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Clotrimazole (Canesten)* in the treatment of candidal balanitis in men

With incidental observations on diabetic candidal balanoposthitis

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SUMMARY Clotrimazole 1% (Canesten) cream was used in a trial comprising 138 men with candidal balanitis. Eighty-six (91%) out of 94 men were asymptomatic after seven days and 57 (98%) of 58 men were asymptomatic after three weeks' treatment. After seven days, *Candida albicans* could no longer be cultured from 86 (90%) of 96 men, nor from 55 (95%) of 58 men three weeks after treatment. Microscopical examination gave varying results. Fifteen (10·9%) of 138 men were found to have diabetes mellitus; this group was significantly older than the non-diabetics. It is concluded that treatment with clotrimazole for seven days is effective in the treatment of candidal balanitis.

Introduction

In recent years, the importance of genital candidosis in men has been stressed. The patient with genital yeasts may be asymptomatic, but such yeasts are found if a diligent search is made in sex partners of women with vaginal candidosis. The male may complain of burning and itching of the penis which will develop within hours of sexual intercourse, and a generalised erythema of the glans and prepuce may be noted (Oates, 1976). This may be caused by hypersensitivity to *Candida albicans*.

In other patients symptoms are less acute. Perhaps a complaint is made of some redness of the glans and prepuce, and there is a whitish subpreputial discharge. The typical case is mild, with a dry, glazed, erythematous surface to the glans penis and on the undersurface of the prepuce. In addition, there may be very small, irregular, eroded papules and a dispersed vesicular eruption, often with plaques of white cheesy matter. The fossa navicularis may be involved and there may be a transient urethritis. Itchy and scaly erythematous lesions may also be present on the penile and scrotal skin, and in the obese, the groins may be involved. An acute fulminating oedematous type of balanoposthitis may occur with ulceration of the penis and a swollen fissured prepuce. This is often associated with diabetes mellitus.

Clotrimazole is a tritylimidazole derivative which acts on the cell membrane. Iwata *et al.* (1973) suggested that fungicidal concentrations of clotrimazole damaged the permeable membrane allowing leakage of intracellular phosphorus compounds and potassium ions, leading to inhibition of macromolecular synthesis. The drug is active *in vitro* against *C. albicans*, most strains being inhibited by 2 mg/l or less, and killed by less than 10 mg/l of the drug (Holt, 1974). It is available as a cream for topical treatment.

Material and methods

An uncontrolled trial was conducted to study the cure rate of patients with candidal balanitis or balanoposthitis and treated with 1% clotrimazole (Canesten) cream.

The 138 patients studied were treated between 1 January 1976 and 30 April 1977. They were included only if culture of *C. albicans* on Sabouraud's medium confirmed the initial findings of mycelia or if spores were found by microscopical examination of Gram-stained material taken from the glans penis, coronal sulcus, or subpreputial sac.

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Two dry cottonwool swabs were taken from the coronal sulcus. A smear was made from the first, stained by Gram's method, examined microscopically using a $\times 100$ objective, and sent to the mycology unit for confirmation. The second swab was inoculated on to Sabouraud's culture medium in the clinic and sent on to the mycology laboratory, where it was examined by microscopy and Sabouraud's culture for *C. albicans*.

Urine from all patients was tested using clinistix (Ames) and all patients with glycosuria had an oral glucose tolerance test.

On the initial visit, note was taken of the duration of balanitis; previous treatment had to have stopped at least seven days earlier if the patient was to be included in the trial. Note was made of concurrent oral antibiotics, corticosteroids, or other treatment.

The patient was asked if the sex partner had vaginal irritation, discharge, or was being treated for a vaginal condition, and if so, did he know her diagnosis. Subsequently, the case notes of these sex partners confirmed this and gave more clinical information.

On the initial visit, note was made of the area affected—glans or prepuce, shaft, scrotum, or groin.

Observations were to be made on the patient before treatment, at the end of the first week of treatment, three weeks after the end of treatment, and at long-term follow-up (mean 9·23 weeks, SD 6·10, s.e.m. 1·36). On each visit, symptoms of irritation, if present, were tabulated. Swabs were collected and examined as before.

After the investigations in the clinic had given positive results the patient was told to apply clotrimazole 1% cream gently, each morning and at night for seven days, washing off the cream the night before attending the clinic for the follow-up visit.

At the end of one week of treatment, the patient was asked if he had benefited from treatment at all and his answers were noted on a graded reply chart. He was asked if he had completed treatment, had had sexual intercourse since starting treatment, and if treatment had upset him in any way (graded reply chart). The clinical impression was also recorded using the following grades—cured, improved, no change, worse, or don't know.

Results

CLINICAL DATA

One hundred and thirty-eight patients (age range 16–68 years, mean 27·7, SD 9·9, s.e.m. 0·8) were admitted to the trial, but 39 (28·2%) (mean 28 years, SD 9·6, s.e.m. 1·5) defaulted after the initial visit. Therefore, 99 patients completed the study.

Associated genital conditions were nongonococcal urethritis in 26 (18·8%) patients, condylomata acuminata in six (4·4%), trichomoniasis in three (2·2%), gonorrhoea in two (1·4%), Reiter's syndrome in one, and balanitis xerotica obliterans in one.

Concurrent treatment was prescribed in 34 patients, oral antibiotics in 20 (14·5%), oral corticosteroids in three (2·2%), and other medication in 11 (8%) patients.

AREA AFFECTED

Of 138 men in the trial, the glans or prepuce was affected in 137 (99·3%), the shaft of the penis in 17 (12·3%), groin in four (2·9%), and the scrotum in two (1·4%) patients.

DETAILS OF SEX PARTNER

Vaginal irritation was present in 41 (29·7%) of the sex partners, and vaginal discharge in 39 (28·3%). A diagnosis of vaginitis was made in 33 (23·9%) women and in 29 (21%) of these this was caused by candidosis. Vaginal treatment was given to 33 of the sex partners for whom details were obtained. Twenty-nine were treated for candidosis, 22 with clotrimazole and seven with nystatin.

Results

TREATMENT OF CANDIDAL BALANITIS WITH CLOTRIMAZOLE 1% CREAM

Final analysis was on the results for 99 patients who completed the study. Symptoms had gone in 89 (93%) of 96 after seven days of treatment. Of those followed up three weeks after the end of treatment 57 (98%) of 58 were asymptomatic and on long-term follow-up, 18 (90%) of 20 remained so. There were no serious side effects.

Yeast cells could no longer be seen by microscopical examination after seven days in 69 (73%) of patients, three weeks after the end of treatment in 43 (75%), and at long-term follow-up in 14 (74%) of patients. In no cases were mycelia found after treatment. They were found in only 54 (59%) before treatment, on initial microscopy.

After culture on Sabouraud's medium 86 (91%) of 94 gave negative results after one week, 55 (95%) of 58 three weeks after the end of treatment, and 18 (90%) of 20 on long-term follow-up.

Eight (8%) of 94 cultures still gave positive results at the end of one week, two (4%) of 58 three weeks after the end of treatment, and two (10%) of 20 on long-term follow-up.

Treatment of the symptoms of candidal balanitis using clotrimazole 1% cream was successful in 93% of patients, and follow-up negative cultures for

C. albicans varied from 91% after one week to 96% of those patients followed up three weeks after the end of treatment.

Associated study on diabetes mellitus presenting with candidal balanitis/balanoposthitis

Of 138 patients with candidal balanoposthitis 15 (10·9%) were found to be diabetic. Their ages ranged from 19–68 years, mean 39·4, SD 17·8, s.e.m. 4·6. Two defaulted after the initial visit but six were in the group that was followed up the longest. These patients were found to be significantly older than non-diabetics presenting with candidal balanitis/balanoposthitis ($t=2·833$, $P<0·02$). In addition two patients were found to have renal glycosuria.

After one week of treatment the diabetic patients had a higher proportion of positive culture results (four of 13) than the non-diabetics (four of 81) ($\chi_1^2=6·565$, $P<0·01$).

During the period of the study a total of 6971 new cases were diagnosed in men, but only six diabetics were found among men who were not in the study.

Discussion

Estimates of the infectivity of *C. albicans* to the male have varied from about 10% (Oriel *et al.*, 1972; Morton and Rashid, 1977) to 33% by smear or culture or to 49% by culture only (Willmott, 1975). Considering that many women are treated by other doctors for candidal vaginitis the infectivity rate of the female is probably much higher than is realised. As vaginal candidosis is the infective gynaecological condition that is most commonly seen, investigation and treatment of the male partner becomes important if this distressing condition is to be contained.

Unfortunately the motivation for follow-up disappears fairly rapidly once the patient realises he has had a relatively benign complaint and has got over his early anxiety of an abnormal genital condition. The default rate was similar to that found by Masterton *et al.* (1975) when treating genital candidosis with natamycin cream.

On the other hand, it could be argued that treatment which has considerable success even when given for such a short time as a week may have beneficial results in preventing the transmission of candidosis in sexually active patients.

Fifteen (10·9%) of 138 patients were found to have diabetes mellitus. Diabetic candidal balanitis occurred in an older age group and, in the uncircumcised male, balanoposthitis presented with an oedematous fissured prepuce which in some cases had become almost impossible to retract. There were often symptoms of vague ill health preceding this for a few months, rather than the characteristic well-known presenting symptoms of diabetes mellitus.

After treatment, yeasts could be seen on microscopical examination while none grew on culture. An explanation for this may be that the yeasts were no longer viable. In this trial, clotrimazole had no serious side effects such as a sensitivity reaction. It was acceptable to the patient even when he persisted in his sexual activities while undergoing treatment. It did not stain bed clothes or underwear.

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