

Treatment of vaginal candidiasis in pregnancy with a single clotrimazole 500 mg vaginal pessary

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Summary

A single vaginal pessary containing clotrimazole 500 mg (Canesten; Bayer-Miles) was used to treat candidiasis during a prospective, mycologically controlled trial among 46 patients in the second and third trimesters of pregnancy. Positive cultures were obtained from vaginal swabs before commencement of treatment. Swabs were taken 1 week and 1 month after treatment. Four patients were lost to follow-up. One week after treatment 83,3% of the patients were cured on microscopic and mycological examination, and all of the patients had relief of symptoms. The recurrence rate was 5,7% after 1 month. Of the 7 patients in whom treatment was unsuccessful, 3 were available for repeat treatment and all 3 responded successfully to a second course.

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Vaginal candidiasis is one of the most commonly encountered infections among obstetric patients. The incidence of vaginal candidiasis in pregnancy is higher than that among non-pregnant women.^{1,2} The hormonal milieu of pregnancy, with a fall in vaginal pH and increased vaginal epithelial cell oestrogen and glycogen contents, favours fungal growth.³ The impaired cellular immunity⁴ and decreased candidacidal effects of leucocytes associated with pregnancy⁵ may also contribute to the increased incidence. Other predisposing factors include obesity, diabetes mellitus, iron deficiency anaemia, immunosuppressive therapy and the prolonged use of broad-spectrum antibiotics.⁶

Several forms of therapy have been developed and are in current use. However, candidiasis is known often to be chronic or recurrent.¹ Furthermore, Masterton *et al.*⁷ noted that 4% of patients with vaginal candidiasis given a 14-day course of local therapy did not even start using their medication, and that approximately 50% of these patients discontinued therapy before completion of the full course. The ideal method of therapy should be effective with a low risk of recurrence of vaginitis and associated with good patient acceptance and compliance.

For the first time a single vaginal pessary containing clotrimazole 500 mg (Canesten; Bayer-Miles) was used as complete therapy for vaginal candidiasis in pregnancy in an open, prospective, mycologically controlled study. The aim of the study was to assess by clinical and mycological criteria the cure rate for vaginal candidiasis using this treatment.

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Patients and methods

Forty-six patients in the second and third trimesters of pregnancy who had clinical and microscopic evidence of vaginal candidiasis were included in the study. High vaginal swabs were taken and positive cultures for *Candida* were obtained in each case before commencement of treatment. The culture medium used was Sabouraud agar.

Patients in the first trimester of pregnancy were excluded from the study in order to exclude the possibility of possible teratogenic effects of the drug. Other criteria for exclusion were concurrent trichomoniasis and the use of local or oral antifungal therapy in the preceding 4 weeks.

After positive cultures for *Candida* had been obtained the pessary containing clotrimazole 500 mg was inserted into the vagina by one of the investigators. Patients were advised to abstain from intercourse for 1 week after treatment in order to avoid reinfection. Patients' sexual partners were requested to treat the glans penis with topical clotrimazole cream during this period.

Examinations were repeated 1 week and 1 month after treatment. Clinical and microscopic examinations were performed at each visit, and high vaginal swabs were taken for culture. Patients were requested to notify the investigators if local irritation or other untoward effects occurred.

Patients with primary vaginal candidiasis, recurrent infection and other concomitant disease, e.g. diabetes mellitus, were all included in the study group.

Results

Of the 46 patients included in the study, 4 were lost to follow-up, mostly owing to delivery. The data on the remaining 42 patients were used in the analysis. The most commonly encountered symptom was vaginal discharge, occurring in 65% of the patients. Pruritus and a burning sensation were other frequent complaints. In only 17% of patients was the diagnosis of vulvitis made. The *Candida* species isolated are listed in Table I.

TABLE I. *CANDIDA* SPECIES ISOLATED

	No. of patients
Primary infection	
<i>C. albicans</i>	44
<i>C. tropicalis</i>	1
<i>C. parapsilosis</i>	1
	<hr/>
	46
Second positive culture	
<i>C. albicans</i>	4
<i>C. parapsilosis</i>	2
<i>C. guilliermondi</i>	1
	<hr/>
	7

One week after treatment 35 patients (83,3%) were cured on microscopic and mycological examination. All patients experienced relief of symptoms. Of the 7 patients (16,7%) who failed to respond, 3 were available for repeat treatment and all 3 responded to a second course. In 2 of these patients the causative organism found after a second culture was a *Candida* species different from the original one, indicating that re-infection had taken place.

One month after treatment 2 of the patients who had originally been treated successfully again had positive cultures for *C. albicans*. The recurrence rate was therefore 5,7%. No patient experienced any adverse effects of treatment.

Discussion

Vaginal candidiasis in pregnancy is often recurrent or chronic, probably because of the continuation of hormonal changes. The patient experiences severe irritation and pruritus, even to the extent of developing the psychological problems of chronic illness.⁶

The importance of vaginal candidiasis in pregnancy, however, is the fact that the fetus can also be affected, either transplacentally, a rare occurrence which is usually fatal, or in the vagina at birth.² Ascending infection from the birth canal spreading to the fetus and amniotic fluid is also possible but not yet proved.^{2,8}

The most common *Candida* infection of neonates is oral thrush, but extensive infection — dermatitis and disseminated neonatal candidiasis — may occur.^{2,9} Sixty-six per cent of babies born to mothers with vaginal candidiasis have positive cultures for *Candida* from the oral cavity after birth,^{6,10,11} but not all develop clinical thrush. Approximately 5% of all newborns are estimated to develop thrush.² Some predisposing factors include prematurity, intra-uterine growth retardation, certain resuscitation procedures and especially a poor immunological response against *Candida*.² Protection against thrush is offered by colostrum cells in breast milk, which have been found to have greater phagocytic effects on *Candida* than leucocytes have.¹²

The aim of therapy for vaginal candidiasis is eradication of the organism, which would cure the patient and protect the baby. Clotrimazole is a synthetic imidazole derivative which acts by changing fungal membrane permeability and thus causing loss of essential substances from the fungal cell. Fungal protein synthesis is also inhibited.^{13,14} After vaginal application of clotrimazole pessaries epithelial penetration takes place, but no systemic absorption of the drug has been found. The drug has been used in pregnant patients without any reported ill-effects on the fetus.¹⁵

The efficacy of clotrimazole has been proved in several reported studies (Table II).^{7,16-20} In pregnant patients cure rates comparable to the results of the present study have been reported (Table III).^{19,21}

TABLE II. REPORTED CURE RATES WITH CLOTRIMAZOLE IN NON-PREGNANT PATIENTS

	% cure
100 mg/d for 6 days, intravaginally	
Lohmeier (1974) ¹⁶	71
Widholm (1974) ¹⁷	81
Masterton et al. (1975) ¹⁸	93
Haram and Digranes (1978) ¹⁹	89
Robertson (1978) ²⁰	75
100 mg 2x/d for 3 days, intravaginally	
Masterton et al. (1976) ⁷	89

TABLE III. REPORTED CURE RATES WITH CLOTRIMAZOLE IN PREGNANT PATIENTS

	% cure
100 mg/d for 6 days, intravaginally	
Frerich and Gad (1977) ²¹	83
Haram and Digranes (1978) ¹⁹	82
500 mg, single dose intravaginally	
Present study	83,3

The reported incidence of recurrence varies from 4,2% to 24% with 6-day courses of therapy.^{2,22} In the current study a recurrence rate of only 5,7% was found. No resistance of *Candida* to any imidazole derivative has been reported,¹ and all investigators have recorded good patient acceptance and a very low incidence of side-effects.

Conclusion

The results of this study compare very favourably with other reported results, indicating that treatment of vaginal candidiasis in pregnant patients with a single clotrimazole 500 mg vaginal pessary is effective and associated with a low rate of recurrence.

Specific advantages of the single-dose therapy include: (i) proven effectiveness; (ii) absence of adverse effects; (iii) rapid relief of symptoms for all patients; (iv) very good patient acceptance and compliance; (v) no increased risk of recurrence; and (vi) simplicity.

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