

# The Relationship Between Hormone Therapy and Vaginal Candidiasis in Postmenopausal Patients

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**OBJECTIVE:** To evaluate the role of hormone therapy on vaginal *Candida* infection and colonization.

**STUDY DESIGN:** The patients in postmenopausal period attending to gynecology clinics were entered the study prospectively. The patients were classified as hormone therapy and control groups. Patients who used hormonal therapy, immunocompromised and having hysterectomy were excluded from the study. Sample for yeast culture was taken at the beginning and again at the end of 3rd and 6th months of the study. Sabouraud dextrose agar medium was used for yeast culture and positive culture showing yeast morphology was typed with conventional and full automatic yeast identification systems. Two groups were compared with Chi-Squared and T test using SPSS 10 statistical software program and  $p < 0.05$  was accepted to be statistical significant.

**RESULTS:** Totally, 112 patients completed the study. Hormonal therapy group consisted of 52 patients and control group consisted of 60 patients. There was no statistical significant difference in demographic characteristics between two groups. *Candida* culture positivity was more frequent in the hormonal therapy group at the 3rd and 6th months of the treatment and follow up ( $p < 0.05$ ). But, clinical infections were not different in two groups ( $p > 0.05$ ). The most frequent type of *Candida* isolated culture was *Candida glabrata*.

**CONCLUSION:** Hormonal therapy increases vaginal *Candida* colonization but not infection.

**Key Words:** *Candida* colonization, Hormonal therapy, Vaginal candidiasis

*Gynecol Obstet Reprod Med;14:2 (107 - 109)*

## Introduction

Hormone therapy (HT) is used to relieve postmenopausal symptoms related to vasomotor and urogenital systems. Also it is known that HT increases risk of breast cancer<sup>1,2</sup> and there is no proved cardiovascular benefit of HT.<sup>3</sup> The other secondary benefits of HT such as preventing osteoporosis, decreasing incidence of colon cancer are known, but HT is not used primarily for these benefit effects.

Vulvovaginal candidiasis is common infection in women in the premenopausal period. But, it is diagnosed rarely in postmenopausal patients. The low incidence of candidiasis in postmenopausal period may be arisen by estrogen deficiency. On the other hand, many women are used HT in this period. There is no prospective study to evaluate candidiasis in postmenopausal patients using HT. Aim of this study is to evaluate the relationship between HT and vaginal candidiasis.

## Material and Method

One hundred sixty three patients, in the postmenopausal period, attending to Department of Obstetrics and Gynecology, Akdeniz University School of Medicine between January 2003 and July 2003 because of postmenopausal period were entered the study. The patients had inform-consent about the study, menopause and menopausal treatment. The patients who preferred to use HT consisted of one group and the others control group, respectively. Microbiologists were not informed about the patients group. The patients using HT, antibiotics or hysterectomies or immunocompromised were excluded from the study. Totally 50 patients entered the study initially were excluded from the study because of lost follow up. HT group consisted of 52 patients and used HT (Estradiol hemihydrate 2mgr/day and Norethisterone acetate 1 mgr/day). Control group consisted of 60 patients.

After taking history, all of the patients were examined systemically and vaginally. During vaginal examination samples for yeast culture and fresh preparation were taken and vaginal pH was evaluated with nitrazine test initially, 3<sup>rd</sup>, 6<sup>th</sup> months of therapy and follow-up. Example for yeast culture was taken from posterior fornix with sterile swab and transferred to transport medium in 24 C°. After than, sample were taken for fresh preparation and stained with gram dye as a standard method. After transporting medium, samples were seed

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Submitted for Publication: 07. 04. 2008

Accepted for Publication: 26. 06. 2008

Sabouraud dextrose agar medium and incubated in 30°C for 7 days. Positive colonies were stained with gram and the colonies showed yeast morphology were typed with conventional and full automatic yeast identification systems (API ID 32 C bio Merieux SA, Mercy l'Etoile, France).

Risk factors for Candida infection including high blood pressure and diabetes mellitus were evaluated separately. Two groups (group 1 and 2) were compared according to the results. Statistical analyses were performed with Chi Squared and T Test using SPSS 10 statistical soft-ware package.

## Results

There was no statistically significant difference between two groups in demographic characteristics (Table 1). However, there were statistically significant differences between two groups in Candida culture positivity and vaginal pH after 3<sup>rd</sup> and 6<sup>th</sup> months ( $p < 0.05$ ) of HT and follow-up (Table 2). The most common type of Candida was *C. glabrata*, secondly *C. albicans* (Table 3). Statistically significant difference in vaginal pH changes was shown in table 4. Also there was significantly increase vaginal discharge in group 1 ( $p < 0.05$ ). But, no treatment was given to any patients because of vaginal discharge and positive culture for candidiasis.

Table 1. Demographic characteristics of the patients.

Characteristics	HT group	Control group	p
Mean age	51.8 (45-60)	49.7(44-58)	>0.05
Mean menopause duration	2.4 (1-7)	2.2(1-6)	>0.05

Table 2. Yeast culture results according to groups.

	Culture	HT Group	Control Group	p	Total
Initial	Negative,n (%)	42 (80.7)	52 (86.6)	0.05<	94 (83.9)
	Positive,n (%)	10 (19.2)	8 (13.3)		18 (16.0)
3 months	Negative,n (%)	39 (75)	60 (100)	0.05>	99 (88.3)
	Positive,n (%)	13 (25)	0		13 (11.6)
6 months	Negative,n (%)	36 (69.2)	55 (91.6)	0.05>	91 (81.2)
	Positive,n (%)	16 (30.7)	5 (8.3)		21 (18.7)

Table 3. The relationship between Candida type and treatment.

	Type	Initial, n (%)	3 months, n (%)	6 months, n (%)
Control Group	<i>C. glabrata</i>	5 (8.3)	--	3 (5.0)
	<i>C. albicans</i>	2 (3.3)	---	1 (1.7)
	<i>C. saprofiticus</i>	1 (1.7)	--	1 (1.7)
	<i>C. kefry</i>	----	--	---
HT Group	<i>C. glabrata</i>	5 (9.6)	5 (9.6)	6 (11.5)
	<i>C. albicans</i>	4 (7.7)	5 (9.6)	5 (9.6)
	<i>C. saprofiticus</i>	1 (1.9)	1 (1.9)	4 (7.7)
	<i>C. kefry</i>	--	2 (3.8)	1 (1.9)

Table 4. Changes in vaginal pH according to HT.

Months	Mean pH in HT group	Mean pH in control group	P
0	6.9	6.8	0.05<
3	5.8	7.3	0.05>
6	5.5	10.1	0.05>

## Discussion

Menopause and HT have been discussed entity frequently in gynecology recently. There are many local and systemic changes in body in that time. Symptoms related postmenopausal period is only relieved well with HT. But long term benefits and risks of HT are discussed.

Estrogens related changes in vaginal epithelium have been described. Vaginal epithelium is the most common area rich for nuclear estrogen receptors. These receptors are more frequent in the perimenopausal period. Estrogens increase superficial cells and karyopycknotic index.<sup>4</sup> The other vaginal effect of estrogens is on the vaginal colonization. Lactobacillus colonization increases with HT and it improves vaginal health.<sup>5,6</sup> As known, lactobacilli are responsible for vaginal acidity. These changes decrease vaginal bacteriologic nonspecific infection and increase local resistance. In this study, vaginal acidic changes were observed in the HT group.

Vaginal discharge consists of vaginal transudation, cervical secretion, cell fragments originated from cervix, endometrium or vagina. There are no glands in the vagina. Estrogens increase vaginal discharge as observed in the study.

*Candida albicans* is the frequent agent lead to vulvo-vaginal infection and this is unique infection having vaginal acidic pH. There is no prospective study to present relationship between HT and vaginal Candida infection or colonization. So, how does HT increase vaginal candidiasis? Some explanations are possible. First Candida reproducibility needs to adhere vaginal epithelium and germination. Estrogens cause the proliferation of vaginal epithelium and increase glycogen in the vaginal epithelial cells. These changes increase proliferation, germination and adhesion capability of *Candida albicans*. Secondly, yeast cells containing estrogen receptors have been described.<sup>7</sup> Receptors are important for germination. Also, lower prevalence of candidiasis in postmenopausal period may be explained with relationship between estrogens and vaginal epithelial changes partly. Some patients in postmenopausal period have the same vaginal flora with premenopausal years.<sup>8</sup> But these patients are obese and have higher plasma estrogen levels. Candida infection is more frequent in these women.

Diagnosis of Candida infection is discussed because of

some problems. Some patients have symptoms but no findings in fresh preparation and no culture positivity, but treated clinically as candidiasis and relieved. Some times, culture is positive but no findings of Candida infection. Also some cases have positive findings in fresh preparation but no positive culture detected etc. On the other hand, the most common positive test is yeast culture. Mc Cormack et al.<sup>9</sup> found that 25% (42/144) of patients had positive culture. But 25 of 42 patients had vulvovaginal pruritus, 8 of 25 patients had positive KOH preparation. Seven of 8 had clinical findings. Thirty four patients were KOH negative, but 18 of 34 (34%) were symptomatic. One hundred two cases were culture and KOH negative and 16/102 cases had vulvovaginal pruritus.

Colonization of Candida species in the vagina does not mean Candida infection. Clinical findings should be present. Because Candida species can be present in vaginal flora without any harmful effects or infection. In this study, no increase in incidence of Candida infection was encountered and no treatment was given to any patients due to culture positivity.

Many studies<sup>10,11</sup> showed that Candida albicans is the most frequent type isolated from vaginal yeast culture. But in our study, C. glabrata was the most frequent type. This may be related to changes in postmenopausal period and studied population.

Conclusion: The incidence of vaginal Candida colonization increases during HT in postmenopausal patients. But there is no increase in the frequency of clinical infection.

## Postmenopozal Hastalarda Vaginal Kandidiyaz ile Hormon Tedavisi Arasındaki İlişki

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Hormon tedavisinin vaginal kandida enfeksiyonu ve kolonizasyonu üzerindeki rolünü değerlendirmek.

Postmenopozal dönemde olup jinekoloji kliniğine başvuran hastalar prospektif olarak çalışmaya alındı. Hastalar hormon tedavisi grup ve kontrol grubu olarak ikiye ayrıldı. Hormon tedavisi alanlar, immün sistemi bozuk olanlar ve histerektomize hastalar çalışmaya dahil edilmedi. Mantar için kültür çalışma başında, izlemin 3. ve 6. aylarında alındı. Saburoid dextroz agar besi yeri mantar kültürü için kullanıldı ve üreme olan örnekler konvansiyonel ve tam otomatik mantar identifikasyon sistemi ile tiplendirildi. İki grup SPSS 10 istatistik programı kullanılarak Ki-Kare ve T testi ile karşılaştırıldı ve p<0.05 istatistiksel anlamlı olarak kabul edildi.

Toplam 60'ı kontrol ve 52'si hormon tedavisi alan grupta olmak üzere 112 hasta çalışmayı tamamladı. Her iki grup arasında demografik özellikler açısından fark bulunmamaktaydı. Kandida kültürlerinde üreme hormon tedavisi grubunda 3. ve 6. aylarda daha fazla idi(p <0.05). Fakat klinik enfeksiyon oranları iki

grupta farklılık göstermemekteydi(p >0.05). Kültürde izole edilen en sık tip kandida glabrata idi.

Hormon tedavisi kandidal kolonizasyonu artırmaktadır. Ancak klinik enfeksiyon sıklığına etki etmemektedir.

**Anahtar Kelimeler:** Kandida kolonizasyonu, Hormon tedavisi, Vaginal kandidiazis

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