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Evaluation and Treatment of Chronic Nonbacterial Prostatitis

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Abstract:-
Context: Prostatitis, is a typical condition including irritation of the prostate organ. It is perhaps the most generally analyzed condition influencing men in a wide age range as well as impacting them negatively on their quality of life. Moreover, Chronic nonbacterial prostatitis in men who are believed to be affected, shows severe symptoms with 8.2% impact on their quality of life.
Method Medline, Web of Science, PubMed, Google Scholar, Wang-Fang were the database used to search for relevant studies. What's more, the accompanying keywords were utilized to look for important information: non-bacterial prostatitis; persistent pelvic torment disorder; prostatitis treatment.
Result: Studies point to several therapies being used as the method of treatment for CNBP such as antibiotics, anti-inflammatory drugs, neuromodulators, alpha-blockers, physiotherapy. despite the use of these treatment strategies, no normalized treatment is at present accessible for CNBP.
Conclusion To our best knowledge, there is no cure for CNBP yet. All studies on the subject show a reduction in some side effects and the patient's personal health improvement. However, in most cases there is a recurring illness after treatment.

Keywords:- *Chronic Nonbacterial Prostatitis, National Institutes of Health (NIH), Treatments.*

I. INTRODUCTION

Prostatitis is a typical condition including irritation of the prostate organ. It is perhaps the most generally analyzed condition influencing men in a wide age range as well as impacting them negatively on their quality of life[1]. As indicated by the National Institutes of Health (NIH), prostatitis is sorted into four kinds, bacterial prostatitis (category I), persistent bacterial prostatitis (category II), chronic nonbacterial prostatitis (CNBP), likewise called Chronic prostatitis/ Chronic pelvic pain syndrome (CP/CPPS) (category III), and asymptomatic prostatitis (category IV)[2]. In this study we focused on chronic nonbacterial prostatitis (CNBP), defined as chronic abdominal pain that can be caused by another undiagnosed disease, frequently connected with genital agony, release torment, pelvic torment, poor quality urinary parcel (LUTS) indications, and having problems with erection, is a frustrating experience for numerous doctors and patients[3]. Ongoing bacterial prostatitis is a urologic torment that goes on for something like three months in the pelvic district related with hindrance [4]. NIH stage III prostatitis is a very common condition that affects men of advanced age and impairs good health (QoL)[2]. CNBP, is the most widely recognized urogenital illness in men under 50, and records for in excess of 90% of all prostatitis cases and influences men from 8.4% to - 14%[5]. As identified potential causes of CNBP numerous studies points to levels of sex hormones, allergies, marital and psychological status, diet, stress, and history of urogenital infections[2, 6]. In addition, explicit treatment for prostatitis is currently unknown to researchers.

Widely primary indicator used for male fertility includes conventional semen analysis, sperm concentration, motility, and morphology. Sperm motility has for some time been perceived as a utilitarian characteristic that ought to be evaluated as a fundamental piece of semen investigation[7]. Motility is an important variable to assess the quality of sperm in various species, including humans[8].

Male reproduction requires the cooperation of different organs of the male urogenital framework, thus all of them playing their significant role. Prostate is the main male reproductive system, which depends on the contents of the prostatic fluid[9]. Semen is made up of sperm, which make up 2-5% ejaculation volume and seminal plasma. Ejaculation volume is mainly comprised of different liquids discharged by the fundamental vesicles, bulbous glands-urethral, and prostate epithelium[10]. Sperm formation is affected by the physical and mental state of the body[10, 11] and directs the formation of all the various organs involved in reproduction inside the male reproductive framework[12, 13]. In addition, sperm motility is influenced by physiological, diet, and enviromental elements[14]

In all bladder illnesses, prostatitis has the best potential to influence fertility particularly aggravation of the uterus as it is directly related to males' infertility[15]. In addition, ongoing information support the role of prostate aggravation as an inclining factor for the improvement of benign prostatic hyperplasia (BPH)[16], prostate cancer but also prostatitis[17]. Surgical and Medical treatment for prostatitis and bladder cancer can cause birth defect, especially relevant for patients with fertility issues in old age[9]. Jianguo reveals that CNBP can affect sperm quality and decrease fertility[18]. Even so, other comprehensive therapies for ending the syndrome are used to diminish patient agony and work on personal health. These

therapeutic interventions includes antibiotics, medications, alpha-blockers, neuromodulators, phytotherapy, physical therapy (PFPT), and behavioral psychotherapy[2, 7].

Currently it is well known that there are no settled treatments to mitigate side effects for CNBP, hence only the helpful mediations are utilized to lessen the aggravation of the patient and work on the personal health[19]. This review was aimed to discuss current chronic nonbacterial prostatitis treatment.

II. SEARCH STRATEGY

The data for this review was obtained by searching using the following keywords: non-bacterial prostatitis; chronic pelvic pain syndrome; prostatitis treatment, while the following databases were searched for relevant studies using Web of Science, PubMed, Google Scholar, Medline and Wang-Fang Database. There was no language restrictions. We reviewed the list of indicators recognized by this pursuit technique and chose the ones we thought were appropriate, based on our keywords. We only focused on type III prostatitis, its manifestations, and treatments. Furthermore, we suggest that chronic inflammation of the prostate, initially caused by infection, autoimmune response may have implications for prostate function.

Tableau I: National institutes of Health Classification system for prostatitis syndrome (NIH)

Type	Nomenclature
I	Acute bacterial prostatitis
II	Chronic bacterial prostatitis
III	Chronic nonbacterial prostatitis
IV	Asymptomatic prostatitis

CHRONIC NONBACTERIAL PROSTATITIS.

Persistent nonbacterial prostatitis CNPP is an inadequately perceived normal type of prostatitis. It is characterized as urologic torment in the pelvic area, joined by side effects of pee or sexual dysfunction, enduring no less than three of the most recent half a year[19]. Based on the presence of leukocytes in the prostatic fluid, CNBP is categorized into inflammatory and noninflammatory structures[20]. Various judgments of pelvic discomfort like urinary contagions, malignancy, anatomic irregularities, or neurological problems should be precluded[21].

CLINICAL PRESENTATION

The principle manifestations of CNBP are perineal, lower mid-region, testicular, penile, and ejaculatory pain associated with paralysis and irritating arousal[22].

Patients with symptoms such as prostatitis report perineal, testicular, and penile uneasiness their aggravation is additionally connected with LUTS and sexual brokenness which continue for somewhere around 90 days. Negative intellectual, conduct, sexual, or enthusiastic side effects is often associated to CNBP that should be considered as part of medical history. Legitimate order requires efficient symptomatic testing.

DIAGNOSIS

Patients with persistence pelvic pain who have no symptoms of infection may be CNBP. In reality, there are no benchmark tests for CNBP[23]. The presence of constant bacterial prostatitis can be recognized in a rehashed history of urinary tract disease. Patient testing should start with the side effects of prostatitis utilizing cautious actual assessment, and clinical history tests[2]. It is additionally prudent to get a total rundown of other wellbeing related problems to acknowledge any neurological issues.

Patient testing with CPPS depends on broad arrangement and incorporates essential tests, urine and culture tests, NIH-CPSI, low urinary plot tests, urodynamics, and urinary cytology, and a few discretionary tests[24]. As much as an exclusion diagnosis, efforts to prevent the diagnosis of competing conflicts such as infection, risk, and urolithiasi should be made. The conclusions ought to incorporate the beginning, seriousness, and term of indications, just as intensifications and manifestations. CNBP is a disorder portrayed by persistent pelvic agony that is frequently connected with LUTS, with pain on the back and private parts, lower mid-region and waist. In addition, pelvic floor muscle pathology is often indicated by Postejaculatory pain[25].

Serious LUTS, particularly with pain related with the voiding cycle, should build the odds of fostering an excruciating bladder infection. Manifestation seriousness ought to be evaluated utilizing the NIH Chronic Prostatitis Symptom Index (CPSI), which is an approved investigation of nine inquiries covering area, recurrence and seriousness of pain, urinary indications and personal health[8]. Six-point improvement in complete scores is considered significant clinically connections to patient-revealed improvement. Introducing CNBP protests can incorporate penile, pelvic, perineal, lower stomach pain, pain during or after discharge and/or pee, recurrence of pee and/or fragmented discharge, and erectile dysfonction[19]. To preclude different sicknesses, which can cause covering indications, actual assessment ought to mostly zero on the genitourinary framework, in this way, review of the midsection, crotch, outer genitalia, perineum, and prostate by means of advanced rectal assessment. Uncommon consideration ought to be given to weakness, paresthesia and pain. Except for tenderness in other tissues of the body, pathology is rarely found. During rectum examination, cautious palpation of the pelvic muscles on the sides and outside of the prostate will regularly show a rash and tight bunches or focuses causing its palpation frequently to deliver the underlying aggravation of the patient. It is vital to be able to tell the difference of muscle delicacy from direct prostatic pain because of irritation.

Laboratory management should include minimally invasive urinalysis, general urine culture, and post-massage or prostatic fluid culture. Assuming pre-or post-massage urine culture exists, by definition, the patient doesn't have CNBP and ought to be treated with another calculation.

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Laboratory tests involving total blood counts, incendiary boundaries, and serum prostate-explicit antigen (PSA) are not suggested for CPPS testing. Public service announcement can be thought of in case patients are in danger for bladder disease. Except if there is a particular sign in chosen patients, for example, intraprostatic growth, calcification, or development of the ureaplasma urealyticum, mycoplasma hominis transrectal ultrasound does not help diagnose CNBP[19]. The patient's urine ought to be inspected, not to assist with diagnosing prostate but rather to control different conditions. For instance, the chance of carcinoma in situ of the bladder, just as other incendiary conditions, should be wiped out. Urinalysis ought to be directed to evaluate for hematuria, pyuria, proteinuria, and glycosuria. A urine culture ought to be directed to preclude UTI. Notwithstanding, by far most of these patients don't have a UTI[24].

ETIOLOGY & PATHOGENESIS

Another research project proposes that a potential reason for CPPS might be an idle bacterial prostatic infection [26]. In addition to another study, about half of Korean urologists pointed out that a possible cause of chronic bacterial prostatitis could be a latent viral infection[27]. This result suggests that bacterial infections are considered to be the most important wellspring of persistent pelvic agony disorder by Korean urologists. As per the etiology of type III prostatitis psychological factors should be considered as contributing factors , therefore, patients should be supported through psychotherapy as it may benefit them[28]. Numerous studies have shown that the third stage of prostatitis is caused by inflammation from a stimulant inside the prostate gland, which in high-risk individuals causes regeneration of the fringe sensory system in the prostate and encompassing regions [29]. However, due to a lack of in-depth and accurate information about the initiator stimulus, it is not yet clear if CPPS may be caused due to more than one factor[29]. Conditions like actual injury, contamination, or extreme mental trauma caused by stress may affect Predisposed patients[30].

TREATMENTS

Medical therapy for chronic non-bacterial prostatitis is primarily empiric. Among the most widely used medicines incorporate anti-toxins; calming drugs; neuromodulators; alpha-blockers; non-intrusive treatment (PFPT); and cognitive social treatment. Plus, all of these treatments Radial shock wave therapy is recently used to simultaneously relieve pain as well as improving the patient’s quality of life. CNBP is a poorly understood, multifaceted condition characterized by pelvic pain and voiding symptoms[24].

ANTIBIOTICS

Antibiotics are recommended as CNBP treatment option, these suggestions depended on realistic experience as opposed to prove based investigations[19]. Various physician use antibiotics as their first-line treatment. It is probably due to the belief that a causal agent unknown to the body may play a role in the symptoms of patients. In fact, according to Murphy et al, at the point when patients have viral infections in their prostate liquid and proof of persistent bacterial prostatitis, anti-infection agents, for example, fluoroquinolones and macrolides, can be compelling in restoring these microorganisms and in assuaging pain and indications[31, 32]. Studies have been conducted to prove the effectiveness of antibiotics as a treatment that can relieve pain in patients with CNBP. Zhou et al, clinical trial comparing the efficacy of treatment with tetracycline (500 mg twice daily) over 12 weeks versus placebo[33]. After administration of treatment, the authors reported a significant decrease of 18.5 points on NIH-CPSI. In general, available RCT have failed to support recommendation usage of antimicrobial agents as a first-line treatment[34]. The administration of ciprofloxacin or levofloxacin treatment for six-week did not lead to any response as measured by NIH-CPSI compared with placebo[35]. Many patients with CNBP take antibiotics, but often without a positive result. few patients might be persuaded to think that they have a repetitive infection in spite of the incidental effects since when given anti-toxins, their indications improve briefly.

ANTI-INFLAMMATORIES

Symptoms of CNBP include inflammation and autoimmune disorders so their role is enhanced by the pathophysiology of CNBP and seems, by all accounts, to be apparent in the NIH Phase IIIA CPPS. To this, RCT were included to assess the therapeutic effect of anti-inflammatory drugs. With an end goal to battle this aggravation, some RCT's have analyzed the viability of standard mitigating drugs, in which have shown no critical incidental effects. HSP70 expression is very low and exhibits IL-1beta protein exposure higher in CNBP patients compared to controls[36]. In an investigation of 463 men determined to have CNBP, half had 45 WBC for each HPF per EPS, which was measurably higher than the control populace where 40% had such a finding [37].

A study by Nickel et al reported that only 27 men out of 161 men randomly assigned to receive rofecoxib compared to placebo showed a slight improvement in CPSI levels, while a bigger level of patients saw an improvement in personal health with treatment contrasted with control treatment, thus 56% versus 27%. Another study conducted by Zhao on 64 patients with CNBP patients randomized to receive 200 mg celecoxib or control treatment exhibited upgrades in ICSP from 23.9 to 15.8 in the treatment arm and from 24, 2 to 19.5 in the control treatment arm following a month and a half of treatment. But this difference could not last for 2 weeks of stopping treatment indicating that this could be limited to long-term development[38]. Even though their mechanism of activity isn't completely perceived, their mitigating properties have been very much recorded in numerous animal examines. Bioflavonoids May Reduce Prostatic Inflammation CNBP, a bioflavonoid such as quercetin improves inflammation related to administration of lipopolysaccharides and obesity-induced inflammation in rat models[39, 40].

Zhao et al managed to disclose the clinical efficacy of celecoxib in patients determined to have type IIIA CPPS. However, response to treatment was limited to the duration of treatment. all of these studies showed no genuinely huge contrast between the treatment group and the control treatment group on clinical adequacy[38]. Hence, clinical trials strongly suggest that monotherapy containing anti-inflammatory or immunomodulatory agents is ineffective.

ALPHA-BLOCKERS

The first use of alpha-blockers in CNBP treatment focuses on the development of urinary and other pelvic symptoms. Alpha-adrenergic receptor blockers are a significant medication for the treating LUTS patients with prostate malignant growth and are helpful in CNBP. A 2002 study conducted by Evliyaoğlu in a randomized controlled trial of 60 men with non-bacterial prostatitis showed a significant improvement (32.9 ± 5.27%) in worldwide, associated with improved pain and quality of life[41]. A similar RTC done in 91 patients assessing the impact of terazos in on urine indications in CNBP showed a critical improvement in urine side effects contrasted to control treatment [42]. Likewise with these past investigations, there have been various randomized controlled preliminaries inspecting the impact of alpha-blockers on all CNBP indications as estimated by CPSI. An investigation of 100 men matured 20 to 50 years took a gander at the impacts of Terazosin on CPSI schools contrasted with control treatment; tracked down that 56% of patients contrasted with 36% had a 45% decrease in CPSI schools with terazosin[43]. However, all of these studies point to a return of symptoms when treatment is stopped after some time in patients, meaning that this category of drugs is at the forefront of symptom control but does not have a causal mechanism of disease[44].

According to Yang G, this improvement was vital for symptoms of urination than pain, thus these drugs ought not be utilized in CPPS patients without proof of urinary issues[45]. Moreover, because of the distributed information, α-blockers ought not be suggested as first-line monotherapy. However, long-term 12-week treatment with problematic LUTS and in addition to previous treatment with α-blockers can be considered in the treatment program[19].

NEUROMODULATORY THERAPY/ NEUROMODULATORS

Neuromodulators are part of the treatments for CNBP, Thus Neuromodulatory drugs for example, amitriptyline and gaba pentin have been generally utilized in the treatment of neuropathic pain and their role in the treatment of CNBP is increasingly defined by researchers. Amitriptyline is an antidepressant used to work on both conclusion and pain manifestations in patients with CNBP. It has been broadly examined in the treatment of interior cystitis and intense bladder illness, what imparts many elements to CNBP. Recent studies have shown adequacy in CNBP-related conditions, like interstitial cystitis, intense bladder disorder, and idiopathic pelvic pain. Preliminary studies have shown a positive response rate for these urinary tract signals and may be genital, pelvic, or suprapubic pain[46]. An ensuing placebo treatment controlled preliminary of 50 patients showed improvement in indications as estimated by the O'Leary-Sant IC score, especially in the space of pain and urinary recurrence. Scores expanded from 26.9 to 18.5 in the treatment arm and from 27.6 to 24.1 in the placebo treatment arm ($P < 0.005$)[47]. Pain relieving neuromodulator specialists have all the earmarks of being a promising methodology to reduce pain as a dominant symptom of CNBP. NIH-CPSI confirmed the positive effects of gaba pentin as an adequate treatment for pain subdomain, but at the same time as the neurological side, the effects were more likely to occur in the pregabalin group. Furthermore, this therapy did not show any clinically beneficial effects compared to placebo based on a primary endpoint analysis, albeit significant outcomes were positive[48]. Therefore, distributed information don't suggest pregabalin as the only treatment for CNBP.

PHYTOTHERAPY

Nowadays, herbal therapies as a treatment for CNBP have become very popular; in his study, Shoskes showed that quercetin has statistically and clinically substantial benefit over placebo, he tested the clinical effectiveness of the drug. quercetin, a bioflavonoid with antioxidant properties[49]. Another study using Quercetin (500 mg twice daily) for 4 weeks provided significant improvement in symptoms compared to placebo as determined by the NIH-CPSI[50]. Likewise, a 3 months treatment of cernilton also showed an improvement in the NIH-CPSI score contrasted with placebo treatment. However, some herbal agents are said to lack clinical evidence in treatment modalities.

SHOCK WAVE THERAPY

Diabetic wounds and other diseases has used shock wave as a treatment[51] and tendonitis[52] whereas extracorporeal shock wave most effective and current treatment method used in CNBP [53]. The frequency has single sound heartbeats and can make cavitation because of high pressing factor and adaptable vacuum[54]. A recent study by Zimmerman et al. showed significant improvement in pain, quality of life, and urination in the ESWT group, while the sham group experienced continued disintegration during the subsequent period[51]. Guu et al. designed a study with ESWT for those who did not pass traditional treatment and experienced significant improvement in clinical practice after administering ESWT with three types of drug treatment for a month and most patients maintained good performance for 3 months. A total of 33 patients receiving at least a month and 2 weeks trial of 3 antibiotic treatments, including fluoroquinolone, alpha-blocker, and acetaminophen, were remembered for the review. These patients experienced significant improvements in clinics shortly after ESWT treatment as compared to the counterpart who used traditional methods of treatment[55]

Darijus Skaudickas showed that the total number of NIH-CPSI,pain and urinary manifestations, and QoL worked on essentially in the ESWT bunch contrasted with the deceiving bunch, in spite of the fact that they saw some decrease in all spaces by week 12 contrasted with week

3[56]. A reasearch by Moayednia et al demonstrated ESWT to be a protected and powerful system for patients with CPPS during present moment follow-up, in any case, no drawn out ESWT execution was recorded [57]. In contrast to Al Edwan et al. He reported that the long-term performance of ESWT lasted for 12 months despite the slightest deterioration observed two weeks later[52]. In a randomized report by Yan et al. including 80 patients with CNBP, a huge improvement in the NIH-CPSI, QoL, and pain was seen in examination with the standard at all post-treatment brings about the ESWT group[58]. Despite the significant results that all these studies show, the mechanism of ESWT is little known and still uncertain because there are not enough studies on ESWT as a treatment for CNBP and few hypotheses are discussed. We can thus say that the treatment by extracorporeal shock wave therapy (ESWT) shows significantly good results despite fewer studies on this very complex topic of the treatment of chronic non-bacterial prostatitis.

III. CONCLUSION

Chronic nonbacterial prostatitis (CNBP) is one of the most well-known urologic determinations and its rate is developing yearly. It is a major health problem that frustrates both patients and practitioners due to the lack of a cure. With the exception of several therapies, no causative or general treatment is available for CNBP. While this is not yet fully understood, significant progress has been made in its diagnosis and treatment over the past few decades. this review aimed to highlight the different treatments most commonly used by patients suffering from CNBP. several treatments can decrease the symptoms of CNBP and improve the quality of life of patients. After several readings we realize that because of the heterogeneity and elusive pathophysiology of CNBP, the implementation of an effective treatment remains difficult. even though a wide range of treatments have been investigated, CNBP still exhibits a diverse sympmatology resulting from multiple probable etiologies. Moreover, there is not yet a standard treatment to treat CNBP because the pathogenesis is not yet elucidated and besides there are some treatments to alleviate the syndrome that is used to reduce patient pain and improve quality of life.

AUTHORS CONTRIBUTIONS

ACMP visualized the idea, managed the exploration of the paper, was the guarantor, and prepared the first draft. KKK and JPM participated in the design and revised the manuscript. LXY provides research funding. All authors supported the submission of this original copy.

REFERENCES

[1]. Mo, X., et al., *Prevalence and correlates of Mycoplasma genitalium infection among prostatitis patients in Shanghai, China.* Sex Health, 2016.
[2]. Khan, F.U., et al., *Comprehensive overview of prostatitis.* Biomed Pharmacother, 2017. **94**: p. 1064-1076.
[3]. Polackwich, A.S. and D.A. Shoskes, *Chronic prostatitis/chronic pelvic pain syndrome: a review of evaluation and therapy.* Prostate Cancer Prostatic Dis, 2016. **19**(2): p. 132-8.
[4]. Wazir, J., et al., *Efficacy of acupuncture in the treatment of chronic prostatitis-chronic pelvic pain syndrome: a review of the literature.* 2019. **51**(12): p. 2093-2106.
[5]. Liang, C.Z., et al., *The prevalence of prostatitis-like symptoms in China.* J Urol, 2009. **182**(2): p. 558-63.
[6]. Roberts, R.O., et al., *A review of clinical and pathological prostatitis syndromes.* Urology, 1997. **49**(6): p. 809-21.
[7]. Sukcharoen, N. and J. Keith, *Evaluation of the percentage of sperm motility at 24 h and sperm survival ratio for prediction of in vitro fertilization.* Andrologia, 1996. **28**(4): p. 203-10.
[8]. Yan, W., et al., *Enhancement of sperm motility and viability by turmeric by-product dietary supplementation in roosters.* Anim Reprod Sci, 2017. **185**: p. 195-204.
[9]. Verze, P., T. Cai, and S. Lorenzetti, *The role of the prostate in male fertility, health and disease.* Nat Rev Urol, 2016. **13**(7): p. 379-86.
[10]. Gilany, K., et al., *Exploring the human seminal plasma proteome: an unexplored gold mine of biomarker for male infertility and male reproduction disorder.* J Reprod Infertil, 2015. **16**(2): p. 61-71.
[11]. Nargund, V.H., *Effects of psychological stress on male fertility.* Nat Rev Urol, 2015. **12**(7): p. 373-82.
[12]. Rey, R.A., et al., *Male hypogonadism: an extended classification based on a developmental, endocrine physiology-based approach.* Andrology, 2013. **1**(1): p. 3-16.
[13]. Nieto, C.M., L.C. Rider, and S.D. Cramer, *Influence of stromal-epithelial interactions on androgen action.* Endocr Relat Cancer, 2014. **21**(4): p. T147-60.
[14]. Al-Qarawi, A.A., *Infertility in the dromedary bull: a review of causes, relations and implications.* Anim Reprod Sci, 2005. **87**(1-2): p. 73-92.
[15]. Wagenlehner, F., et al., *Prostatitis and andrological implications.* Minerva Urol Nefrol, 2013. **65**(2): p. 117-23.
[16]. Ficarra, V., et al., *The role of inflammation in lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH) and its potential impact on medical therapy.* Curr Urol Rep, 2014. **15**(12): p. 463.
[17]. Wagenlehner, F.M., et al., *The role of inflammation and infection in the pathogenesis of prostate carcinoma.* BJU Int, 2007. **100**(4): p. 733-7.
[18]. Zhang, J., Y. Wang, and S. Zhou, *[Effect of chronic abacterial prostatitis on semen quality and efficacy of antibacterial agents].* Zhonghua Nan Ke Xue, 2004. **10**(8): p. 598-600.
[19]. Magistro, G., et al., *Contemporary Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome.* Eur Urol, 2016. **69**(2): p. 286-97.

[20]. Bhavsar, A. and S. Verma, *Anatomic imaging of the prostate.* Biomed Res Int, 2014. **2014**: p. 728539.
[21]. Krieger, J.N., L. Nyberg, Jr., and J.C. Nickel, *NIH consensus definition and classification of prostatitis.* Jama, 1999. **282**(3): p. 236-7.
[22]. Nickel, J.C., *Prostatitis: evolving management strategies.* Urol Clin North Am, 1999. **26**(4): p. 737-51.
[23]. McNaughton Collins, M., R. MacDonald, and T.J. Wilt, *Diagnosis and treatment of chronic abacterial prostatitis: a systematic review.* Ann Intern Med, 2000. **133**(5): p. 367-81.
[24]. ANTHONY, *ETIOLOGY AND MANAGEMENT OF CHRONIC PELVIC PAIN SYNDROME IN MEN.* j.urology, 2004. **04**: p. 0090-4295.
[25]. Shoskes, D.A., et al., *Muscle tenderness in men with chronic prostatitis/chronic pelvic pain syndrome: the chronic prostatitis cohort study.* J Urol, 2008. **179**(2): p. 556-60.
[26]. Krieger, J.N. and D.E. Riley, *Chronic prostatitis: Charlottesville to Seattle.* J Urol, 2004. **172**(6 Pt 2): p. 2557-60.
[27]. Ku, J.H., J.S. Paick, and S.W. Kim, *Chronic prostatitis in Korea: a nationwide postal survey of practicing urologists in 2004.* Asian J Androl, 2005. **7**(4): p. 427-32.
[28]. Mehik, A., et al., *Fears, sexual disturbances and personality features in men with prostatitis: a population-based cross-sectional study in Finland.* BJU Int, 2001. **88**(1): p. 35-8.
[29]. Nickel, J.C., *The biomedical model has failed! So whatis next, Contemp.* Urol Clin North Am, 2006. **1**: p. 31–39.
[30]. Dadabhoy, D. and D.J. Clauw, *Fibromyalgia: progress in diagnosis and treatment.* Curr Pain Headache Rep, 2005. **9**(6): p. 399-404.
[31]. Murphy, A.B. and R.B. Nadler, *Pharmacotherapy strategies in chronic prostatitis/chronic pelvic pain syndrome management.* Expert Opin Pharmacother, 2010. **11**(8): p. 1255-61.
[32]. Magri, V., et al., *Fluoroquinolone-macrolide combination therapy for chronic bacterial prostatitis: retrospective analysis of pathogen eradication rates, inflammatory findings and sexual dysfunction.* Asian J Androl, 2011. **13**(6): p. 819-27.
[33]. Zhou, Z., et al., *Detection of nanobacteria infection in type III prostatitis.* Urology, 2008. **71**(6): p. 1091-5.
[34]. Alexander, R.B., et al., *Ciprofloxacin or tamsulosin in men with chronic prostatitis/chronic pelvic pain syndrome: a randomized, double-blind trial.* Ann Intern Med, 2004. **141**(8): p. 581-9.
[35]. Nickel, J.C., et al., *Levofloxacin for chronic prostatitis/chronic pelvic pain syndrome in men: a randomized placebo-controlled multicenter trial.* Urology, 2003. **62**(4): p. 614-7.
[36]. Guo, *Levels of cytokines and heat-shock protein 70 in the seminal plasma of patients with chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome.* 2012. **18**: p. 1088–1092.
[37]. Nickel, J.C., et al., *Leukocytes and bacteria in men with chronic prostatitis/chronic pelvic pain syndrome compared to asymptomatic controls.* J Urol, 2003. **170**(3): p. 818-22.
[38]. Zhao, W.P., et al., *Celecoxib reduces symptoms in men with difficult chronic pelvic pain syndrome (Category IIIA).* Braz J Med Biol Res, 2009. **42**(10): p. 963-7.
[39]. Seo, M.J., et al., *The inhibitory effects of quercetin on obesity and obesity-induced inflammation by regulation of MAPK signaling.* J Nutr Biochem, 2015. **26**(11): p. 1308-16.
[40]. Liao, Y.R. and J.Y. Lin, *Quercetin intraperitoneal administration ameliorates lipopolysaccharide-induced systemic inflammation in mice.* Life Sci, 2015. **137**: p. 89-97.
[41]. Evliyaoğlu, Y. and R. Burgut, *Lower urinary tract symptoms, pain and quality of life assessment in chronic non-bacterial prostatitis patients treated with alpha-blocking agent doxazosin; versus placebo.* Int Urol Nephrol, 2002. **34**(3): p. 351-6.
[42]. Gül, O., M. Eroğlu, and U. Ozok, *Use of terazosine in patients with chronic pelvic pain syndrome and evaluation by prostatitis symptom score index.* Int Urol Nephrol, 2001. **32**(3): p. 433-6.
[43]. Cheah, P.Y., et al., *Terazosin therapy for chronic prostatitis/chronic pelvic pain syndrome: a randomized, placebo controlled trial.* J Urol, 2003. **169**(2): p. 592-6.
[44]. Chen, Y., et al., *Effects of a 6-month course of tamsulosin for chronic prostatitis/chronic pelvic pain syndrome: a multicenter, randomized trial.* World J Urol, 2011. **29**(3): p. 381-5.
[45]. Yang, G., et al., *The effect of alpha-adrenergic antagonists in chronic prostatitis/chronic pelvic pain syndrome: a meta-analysis of randomized controlled trials.* J Androl, 2006. **27**(6): p. 847-52.
[46]. Pranikoff, K. and G. Constantino, *The use of amitriptyline in patients with urinary frequency and pain.* Urology, 1998. **51**(5A Suppl): p. 179-81.
[47]. van Ophoven, A., et al., *A prospective, randomized, placebo controlled, double-blind study of amitriptyline for the treatment of interstitial cystitis.* J Urol, 2004. **172**(2): p. 533-6.
[48]. Aboumarzouk, O.M. and R.L. Nelson, *Pregabalin for chronic prostatitis.* Cochrane Database Syst Rev, 2012(8): p. Cd009063.
[49]. Shoskes, D.A., et al., *Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial.* Urology, 1999. **54**(6): p. 960-3.
[50]. Wagenlehner, F.M., et al., *A pollen extract (Cernilton) in patients with inflammatory chronic prostatitis-chronic pelvic pain syndrome: a multicentre, randomised, prospective, double-blind, placebo-controlled phase 3 study.* Eur Urol, 2009. **56**(3): p. 544-51.
[51]. Zimmermann, R., et al., *Extracorporeal shock-wave therapy for treating chronic pelvic pain syndrome: a feasibility study and the first clinical results.* BJU Int, 2008. **102**(8): p. 976-80.

[52]. Al Edwan, G.M., M.M. Muheilan, and O.N. Atta, *Long term efficacy of extracorporeal shock wave therapy [ESWT] for treatment of refractory chronic abacterial prostatitis.* Ann Med Surg (Lond), 2017. **14**: p. 12-17.
[53]. Pajovic, B., et al., *Comparison of the efficiency of combined extracorporeal shock-wave therapy and triple therapy versus triple therapy itself in Category III B chronic pelvic pain syndrome (CPPS).* Aging Male, 2016. **19**(3): p. 202-207.
[54]. Speed, C.A., et al., *Extracorporeal shock wave therapy for plantar fasciitis. A double blind randomised controlled trial.* J Orthop Res, 2003. **21**(5): p. 937-40.
[55]. Guu, S.J., et al., *Efficacy of Low-Intensity Extracorporeal Shock Wave Therapy on Men With Chronic Pelvic Pain Syndrome Refractory to 3-As Therapy.* Am J Mens Health, 2018. **12**(2): p. 441-452.
[56]. Skaudickas, D., et al., *Extracorporeal shock wave therapy for the treatment of chronic pelvic pain syndrome.* Open Med (Wars), 2020. **15**(1): p. 580-585.
[57]. Moayednia, A., et al., *Long-term effect of extracorporeal shock wave therapy on the treatment of chronic pelvic pain syndrome due to non bacterial prostatitis.* J Res Med Sci, 2014. **19**(4): p. 293-6.
[58]. Yan, X., et al., *[Effect of extracorporeal shock wave therapy on diabetic chronic wound healing and its histological features]*. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi, 2012. **26**(8): p. 961-7.