

Natamycin in genital candidosis in men

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Vaginal candidosis is probably the most prevalent gynaecological condition to-day (Newcomer, Sternberg, Wright, Reisner, McNall, and Sorensen, 1960). *Candida albicans*, a spore-forming Gram-positive fungus, forms branching pseudo-hyphae which thrive in an acid medium with a high glycogen content. Patients in the high oestrogen state of pregnancy and those taking oral contraceptives are particularly affected (Walsh, Hildebrandt, and Prystowsky, 1968).

Candidal balanitis or balanoposthitis may occur as a contagious lesion or as a hypersensitive reaction to *Candida albicans* present in the vagina of the consort. The causes of balanitis and balanoposthitis are varied, and exclusion of glycosuria is essential in all patients. Although candidal balanitis may be caused by an underlying diabetes, it may also follow antibiotic therapy. In the majority of cases, however, it arises from coitus with an already infected sexual partner. The male consort is at particular risk if his sexual partner is pregnant or diabetic, or has recently been treated with a broad-spectrum antibiotic, corticosteroids, or anti-trichomonal agents, or is taking an oral contraceptive. In recent years, the increasing popularity of the oral contraceptive pill has been linked with the rising incidence of vaginal candidosis (Catterall, 1971). As the male partner much less often uses a condom nowadays, there is an understandable parallel increase in genital candidosis in the male. Candidal balanitis is not, in itself, of serious import, but the distressing symptoms and the associated discomfort of the infection call for prompt and effective treatment. It is, of course, important that the sexual partner be examined and treated for vaginal candidosis if this is found to be present.

A number of antifungal antibiotic preparations for the treatment of candidal balanitis are available, and one of the more recent additions is natamycin (Pimafucin) which, like other antifungal antibiotics, such as amphotericin and nystatin, belongs to the polyene group. Natamycin is a tetraene substance, containing four conjugated double bonds.

Although its exact antifungal action is unknown, it acts like other members of the polyene group of antifungal antibiotics on the cell surface, causing a

loss of important plasmatic substances from the cell (York, 1966; Weissmann and Sessa, 1967). Natamycin is not ordinarily absorbed from the gastrointestinal tract in humans, and no antifungal activity in serum could be demonstrated in eight patients after the daily oral intake of 125–500 mg. of natamycin (Lynch, Furcolow, Yates, Tosh, and Larsh, 1961).

Natamycin is well tolerated by the skin and shows no sensitizing activity. Allergy tests in a group of 73 industrial workers with regular contact with natamycin over a period of 5 years failed to reveal any sensitization (Malten, 1968).

Scope of investigation

A trial was conducted to study the clinical efficacy of a topical preparation containing 2 per cent. natamycin in a vanishing cream base (Pimafucin cream) on 93 male patients with clinical candidosis of the genitalia or anus or both.

Tentative diagnosis was based on clinical findings, but in the majority of patients supportive laboratory evidence was obtained. Initially, mycelia and spores were identified by Gram-staining in routine microscopy of scrapings taken from lesions. Also, further specimens were inoculated into Stuart's transport medium and thereafter cultivated on Sabouraud's medium. Each patient was instructed to apply the cream twice daily for 14 days and a 2-month follow-up period was planned. This proved impracticable because a large number of patients defaulted. There were 41 patients with other conditions, some of which, such as glycosuria or recent broad-spectrum antibiotic treatment, predisposing towards candidosis. Others were concomitant infections like herpes genitalis and warts. 41 patients were married and two divorced, and fifty claimed to be single. Their most recent sexual activity was stated to be marital by 26 patients (28 per cent.), with a regular sexual partner by fifteen (16 per cent.), and casual by 52 (56 per cent.).

CLINICAL DIAGNOSIS

Reddened, intact, discrete maculopapular lesions which were frequently itchy were the commonest and earliest clinical manifestations. These often eroded, leaving large areas completely denuded of mucous membrane. The uncircumcised patient was particularly affected and a secondary inflammatory phimosis occurred in nine men.

In other patients, with a longer history of infection, a different and distinctive clinical picture emerged. Extensive

reddened moist areas—approaching the eczematous—affected the genitalia. In 67 patients the genital mucosa was affected alone, but in 21 patients, genital and perianal lesions co-existed, and in five others only the perianal skin was infected.

Results

93 patients were initially treated with local natamycin cream 2 per cent.

Not surprisingly, in a study of this nature, the default rate was high. 27 of those patients considered suitable for entry within the terms of the protocol failed to return for follow-up examination; eighteen had genital candidosis, eight had genital and anal candidosis, and one had anal candidosis alone. The results in the 66 patients finally available for assessment are shown in the Table. When treatment was successful, the local itching and burning subsided within 72 hrs of the start of treatment, but the inflammation itself did not clear up for 10 to 12 days.

Natamycin cream was entirely acceptable to our patients and no side-effects were noted.

Discussion

Topical natamycin treatment proved much more satisfactory—with a 2 per cent. failure rate—in those patients in whom the candidal infection was confirmed on culture. In contrast, one out of every two patients failed to benefit from treatment when the original diagnosis was made on purely clinical grounds and was not supported by culture.

It seems more realistic to doubt the accuracy of the initial diagnosis rather than the efficacy of the antifungal treatment. Similar diagnostic pit-falls may explain some of the disappointing results obtained during the treatment of local candidosis in general practice.

Obviously, whenever possible, the clinical diagnosis of candidosis should have cultural confirmation. Furthermore, only such proven cases should be included in therapeutic trials—otherwise impressions may be distorted and illfounded and inaccurate conclusions may be drawn.

In the group of patients who had lesions of the "eczematous" type, we found neither mycelia or candidal spores. We do not know the exact aetiology—whether they were due to a sensitization to the yeasts themselves or whether an endotoxin from the *Candida* was at work. Antifungal treatment failed to improve the condition; indeed, some patients were actually made worse by local therapy. In fact, these lesions did not respond to any subsequent treatment be it antibiotic, antihistaminic, or steroidal. In three cases, a candidal vaginitis was successfully treated in the consorts without obtaining any improvement.

Although candidal balanitis may occur after the use of antibiotic treatment, or steroid treatment, and may be associated with an underlying diabetes, the majority of cases are caused by the simple transmission of the infection from the sexual partner. Hence, eradication of *Candida* must be undertaken simultaneously in both sexual partners. Patel (1973) recently reported the use of natamycin in the treatment of vaginal candidosis in the pregnant patient with the impressive result of a 94 per cent. success rate. The results of this study as well as the work done by Patel show natamycin to be a highly effective treatment for candidosis and both natamycin cream and natamycin vaginal tablets can be considered a most efficient treatment for these increasingly common clinical states.

Avoidance of sexual activity during the course of treatment is desirable but the patient does not always obey such advice. Appreciating this, we advise the patient to apply antifungal cream liberally to his penis before intercourse. We believe that this reduces the risk of re-infection.

Although candidal balanitis is not a serious infection, patients suffer a great deal of discomfort and mental anguish, so that swift and effective treatment is necessary.

Since the condition itself is one of intense irritation and discomfort, the avoidance of the use of any substance known to produce a sensitivity reaction is important, and the complete absence in this study of any side-effects at all brings the use of natamycin very much to the fore. Also, unlike some other

TABLE Results of treatment

Diagnosis	Number of patients	Results			
		In patients with culturally proven candidosis		In patients without culturally proven candidosis	
		Cured	Failed	Cured	Failed
Genital candidosis	49	37 (97%)	1 (3%)	2	9
Combined skin and anal candidosis	13	3	0	9	1
Anal candidosis alone	4	2	0	1	1
Total	66	42 (98%)	1 (2%)	12 (52%)	11 (48%)

antifungal preparations in current use, natamycin does not cause yellow staining of the underwear. Being odourless, it is aesthetically acceptable to the patient—by no means a trivial point in a patient who is already upset because of a 'strange' genital condition.

Summary

In a trial of natamycin, an antifungal antibiotic in a vanishing cream base, assessment was possible in 66 men with genital or anal candidosis.

The overall cure rate was 82 per cent. In 43 patients with culturally proven candidosis it was 98 per cent. but in 23 patients treated solely on clinical impression it was only 52 per cent. Symptoms were rapidly relieved in those who responded and there were no side-effects.

In our hands, natamycin 2 per cent. cream has proved to be a valuable preparation in the treatment of candidal balanitis.

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