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[Intervention Review]

Interventions for chronic abacterial prostatitis

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ABSTRACT

Background

Chronic abacterial prostatitis is a common disabling but enigmatic condition with a symptom complex of pelvic area pain and lower urinary tract symptoms. The scope of treatments recommended for chronic abacterial prostatitis is a testament to how little is known about what causes the condition and how to treat it. As a result, chronic abacterial prostatitis often causes physician frustration, patient confusion and dissatisfaction, variable thresholds for referral, and potentially inappropriate antibiotic use.

Objectives

Examine the evidence regarding the effectiveness of therapies for chronic abacterial prostatitis.

Search methods

Studies were identified through a search of MEDLINE (1966 to 2000), the Cochrane Library, bibliographies of identified articles and reviews, and contact with an expert.

Selection criteria

Studies were eligible if they: (1) are randomized controlled trials (RCTs) or controlled clinical trials (CCTs) (2) involve men with chronic abacterial prostatitis (3) control group receives placebo, sham intervention, active pharmacologic or device therapy for chronic abacterial prostatitis and (4) outcomes data are provided. Eligibility was assessed by at least two independent observers.

Data collection and analysis

Study information on patients, interventions, and outcomes was extracted independently by two reviewers. The main outcome was the efficacy of treatment for chronic abacterial prostatitis versus control in improving urologic symptom scale scores or global report of urinary tract symptoms. Secondary outcomes included changes in the prostate examination, uroflowmetry, urodynamics, analysis of urine, expressed prostatic secretions and seminal fluid, and prostate ultrasonography.

Main results

The 15 treatment trials involved: medications used to treat benign prostatic hyperplasia (n = 4 trials); anti-inflammatory medications (n = 2 trials); antibiotics (n = 1 trial); thermotherapy (n = 5 trials); and miscellaneous medications (n = 3 trials). The disparity between studies did not permit quantitative analysis. There were a total of 600 enrollees (age range 38 to 45). All but one of the trials were done outside the United States.

Authors' conclusions

The treatment trials are few, weak methodologically, and involve small sample sizes. The routine use of antibiotics and alpha blockers for chronic abacterial prostatitis is not supported by the existing evidence. The small studies examining thermal therapy appear to demonstrate benefit of clinical significance and merit further evaluation. Additional treatment trials are required and they should report important patient characteristics (e.g., race), study design details and utilize clinically relevant and validated assessment measures.

PLAIN LANGUAGE SUMMARY

Little evidence that antibiotics or alpha-blocker drugs help to relieve chronic abacterial prostatitis, but heat treatments might be effective and more research is needed.

Chronic abacterial prostatitis (CAP) involves inflammation of the prostate gland and commonly affects men of all ages. It can cause problems urinating, including discomfort and pain, increased frequency and urge, or problems emptying the bladder. In most cases, the cause is unknown. Treatments for CAP include heat treatments (using microwaves) and several different types of drugs. The review found that there is little evidence to support the routine use of antibiotic or alpha-blocking drugs for CAP. Heat treatments in comparison may be useful. However, the few studies that have been performed are generally of poor quality. More studies are needed.

BACKGROUND

Chronic abacterial prostatitis is a common but enigmatic condition (Pfau 1986) that has been termed "a wastebasket of clinical ignorance" (Stamey 1980). The hallmark of chronic prostatitis is its symptom complex of pelvic area pain and lower urinary tract symptoms (Nickel 1998a; Krieger 1996). There were almost 2 million outpatient visits per year in the United States from 1990-94 with a diagnosis of prostatitis (McNaughton Collins 1998). Prostatitis affects men of all ages, unlike BPH and prostate cancer which are predominantly diseases of older men. There are several types of prostatitis, each with different characteristics and proposed treatments. The umbrella term, prostatitis, is frequently used to cover all these conditions. The etiology of prostatitis is unknown in over 90% of cases; the remaining 5-10% of cases are bacterial (de la Rosette 1993a). Previous literature describes potential determinants of prostatitis, including: sex hormone levels, diet, past genitourinary disease, stress, psychological factors, allergy, and marital status (Roberts 1997). More recent studies have examined age (Berger 1989; McNaughton Collins 1998; Roberts 1998), race (McNaughton Collins 1998), infectious agents (including viral and sexually transmitted diseases) (Berger 1997; Dominique 1998; Lowentritt 1995), uric acid (Persson 1996a; Persson 1996b), sexual activity (Alexander 1996; Berger 1989; Drabick 1997), autoimmunity (Alexander 1997; Moon 1998), prostatic cysts and calculi (de la Rosette 1995; Thin 1997), proinflammatory cytokines (Alexander 1998), and prostate biopsy (Aus 1996).

The traditional classification of prostatitis by Drach (Drach 1978) is popular, although the validity has never been tested. In addition, this etiologic-based classification system may contribute to the confusion (Nickel 1998a). A newly established (also not validated) NIH chronic prostatitis classification system (Krieger 1999), based closely on the traditional classification, incorporates the terminology "chronic pelvic pain syndrome" to reflect the uncertainty about whether the categories of chronic nonbacterial prostatitis and prostatodynia are, in fact, related to the prostate gland. The NIH definition of Type III chronic abacterial prostatitis/chronic pelvic pain syndrome (CAP/CPPS) is defined as "no demonstrable infection," broken down further to reflect inflammatory ("white cells in semen, expressed prostatic secretions or post-prostatic massage urine") and non-inflammatory ("no white cells in semen, expressed prostatic secretions or post-prostatic massage urine") components. The scope of treatments recommended for chronic abacterial prostatitis is a testament to how little is known about what causes the condition, and how to diagnose and treat it. Since the symptom complexes of chronic abacterial prostatitis and benign prostatic hyperplasia overlap, investigators have hypothesized that benign prostatic hyperplasia treatments (i.e., finasteride and alpha blockers) may help some men with chronic abacterial prostatitis. Other treatment options have ranged from antibiotics to thermotherapy. As a result, chronic abacterial prostatitis often causes physician frustration (Meares 1991; Nickel 1998b), patient confusion and dissatisfaction (Keltikangas 1989; Meares 1973), variable thresholds for referral (de la Rosette 1993b), and potentially inappropriate antibiotic use (McNaughton Collins 1998).

OBJECTIVES

The optimal management of chronic abacterial prostatitis is not known. Our goal was to systematically review the effectiveness of therapies for chronic abacterial prostatitis.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials (RCTs) or controlled clinical trials (CCTs).

Types of participants

Men with NIH type III chronic abacterial prostatitis/chronic pelvic pain syndrome. Since > 90% of prostatitis is type III, we focused our review on this type. We did not examine Type IV (asymptomatic inflammatory prostatitis) because these patients are diagnosed incidentally during evaluation for other disorders.

Types of interventions

The control group received placebo, sham intervention, active pharmacologic or device therapy for chronic abacterial prostatitis.

Types of outcome measures

The primary outcome was the efficacy of treatment for chronic abacterial prostatitis vs. control in improving urologic symptom scale scores or global report of urinary tract symptoms. Secondary outcomes will included changes in the prostate examination, uroflowmetry, urodynamics, analysis of urine, expressed prostatic secretions and seminal fluid, and prostate ultrasonography.

Search methods for identification of studies

See: Prostatic Diseases and Urologic Cancers Group methods used in reviews.

Randomized or controlled clinical trials for abacterial prostatitis were identified through MEDLINE from 1966 to March 1999 by crossing an optimally sensitive search strategy for trials developed for the Cochrane Collaboration with the MeSH headings (including all subheadings) prostatitis, chronic nonbacterial prostatitis, chronic abacterial prostatitis, chronic pelvic pain syndrome, and prostatodynia (Dickersin 1994). The Cochrane Library, reference lists of identified trials, and previous reviews were also searched for additional trials. An expert in prostatitis (J. Curtis Nickel, MD) was asked to identify additional trials. There was no language restrictions.

Data collection and analysis

Eligibility:
At least two reviewers (MMC, RM) independently decided on eligibility.

Extraction:
Data extraction, including study characteristics, was performed independently by two reviewers. Extracted data was reviewed by the principal reviewer and discrepancies resolved by discussion.

Assessment of methodological quality:

As a measure of overall methodologic study quality we assessed the quality of concealment of treatment allocation according to a scale developed by Schulz (Schulz 1995) assigning 1 to poorest quality and 3 to best quality: 1 = trials in which concealment was inadequate (e.g. such as alternation or reference to case record numbers or to dates of birth); 2 = trials in which the authors either did not report an allocation concealment approach at all or reported an approach that did not fall into one of the other categories; and 3 = trials deemed to have taken adequate measures to conceal allocation (e.g. central randomization; numbered or coded bottles or containers; drugs prepared by the pharmacy; serially numbered, opaque, sealed envelopes etc. that contained elements convincing of concealment). Additionally, we assessed whether study participants and investigators were blinded to the treatment provided.

Outcomes:
Symptomatic changes measured by urologic symptom scale scores (AUA, Boyarsky, Prostatitis Symptom Severity Index), global assessment, pain scores, quality of life score, or subjective rating; uroflowmetry (peak or mean urine flow rate ml/sec); prostate examination (volume); analysis of urine (leukocyte or erythrocyte counts, urate concentrations); analysis of expressed prostatic secretions and seminal fluid (leukocyte counts, urate and xanthine concentrations); prostate ultrasonography (volume); and analysis of prostate specific antigen (PSA - serum volume). The number and percent of men reporting specific side effects and/or withdrawing from the study were recorded.

Meta-analysis:
For the clinical trials meeting criteria, there were a range of differences in the interventions, study duration, assessment measures, and clinical outcomes. The disparity between studies and reported outcomes did not permit quantitative analysis or pooling of findings across trials.

RESULTS

Description of studies

The MEDLINE search retrieved 60 potential studies for inclusion. Thirteen studies met inclusion criteria, and an additional four were identified through the alternative searching methods. Two studies were excluded because they included subjects with bacterial prostatitis (Baert 1974; Sagliaschi 1987). The 15 articles that met our inclusion criteria involved: 1) medications used to treat benign prostatic hyperplasia (Leskinen 1999; de la Rosette 1992; Dunzendorfer 1983; Osborn 1981); 2) anti-inflammatory medications (Muraro 1995; Wedren 1987); 3) antibiotics (Simmons 1985); 4) thermotherapy (Nickel 1996a; Montorsi 1993; Vassily 1999; Shah 1993; Strohmaier 1988); and 5) miscellaneous medications (Shoskes 1999; Persson 1996; Okada 1985). Five studies used placebo and three used sham. There were a total of 600 enrollees with mean age range 38 to 45. No studies reported the racial characteristics of participants. Study duration range was 2 weeks to 1 year; maximum follow up to 26 months. One study was done in the United States. Four were published in a non-English language (Muraro 1995 - Italian; Dunzendorfer 1983, Strohmaier 1988 - German; Okada 1985 - Japanese). All included information on symptom improvement, which was the primary outcome.

Risk of bias in included studies

None of the 15 trials met the Schulz criteria for adequate quality of concealment of treatment allocation. Of the 15 treatment trials meeting inclusion criteria 13 trials reported that subjects were "randomized" or used randomization methods (Shoskes 1999; Leskinen 1999; Vassily 1999; Nickel 1996a; Persson 1996; Muraro 1995; Montorsi 1993; Shah 1993; de la Rosette 1992; Strohmaier 1988; Wedren 1987; Dunzendorfer 1983; Simmons 1985). One crossover trial reported treatments were randomly assigned (Osborn 1981). One comparative study reported using double-blinding with no mention of randomization (Okada 1985). Ten studies reported double-blinding (Shoskes 1999; Leskinen 1999; Nickel 1996a; Persson 1996; Shah 1993; Wedren 1987; Okada 1985; Simmons 1985; Dunzendorfer 1983; Osborn 1981).

Effects of interventions

Medications Used to Treat Benign Prostatic Hyperplasia - Table 1:
Finasteride, a 5 alpha reductase inhibitor, has been investigated as a treatment option to reduce symptoms associated with inflammatory chronic pelvic pain syndrome (Leskinen 1999). Compared to placebo, finasteride reduced prostatitis and benign prostatic hyperplasia symptom scores, using validated symptom indices for prostatitis (Nickel 1996a) and for benign prostatic hyperplasia (Barry 1992), as well as a one-question, unvalidated pain evaluation. There was no statistically significant difference in pain between the two groups. Three men on finasteride experienced partial impotence. The mechanism by which finasteride would improve symptoms in patients with chronic abacterial prostatitis remains unknown although it is speculated that it may be relayed to reduction in prostate volume.

Three studies utilized alpha blockers to treat chronic abacterial prostatitis. De la Rosette (de la Rosette 1992) examined the use of the alpha blocker, alfuzosin, in men with both inflammatory and noninflammatory chronic pelvic pain syndrome. Compared to placebo, the treated group did not have a significant reduction in symptoms. Duzendorfer (Dunzendorfer 1983), investigating the use of diphenoxybenzamine, found statistically significant improvements in several pain outcomes at 6 weeks follow up. Although the treated group had orthostatic complaints, the number of patients with this side effect and the duration or severity were not described. In another study involving alpha blockers, 37 patients were enrolled in a double blind, cross-over trial of phenoxybenzamine, baclofen, and placebo; treatments were given in random order and were each given for one month. Phenoxybenzamine resulted in symptomatic improvement in 50% of patients (Osborn 1981).

Anti-inflammatory medications:
Muraro (Muraro 1995) examined the efficacy and safety of treatment with Seaprose S (a proteolytic enzyme reported to have anti-inflammatory action) in combination with local prostatic hyperthermia versus monotherapy with hyperthermia in 20 men with chronic abacterial prostatitis. No adverse effects were encountered. The study found that spontaneous pain and pain on palpation were reduced more in the combination treated group compared to the hyperthermia alone group. Wedren (Wedren 1987) examined the efficacy of Elmiron, an anti-inflammatory agent which has been used in the treatment of interstitial cystitis. Although the treated group (N=15) was noted to have improvement in symptoms, the only symptoms that improved were physician

rated non-specific myalgias and arthralgias. One-third of men in the Elmiron group dropped out of the study.

Antibiotics:
Although antibiotics are frequently used in the treatment of chronic abacterial prostatitis, only one small randomized controlled trial has addressed the efficacy and safety of antibiotic treatment for use in men with this condition (Simmons 1985). The investigators found no difference in symptom improvement between the antibiotic (minocycline) and the control (Valium) groups.

Thermotherapy:
Five studies have evaluated different types of heat treatment (either transrectal microwave hyperthermia (TRMH) or transurethral microwave thermotherapy (TUMT)) for chronic abacterial prostatitis; three of the studies used sham treatments. In a study by Vassily (Vassily 1999) greater symptom improvement was noted in the TRMH treated group (N = 80), compared with the sham treated group (N = 20). In another trial versus sham in 30 men with both inflammatory and noninflammatory chronic pelvic pain syndrome, treatment success, defined as a greater than 50% improvement in symptoms, was documented in 55% of men in the heat treated group at 3 months follow up (Shah 1993). No complications were reported. Montorsi (Montorsi 1993) evaluated different treatment schedules of TRMH in men with both inflammatory and noninflammatory chronic pelvic pain syndrome in which subjects were randomized to one of three therapeutic heat regimens that differed from each other in total dose of heat delivered and in the time interval between each session. Significant symptom improvement was found in all patients at long term follow-up (26 months), as well as quality of life improvement in 50% of men. Strohmaier (Strohmaier 1988) randomized subjects to one of two therapeutic heat regimens that differed from each other in total dose of heat delivered. While objective parameters such as uroflow, residual volume, and urinalysis were not effected by TRMH, marked symptom improvement was noted at six months.

The safety and efficacy of TUMT was investigated in 20 men (Nickel 1996a). The strengths of the study included the use of validated prostatitis symptom indices, a validated benign prostatic hyperplasia symptom score (Barry 1992) and a quality of life question. Heat-treated patients had significantly improved symptom scores compared with sham-treated patients at the 3 month follow up. However, 20% of patients exhibited an array of temporary side effects, including hematuria, impotence, premature ejaculation, urinary tract infection, urinary retention, and urinary incontinence.

Miscellaneous medications:
Persson (Persson 1996) theorized that back flow of urine into prostatic ducts causes prostatic inflammation by increasing concentrations of metabolites containing purine and pyramidine bases and, subsequently, conducted a double-blind controlled study of allopurinol treatment in 54 men with 330 days of follow up. Although this small trial showed improvements in patient-reported symptoms, investigator-graded prostate pain, and biochemical parameters, the data provided, the measures used, and the statistics presented, do not make these findings conclusive that changes in urine and prostatic secretion composition regarding purine and pyrimidine bases relieves symptoms (Nickel 1996b; McNaughton Collins 2000).

Okada (Okada 1985) examined the use of an amino acid preparation, PPC, in comparison with a control group who was treated with a pollen extract. Fifty-one percent of the PPC treated group (N = 32) compared with 37% of the pollen treated group (N = 30) noted "moderate to excellent" symptom improvement. The statistical significance of this finding was not reported. The authors report no severe side effects, but do not elaborate on other side effects that may have been demonstrated.

Quercetin is a naturally occurring bioflavonoid with anti-oxidant and anti-inflammatory activities. In a placebo-controlled trial (Shoskes 1999), Quercetin was investigated as a treatment in 30 men with NIH category III prostatitis syndromes (chronic abacterial prostatitis and prostatodynia). Symptom improvement, measured by the NIH chronic prostatitis symptom score, was significant in the Quercetin group (mean score improved from 21.0 to 13.0, 35%) but not in the placebo group (mean score improved from 20.2 to 18.8, 7.2%). With Quercetin, one subject reported a headache and one subject reported mild tingling of the extremities, both resolving after cessation of therapy.

DISCUSSION

This systematic review has summarized a diverse range of randomized and controlled trials of treatment options for chronic abacterial prostatitis. The results of the review revealed that the trials are few and weak methodologically with small sample sizes. The heterogeneity of the treatments examined precluded a formal meta-analysis and a quantitative estimate of efficacy.

Several studies had methodologic flaws. For the study conducted by Shah (Shah 1993) (reported as an abstract), the symptom assessment instrument was not described. While a validated prostatitis symptom index was used (Nickel 1996b) in the study by Vassily (Vassily 1999) (also reported as an abstract), the authors reported the index was "modified", raising concern about the validity of the modified version. The symptom index used in the Montorsi study (Montorsi 1993) was an unvalidated modification of a BPH symptom index, the Boyarsky index. The duration of follow up was not reported for one study and whether the pain instrument used was validated is unclear [Muraro 1995].

Simmons used a control group that was treated with diazepam rather than placebo and there is no evidence that diazepam is superior to placebo in chronic abacterial prostatitis. The Okada (1985) study utilized a pollen extract as the control. Since there is no evidence that pollen extract is effective in the treatment of chronic abacterial prostatitis, this control group is unsatisfactory. Symptom improvement was measured, although it is unclear whether a validated instrument was used.

Although experts may recommend or support an empiric course of antibiotics for chronic abacterial prostatitis (Nickel 1998a, Lipsky 1999, Bjerklund Johansen 1998), this practice is not supported by the existing evidence regarding disease etiology and treatment outcomes and deserves further scrutiny. Additionally, while a recent review has categorized alpha blocker treatment as "likely to be beneficial" in chronic abacterial prostatitis (Stern 1999), the routine use of alpha blockers was not supported by the available evidence.

AUTHORS' CONCLUSIONS

Implications for practice

The routine use of antibiotics and alpha blockers for chronic abacterial prostatitis are not supported by existing evidence and deserve further scrutiny. The small studies examining thermal therapy appear to demonstrate benefit of clinical significance and merit further evaluation.

Implications for research

Future methodologically robust randomized controlled treatment trials with larger sample sizes are needed. Future trials should report important patient characteristics (e.g., race), study design details and utilize clinically relevant and validated assessment measures.

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McNaughton Collins 2000

McNaughton Collins M, MacDonald R, Wilt TJ. [Diagnosis and treatment of chronic abacterial prostatitis: a systematic review]. *Ann Intern Med* 2000;**133**:367-81.

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

de la Rosette 1992

Methods	Randomized, parallel, double-blind, placebo-controlled study.
Participants	N=20†; Geographic region: The Netherlands Mean age: 39.4 Discontinuations/Not available to follow-up: none reported
Interventions	Alfuzosin 2.5 mg (n=10) three time daily vs. placebo (n=10). Study duration: 6 weeks
Outcomes	Symptomatic changes, symptom score; urodynamics; adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Dunzendorfer 1983

Methods	Randomized, parallel, double-blind, placebo-controlled study.
Participants	N=30; Geographic region: Germany Mean age: 39 Discontinuations/Not available to follow-up: none reported
Interventions	Study duration: Phenoxybenzamine (Dibenzyran) 10 mg (n=17) twice daily vs. placebo (n=13). Study duration: 12 weeks
Outcomes	Symptomatic changes (pain evaluation); Erythrocyte and leukocyte counts in the urine following prostate palpation; adverse events.
Notes	Block randomization

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Leskinen 1999

Methods	Randomized, parallel, double-blind, placebo-controlled study.
Participants	N=41; Geographic region: Finland Mean age: 46.8 Discontinuations/Not available to follow-up: 6, finasteride=4, placebo=2
Interventions	Finasteride 5 mg daily (n=31) vs. placebo (n=10). Study duration: 12 months
Outcomes	Symptomatic changes - Prostatitis Symptom Severity Index, prostatism score, pain evaluation; uroflowmetry; prostate specific antigen level; prostate volume; adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Montorsi 1993

Methods	Randomized study comparing three different therapeutic protocols.
Participants	N=54†;

Montorsi 1993 *(Continued)*

	Geographic region: Italy Mean age: 38.2 Discontinuations/Not available to follow-up: none
Interventions	TRMH, 3 groups. (a) 1 session/wk x 4 weeks; (b) 1 session/wk x 6 wks; (c) 2 sessions/wk x 3 wks. [42.5 ± 0.5C]. Mean follow-up: 26 months
Outcomes	Subjective symptoms (modified Boyarsky scale); self-rated quality of life improvement; uroflowmetry; ultrasonography of the prostate; adverse events.
Notes	"Randomly assigned"

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Muraro 1995

Methods	Randomized, parallel, single-blind, controlled study.
Participants	N=20; Geographic region: Italy Mean age: 42.5 Discontinuations/Not available to follow-up: none reported
Interventions	Seaprose S (a proteolytic enzyme reported to have anti-inflammatory action) 30 mg + hyperthermia (combo)(n=10) vs. Hyperthermia (mono) [1 hr session x 7 each; 42.5 - 43.5C] (n=10). Study duration: 2 weeks
Outcomes	Symptomatic changes; Instrumental tests (uroflowmetry; transurethral prostatic echography).
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Nickel 1996a

Methods	Randomized, parallel, double-blind, placebo (sham)-controlled study.
Participants	N=20; Geographic region: Canada Mean age: 45.3

Nickel 1996a *(Continued)*

	Discontinuations/Not available to follow-up: none reported
Interventions	Transurethral microwave hyperthermia (TUMT) (n=10) 45-60C vs. sham (n=10). Study duration: 1 hr session each.
Outcomes	Symptomatic changes, quality of life score, American Urological Association index, prostatitis symptom frequency and severity; subjective global assessment; adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Okada 1985

Methods	Double-blind, comparative study.
Participants	N=62; Geographic region: Japan Mean age: not reported Discontinuations/Not available to follow-up: none reported
Interventions	PPC (amino acid preparation) (n=32) vs. 2 Pollen extracts (n=30). Study duration: 4 weeks
Outcomes	Subjective symptoms; changes in prostate (tenderness, swelling, and sclerotic change); adverse events
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Osborn 1981

Methods	Crossover trial-treatments given in random order.
Participants	N=37†; Geographic region: UK Mean age: 42 Discontinuations/Not available to follow-up: 10
Interventions	Phenoxybenzamine 10 mg daily x 3 days then 10 mg twice daily vs. Baclofen 5 mg three times daily x 3 days then 10 mg three times daily vs. placebo. Study duration: 1 month
Outcomes	Symptomatic response; peak urine flow; adverse events.

Osborn 1981 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Persson 1996

Methods	Randomized, parallel, double-blind, placebo-controlled study.
Participants	N= 54; Geographic region: Sweden Mean age: not reported Discontinuations/Not available to follow-up: 20 dropouts across all groups
Interventions	(a) Allopurinol 300 mg + placebo (n=18) (b) Allopurinol 300 mg two times daily (n=16) (c) placebo (n=20). Study duration: 240 days
Outcomes	Subjective discomfort scale; urate (serum, urine, expressed prostatic secretion), xanthine, leukocyte concentrations.
Notes	Randomization code was centralized but not described.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Shah 1993

Methods	Randomized, parallel, double-blind, placebo (sham)-controlled study.
Participants	N= 30†; Geographic region: UK Mean age: not reported Discontinuations/Not available to follow-up: not reported
Interventions	Transrectal microwave hyperthermia (TRMH) 43.8C, (n=15) vs. sham 37C (n=15). Study duration: 1 hr session x 4
Outcomes	Symptomatic changes, symptom score, treatment successful if > 50% improvement.
Notes	

Shah 1993 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Shoskes 1999

Methods	Randomized, parallel, double-blind, placebo-controlled study.
Participants	N=30†; Geographic region: USA Mean age: 44.8 Discontinuations/Not available to follow-up: 2 (both placebo)
Interventions	Quercetin (a bioflavonoid) 500 mg twice daily (n=15) vs. placebo. Study duration: 1 month
Outcomes	Symptomatic changes - National Institutes of Health chronic prostatitis symptom score; leukocyte counts; adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Simmons 1985

Methods	Randomized, parallel, double-blind, controlled study.
Participants	N=41; Geographic region: UK Mean age: not reported Discontinuations/Not available to follow-up: 2 (both minocycline)
Interventions	Minocycline 100 mg (n=20) twice daily vs. Diazepam 5 mg (n=21) twice daily. Study duration: 3 months
Outcomes	Symptomatic changes; expressed prostatic secretion (EPS) polymorphonuclear leukocyte counts; adverse events.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Simmons 1985 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	B - Unclear

Strohmaier 1988

Methods	Randomized study comparing two different therapeutic protocols.
Participants	N=17†, 14 analyzed; Geographic region: Germany Age range 30-50; Discontinuations/Not available to follow-up:
Interventions	TRMH [2 groups; 39.5C or 43C; 1 or 2 sessions per week; parallel medication (doxycycline or placebo). Mean follow-up: 6 months
Outcomes	Subjective symptoms; urinalysis; urodynamics.
Notes	Preliminary results.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Vassily 1999

Methods	Randomized, parallel, placebo (sham)-controlled study.
Participants	N=100; Geographic region: Russia Mean age: not reported Discontinuations/Not available to follow-up: none reported
Interventions	TRMH (n=80) vs. sham (n=20). Study duration: 6 sessions over 2 weeks each. All patients received anti bacterial and anti-inflammatory therapy.
Outcomes	Symptomatic changes, symptom scores; prostate secretion analysis and spermogram.
Notes	Randomized 4:1

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

Wedren 1987

Methods	Randomized, parallel, double-blind, controlled study.
Participants	N=30; Geographic region: Sweden Mean age: 37.7 Discontinuations/Not available to follow-up: 6 (5 pentosan, 1 placebo)
Interventions	Sodium pentosanpoly sulphate (Elmiron) 100 mg (n=15) x 2 twice daily vs. placebo (n=15). Study duration: 3 months
Outcomes	Symptomatic changes, physician rating of treatment and symptom score; uroflowmetry; adverse events.
Notes	"Randomized blindly"

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment (selection bias)	Unclear risk	B - Unclear

† Contains men with prostatodynia

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Baert 1974	Includes subjects with bacterial prostatitis.
Sagliaschi 1987	Includes subjects with bacterial prostatitis.

ADDITIONAL TABLES

Table 1. Clinical Trials of Treatment for Chronic Abacterial Prostatitis

Study	Intervention	Subjects, n	Study duration	Results 1	Results 2	Adverse events	Discontinuations
Leskinen 1999	Finasteride 5 mg vs. placebo	N=41; finasteride=31, placebo=10.	12 months	Symptom scores decreased significantly in the finasteride group (Prostatitis Symptom Severity Index P <0.001, prostatism score p <0.05) but no significant differences in pain between groups.	Significant differences in changes of prostate volume and serum prostate specific antigen between the 2 groups (p <0.03, p<0.02, respectively).	Finasteride; partial impotence=3.	Finasteride=4, placebo=2.
de la Rosette 1992	Alfuzosin 2.5 mg three time daily vs. placebo	N=20; alfuzosin=10, placebo=10	6 weeks	Alfuzosin group, improvements: symptom score (p=0.01)	Alfuzosin group, maximal flow (p=0.01), flow time (p=0.03), time to maximal flow (p=0.01). Compared to placebo only change in maximal flow was significant.	Alfuzosin; transient decrease in systolic pressure=4; slight decrease in libido=2.	None reported
Dunzendorfer 1983	Phenoxybenzamine (Dibenzyran) 10 mg twice daily vs. placebo.	N=30; dibenzyran=17, placebo=13.	12 weeks	Improvements in pain outcomes (p<0.05) at 6 weeks.	Decreased erythrocyte count in urine with Dibenzyran (p<0.001) at 12 weeks.	Dibenzyran; orthostatic complaints, aspermia.	None reported
Osborn 1981	Phenoxybenzamine 10 mg daily x 3 days then 10 mg twice daily vs. Baclofen 5 mg three times daily x 3 days then 10 mg three times daily vs. placebo.	N=37; crossover study	1 month	Satisfactory symptomatic response: Phenoxybenzamine 50% (13/27); Baclofen 37% (10/27); placebo 8% (4/10). Phenoxybenzamine vs. placebo p = 0.027 (ns, based on 3-arm trial 0.05/3 = 0.019)	No differences in peak urine flow between groups.	Phenoxybenzamine; reflux ejaculation.	10 ("27 have completed trial to date").
Muraro 1995	Seaprose S (a proteolytic enzyme reported to have anti-inflammatory action) 30 mg + hyperthermia (combo) vs. Hyperthermia (mono) [1 hr session x 7 each; 42.5 - 43.5C] (n=10).	N=20; combo=10, mono=10	2 weeks	Decrease in spontaneous pain: Combo 70%; mono 11.1%. Decrease in pain on			None reported

Table 1. Clinical Trials of Treatment for Chronic Abacterial Prostatitis *(Continued)*

				palpation: combo 70.6%; mono 20%.			
Wedrén 1987	Sodium pentosanpoly sulphate (Elmiron) 100 mg (n=15) x 2 twice daily vs. placebo (n=15).	N=30; Elmiron=15, placebo=15	3 months	Physician rated improvement of myalgia/ arthalgia (p<0.01).		Elmiron; diarrhea 2 men.	Elmiron=5, placebo=1.
Simmons 1985	Minocycline 100 mg twice daily vs. Diazepam 5 mg twice daily.	N=41; Minocycline=20Diazepam=21.	3 months	No difference in symptom improvement between the two groups.	Percentage fall in EPS leukocyte count was 35.2% with Minocycline compared to 8% with diazepam.	Minocycline; esophagitis=1.	Minocycline=2.
Nickel 1996	Transurethral microwave hyperthermia (TUMT) 45-60C vs. sham.	N=20, TUMT=10, sham=10.	1 hr session each.	Symptomatic improvement, 3 months follow-up: quality of life score (p<0.05); prostatitis symptom severity (p<0.05).	Subjective global assessment - TUMT 70% (7/10), sham 10% (1/10).	Transient and resolved in 4 men (e.g. hematuria).	None reported
Montorsi 1993	Transrectal microwave hyperthermia (TRMH), 3 groups. (a) 1 session/wk x 4 weeks; (b) 1 session/wk x 6 wks; (c) 2 sessions/wk x 3 wks [42.5 ± 0.5C].	N=54; Group 1=18, Group 2=17, Group 3=19.	Mean follw-up was 26 months.	Subjective symptom score significantly improved in all patients at long term follow-up; self-reported improvement of quality of life in 50% of men.		"Almost all" men had transient hematuria, UTI=2, epididymitis=1, hemospermia=1.	
Vassily 1999	TRMH vs. sham. All patients received anti bacterial and anti-inflammatory therapy.	N=100; TRMH=80, sham=20.	6 sessions over 2 weeks.	Symptomatic improvement: TRMH 75%, sham 52.5%.	Prostate secretion analysis: "significant improvements in both groups."	Not reported.	Not reported.
Shah 1993	TRMH 43.8C vs. sham 37C.	N=30; TRMH=15, sham=15.	4 sessions each. Mean follw-up was 3 months.	Treatment success for TRMH: 68%, 57%, and 55% at end of treatment, 6 weeks, 3 months follow-up, respectively. Placebo effect of 10%.		"No significant complications reported."	Sham=2.

Table 1. Clinical Trials of Treatment for Chronic Abacterial Prostatitis *(Continued)*

Strohmaier 1988	TRMH [2 groups; 39.5C or 43C] parallel medication (doxycycline or placebo).	N=17; 14 analyzed	1 or 2 sessions per week. Mean follw-up was 6 months.	Marked subjective improvement in all subjects.	Urodynamic parameters unchanged.	None reported.	None reported.
Persson 1996	(a) Allopurinol 300 mg + placebo; (b) Allopurinol 300 mg twice daily; (c) placebo.	N=68, a=18, b=16, c=20.	240 days.	Subjective discomfort improvement (p=0.003).	"Significant effects" on urate and xanthine concentrations.	None reported.	20 dropouts across all groups.
Okada 1985	PPC (amino acid preparation) vs. 2 Pollen extracts (PE).	N=62, PPC=32, PE=30.	4 weeks.	Moderate-excellent improvement, subjective symptoms: PPC 50.5%, PE 36.7%.	Alleviated prostate swelling - rated excellent, PPC 76.9%, PE 35.7%.	"No severe side effects"	None reported.
Shoskes 1999	Quercetin (a bioflavonoid) 500 mg twice daily vs. placebo.	N=30; Quercetin=15, placebo=15.	1 month.	Symptomatic changes - National Institutes of Health chronic prostatitis symptom score, significant improvement for men on Quercetin (from 21.0 to 13.1 vs. 20.2 to 18.8 for placebo, p=0.003).	Significant decrease in leukocyte count in men on Quercetin (p=0.01).	Quercetin; headache=1,	Placebo=2.

WHAT'S NEW

Date	Event	Description
4 April 2011	Amended	Authors have indicated the review will not be updated.

HISTORY

Protocol first published: Issue 2, 2000
Review first published: Issue 1, 2001

Date	Event	Description
30 May 2008	Amended	Converted to new review format.
20 August 1999	New citation required and conclusions have changed	Substantive amendment

DECLARATIONS OF INTEREST

None.

SOURCES OF SUPPORT

Internal sources

- Department of Veterans Affairs Health Services Research and Development (HSRD) Office, USA.
- Agency for Health Care Policy and Research (Grant No. HS 08397), USA.

External sources

- NIH/NIDDK (Grant No. DK53736), USA.

NOTES

Authors have indicated the review will not be updated.

INDEX TERMS

Medical Subject Headings (MeSH)

Chronic Disease; Clinical Trials as Topic; Pelvic Pain [etiology] [therapy]; Prostatic Hyperplasia [therapy]; Prostatitis [etiology] [*therapy]; Treatment Outcome

MeSH check words

Humans; Male