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Changes in white blood cell counts in men undergoing thrice-weekly prostatic massage, microbial diagnosis and antimicrobial therapy for genitourinary complaints

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Objective To report changes in the white blood cell (WBC) counts in expressed prostatic secretions (EPS) in men with pelvic symptoms undergoing thrice-weekly prostatic massage combined with antimicrobial therapy.

Patients and methods The study comprised a retrospective analysis of the records of 35 patients (mean age 45.3 years, range 28–70, SD, 12.03) with pelvic pain, pain in the lower back, obstructive urinary symptoms, irritative urinary symptoms, or sexual dysfunction, who had undergone the same diagnosis and treatment protocol in a genitourinary clinic in Manila, Philippines, from September 1992 to September 1995.

Results EPS were obtained 347 times in 35 patients (median 9 times per patient, range 6–16). In 26 of the 35 (74%) patients the WBC count in the EPS was <10 per oil-immersion field (OIF, $\times 1000$) at the first prostatic massage. In 34 of 35 (97%) patients the WBC count rose to $\geqslant 10$ as prostatic massage continued on a thrice-weekly schedule. The mean (range, SD) initial WBC count in the EPS was 8.4 (1–48, 8.43) and the maximum was 40.9 (6–60, 19.05); the difference between these values was 32.5 (3–57, 18.78; 95% confidence interval 26.1–40.1) and the difference was statistically significant (paired *t*-test, $P<0.001$).

Conclusions The classification of patients into those with prostatodynia or prostatitis based on one EPS examination is misleading and thrice-weekly massage of the prostate is better than a single collection of EPS to obtain the most purulent sample for Gram staining and culture.

Keywords Prostatitis, prostatodynia, sexual dysfunction, benign prostatic hyperplasia, impotence, clinical series

Introduction

Four categories of prostatitis are recognized, i.e. acute bacterial, chronic bacterial, nonbacterial and prostatodynia. The generally accepted threshold between prostatodynia and prostatitis is $\geqslant 10$ white blood cells (WBC) per oil immersion field (OIF, $\times 1000$) [1–4]. The Meares and Stamey localization test [5] has been considered the 'gold standard' for diagnosing the prostatitis syndromes. Using the Meares and Stamey classification, $\approx 90\%$ of patients with chronic pelvic symptoms are categorized as nonbacterial prostatitis or prostatodynia, which are thought to be incurable diseases [6]. Published in 1968, the original report by Meares and Stamey [5] was based on only six patients and the procedure has been largely abandoned by practising urologists and GPs [7]; it has been estimated that $<5\%$ of urologists routinely use the Meares and Stamey localization procedure [8].

The protocol of the Manila Genitourinary (GU) clinic for treating prostatitis syndromes consists of thrice-weekly prostatic massage, microbial testing and antimicrobial therapy, and was first described in 1982 [9]. In this clinic, patients with acute or chronic bacterial prostatitis, nonbacterial prostatitis, prostatodynia, sexual dysfunction or BPH receive the same treatment. This paper reports the changes in the WBC counts in the EPS in 35 men with pelvic symptoms undergoing thrice weekly prostatic massage as part of this treatment protocol.

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Patients and methods

The medical records were reviewed for 35 patients (mean age 45.3 years, range 28–70, SD 12.03) with pelvic symptoms treated using the same protocol between September 1992 and September 1995. Six (17%) of the patients reported being single and 29 (83%) reported being married. The primary and subsidiary complaints were recorded from the charts when available, symptoms being recorded using terminology based on the symptom scores developed by the AUA [10] and the University of Washington [11].

All patients stayed in the protocol for at least six EPS massages and comprised a unique group undergoing the same treatment protocol and testing regimen; no patients had only 2–5 massages. The urethra was tested for *Chlamydia* by the direct immunofluorescence (DIF) test (Chlamydia Direct IF, bioMerieux, France). All the patients underwent thrice-weekly prostatic massages by DRE, carried out by one of two clinic physicians. For consistency, the first drop of EPS was collected at each massage and Gram stained by one of two laboratory technicians. The maximum WBC count per OIF was recorded at every massage; when the OIF contained too many WBC to count it was recorded as 60 WBC/OIF. The EPS were cultured for aerobic bacteria (brain-heart infusion broth), anaerobic bacteria (cooked-meat medium), *Ureaplasma* and *Mycoplasma* (*Mycoplasma* IST broth) and *Trichomonas* (medium consisting of liver digest, glucose and sodium chloride).

Patients were simultaneously treated with ofloxacin 400 mg and minocycline 100 mg (both orally, twice daily) during the protocol. After the fourth massage, metronidazole 2 g orally was given once. After the antibiotics were stopped, the patients were given ketaconozole 400 mg for 5 days. Any patient not tolerating a drug was given a substitute, i.e. another quinolone antibiotic, usually ciprofloxacin, for ofloxacin, doxycycline for minocycline, and itraconazole for ketaconazole.

Results

Sixteen different symptoms were present in the study population, those most frequently recorded in the patient's charts being pain symptoms, but also including obstructive and irritative urinary symptoms, sexual dysfunction, urethral discharge and fatigue. The most common chief complaints were pain during urination, pain in the penis, pain in the lower back, and pain in the perineum. The most common complaints overall were pain during urination, difficulty obtaining an erection, and the need to urinate again <2 h after urinating (Table 1). That these symptoms are commonly seen in men with prostatitis has been reported recently [12,13].

Using >3 months as the threshold between designating cases as acute or chronic, seven (20%) of the 35 patients were acute and 28 (80%) chronic, based on their primary complaint on presentation. Patients experienced their primary complaints for periods ranging from 3 days to 20 years, with a median duration of symptoms of 12 months.

Table 2 lists the 35 patients and their WBC count in the EPS as it changed with thrice-weekly massages, with the number of massages that each patient underwent. All patients completed six prostatic massages, one patient underwent 16, the median being 9 (range 6–16, mean 9.9, SD 2.3). At the first massage, 26 of 35 (74%) patients had <10 WBC/OIF and of these 26 patients, 25 (96%) had a WBC count of >10 in subsequent EPS (95% CI, 0.78–0.98). By the end of the study, 34 of 35 (97%) patients had $\geqslant 10$ WBC/OIF as the thrice-weekly prostatic massage continued. As $\geqslant 10$ WBC/OIF is usually used as the threshold to distinguish prostatodynia or prostatitis, the diagnostic category of these patients changed with continued massage.

The initial WBC count in the EPS was never the maximum; most patients had a maximum count between their third and fifth massage, with a wide variation in this peak. At least 10 massages were required for every patient in this study to reach the peak WBC count in

Table 1 The frequency of complaints in 35 patients attending the Manila Genitourinary Clinic

Complaint	*Total*	*Main*	*Second*	*Third*	*Fourth*
Pain during urination	9	7	2		
Difficulty obtaining an erection	8	2	3	1	2
Need to urinate again <2 h after urinating	7	3	3	1	
Urethral discharge	7	2	4	1	
Arousing to urinate $\geqslant$ once a night	6	1	2	2	1
Pain in lower back	6	4	1	1	
Pain in the penis	6	5	1		
Pain between the testicles and anus	5	4	1		
Pain in the lower abdomen	4	2		2	
Pain in the testicles	4	2	2		
Having to push or strain to begin urination	3	1	1		1
Pain with ejaculation	3		1	1	1
Weak urinary stream	2			2	
Bladder does not feel completely empty after urinating	1	1			
Premature ejaculation	1	1			
Fatigue	1		1		

Table 2 Patients and changes in their WBC counts with successive drainages; 35 patients underwent drainage from six to 16 times

Patient no.	WBC count at massage number																No. of massages	First	Counts		Ratios	
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16			Min	Max	Max/Min	Max/First
1	15	35	26	3	4	15	8	2									8	15	2	35	17.5	2.33
2	6	45	20	3	3	4	1	7	8	10	10						11	6	1	45	45.0	7.5
3	3	4	52	30	14	30											6	3	3	52	17.3	17.3
4	6	4	18	20	7	25	12	8	12	15	6	13					12	6	4	25	6.25	4.17
5	4	1	17	5	10	6	10	5	4	3	3	4	2				13	4	1	17	17.0	4.25
6	15	30	3	42	5	4	35	8									8	15	3	42	14.0	2.80
7	20	20	30	60	50	60	25	35	20								8	20	15	60	4.0	3.0
8	15	20	30	30	50	10	3	12									8	15	3	50	16.67	3.33
9	3	3	3	3	6	4	5	2	3								9	3	2	6	3.0	2.0
10	8	17	30	60	50	60	55	20	60	60	45	52					12	8	8	60	7.5	7.5
11	16	10	38	35	5	2	3	8	5								9	16	2	38	19.0	2.35
12	5	2	3	2	15	2	5	2									8	5	2	15	7.5	3.0
13	3	3	3	60	60	60	60	30	10	26	16						11	3	3	60	20.0	20.0
14	5	7	40	14	24	30	15	56	36	8	7	5					12	5	5	56	11.2	11.2
15	7	3	3	5	10	1	3	5	2								9	7	1	10	10.0	1.43
16	3	3	7	3	12	15	5	1	2								9	3	1	15	15.0	5.0
17	5	4	7	10	5	5	18	8									8	5	4	18	4.5	3.6
18	5	8	5	12	1	4	6										7	5	1	12	12.0	2.4
19	3	6	16	60	34	5	5	3	7	3	5						11	3	3	60	20.0	20.0
20	4	3	6	25	18	25	10	4	2	6							10	4	2	25	12.5	6.25
21	4	8	60	20	2	3	5										7	4	2	60	30.0	15.0
22	6	4	5	20	5	8	3	0	3	6	3	4	1				13	6	1	20	20.0	3.3
23	3	4	8	34	12	3											6	3	3	34	11.3	11.3
24	10	3	3	24	28	8	8	6	5	5	4	2					12	10	2	28	14.0	2.8
25	5	5	10	16	10	2	5	3	8	25	15	6					12	5	2	25	12.5	5.0
26	15	60	60	30	15	15	12	15	10	30	20	22					12	15	10	60	6.0	4.0
27	7	20	8	5	60	25	30	40	45	60	35	35	60	45	5	2	16	7	2	60	30.0	8.57
28	48	60	6	20	20	45	12	12									8	48	6	60	10.0	1.25
29	6	8	35	37	60	10	7	5	45	15							10	6	5	60	12.0	10.0
30	1	10	50	60	30	20	5	30	15								9	1	1	60	60.0	60.0
31	7	35	30	30	35	58	24	12	10	5	15	6	14				13	7	5	58	11.6	8.29
32	15	30	60	25	20	35	29	14	34								9	15	14	60	4.29	4.0
33	6	3	13	10	54	45	55	15	15	30	38	25	4				13	6	3	55	18.3	9.17
34	1	5	8	15	35	13	60	4									8	1	1	60	60.0	60.0
35	8	28	30	15	12	20	16	20	18	6							10	8	6	30	5.0	3.75

the EPS. The changes in WBC with continued thrice-weekly prostatic massage were statistically significant (Fig. 1). The mean (SD) WBC count at the first massage was 8.4 (8.43) and at the second was 14.6 (16.24), giving a mean change of 6.2 (12.03, 95% CI 2.1–10.4); the difference was statistically significant (paired *t*-test, $P=0.0043$). The count at the fourth massage was 24.1 (18.47) and the mean change from the first to fourth massage was 15.7 (19.73; 95% CI 8.9–22.5; $P<0.001$, paired *t*-test). The most important change clinically in the WBC count was from the first to the maximum, the mean (SD) of which was 40.9 (19.05), giving a mean change from the first of 32.5 (18.78; 95% CI 26.1–39.0; $P<0.001$, paired *t*-test); thus the maximum WBC exceeded the first by a factor of 5.

All patients had a complete set of cultures and urethral chlamydial DIF testing at the first EPS examination, the tests being repeated throughout treatment. None of the cultures or slides for *Trichomonas* or anaerobic bacteria were positive. Two patients (nos 9 and 11) were negative on chlamydial DIF testing and on all bacterial cultures; patient no. 9, 45 years old, had pain in his lower abdomen of 4 years' duration. His WBC in the EPS never exceeded 10 over nine massages; his initial WBC count was 3 and the maximum 6. For a year, patient no. 11 (44 years old) had had pain in the lower back, pain with ejaculation, difficulty obtaining an erection, and had to push or strain to urinate; his first WBC count was 16 and his maximum 38. The remaining patients had positive bacterial cultures or a positive chlamydial DIF (Table 3).

After six massages, the patients began to discontinue

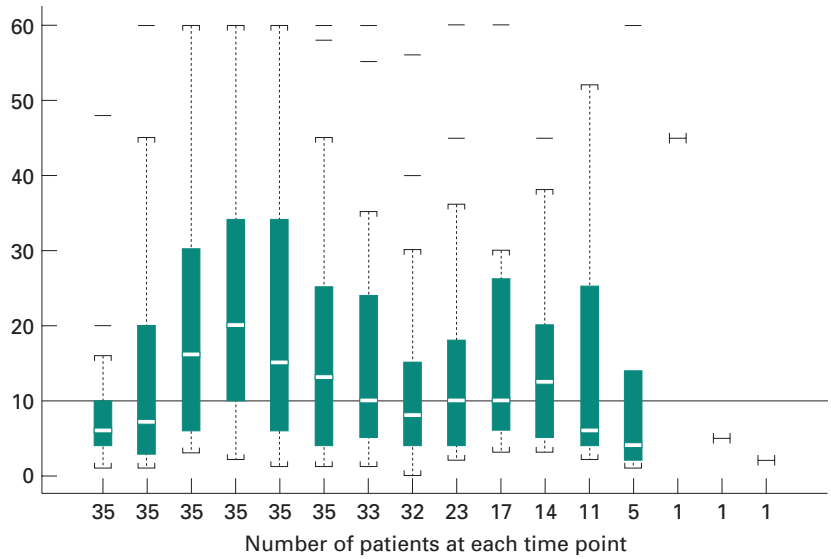

Fig. 1. Changes in the WBC counts of 35 patients at each successive massage. From left to right, the graph shows the 16 massages with the number of patients at each massage listed on the abscissa. The median WBC count is shown as the small (coloured) rectangle inside each bar, the solid bar represents the 25th to the 75th percentile and the whiskers represent the entire range of the data, excluding outlying data shown as horizontal lines.

the thrice-weekly massage regimen, the records suggesting that this was because the symptoms resolved, the thrice-weekly treatment was inconvenient, or because of the expense of treatment compared with the patient's income. Follow-up of the patients by telephone was inadequate; only nine of the 35 patients had telephones and only five of the nine (14% of the study group) could be contacted for an interview by the first author. Four of the five patients (nos 4, 10, 12, 24 and 25) reported being completely cured of all symptoms by the protocol. Patient no. 25, a diabetic who had undergone a TURP, reported being only partially cured by the protocol. All five of those contacted by telephone reported being unharmed by the protocol and none of the 35 patients had complications from prostatic massage recorded in their charts.

Discussion

Before the production of antibiotics for medical use in the 1940s, and even after the introduction of the sulpha antibiotics and penicillin, the 'gold standard' for the treatment of prostatitis was prostatic massage [14]. After antibiotics were introduced, they became the 'gold standard' treatment for prostatitis [15]. Prostatitis is the major cause of antibiotic treatment in men [16].

Using Medline and manual library searches, we have found no studies on the effect of thrice-weekly prostatic massage on WBCs in the EPS from healthy or diseased men, no studies on what frequency of prostatic massage maximizes the clinical response, nor studies on the combination of the two 'gold standards', i.e. prostatic massage and antibiotics, for prostatitis.

Obstruction of the prostatic ducts and inflammation of the prostate are both recognized components of prostatitis [17]. The treatment protocol in Manila is based on the theory that the prostatitis syndromes are caused by obstruction of prostatic ducts with or without concomitant infection. Experience suggests that antibiotic failure in patients with chronic bacterial or nonbacterial prostatitis and prostatodynia is caused by infection behind the obstructed prostatic ducts, where antibiotics may have a transient benefit but ultimately fail because of the surgical principle that obstruction and infection cannot be cured without curing the obstruction first [18].

We do not discount the idea that unidentified bacteria may be responsible for prostatitis in many cases. In lieu of the use of DNA technology to treat other inflammatory diseases [19], e.g. cat-scratch disease, bacillary angiomatosis, Whipple's disease and ulcers, we suggest using DNA technology on the most purulent prostatic fluid secretions to determine whether unculturable organisms are involved. A dramatic first step was reported by Krieger *et al.* [20] using PCR assays to detect bacterial 16s rRNA in 85% of patients with 'nonbacterial' prostatitis from perineal prostatic biopsy specimens, in which skin contamination was controlled.

In the present series, the patients' samples were cultured for anaerobes and although the cultures were negative, the patients were still treated with metronidazole [21], on the premise that fastidious anaerobes are too difficult to culture and that prostatitis is multibacterial. This is similar to the way in which pelvic inflammatory disease is treated in women. Anaerobes are a known cause of prostatic abscess [22] and have been implicated in diseases of the genitourinary tract, especially in male infertility and prostatitis [23–27]. Because anaerobes are fastidious organisms, difficult and expensive to culture, there is controversy about how much technology to use in an attempt to find anaerobes [28]. During the

Table 3 A summary of the culture results and chlamydial DIF for the 35 patients

Patient no.	*Chlamydia*	*Staph Aureus*	*Staph Epidermidis/ Saphrolyticus*	*Pseudomonas*	*E. Coli*	*Ureaplasma*	*Mycoplasma*
1	Y		Y				
2	Y	Y					
3			Y				
4			Y				
5		Y					
6		Y					
7		Y					
8			Y	Y			
9							
10		Y					
11				Y			
12		Y					
13		Y					
14		Y					
15					Y		
16		Y					
17		Y					Y
18		Y					
19		Y					
20		Y					
21			Y				
22		Y					
23		Y					
24		Y					
25	Y		Y			Y	Y
26	Y	Y				Y	
27		Y					
28		Y					
29		Y					
30	Y	Y					
31			Y				
32			Y				
33			Y				
34		Y		Y			
35	Y						
total positive	6	20	10	3	1	3	1

Y means 'yes' a positive culture or DIF test.

development of the current protocol, when antibiotics were stopped antifungal agents were prescribed, because budding yeast cells were found in the Gram stains of the EPS or in cultures (unpublished data).

The Manila GU physicians reported softening of the prostate during repeated massage and remodelling of the palpable architecture of the prostate. The physical size of the prostate was also reportedly decreased in many patients undergoing thrice-weekly prostatic massage. This was also noted by Homonnai *et al.* [29] in a study of 123 men undergoing twice-weekly prostatic massage, in which it was concluded that there was a marked reduction in size of the prostate and a better consistency in many of the patients. Furthermore, the concept of massage of pus from glands is not new; another example of digital massage is the treatment of the female breast with mastitis [30].

The physicians in the Manila GU clinic call their procedure 'prostatic drainage' rather than 'prostatic massage'. Drainage is carried out in the direction in which the glands drain at the microscopic level and is meticulous, with every aspect of the reachable prostate being drained. Increasing pressure is applied during the thrice-weekly drainage, as much as can be tolerated by the patient. The ductal and glandular anatomy of the three prostate zones, from which the technique of prostatic drainage is derived, has been described [17,31].

We suggest that much of what is designated 'BPH' is

confused with prostatitis and therefore can be treated as prostatitis. Indeed, prostatitis as a histological lesion has been found in 98% of patients with BPH [32]. Microbial tests on BPH tissue have detected significant rates of infectivity; in one study, >70% of TURP specimens showed clinical or microscopic signs of infection [33] and in another, using only limited cultures, 21% of men with BPH had infected prostate tissue removed at surgery [34]. Dan *et al.* found *Chlamydia* in three of 100 men undergoing TURP, using only simple culture techniques [35]. The ideal endpoint for the GU clinic protocol is two successive WBC counts in the EPS of <10, negative culture of the EPS and the resolution of symptoms.

In conclusion, the classification of patients into those with prostatodynia or prostatitis based on one EPS examination may be misleading. Thrice-weekly massage of the prostate appears better than a single sample to obtain the most purulent EPS for Gram stain and culture. Diseases that can be associated or confused with prostatitis, e.g. prostatodynia, interstitial cystitis, infertility, sexual dysfunction, impotence, BPH, bladder neck obstruction, urethritis, epididymitis, ejaculatory duct obstruction and orchitis, should be re-evaluated using thrice-weekly prostatic massage.

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