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Chronic prostatitis/chronic pelvic pain syndrome: the role of an antifungal regimen

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Introduction. The role of fungal infection as a causative factor for prostatitis is currently underestimated. The aim of our work was to evaluate the response to an antifungal regimen in the setting of patients presenting with symptoms of chronic pelvic pain syndrome that have been refractory to treatment with antibiotics and alpha–blockers.

Material and methods. We included 1,000 consecutive patients. The inclusion criteria included failure of response to four consecutive weeks of antibiotic and alpha–blockers. The antifungal regimen was continued for two weeks. It included a low carbohydrate diet, the alkalinization of urine, and administration of fluconazole.

Results. The mean age of the patients was 34 years. Mean serum total PSA and PSA density (PSAd) were 0.6 ng/ml and 0.03 ng/ml/gram, respectively. The mean age, PSA, prostate volume, and PSAd for patients that showed good response were 33, 0.5, 17, and 0.031, respectively. Values for patients that did not show good response were 36, 0.8, 23, and 0.037, respectively ($p < 0.0001$ for all of the variables). Improvement was observed in 80% of cases treated with the antifungal regimen.

Conclusions. Antifungal regimen should be considered for the majority of young adult men, presenting with chronic prostatitis/ chronic pelvic pain syndrome and incomplete response to antibiotics.

Key Words: prostatitis ‹› chronic pelvic pain syndrome ‹› candida ‹› antifungal

INTRODUCTION

Prostatitis is a common health problem, affecting around 8% of men presenting to urologists with genitourinary problems [1]. Data in the literature regarding fungal prostatitis are sparse and mostly in the form of isolated case reports [2–5]. One should expect fungal prostatitis to be increasingly recognized in the era of broad–spectrum antibiotics.

Many studies have been published, confirming the association of bacterial prostatitis and the rise in serum PSA. Pansadoro et al. [6] reported that there is an increase in PSA in the blood of 71%, 15%, and 6% of men with acute bacterial prostatitis, chronic bacterial prostatitis, and nonbacterial prostatitis, respectively. Lee et al. [7] reported recently that chronic prostatitis may interfere with the interpretations for PSA level for prostate cancer screening.

The aim of our work was to report our experience in managing 1,000 Egyptian men, presenting with chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) and not responding to a combination of antibiotic and alpha–blocker treatment.

MATERIAL AND METHODS

In our study we included all patients who presented during the period of one year to our urology outpatient clinic with CP/CPPS, which failed to improve with medical treatment. Our university hospital is a tertiary care hospital that serves our province and all the surrounding territories. Medical care here is totally free of charge, which allows us to manage a high volume of cases.

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Patients were included in the study if they were adult men, presenting with non–specific pelvic, genital, or perineal pain, with or without LUTS. They should also have received four continuous weeks of treatment with fluoroquinolones and alpha–blockers, without showing improvement of their symptoms. In our institution we usually use a combination of ciprofloxacin and tamsulosin. Urine culture and abdominopelvic ultrasound should be performed to exclude bacterial infection or any other possible pathology. The use of the abovementioned criteria allowed us to include into our study around 20% of cases presenting to our institution with prostatitis symptoms, while the others showed a good response to the combination treatment of antibiotics and alpha–blockers.

Our patients were continued on a low carbohydrate diet, had their urine alkalinized with potassium citrate, and were administered fluconazole daily for two weeks.

An improvement in a patient's symptoms was defined subjectively according to the patient's testimony as to the disappearance of their symptoms or the achievement of at least an 80% improvement of their pre–treatment symptoms. The improvement percentage was based on the patient's assessment of symptom improvement on a scale of 1 to 10. The data was recorded as improved or not improved.

Follow–up was performed two weeks after the end of the treatment period and three months after treatment initiation. The response to treatment was measured at the three–month follow–up. The patients that showed a good response did not revisit our outpatient clinic, which we believe denoted the persistence of symptom improvement.

The data collected included patients age, prostate volume, serum total PSA, history of previous antibiotics treatment for the same or other condition, and the response to the antifungal treatment.

Statistical analysis was done using the SPSS program. Categorical variables were calculated using the two–tailed Fisher's exact test. Continuous variables were calculated using a two–tailed independent t test.

RESULTS

The mean age of the patients was 34 years. Mean serum total PSA and PSA density (PSAd) were 0.6 ng/ml and 0.03 ng/ml/g, respectively. Table 1 illustrates the descriptive data for our patients.

Patients were mainly complaining of irritative lower urinary tract symptoms – mainly frequency and urgency. Discomfort and vague pain related to the genital area was usually an associated complaint.

Table 1. *Descriptive data for our CP/ CPPS patients*

Variable		Value
Mean age		34 ±5
Mean serum total PSA		0.6 ±0.2
Mean prostate volume		18 ±4
Mean PSAd		0.03 ±0.009
History of previous antibiotics courses	Yes	698
	No	302
Improvement with antifungal regimen	Yes	803
	No	197

Lower serum total PSA, prostate volume, and PSAd were significantly associated with improvement of CP/CPPS symptoms after the antifungal regimen. Patients who were previously treated with multiple courses of antibiotics also showed significant improvement after the antifungal regimen. A better response to the antifungal regimen was significantly associated with younger age. Table 2 illustrates the statistical results.

DISCUSSIONS

In the last decades, fungal urinary tract infections (UTI) due to candida yeasts have increased significantly [8, 9]. Recently, Behzadi et al. [10] reported the incidence of UTI associated with *Candida albicans* to be 6.8% of all microbial UTIs. Fisher et al. [11] have recently published a review article on *Candida* infection of the urinary tract. They could conclude that *Candida* organisms are very well equipped for colonization and invasion of the urinary tract, and little is currently known about the regulating factors for *Candida* virulence. Some studies have shown that an *E. coli* infection of the urinary tract can act as a bridge, facilitating the colonization of *Candida*

Table 2. *Correlation of response to antifungal regimen with patients' variables*

Variables		Improvement		P value
		Yes	No	
Age (mean & SD)		33 ± 4	36 ±6	<0.0001
PSA (mean & SD)		0.5 ±0.2	0.8 ±0.1	<0.0001
Prostate volume (mean and SD)		17 ±2.5	23 ±5.4	<0.0001
PSAd (mean & SD)		0.031 +0.01	0.037 +0.03	<0.0001
Antibiotics	Yes	612	86	0.0001
	No	191	111	

albicans [12, 13]. Anothaisintawee et al. (14) conducted a systematic review and meta–analysis of literatures on management of CPPS. Interestingly they concluded that although CPPS had to represent a spectrum of cases that are free of microbial infection, antibiotics administered alone or in combination with alpha–blockers represent the best current modality of treatment for such cases.

In our study patients who received multiple previous courses of antibiotics did show a better response to the antifungal regimen. As previously shown, *Candida* colonization and invasion of the urinary tract occurs with difficulty except when associated with a bacterial colonization. Other factors that do not exist in our study group include diabetes mellitus and prolonged catheterization. An explanation may be that previous bacterial infection acts as a factor facilitating *Candida* colonization of the prostate. Different courses of antibiotics may help in properly eliminating the urinary bacterial infection, facilitating the action of antifungal medications. Another explanation may be that recurrent antibiotic courses block the local immune mechanisms, facilitating the invasion and virulent behavior of the colonized *Candida* infection.

In our study, a better response to the antifungal regimen was achieved in younger men. A possible explanation may be the possible association with sexually transmitted pathogens. *Gonorrhea* and *Chlamydia* may result in destruction of the urothelium, facilitating *Candida* colonization and invasion. In our study group we could not get a history of such occurrence. However, in Egypt, due to religious and social reasons, people are very ashamed to discuss their sexual relations. Most of them take antibiotics empirically without visiting a doctor, a treatment that is not likely to be efficient.

Chronic prostatitis is a well–known cause of high serum total PSA. Nadler et al. [15] reported that prostatitis and BPH can cause high PSA, in the absence of prostate cancer. More recently Nadler et al. [16] studied 421 patients with CPPS and could detect that the mean total PSA of the studied group was 1.97 ng/ml, which is significantly higher than the value in the normal population. Schaeffer et al. [17] added that treatment of chronic prostatitis with antibiotics like ciprofloxacin results in a significant reduction of the elevated PSA. In our study we did not investigate serum total PSA at the start of encountering the patients in the outpatient clinic. The available PSA data represents the values only obtained for the patients included in the study, following a four week course of ciprofloxacin. The mean serum PSA was 0.6 ng/ml, mean prostate volume was 18 grams, and the mean PSAd was 0.003. Patients that showed a response to the antifungal regimen had significantly lower serum total PSA and lower prostate volume. Lower PSA values in the improved group do not represent an error caused by the lower prostate volume, as proved by the statistically significant lower levels of PSAd as well. We could not find an association between fungal prostatitis and serum PSA in literature. In our cohort the mean PSA was 0.5 and 0.8 ng/ml ($p < 0.0001$) for patients that showed and did not show good response to antifungal regimen respectively. So it seems that fungal prostatitis may be associated with lower PSA values. The explanation of this finding is to be investigated.

Although in our study there is lack of a urine culture documenting fungal infection, 80% of our cases showed significant improvement of their prostatitis symptoms, when followed on the antifungal regimen. The antifungal regimen may be considered for young adults who present with symptoms of chronic prostatitis and those with failed or incomplete response to antibiotics. The lower the serum total PSA and the smaller the prostatic volume, the more response one can anticipate with the antifungal regimen. Further, better–structured studies will be needed to confirm our findings.

CONCLUSIONS

The antifungal regimen may be considered for the majority of young adults, presenting with chronic prostatitis/chronic pelvic pain syndrome and incomplete response to antibiotics.

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