Denture stomatitis

The clinical effects of chlorhexidine and amphotericin B

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The clinical effects of an antibacterial substance with antifungal activity (chlorhexidine) and a specific antimycotic (amphotericin B) in denture stomatitis were studied in 100 patients. Five 14-day regimens of chlorhexidine, amphotericin B or placebo lozenges combined with denture immersion in 0.2 % chlorhexidine or water were tested. The efficiency of amphotericin B and chlorhexidine was comparable. This indicates that chlorhexidine has a considerable antifungal effect in the oral cavity and, further, that fungi are the responsible micro-organisms in denture stomatitis rather than bacteria. Chlorhexidine frequently discoloured the dentures. A high incidence of local and general predisposing factors to denture stomatitis, as well as of relapse 14 days after treatment, was observed.

Key-words: stomatitis; antifungal agents; chlorhexidine; amphotericin B

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The aim of the present investigation was to study the clinical effects of chlorhexidine and amphotericin B in denture stomatitis. *Heyden et al.* (1971) reported chlorhexidine to be efficient in the treatment of this disorder, attributing it to the antibacterial activity of the compound, whereas *Budtz-Jörgensen & Löe* (1972) ascribed this to the antifungal effect of chlorhexidine. By comparing an antibacterial substance with antifungal activity (chlorhexidine) to a specific antimycotic with no effect on bacteria (amphotericin B) (*Kinsky*, 1967) it was intended to obtain information, at least indirectly, on the relative etiologic significance of bacteria and fungi in denture stomatitis.

Further, this trial was performed to test the disposition of chlorhexidine to discolour dentures, as stain on the teeth has been claimed to be the main problem in using this drug in the oral cavity (*Löe*, 1973).

MATERIAL AND METHODS

1. Patients

One hundred patients with generalized simple or granular denture stomatitis, described previously (*Olsen*, 1974—1975), entered the trial. A medical and dental history was taken from each participant according to a checklist of factors relevant to the development of denture stomatitis.

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The patients, matched in series of 5 (*Olsen*, 1975), were randomly assigned to 5 treatment groups so that each contained 20 patients.

2. Treatment

The combinations of tested drugs are shown in Table I. For a period of 14 days each patient took one lozenge 4 times daily. During sucking the dentures were kept in a soaking agent (*Olsen*, 1975).

Table I. *Combinations of treatment tested in 5 groups of 20 patients with denture stomatitis*

Lozenges	Soaking agent
Placebo	Water
Amphotericin B 10 mg	Water
Placebo	Chlorhexidine 0.2 %
Amphotericin B 10 mg	Chlorhexidine 0.2 %
Chlorhexidine 5 mg	Chlorhexidine 0.2 %

3. Appointments

The patients were examined by the same methods at the same hour the day before onset of the treatment (day 0), after 14 days of treatment (day 15), and at the relapse control 14 days after discontinuation of the treatment (day 29).

4. Inflammation

The intensity of the mucosal erythema in the palate and the tongue, and the inflammatory reaction in each of the mouth angles were rated clinically according to the following scale:

no = 0
slight = 1
moderate = 2
severe = 3

Colour photographs (Medical-Nikkor Auto® camera, Kodak Ektachrome-X® film) were taken from the same sites. At the termination of the trial the slides were scored blindly, employing the clinical 0—3 scale. Summarized clinical and photographic scores were used for the final evaluation. (In addition, the dentures were photographed at each sitting.)

5. Symptoms

The intensity of the subjective symptoms of denture stomatitis (soreness, itching and burning pain) was graded, using the same rating scale as in the evaluation of inflammation.

6. Fungal cultures

Fungi were grown on agar models of the upper jaw and upper denture and identified as described previously (*Olsen*, 1974).

7. Statistical procedures

Multinomial test series were derived from the material (*Sverdrup*, 1967). The homogeneity test with ranked observers (*Feller*, 1968) was used to indicate differences at the 5 % probability level.

RESULTS

1. Fungal cultures

Before treatment yeasts were isolated from the palatal mucosa and the fitting surface of the upper denture in all the 100 patients. The quantitative and the qualitative effects of the treatment on the mycotic flora have been described (*Olsen*, 1975).

2. Inflammation

Before treatment 31 of the patients had generalized simple and 69 granular inflammation in the palate. Signs of lingual inflammation and rhagades were present in 88 and 30 patients respectively. In some

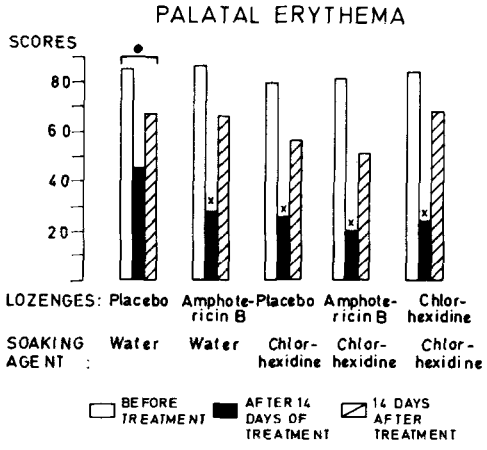

Fig. 1. Summarized clinical and photographic scores on the erythema in the palate of 100 patients with denture stomatitis (No = 0, slight = 1, moderate = 2, severe = 3). x significantly reduced scoresc ompared to the control•. (5 % level of significance.)

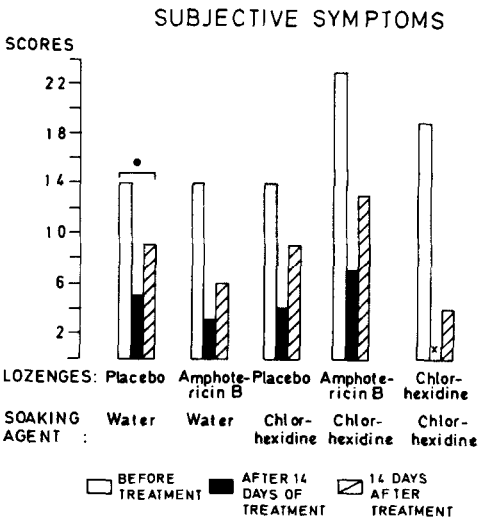

Fig. 2. Summarized scores on subjective symptoms (soreness, itching and burning pain) in 100 patients with denture stomatitis (No = 0, slight = 1, moderate = 2, severe = 3). x significantly reduced scores compared to the control•. (5 % level of significance.)

of the cases the mucosa of the lower jaw or cheeks was also erythematous.

At the end of the treatment the palatal erythema had been reduced in the control (placebo/water) as well as in the 4 groups treated with active drugs (Fig. 1). However, the reductions were significantly higher in the last-mentioned groups. The relative effects of the active medications were essentially the same in the palate and the tongue. In the treatment of angular cheilitis, denture disinfection in chlorhexidine proved significantly less efficient than the other active treatments, including mere sucking of amphotericin B tablets.

Relapse was observed in all groups 14 days after the end of the treatment. Thus, the scores on the palatal erythema did not differ significantly in any of the 5 groups. In treated rhagades, however, the effect obtained with the amphotericin B/chlorhexidine combination proved significantly more effective than that of any other medication.

3. Subjective symptoms

Symptoms of denture stomatitis such as soreness, itching and burning pain were recorded in 44 of the 100 patients before treatment.

At the end of treatment all patients treated with the combination of chlorhexidine lozenges and denture disinfection were symptomless, while the symptoms had been reduced in the 4 remaining groups (Fig. 2).

Fourteen days after treatment recurrence was observed in all groups, and the scores on the subjective symptoms were no longer statistically different from pretreatment evaluations.

4. Palatal erythema as related to subjective symptoms

Before treatment the palatal erythema and the subjective symptoms were given the same score in 18 of the 100 patients (Fig. 3). Even patients with severe ery-

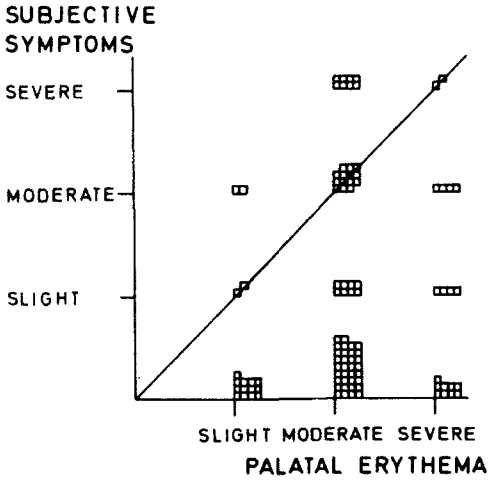

Fig. 3. Correlation between objective (clinical) scores on the palatal erythema and subjective scores on the symptoms of 100 patients with denture stomatitis.

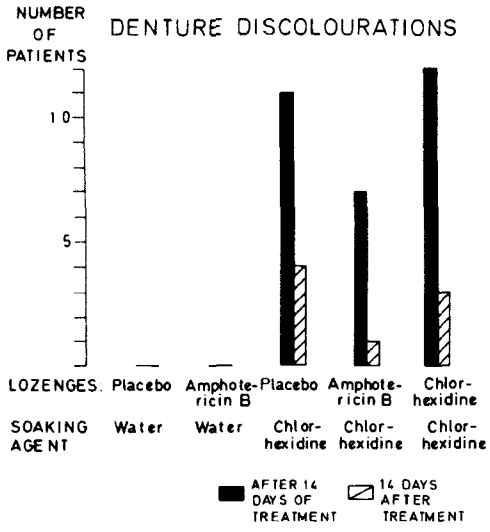

Fig. 4. Patients in a sample of 100 with denture discolouration as a side effect after 14 days' treatment of denture stomatitis.

thema could be asymptomatic. On the other hand, all patients except 2 with severe or moderate symptoms had either severe or moderate erythema.

5. Side effects/complaints

Half of the patients performing denture soaking in chlorhexidine developed stains on their acrylic dentures (Fig. 4). Only 17 % of these patients commented on their discoloured dentures. The deposits, dark brown to blackish, appeared primarily in cracks, along the 'gingival margin' of the denture, on the approximal surfaces of its teeth, or on the fitting side. Most of the stain had disappeared at the relapse control (29th day). Non-chlorhexidine-treated prostheses were unaffected. Two patients in the chlorhexidine/chlorhexidine group developed discolourations on their dorsal tongue surfaces. After the regular period of drug intake (placebo/chlorhexidine) one patient started to apply 0.2 % chlorhexidine solution to her rhagades and acquired a blackish stain on the adjacent facial skin. Up to 60 % of the patients in the groups immersing their dentures in chlorhexidine (placebo/chlorhexidine) made comments on its taste.

6. Exclusions and dropouts

Four patients were excluded for failing co-operation, and 2 because no culture could be obtained from their palatal mucosa. Two patients were hospitalized during the experimental period due to intercurrent general disease. All these patients were replaced.

DISCUSSION

It seems widely accepted that denture stomatitis may be *Candida*-induced, but bacteria have also been suggested as an etiologic factor. Thus, *Budtz-Jörgensen* (1970) ascribed to micro-organisms other than yeast-like fungi the persisting sub-epithelial inflammation in granular type lesions after antifungal therapy. Further, *Van Reenen* (1973) held that, rather than a specific pathogen, a number of micro-

organisms, bacteria as well as yeasts, participate in the pathogenesis of denture stomatitis. In the present series bacteria were not studied. However, the fact that the anti-inflammatory effects of amphotericin B and chlorhexidine proved equal in the palate, indirectly suggests that bacteria are of no major importance in denture stomatitis.

A lower anti-inflammatory effect of the amphotericin B lozenges might have been expected than of the chlorhexidine denture disinfectant as the former have been shown to affect organisms mainly on the palatal mucosa, whereas the disinfectant reduces the amounts of fungi both on the palate and on the denture (*Olsen*, 1975). Leaving the denture out during tablet sucking may have compensated for the insignificant effect on the denture microorganisms. The importance of this procedure was clearly demonstrated in the control where, regardless of the lack of antifungal effect, a noticeable reduction of the palatal erythema occurred. Removal of the denture probably implied elimination of the main promoting factor and, further, a free access of oxygen and an unobstructed flow of saliva to a denture bearing tissue at rest.

Although the active drugs failed to abolish the inflammatory signs in all patients, a marked improvement was always obtained in those only partly cured. Prolongation of the treatment might have caused further amelioration as chronic oral candidosis may be rather resistant to local therapy. On the other hand, the persisting erythema sometimes appeared so localized that denture trauma was suspected (*Budtz-Jörgensen & Bertram*, 1970).

In the treatment of rhagades, denture disinfection with chlorhexidine proved less effective than the other active medications. This agreed with the observations from smears (*Olsen*, 1975). As the combination of chlorhexidine lozenges and denture disinfection was significantly more efficient than disinfection alone, the observed difference may simply depend upon the concentration of chlorhexidine in the affected area. Denture disinfection in chlorhexidine also reduced the intensity of inflammation of the tongue and cheek mucosa. The effect of the disinfectant on oral tissue may be due to the reduction of the denture yeast flora as the main fungal reservoir. It may also be ascribed to an intra-oral release of chlorhexidine. Findings in oral scrapings suggested similar effects (*Olsen*, 1975). *Bonesvoll & Olsen* (1974) found that chlorhexidine was readily bound to acrylic dentures and that it could be traced in the saliva afterwards during a 24-hour period. Immersion for 16 minutes, i.e. the approximate time needed to dissolve an antifungal tablet, allowed a near maximum binding of the drug.

Budtz-Jörgensen & Löe (1972) maintained that the antifungal effect of chlorhexidine is comparable to that of specific antimycotics in the treatment of palatal candidosis associated with dentures. This is supported by the present study. The efficiency of chlorhexidine in the treatment of oral candidosis was recently demonstrated also in thrush (*Langslet, Olsen & Lökken*, 1974).

The frequent denture stains in the present experiment were restricted to prostheses which had been immersed in chlorhexidine. The deposits were minor in most cases and had been reduced by the patients' efforts at the relapse control. Nevertheless, denture stain may prove an obstacle to regular, overnight soaking. Further investigations are being carried out into this particular aspect.

Local and general predisposing factors to denture stomatitis were often recorded in the present sample. Thus, the denture fit was considered poor in 57 patients. Nocturnal denture wearing was reported by 83 participants. Sixty of the 69 patients with papillary hyperplasias in the palate were among these 83 patients. *Love, Goska & Mixson* (1967) found the incidence of severe inflammation and papillary hyperplasias significantly higher in patients not keeping their prostheses out for the night. Use of drugs with xerostomic side effects was frequently noted. *Pollack, Buck & Kalnins* (1964), treating about 600 patients with oral mycoses as a complication of psychopharmacological therapy, asserted that dryness of the mouth vanished after antifungal treatment. This was also reported by 12 patients in the present study. One of these had received the placebo/water combination.

The control 14 days after treatment established a pronounced relapse tendency. This may be due to the predisposing factors and even to auto-infection from yeast-like fungi persisting in the oral cavity or inhabiting other sites.

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