
IMPACT OF COMPLEX PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENT IN PATIENTS WITH CHRONIC PROSTATITIS/CHRONIC PELVIC PAIN SYNDROME

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Abstract: Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) is a common condition in men and a serious problem affecting the health of adults men. It is considered that symptoms persisting for more than one year may lead to a decrease in quality of life. It is accepted that older men may be affected at different age by symptoms of CP/CPPS. Men under 50 years old are diagnosed frequently. It is characterized by pain and discomfort in the pelvis, symptoms of the lower urinary tract and a high incidence of depression. CP can evolve without symptoms or with only weakening of sexual function. It never heals spontaneously. The disease poses significant psychological and social problems for men of sexually active age. The diagnosis and treatment create many difficulties. CP/CPPS combines several different prostate diseases and syndromes that differ in their characteristics and methods of treatment. CP/CPPS requires multimodal therapeutic behavior. It is recommended for the individual therapy plans to be developed based on multimodal therapy. The treatment is complex and aims at influencing the infectious agent and inflammatory processes, improving the quality of life, reducing symptoms and complications. Depending on the clinical manifestation, antibiotic therapy, Alpha-blockers, non-steroidal anti-inflammatory drugs, 5-alpha reductase inhibitors, antidepressants, phytopreparations, standardized pollen extract, other drugs that improve local and general immunity and function, Botulinum toxin A (BTA), Injection of local anesthetic, neuropathic pain medications, Phosphodiesterase type 5 (PDE-5) inhibitors and others are recommended. Non-pharmacological treatment includes lifestyle change, psychotherapy and cognitive behavioural therapy, prostate massage, therapeutic exercise, myofascial release, manual therapy, diaphragmatic breathing, biofeedback, postural training, education and training for home exercise program, traditional Chinese medicine (acupuncture), balneotherapy, peloid therapy. Reformed physical factors are affordable and safe to administer and do not have the usual adverse events observed with pharmacological therapy. These include TENS, interferential and sinusoidal modulated currents, high frequency currents, microwave currents, magnetic field, extracorporeal shock-wave therapy, Light therapy-infrared and red radiation LASER therapy. Due to the lack of high quality, randomized clinical studies, the effects of the physical factors applied need further clinical studies to determine their effectiveness.

Keywords: Chronic prostatitis / chronic pelvic pain syndrome (CP / CPPS), pharmacological treatment, non-pharmacological treatment, quality of life

1. INTRODUCTION

Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) is a common condition in men and a serious health problem (Zhang, Liang, Shang & Li (2020)). The incidence rate ranges from 8.2% to 25% (Krieger, Lee, Jeon et al. (2008); Zhang et al. (2020)). Symptoms that persist for more than one year are thought to lead to a decrease in quality of life (Doiron, R.C., & Nickel, J.C. (2018)). It is assumed that 35% to 50% of men are affected at different periods in their lives by symptoms of CP (Rees, Abrahams, Doble, Cooper & Prostatitis Expert Reference Group (PERG) (2015). Prostatitis is the third most common diagnosis in men under 50 years of age (Bergman J, Zeitlin S. (2007)). It is characterized by pain and discomfort in the pelvis, lower urinary tract symptoms and high incidence of depression (Tripp, Nickel, Wang, et al. (2006). CP can evolve without symptomatology or with only diminished sexual function and treatment create many difficulties (McNaughton, Pontari, O'Leary, et al. (2001) Rees et al. (2015)). CP/CPPS bring together several different prostate diseases (bacterial and abacterial) and syndromes that differ in treatment characteristics and methods (Krieger et al. (2008)). In 1995, the NIH (US National Institute of Health) adopted a new classification for prostate inflammation (Krieger, Nyberg, Nickel (1999)). The European Association of Urology (EAU) recommends using the NIH classification:

Category I, acute bacterial prostatitis.

Category II, chronic bacterial prostatitis, is a persistent bacterial infection of the prostate leading to recurrent urinary tract infections caused by the same bacterial strain.

Category III, chronic prostatitis/chronic pelvic pain syndrome

A. Inflammatory chronic prostatitis/chronic pelvic pain syndrome is associated with leukocytes in the expressed prostatic fluid, post-prostate massage urine or seminal fluid.

B. Non-inflammatory chronic prostatitis/chronic pelvic pain syndrome with no evidence of urogenital inflammation.

Category IV, asymptomatic inflammatory prostatitis.

CP/CPPS has a multifactorial etiology and requires multimodal therapeutic behavior (Shoskes & Katz (2005); Shoskes, Nickel & Kattan (2010)). A thorough evaluation of patients with CP/CPPS is important for adequate therapy, given the heterogeneity of patients. It is recommended that individual therapy plans to be developed based on multimodal therapy. Doiron 2018 does not recommend sequential monotherapy as this approach is too simplistic and does not lead to successful treatment (Doiron & Nickel (2018); Magistro, Wagenlehner, Grabe et al. (2016)). Only 5% to 10% of cases of prostatitis are of bacterial origin (Bartoletti, Cai, Mondaini et al. (2007); Franco, Turk, Jung et al. (2020)). The treatment is complex and aims at influencing the infectious agent and the inflammatory processes, improving the quality of life, reducing symptoms and complications.

2. PHARMACOLOGICAL TREATMENT

1. Antibiotic therapy Antibiotics (quinolones) may reduce prostatitis symptoms compared to placebo and may not be associated with an increased incidence of adverse events. They probably do not affect sexual dysfunction and quality of life. There is no information on their effect on anxiety or depression (Franco, Turk, Jung et al. (2019)). Fluoroquinolones are a treatment of choice for acute inflammation (Schaeffer (1999)) and CP/CPPS IIIA (Grabe, Bjerklund-Johansen, Botto, et al. (2013); Rees et al. (2015)) Treatment should last at least 4 to 6 weeks. In case of resistance, treatment with sulfonamides, the duration is from 8 to 12 weeks, is prescribed. In certain indications, tetracyclines and macrolides are administered due to their activity against Chlamydia and Mycoplasma. The sexual partner should be treated at the same time as the patient.

2. Alpha-blockers including terazosin, doxazosin, phenoxybenzamine, tamsulosin, alfuzosin and silodosin (Franco et al. (2020)). They reduce the smooth muscle tone in the urethra and improve urination (Patrashkov T, 2005). Increase in prostate pressure in the urethra at CP is proved by urodynamic studies (Schaeffer A. J., (1999)). Alpha-blockers are recommended for initial treatment of moderately severe obstructive symptoms (Rees et al. (2015)). If symptom reduction is not achieved within 4-6 weeks, treatment should be discontinued and a different pharmacotherapy considered (Rees et al. (2015)). According to a 2019 meta-analysis, there is no conclusive data on the effect of alpha-blocker in comparison with placebo in short-term follow-up. They probably do not lead to nearly any difference in sexual dysfunction, quality of life, anxiety and depression (Franco et al. (2019)). In case of CP/CPPS they are not recommended as first-line monotherapy. Treatment - not less than 3 months.

3. Nonsteroidal anti-inflammatory drugs reduce pain and suppress inflammation, especially with CP/CPPS IIIA. Anti-inflammatories (corticosteroids, nonsteroidal anti-inflammatory drugs and thiocolchicoside) may reduce prostatitis symptoms compared to placebo and may not be associated with an increased incidence of adverse events and are unlikely to be associated with an increased incidence of adverse reactions. Information on sexual dysfunction, quality of life, anxiety and depression has not been established (Franco et al. (2019)).

4. 5-alpha reductase inhibitors. Finasteride is likely to reduce the symptoms of CP compared to placebo and is unlikely to be associated with an increase in adverse reactions (Franco et al. (2019), (2020)). A reduction in prostate volume was reported in 20–39% of cases (Patrashkov 2005). There is no information on the effects on sexual dysfunction, quality of life or anxiety and depression (Franco et al. (2019)). There is insufficient evidence of monotherapy with 5 α -reductase inhibitors at CP/CPPS, except in the case of concomitant BPE (Rees et al. (2015)).

5. Antidepressants. In the case of CP, hypochondria, somatization, depression, mental impotence are present. Franco (2020) reported no conclusive evidence of the efficacy of duloxetine, sertraline and dapoxetine in CP/CPPS IIIA. Tricyclic antidepressants are also suitable for neuropathic pain (Rees et al. (2015)).

6. Phytopreparations (Pollen extract, Prolit Super Pro®, calendula and curcuma, quercetin and cranberry) are likely to have a positive effect on CP/CPPS IIIA and do not increase the risk of side effects but do not improve sexual dysfunction. There are no data on the effects on anxiety, depression and quality of life (Franco et al. (2020)).

7. Standardized Pollen Extract Graminex G63. It is recommended for a period of 90-120 days for all types of prostatitis. A 2017 meta-analysis reports that it can improve quality of life without significant adverse events. Long-term RCTs could provide more evidence of the efficacy of pollen extracts at CP/CPPS (Cai, Verze, La Rocca, et al (2017)).

8. Other medicines that improve local and general immunity and functional status of the prostate, including Vitamins (C,E), Microelements (Zn,Se), Omega-3 fatty acids, and the use of Urovaxins are also recommended.

9. Botulinum toxin A (BTA). Intraprostatic BTA injection in refractory symptomatology is a potential therapeutic option that reduces pain (Falihatkar, Shahab, Gholamjani Moghaddam et al. (2015); Abdel-Meguid, Mosli, Farsi, et al. (2018)) and improves quality of life (Falihatkar et al. (2015)). Injection of pelvic floor muscles does not reduce

symptoms. There is no evidence of adverse reactions. Information on sexual dysfunction, quality of life, depression, and anxiety is not available (Franco et al. (2020)).

10. Injection of local anesthetic for trigger point pain or localized myofascial pain. It is suitable for neuropathic pain, only in some patients with true organ-specific prostate pain. It may be appropriate therapy in pudendal neuropathy, unilateral perineum pain, the pudendal nerve block (Doiron & Nickel (2018)).

11. Medications for neuropathic pain. Pregabalin may be included if needed (Franco, J.V.A. et al. (2020)) or amitriptyline, gabapentinoids (or even the combination of them). They can be effective as part of multimodal therapy for non-responding symptoms of CP CPPS (Doiron, R. C., & Nickel, J. C. (2018)).

12. Phosphodiesterase type 5 (PDE-5) inhibitors (Tadalafil) are suitable for sexual dysfunction associated with ejaculatory pain or psychological sexual dysfunction (Doiron & Nickel (2018)).

According to Franco (2019, 2020), part of the pharmacological therapy studies are short-term (4 to 12 weeks) and do not account for the occurrence of adverse reactions and effects on anxiety, depression and quality of life. Some of the therapeutic interventions are likely to be effective on some of the symptoms and do not affect others, for example phosphodiesterase inhibitors affect sexual dysfunction and do not affect the symptoms of prostatitis, the analgesics influence pain in pain syndrome. Some of the side effects can be reduced or eliminated by titrating the dose of the drug. In others, such as alpha-blockers, unwanted retrograde ejaculation stops when the medication is discontinued. Pharmacological therapy needs to be refined based on major complaints of CP/CPPS.

3. NON-PHARMACOLOGICAL TREATMENT

1. Lifestyle change. It is recommended to adjust lifestyle, diet and sexual habits (Zhang, Liang, Shang & Li (2020)). 13 potential risk factors for CP/CPPS were identified, including diet (alcohol, coffee, chilli and spicy foods, excessive diet, bowel dysfunction), sexual habits (delayed ejaculation, sexual restraint, excessive sex, interruption of coitus) lifestyle (sedentary life), perineal trauma (pelvic floor muscle tenderness, sitting position, traumatic sports for perineum, constrictive clothing (Gallo (2014)) Psychological support is part of the multimodal approach to managing CP/CPPS. Chronic pain is a common cause of anxiety and depression. Mental disorders should always be evaluated by a specialist psychologist or psychiatric team in order to pay attention to sensitive patients (Zhang et al. (2020)). Training and communication between sexual partners is essential (Rees et al. (2015)), Cognitive Behavioral Therapy (CBT) and Psychotherapy. Psychological symptoms are considered to be part of CP/CPPS, however, there is no convincing evidence that this therapy is effective (Rees et al. (2015)).

2. Massage of the prostate, of the perineal or pelvic floor, are effective at CP/CPPS with perineal morbidity and difficulty in evacuation of the bladder/rectum (Zhang et al. (2020)). Some authors recommend a massage device. The effects of the therapy are caused by the factors heat, pulsed magnetic field and a soft vibration massage. In transrectal ultrasound in the color Doppler mapping mode, a research proves an improvement in blood circulation in the prostate gland (Zhiborev & Martov (2018)). No convincing evidence has been found on the effectiveness of prostate massage, and there is no data on adverse reactions, effect on sexual dysfunction, quality of life and anxiety. (Franco et al. (2018, 2019)).

3. Kinesitherapy. Exercises to increase the strength and endurance of the abdominal and pelvic muscles, specialized exercises for sphincters and breathing exercises are applied (Ryazkova, (1999)). With increased tone and pain points in the pelvic floor muscles, relaxing techniques of manual therapy, flexibility exercises and aerobic exercises can be effectively applied (Van Alstyne, Harrington, Haskvitz, (2010)). Although there is no consensus on appropriate specialized physiotherapy techniques, in CP/CPPS Myofascial release, Coordination Exercises/Training, Therapeutic Exercise, Manual therapy, Relaxation Exercises, Diaphragmatic Breathing, Behavioral Recommendations, Postural Education/training, Biofeedback, Education/training on home exercise program are recommended (Franco et al. (2020)). Physical activity could probably reduce the symptoms of CP/CPPS, but data of the effects on anxiety, depression, sexual dysfunction and quality of life are not available (Franco et al. (2020)).

4. Traditional Chinese Medicine (TCM) can relieve pain and affect quality of life. In a prospective randomized trial, the effect of Acupuncture and sham-acupuncture was compared. The authors suggest that acupuncture may play a role in the immunomodulation in CP/CPPS by increasing NK cell levels, but further studies are needed to establish the mechanism of action (Lee, Liang, Yuen & Krieger, (2014). Lee et al. (2014) TCM can reduce the symptoms of prostatitis and is not associated with an increased risk of side effects. It is unlikely to improve sexual dysfunction, anxiety and depression, and there are no data on the effect on quality of life (Franco et al. (2020)). High quality RCPs could help to determine the effect of this therapy (Xue et al. (2019)).

5. Balneotherapy is performed after the acute process activity reduction. Balneotherapy with radon mineral water is applied and thus the hemodynamics is activated and the development of sclerotic processes in the gland is inhibited (Mannapova & Dariĭ, (2012)). Mud shorts or rectal pads are applied, and paraffin therapy may be an alternative. Shared and seated baths with sulphide mineral waters are recommended (Ryazkova et al. 1999).

6. Reformed physical factors. Preformed physical factors are accessible and safe to administer and do not have the usual side effects observed with pharmacological therapy. (Popkov et al. (2017)). CP/CPPS is a clinical syndrome with multifactorial etiology and is best responded to by multimodal therapy (Shoskes et al. (2010)).

Low frequency and low voltage currents. Schneider, Tellenbach, Mordasin, et al. (2013) report significant pain reduction (VAS) and improved quality of life after transcutaneous electrical stimulation (TENS). Sikiru, Shmaila, Muhammed, (2008) reported a significant reduction in pain after TENS, compared to the group with pain medication or placebo tablets against antibiotic treatment (ofloxacin 300 mg). Pirola, Verdacchi, Rosadi, et al. (2019) have also reported positive results from the implementation of TENS. Therapy may be preferred instead of analgesics due to their side effects. TENS is not expensive and is not an invasive method and may be an alternative to drug analgesia (Rees et al. (2015)).

Medium frequency current have a good analgesic effect. Sinusoidal Modulated Currents, applied Transcutaneously Abdominally-Sacral in Congestive Prostatitis (Karpukhin et al. (2011)) - improve blood circulation, stimulate spinal erection and ejaculation centers and improve sexual function. Interference currents - applied pubic-sacral - enhance venous flow, improve blood circulation of the cavernous bodies and have an analgesic effect (Mannapova et Darii (2012)).

Microwave therapy is administered in an athermic to oligothermal dosage. The local temperature of the prostate gland is increased, and thus microcirculation improved, congestion reduced and the penetration of drugs improved (Wenninger, Heiman, Rothman et al. (1996)). Good anti-inflammatory effect proves Ultra High Frequency Inductothermia (Mannapova et Darii (2012); Popkov et al. (2017)). A good therapeutic effect is reported by Jin, Wang, Zhai, et al. (2017). Another study, of Chung , Choi, Yoo, et al. (2017) analyzed the clinical results of the use of drug and microwave thermotherapy and found that the combination of pharmacological agents (Ciprofloxacin 500 mg twice daily and nonsteroidal anti-inflammatory drugs (NSAIDs) and microwave therapy improve NIH-CPSI and satisfaction of patients with CP/CPPS more than patients only on medication monotherapy.

Low-intensity pulsed ultrasound (LIPUS) is probably an effective therapy for CP/CPPS. Li, Wang, Han et al. (2013) reported a reduction in CP pain with transperineal administration of US. The methodology is easy to administer and safe and may be recommended for wider clinical use. Lin, Reed-Maldonado, Lin, et al. (2016) suggest that the mechanisms of the therapeutic effect of LIPUS in CP/CPPS are due to the effects on the cyclooxygenase-2 (COX-2) and the monocyte chemo-attractant protein 1 (MCP-1), Omi, Mochida, Iwashina, et al. (2008), which are responsible for the therapeutic effect.

Sono-electromagnetic stimulation is multimodal therapy with low-intensity ultrasound, low-frequency electric field and magnetic field. A randomized, placebo-controlled, double-blind study proves that therapy leads to significantly improved symptomatology in CP and is recommended for patients with complaints \leq 12 months (Kessler, Mordasini, Weisstanner et al. (2014)).

Low-intensity laser irradiation improves bowel movements, reduces pain, and improves quality of life (Mannapova et Darii (2012); Ryazkova (1999); Vsevolod, (1994)) reported improvements in subjective complaints and improved uroflowmetry and ultrasound evaluation following transrectal administration of a low-intensity helium-neon laser. Mowafy et al. (2016) reported a significant reduction in PSSI and UPV in antibiotic and laser therapy.

Low frequency magnetic field. It Improves local circulation and has a mild analgesic effect (Mannapova et Darii (2012); Ryazkova, (1999)); Gavrushev, Strotsky, Malashchitsky et al. (2017)) report about extracorporeal magnetotherapy. The control group received non-steroidal anti-inflammatory drugs (diclofenac) and tamsulosin. No difference in NIH-CPSI was observed within 3 months, with better results in the magnetic field group at 9 months.

Extracorporeal shock-wave therapy ESWT has a pronounced analgesic effect, which manifests itself after 1-2 procedures, reduces painful urination and fibrotic processes, but does not affect calcifications (Rotov, (2008)). Triple therapy α -blocker, anti-inflammatory agent , muscle relaxant, and ESWT, show a significant change in residual urine (PVR) and maximal flow rate (QMAX) and NIH-CPSI compared with drug treatment (Pajovic, Radojevic, Dimitrovski, Vukovic (2016)) ESWT could reduce prostatitis symptoms and may not be associated with an increase in the incidence of prostatitis. (Franco et al. (2018, 2019)).

Light treatment infrared and red radiation in prostate gland projection, followed by mud therapy (intrarectal sapropel tampons) and sinusoidal modulated currents in CP in remission and latent inflammation can improve treatment efficacy and reduce the likelihood of recurrence for one year (Kolmacu &Levickij (2014); Popkov et al. (2017)).

A number of publications prove good therapeutic effect of the application of physical factors in CP/CPPS. It is recommended that physical medicine specialists, psychologists, cognitively behavioral therapists and sexual health counselors to be involved in the management of CP/CPPS (Zhang et al. (2020)). Due to the lack of high quality, randomized clinical studies, the effects of applied physical factors such as TENS, interferential and sinusoidal modulated currents, ultra-high frequency currents (UHF) - short wave diathermy and micro wave currents (SHF) of

centimeter and decimeter wavelength range, magnetic field, extracorporeal shock-wave therapy, Low intensity LASER therapy need further clinical studies to determine their effectiveness.

4. CONCLUSION

The treatment of CP/CPPS aims at influencing the infectious agent and inflammatory processes in the prostate, improving the quality of life, reducing symptoms and complications. It is difficult and long-term. For good results, therapy must be complex. Due to the lack of high quality, randomized clinical studies, the effects of the physical factors applied need further clinical studies to determine their effectiveness. Combining pharmacological with non-pharmacological treatment can increase therapeutic outcomes.

REFERENCES

- Патрашков Т, (2005) „Как да живеем с... проблемите на простатната жлеза“, ISBN: 9545285249
- Ротов, Антон Евгеньевич (2008) Применение ударно-волновой терапии в комплексном лечении и реабилитации больных хроническим простатитом [\[dissercat.com\]](http://dissercat.com)
- Рязкова М, Кирова И, Алексиев А, Михайлов Е, (1999). Практическа физиотерапия“, Издателство „Знание“
- Abdel-Meguid TA, Mosli HA, Farsi H, Alsayyad A, Tayib A, Sait M, Abdelsalam A. (2018). Treatment of refractory category III nonbacterial chronic prostatitis/chronic pelvic pain syndrome with intraprostatic injection of onabotulinumtoxin A: a prospective controlled study. *Can J Urol.* 25(2):9273-9280. [\[PubMed\]](#)
- Bartoletti R, Cai T., Mondaini N., Dinelli N., Pinzi N, Pavone C, Gontero P, Gavazzi A. et al. Italian Prostatitis Study Group. (2007). Prevalence, incidence estimation, risk factors and characterization of chronic prostatitis/chronic pelvic pain syndrome in urological hospital outpatients in Italy: results of a multicenter case-control observational study. *J Urol.* 178(6):2411-5. [\[Google Scholar\]](#)
- Bergman J, Zeitlin S. (2007) Prostatitis and chronic prostatitis/chronic pelvic pain syndrome. *Expert Rev Neurother.* 7(3):301-7. [\[Taylor & Francis Online\]](#)
- Cai, T., Verze, P., La Rocca, R., Anceschi, U., De Nunzio, C., & Mirone, V. (2017). The role of flower pollen extract in managing patients affected by chronic prostatitis/chronic pelvic pain syndrome: a comprehensive analysis of all published clinical trials. *BMC urology*, 17(1), 32. [\[PubMed\]](#)
- Chung H, Choi H, Yoo TK, et al (2017). The Effects of Microwave Thermotherapy for Chronic Prostatitis/Chronic Pelvic Pain Syndrome: A Prospective, Randomized Study. *Urogenit Tract Infect.* 12(1):35-41 [\[Synapse.koreamed\]](#)
- Doiron, R.C., & Nickel, J.C. (2018). Management of chronic prostatitis/chronic pelvic pain syndrome. *Canadian Urological Association journal = Journal de l'Association des urologues du Canada*, 12(6), S161–3. [\[Pub Med\]](#)
- Falahatkar S, Shahab E, Gholamjani Moghaddam K, Kazemnezhad E. (2015). Transurethral intraprostatic injection of botulinum neurotoxin type A for the treatment of chronic prostatitis/chronic pelvic pain syndrome: results of a prospective pilot double-blind and randomized placebo-controlled study. *BJU Int.* 116(4):641-9. [\[PubMed\]](#)
- Franco JVA, Turk T, Jung JH, et al. (2018). Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. *Cochrane Database of Systematic Reviews* (5) [\[Cochrane Databases\]](#)
- Franco JVA, Turk T, Jung JH, et al (2019). Pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome. *Cochrane Database of Systematic Reviews*, Issue 10. [\[Cochrane Database\]](#)
- Franco JVA, Turk T, Jung JH, et al (2019). Non-pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome: a Cochrane systematic review. *BJU Int.* 124:197-208. [\[Google Scholar\]](#)
- Franco JVA, Turk T, Jung JH, et al (2020) Pharmacological interventions for treating chronic prostatitis/chronic pelvic pain syndrome: a Cochrane systematic review. *BJU Int.* [\[PubMed\]](#)
- Gallo, L. (2014). Effectiveness of diet, sexual habits and lifestyle modifications on treatment of chronic pelvic pain syndrome. *Prostate Cancer Prostatic Dis* 17, 238–245 [\[Nature.com\]](#)
- Gavrusev, A. Strotsky, A. Malashchitsky D. Metrics P.X., (2017). Extracorporeal magnetic therapy for the treatment of chronic prostatitis *European urology* 16(5): E2192 [\[Europeanurology\]](#)
- Grabe M, Bjerklund-Johansen TE, Botto H et al. (2013). Guidelines on Urological Infections, European Association of Urology. Available at: http://uroweb.org/wp-content/uploads/18_Urological-infections_LR.pdf. [\[Uroweb\]](#)
- Jin, J. X., Wang, H. Z., Zhai, Z. X., Ma, B. L., Li, Q. F., Xiao, N., ... Rodriguez, R. (2017). Transrectal microwave thermotherapy causing a short-time influence on sperm quality in Chinese chronic nonbacterial prostatitis patients. *Asian journal of andrology*, 19(5), 548–553. [\[PubMed\]](#)
- Karpukhin IV, Li AA, Korzhachkina NB, Kiiatkin VA. *Vopr Kurortol Fizioter Lech Fiz Kult.* (2011) Physical factors for the treatment of patients with chronic bacterial prostatitis. (1):39-43. [Article in Russian] [\[PubMed\]](#)
- Kessler TM., Mordasini L, Weisstanner C, (2014). Sono-Electro-Magnetic Therapy for Treating Chronic Pelvic Pain Syndrome in Men: A Randomized, Placebo-Controlled, Double-Blind Trial. *PLoS One.* eCollection 29;9(12):e113368. [\[PubMed\]](#)

- Kolmacuj IA, Levickij EF. (2014). Optimization of differentiated physiotherapy methods in patients with HP/CPPS and methodological evaluations to its effectiveness. *Experimental and clinical urology* 1:50–54. [[gniiik.ru](#)]
- Krieger JN, Nyberg, Jr L, Nickel JC. (1999). NIH Consensus Definition and Classification of Prostatitis. *JAMA*. 282(3):236–237. [[PubMed](#)]
- Krieger, J. N., Lee, S. W., Jeon, J., Cheah, P. Y., Liong, M. L., & Riley, D. E. (2008). Epidemiology of prostatitis. *International journal of antimicrobial agents*, 31(1), S85–S90. doi:10.1016/j.ijantimicag.2007.08.028 [[PubMed](#)]
- Lee, S. W., Liong, M. L., Yuen, K. H., & Krieger, J. N. (2014). Acupuncture and immune function in chronic prostatitis/chronic pelvic pain syndrome: a randomized, controlled study. *Complementary therapies in medicine*, 22(6), 965–969. [[PubMed](#)]
- Li HS, Wang B, Han L, Wang CH, Xin ZC. (2013). Transperineal ultrasonic therapy for chronic prostatitis.[Article in Chinese].*Zhonghua Nan Ke Xue*. 19(1):49-53. [[Pub Med](#)]
- Lin, G., et al (2016). Effects and Mechanisms of Low-Intensity Pulsed Ultrasound for Chronic Prostatitis and Chronic Pelvic Pain Syndrome. *International journal of molecular sciences*, 17(7), 1057. [[PubMed](#)]
- Magistro G, Wagenlehner FM, Grabe M, Weidner W, Stief CG, Nickel JC. (2016) Contemporary Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome. *Eur Urol*. Feb;69(2):286-97. [[PubMed](#)]
- Mannapova GF, Darii EV. (2012). Physical factors in the treatment of chronic bacterial prostatitis (chronic pelvic pain syndrome), *Urologiia*. (3):74-8. [Article in Russian] [[PubMed](#)]; [[Ivrach.ru](#)]
- McNaughton Collins, M., Pontari, M.A., O'Leary, M.P. et al (2001). Chronic Prostatitis Collaborative Research Network Quality of life is impaired in men with chronic prostatitis: the Chronic Prostatitis Collaborative Research Network. *Journal of general internal medicine*, 16(10), 656–662. [[Springer Link](#)]
- Mowafy, Z.M.E. & Asham, H.N. & Moharam, A.A.-E & Wahed, M.H.M. (2016). Ultrasonographic response to low-intensity laser therapy in chronic prostatitis. 9:51-58. [[ResarchGate](#)]
- Omi H, Mochida J, Iwashina T, Katsuno R, et al (2008).Low-intensity pulsed ultrasound stimulation enhances TIMP-1 in nucleus pulposus cells and MCP-1in macrophages in the rat.*JOrthopRes*.26:865-71. [[GoogleScholar](#)]
- Pajovic B, Radojevic N, Dimitrovski A, Vukovic M. (2016). 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). *The Aging Male* 19(3): 202-207. [[Taylor & Francis Online](#)]
- Pirola, G. M., Verdacchi, T., Rosadi, S., Annino, F., & De Angelis, M. (2019). Chronic prostatitis: current treatment options. *Research and reports in urology*, 11, 165–174. [[Dovepres](#)]
- Popkov VM, Churakov AA, Dolgov AB et al (2017). Physiotherapeutic methods in treating patients with chronic abacterial prostatitis/chronic pelvic pain syndrome: current and development perspectives (review). *Saratov. Journal of Medical Scientific Research*.13(3): 532–536. [[Article in Russian](#)]
- Rees J., Abrahams, M, Doble A, Cooper A.(2015). Diagnosis and treatment of chronic bacterial prostatitis and chronic prostatitis/chronic pelvic pain syndrome: a consensus guideline. *BJU int*,116(4), 509–525. [[PubMed](#)]
- Schaeffer AJ. (1999). Prostatitis: US perspective. *Int Journal of Antimicrobial Agents* (11)205–11. [[Science Direct](#)]
- Schneider, M.P., Tellenbach, M., Mordasin,i L. et al (2013). Refractory chronic pelvic pain syndrome in men: can transcutaneous electrical nerve stimulation help? *BJU Int*. 112(2):E159-63. [[Wiley Online Library](#)]
- Shoskes, D.A. & Katz, E. (2005). Multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome. *Curr Urol Rep* 6: 296. [[Springer Link](#)]
- Shoskes, D.A., Nickel, J.C., & Kattan, M.W. (2010). Phenotypically directed multimodal therapy for chronic prostatitis/chronic pelvic pain syndrome: a prospective study using UPOINT.*Urology*,75(6):1249-53. [[PubMed](#)]
- Sikiru L, Shmaila H, Muhammed SA. (2008). Transcutaneous electrical nerve stimulation (TENS) in the symptomatic management of chronic prostatitis/chronic pelvic pain syndrome: a placebo-control randomized trial. *Int Braz J Urol*. 34(6):708-13. [[Pub Med](#)]
- Tripp D, Nickel J, Wang Y, et al. (2006). Catastrophizing and pain-contingent rest predict patient adjustment in men with chronic prostatitis/chronic pelvic pain syndrome. *J Pain*. 7(10):607–708. [[JPain](#)]
- Van Alstyne L.S., Harrington K.L., Haskvitz E.M., (2010). Physical Therapist Management of Chronic Prostatitis/Chronic Pelvic Pain Syndrome, *Phys Ther*. 2010 Dec;90(12):1795-806 [[PubMed](#)]
- Vsevolod M., (1994). Transrectal Low level LASER therapy in the management of prostatic problems: A pilot study. *J-STAGE LASER THERAPY*. 6(4):203-207. [[Jstage](#)]
- Weninger K., Heiman J. R., Rothman I., Berghuis J. P., Berger R. E. *Sickness* (1996) Impact of chronic nonbacterial prostatitis and its correlates // *J.Urol.*;155 (3): 965–968. [[PubMed](#)]
- Xue, Y., Duan, Y., Gong, X. et al (2019). Traditional Chinese medicine on treating chronic prostatitis/chronic pelvic pain syndrome: A systematic review and meta-analysis. *Medicine*, 98(26), e16136. [[PubMed](#)]

- Zhang, J., Liang, C., Shang, X., & Li, H. (2020). Chronic Prostatitis/Chronic Pelvic Pain Syndrome: A Disease or Symptom? Current Perspectives on Diagnosis, Treatment, and Prognosis. *AmJMH* [\[SagePub\]](#)
- Zhiborev, A.B., Martov, A.G., (2018). The effectiveness of the integrated approach to the treatment of chronic prostatitis, including in patients with benign prostatic hyperplasia. *Urologiia*. (4):81-87. [\[PubMed\]](#)