



Use of prostatic massage in combination with antibiotics in the treatment of chronic prostatitis

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Chronic prostatitis is often refractory to antibiotics, however biopsy and molecular data indicate persistent symptoms may be due to occult infection. Combining antibiotic therapy with regular prostatic massage has been suggested as an effective therapy for some of these men.

From November 1996 to December 1998, 73 men with chronic pelvic pain syndromes were treated with antibiotics and prostatic massage. Antibiotic selection was based on culture and sensitivity of prostatic fluid or empirically if cultures were negative. Prostatic massage was done 1 to 3 times per week and fluid examined for WBCs and cultured for bacteria.

The average age of the group was 43.5 y (range 23–72) and average duration of symptoms 6.7 y (median 3 y, range 3 months–30 y). Prostatic cultures were negative in 19, grew uropathogens in 2, and Gram positive bacteria in 52 patients. Overall 29 patients (40%) had complete resolution of symptoms, 14 (19%) had complete resolution followed by a recurrence, 15 (21%) had some improvement and 15 (21%) had no improvement. All positive cultures were sterilized during treatment.

Combination prostatic massage and culture specific antibiotics can be an effective treatment in a proportion of men with long standing refractory chronic prostatitis.

Keywords: chronic prostatitis; prostatic massage; antibiotic therapy

Introduction

Chronic prostatitis is a common disorder with an uncertain response to conventional treatment that is frustrating for both patient and urologist.^{1,2} Chronic prostatitis is typically treated with prolonged courses of antibiotics, despite a low prevalence of positive cultures, if indeed expressed prostatic secretions (EPS) are collected at all. Many however do not respond to antibiotics or have a rapid recurrence in symptoms when antibiotics cease. In these patients it is unclear whether treatment failure is due to inadequate antibiotic tissue levels or that the symptoms are unrelated to infection but rather derive from an inflammatory or neuromuscular condition.

Prior to effective antimicrobials for chronic prostatitis, the mainstay of therapy was prostatic massage. Presumably, symptoms related to prostatic congestion would be relieved by expelling inflammatory cells and fluid from

obstructed acini of the gland. Recently there has been renewed interest in combining prostatic massage with antimicrobial therapy for patients with recalcitrant chronic prostatitis.³ The purpose of this study was to evaluate regular prostatic massage in combination with culture specific antibiotic therapy in men with chronic prostatitis (NIH chronic pelvic pain syndrome classes II, IIIa and IIIb).

Materials and methods

From November 1996 to December 1998, 195 men were evaluated in our chronic prostatitis clinics at either Harbor-UCLA Medical Centre or the Institute for Male Urology. Of these, 73 men were treated with combined prostatic massage and antibiotics entirely at our clinics and were available for follow up. Evaluation included a complete history and physical examination, uroflow and ultrasound residual and aerobic culture of urethra (VB1 or urethral swab), midstream urine and expressed prostatic secretions (EPS). For the 6 patients in whom EPS was not

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obtainable, a post massage urine (VB3) was cultured. No symptom score was used to quantify the voiding symptoms. All colony counts were reported for any bacteria isolated and sensitivities performed. Chlamydia culture was performed from a urethral swab. EPS was examined under the microscope at 400× magnification (40× lens) and white blood cell (WBC) count per high power field (hpf) reported as the mean of at least four fields. Prostatic massage was performed with the patient in the standing position leaning over the examining table. Each lobe was compressed against the pubic bone with a rolling motion laterally to the midline and then stripped superiorly to inferiorly. There was no specific abstinence period required before each visit.

Patients with a positive EPS or VB3 culture were classified as chronic bacterial prostatitis (CBP) (NIH class II) unless identical bacteria were isolated from VB1. Patients with negative culture were classified as nonbacterial prostatitis (NBP) (NIH class IIIa) if they had 10 or more WBC per hpf in their EPS. Those with negative cultures and fewer than 10 WBC per hpf in their EPS were classified as prostatodynia (NIH class IIIb).

In cases with a positive culture, antibiotics were chosen based on reported sensitivities. In cases without a positive culture, antibiotic selection was guided by prostatic penetration, response to previous therapy and patient allergies and side effects. Prostatic massage was performed 1–3× per week for a median of three weeks (range 2–12 weeks). If interim cultures showed resistance to the chosen antibiotics, these were changed. Endpoints were final EPS culture, WBC count in the EPS and patient symptoms. A complete response was defined as resolution of all pain and urinary symptoms. A partial response was defined as any residual symptom. Patients were followed for a minimum of four months (range 4–15 months).

Statistical comparison of continuous variables was by an unpaired *t* test and of category variables by the Chi squared test. Statistical significance was set at an alpha of 0.05.

Results

The average age of the group was 43.5 y (range 23–72) and average duration of symptoms 6.7 y, (range 3 months–30 y). Patients had previously been treated by a median of four doctors, although 25 (34%) never had a previous post massage culture of EPS or urine. Symptoms included pain in 93%, obstructive urinary symptoms in 56%, irritative urinary symptoms in 50% and erectile dysfunction in 30%. The symptoms were reported as continuous by 10 patients (13.7%), fluctuating but never becoming asymptomatic in 63 patients (86.3%) and intermittent in 10 patients (13.7%).

Based on EPS culture and WBC count, there were 54 NIH class II patients (74%), 17 class IIIa patients (23%) and 2 class IIIb patients (3%). In the 54 class II patients with positive cultures, only two grew a gram negative uropathogen (*E. coli*) while the remainder grew Gram positive bacteria (*Corynebacteria*, *Coagulase* negative *Staphylococci* and *Strep. viridans* were most common). Every positive culture but one had fewer than 100 000

colony counts in the EPS. Antibiotics chosen on the basis of sensitivities included quinolones (17 patients), azithromycin (12 patients), cephalosporins (11 patients), ampicillin+clavulonic acid (6 patients), minocycline (5 patients) and geocillin (3 patients). In 10 patients, resistant strains were detected during therapy prompting a change in antibiotics and in one patient yeast in the EPS prompted the addition of fluconazole. In the remaining 19 patients with negative cultures, antibiotic selection included quinolones (11 patients), clindamycin/metronidazole (3 patients), ampicillin+clavulonic acid (2 patients), minocycline (2 patients) and azithromycin (1 patient).

Prostatic massage was performed 1–3 times per week for a median of three weeks (range 2–8 weeks). Antibiotics were continued for a minimum of four weeks. In all patients with initially positive cultures, the final cultures were sterile. Overall, 29 patients (40%) had complete resolution of symptoms, 14 (19%) had initial resolution but had a recurrence following therapy, 15 (21%) had partial improvement and 15 (21%) had no improvement. Positive initial cultures were associated with a higher complete response to treatment. Neither patient with NIH class IIIb had any improvement and only 24% of class IIIa patients had complete improvement in contrast to 46% complete improvement in the class II patients.

In comparing complete responders to all other, the responders were slightly older (46.0 vs 41.8 y, NS), had a longer average symptom duration (7.9 vs 6.0 y, NS) and were much more likely to have had any prior benefit to antibiotic therapy (76% vs 45%, *P* < 0.001). WBC level in the EPS increased to a peak value over 10 per hpf in 73% and did not correlate with response to therapy. In the NIH category II patients, there was no correlation between type of organism isolated or antibiotic used with response to therapy with the exception that no patient treated with ampicillin/clavulonic acid had a complete and durable response.

For the 44 patients without a complete and durable response to antibiotics and prostatic massage, other forms of treatment were often successful. In the 14 patients with an initial complete response but recurrence, one was cured with a transurethral resection of centrally located prostatic calculi, one had resolution of symptoms with

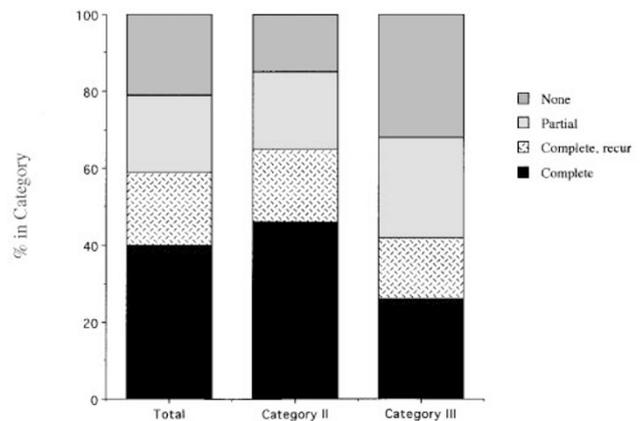


Figure 1 Treatment response by NIH category.

pelvic physiotherapy, three were treated successfully with an alpha blocker (tamsulosin) and two were treated successfully with a bioflavonoid.⁴ In the 15 patients who had partial improvement with antibiotics and massage, complete improvement was achieved with tamsulosin in three patients, bioflavonoids in two patients, gabapentin therapy in one patient and repair of a varicocele in one patient. Finally, in the 15 patients with no response to antibiotics and massage, three responded to bioflavonoids and two responded to tamsulosin. Therefore, of the 73 patients, 48 (63%) had eventual resolution of their symptoms with primary or secondary therapy.

Discussion

Chronic pelvic pain syndromes (CPPS) are common in men, with an estimated prevalence of 10% and lifetime incidence of 50%. Nevertheless, there is little agreement over the pathophysiology and appropriate treatment for the large group of men who do not respond to oral antibiotics. In this study, we have shown that the combination of antibiotics with regular prostatic massage is effective for a proportion of men with longstanding CPPS refractory to other therapies.

Current diagnostic criteria for chronic prostatitis/CPPS rely on the number of WBC in EPS and culture of EPS or post massage urine. Unfortunately, both diagnostic criteria are open to interpretation. In terms of culture, a small percentage of men with CPPS will show a positive culture defined as known uropathogens detected at $> 10^5$ per ml. A much higher proportion however will have positive cultures for Gram positive organisms and other bacterial at $< 10^5$ per ml (74% of our study patients). While some of these positive cultures undoubtedly represent commensal skin organisms, there is clear evidence that organisms such as coagulase negative *Staphylococci*, *Streptococcus viridans* and *Corynebacteria* can cause chronic prostatitis, often residing within an intraprostatic biofilm.^{5,6} In terms of WBC count in the EPS, this value is known to fluctuate over time in men with chronic prostatitis.⁷ Furthermore, many men without inflammation on the first EPS specimen will be found to have significant elevations on later specimens.³ Therefore it is likely that persistent prostatic infection is underdiagnosed in a majority of men with CPPS.

The mechanism whereby prostatic massage helps men with CPPS is not known. If groups of prostatic acini become obstructed by inflammatory cells, massage could assist in the drainage of infected material and assist in antibiotic penetration within the obstructed spaces. For bacteria within a protective biofilm, massage may produce a physical disruption and improve exposure of the bacteria to antibiotics and immune cells. In addition, massage may improve the blood flow and antibiotic delivery to the prostate. Finally, the massage may not be acting directly on the prostate at all, but may help break pelvic muscle spasm by activating local pressure points.⁸

In our patients who failed multiple prior therapies, 40% achieved a durable resolution of symptoms with antibiotic therapy and massage. The chance for success improved with the presence of a positive culture (although the majority were for low counts of Gram

positive organisms) and with a history of prior improvement with antibiotics. Even in category IIIa patients without a positive culture, a cure was achieved in 24% of the patients. In these category IIIa patients, improvement was seen presumably due to the presence of bacteria that were not detectable by culture or due to the effects of the massage alone. We are currently studying these possibilities in a randomized controlled study of prostatic massage with or without antibiotics in category IIIa patients. One experimental technique to identify microorganisms that will not grow in culture is to use PCR to detect bacterial 16S ribosomal RNA sequences which can be sequenced and classified according to a phylogenetic tree.⁹ We have recently used this technique in EPS and identified several new bacterial clones within the *Corynebacteria* genus that were present only in patients with prostatitis and in no control patients.¹⁰ Of particular note, 7 out of 11 patients with positive bacterial signal in the EPS responded to antibiotic therapy + prostatic massage while 0 out of 6 without bacterial signal responded. It may be that this molecular approach could more accurately predict which patients to select for this form of therapy independent of conventional culture results or EPS WBC levels.

Of the 60% of patients that did not have a complete and durable improvement with antibiotic based therapy, an additional 18 patients (25% of the total group) responded to secondary therapy such as alpha blockers, phytotherapy, physiotherapy or surgery for a specific anatomic problem. Men with chronic pelvic pain syndromes and voiding symptoms often have urodynamic evidence of bladder neck dyssynergia, and medical or surgical therapy to relax the bladder neck has often proved successful.¹¹⁻¹³ In our experience, dizziness and postural hypotension have significantly limited their use in the younger chronic prostatitis population. We have found the new alpha blocker tamsulosin to be much better tolerated in this age group. The bioflavonoids are antioxidants with several anti-inflammatory properties.¹⁴ In an unblinded study, we found they significantly reduced the symptoms of 75% of men with CPPS category III.⁴ Confirmation awaits the results of a placebo controlled doubled blinded trial currently in progress.

One limitation of our study was the lack of a validated symptom score to assess the degree of symptomatic improvement. By necessity, we therefore focussed only on complete resolution of symptoms as our primary endpoint. All our patients are currently assessed with the new NIH symptom score¹³ which should allow quantification of changes of symptoms and quality of life impact in our population.

Conclusions

In summary, we found that therapy with the combination of prostatic massage and antibiotics was effective in a proportion of men with longstanding chronic prostatitis categories II and IIIa refractory to previous therapies. Including those men whose symptoms were managed successfully with secondary non-antibiotic therapy, 63% of patients had a resolution of their symptoms.

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