	28.0 (17.0)*	38.0 (18.0)*
Palatability	2.5 (0.1)	2.2 (0.2)
Acceptability	2.6 (0.1)	2.4 (0.2)

*Compared with pretreatment value: $p < 0.001$.

Analysis of associated conditions confirmed the important association between dentures and infection.⁵ Dentures cause tissue trauma, provide sites for colonisation, and diminish salivary flow.¹ Saliva is thought to be necessary for normal oral immune defences,⁶ and five of our patients had poor salivary flow due to anticholinergic treatment or Sjögren's syndrome. Though Sjögren's syndrome is associated with increased infection,⁷ the contribution of atropine analogues has not been reported.

Inhaled corticosteroids predispose to infection⁸ but in our patients antibiotics and oral corticosteroids were more commonly associated, and there are several mechanisms for this association.¹ Use of sedatives (including narcotics) was similarly frequent, and presumably lack of denture cleaning and diminished food intake reducing salivary flow contributed.

Although medical treatment has been influenced little by dentists' concern about dentures, beneficial responses in the eight patients with chronic infection may have been due to chlorhexidine treatment of dentures. None had tried this treatment before, nor been instructed to refrain from eating or drinking after treatment. These manoeuvres may have been critical in obtaining a superior response.

Difficulty in diagnosis occurred in a few patients with symptoms, signs, and microbiological findings showing a lack of correlation. Improvement in microbiologically negative patients given nystatin suggests that antibiotics or other organisms may have inhibited culture. Microbiology remains useful when clinical signs are atypical, and inspection of the oropharynx in patients with predisposing states is recommended.

Patients with respiratory diseases entered into this study were sequentially diagnosed as having oral candidiasis. The distribution of likely predisposing factors among this sample highlights the importance of dentures, antibiotics, steroids, and sedation and suggests that atropine analogues may also be relevant. Of greater importance, however, was the success of nystatin when supported by chlorhexidine treatment of dentures and measures enhancing retention of drug in the oropharynx. Clinically the pastille formulation was as effective as suspension and the potential for enhanced drug delivery to the oropharynx suggests that it may be additionally beneficial for patients in whom poor compliance with therapeutic instructions seems likely.

We thank Mr P Woods, of E R Squibb and Sons Ltd, for his help and Dr J Kirk and Dr R Prince for editorial work.

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(Accepted 10 April 1986)