대한한방내과학회지 제29권 3호(2008년 9월)
Korean J. Orient.Int. Med. 2008:29(3)800-809

The Clinical Effect of *Bosingunyang-tang* on Chronic Non-bacterial Prostatitis/Chronic Pelvic Pain Syndrome : Randomized Double-blind, Placebo-controlled Clinical Trial

Moon-koo Song, Ji-suck Kang, Cheol-ho Kang, Young-min Ahn, Se-young Ahn, Ho-kyung Doo, Byung-cheol Lee
Dept. of Internal medicine, College of Oriental Medicine, Kyung Hee University

The Clinical Effect of *Bosingunyang-tang* on Chronic Non-bacterial Prostatitis/Chronic Pelvic Pain Syndrome : Randomized Double-blind, Placebo-controlled Clinical Trial

Moon-koo Song, Ji-suck Kang, Cheol-ho Kang, Young-min Ahn, Se-young Ahn, Ho-kyung Doo, Byung-cheol Lee
Dept. of Internal medicine, College of Oriental Medicine, Kyung Hee University

ABSTRACT

Objective : Although chronic prostatitis/chronic pelvic pain syndrome(CP/CPPS) is a common disease, there is no consensus on the etiology or pathology and treatment. This was a double-blinded, placebo-controlled, randomized clinical trial, investigating the therapeutic effects of the traditional Korean medicine, *Bosingunyang-tang*(BSGYT).

Method : Participants who met US National Institutes of Health (NIH) consensus criteria for CP/CPPS were entered after applying inclusion/exclusion criteria. They were randomized to the BSGYT or placebo group, and treated three times a day for 6 weeks. NIH-Chronic Prostatitis Symptom Index (NIH-CPSI) was used to estimate the clinical symptoms of CP/CPPS. Prostaglandin E2 and β-endorphin in prostatic fluid, collected by 2-glass pre-massage and post-massage test, were analyzed as factors associated with pain and inflammation.

Result : The mean decrease in NIH-CPSI total score of the BSGYT group was 11.0 points, which is 5.7 points more than the placebo group. (Mann Whitney test P=0.038) Also the BSGYT group showed three times higher response rate than the placebo group in NIH-CPSI pain subscale score. (Fisher's exact test P=0.027) In those responders, prostaglandin E2 decreased significantly. (Wilcoxon's signed-ranks test P=0.037). No specific side effects were observed.

Conclusion : After a 6-week treatment period, BSGYT improved clinical symptoms of CP/CPPS patients by decreasing PGE2 level in prostatic fluid.

Key words : *Bosingunyang-tang*, chronic prostatitis, chronic pelvic pain syndrome, prostaglandin E2, B*ushenjianyang-tang*

Ⅰ. Introduction

Chronic prostatitis/Chronic pelvic pain syndrome (CP/CPPS) is the third most important prostatic disease after Benign Prostatic Hyperplasia(BPH) and prostate cancer[1]. It is associated with high morbidity ; 8% of ambulatory visits with genitourinary symptoms are diagnosed as CP/CPPS, and it is more common in 36~65 years old men[2]. But CP/CPPS is diagnosed only on the basis of symptoms, principally pain or discomfort

· 교신저자: 이병철 서울특별시 동대문구 회기동 1
경희의료원 부속한방병원 한방 6내과
TEL: 02-958-9182 FAX: 02-958-9158
E-mail: hydrolee@korea.com
· 이 연구는 이 논문은 2006년도 경희대학교 한의과대학 부속 한방병원 임상연구비에 의하여 작성되었음.

in the pelvic region, and no objective measures can help define the disease[3].

Urological pain complaints were recognized as a primary component of CP/CPPS by NIH-consensus definition[4]. This pain is a distinctive feature of CP/CPPS among three symptom categories of CP/CPPS(Pain, Voiding complaints, sexual dysfunction), and the effect on a person's life with that pain has been likened to the effect of having myocardiac infarction, angina or Crohn's disease[5-7].

In spite of these high morbidity and effect on Quality of Life(QoL), there is no consensus on its etiology, pathology and therefore treatment[8]. In Korea, urologists use antibiotics and alpha blockers as their first choice without localization even though they do not think hidden bacterial prostatitis is the etiology of CP/CPPS[9]. These discrepancies are due to unclear etiology and ineffectiveness of any established treatments. Whereas Traditional Korean Medicine is popular for conditions not managed sufficiently by Western medicine, like CP/CPPS. We report a double blinded, randomized controlled trial for CP/CPPS with herbal medicine, *Bosingunyang-tang* (BSGYT).

Ⅱ. Methods

1. Subjects of clinical study

This study was carried out between October 18, 2007 and December 22, 2007 in the Oriental Medical Hospital, Kyung Hee University. Participants met NIH CP/CPPS consensus criteria. Eligibility requirements included age from 18 to 50 years-old, NIH Chronic Prostatitis Symptom Index(NIH-CPSI) total score higher than 15(scale 0~43), IPSS total score higher than 8, and symptoms lasting over 3 months during the previous 6 months. After a medical history and physical examination, participants were excluded from the study, if they had some urological disease(acute prostatitis or bacterial prostatitis, benign prostatic hypertrophy, prostatic cancer, urinary tuberculosis, urinary tract infection, bladder stone, urethral stricture, interstitial cystitis, urethritis, neuropathic bladder, bladder cancer, hematuria), drug history(drug therapy with antibiotics, muscle relaxant, nonsteroidal anti-inflammatory drug, analgesics within 1 month or presumed to have it), diseases which influence urological symptoms(brain disease, sexually transmitted diseases, etc.) or any acute disease or disease that should be treated.

2. Clinical Study design

A 6-week double-blinded, placebo-controlled, randomized clinical trial was conducted. Participants were assigned to BSGYT(N=14) or Placebo(N=13) group equally. They were treated with BSGYT (aqueous extracts 6g) or placebo medicine (aqueous extracts 6g) three times a day for 6 weeks without washing out period, because they had not taken any drugs for over a month. Every patients were taught with a paper about lifestyle interventions like hot hip bath or exercise, and they were encouraged to avoid alcohol or caffeine.

The patients were assessed at baseline and after 3 and 6 weeks by using Korean version of the NIH-CPSI and IPSS[27]. Both questionnaires were validated. Laboratory and physical assessments were performed at baseline and after 6 weeks. Expressed prostatic secretion(EPS) samples were collected by 2-glass pre-massage and post-massage test. EPS samples were preserved at -80°C before

analysis[22]. ELISA assays were used to measure β-endorphin and prostaglandin E2, factors associated with pain and inflammation. (prostaglandin E2 : Caymen Chemical Co., Ann Arbor, Michigan, β-endorphin : Peninsula Laboratories, San Carlos, California., USA) Routine urine analysis and cultures were performed on all urine samples. All participants signed a consent form and The Institutional Review Board of the Korean Medical Hospital, Kyung Hee University approved this trial.

3. Preparation of BSGYT aqueous extracts

Bosingunyang-tang (BSGYT) extract powder was obtained from the Department of Pharmaceutical Preparation of Oriental Medicine, Oriental Medical Hospital, Kyung Hee University. BSGYT extract powder is a dried mixture of the following raw materials : 20 gm of Rehmanniae Radix Preparat and Poria, 12gm of Lycii Fructus, 8gm of Dioscoreae Rhizoma and Corni Fructus, 6gm of Eucommiae Cortex, Morindae officinalis Radix, Cynomorii Herba and Achyranthis Bidentatae Radix, 4gm of Citri Pericarpium, Angelicae gigantis Radix and Psoraleae Fructus, 3gm of Polygalae Radix, Schizandrae Fructus and Amomi Fructus(Table 1). Placebo material was made of corn starch and lactose. We used Phenylthiocarbamide and Citric acid for taste, ssanghwa flavour for smell, caramel and sepia color to looks like BSGYT extract. The extract powder of BSGYT and Placebo was manufactured under the Good Manufacturing Practice(GMP) system, and the qualities of these raw materials were tested according to the Korea Food & Drug Administration and hospital standards. The airdried and crushed materials were added to distilled water, and extraction was performed by heating for 4 h at 100°C. Then the extract was concentrated with a rotary evaporator (Model NE-1, EYELA Co., Japan) and dried with a Freeze Dryer (Model FD-1, EYELA Co., Japan). The collection rate of the final aqueous extracts was 11.8 %.

Table 1. The contents of *Bosingunyang-tang*(BSGYT)

Herbal name	Herb medicine	dose(gm)
熟地黃	Rehmanniae Radix Preparat	20.0
茯　神	Poria	20.0
枸杞子	Lycii Fructus	12.0
山　藥	Dioscoreae Rhizoma	8.0
山茱萸	Corni Fructus	8.0
杜冲 鹽水炒	Eucommiae Cortex	6.0
巴戟天 酒蒸	Morindae officinalis Radix	6.0
鎖　陽	Cynomorii Herba	6.0
牛　膝	Achyranthis Bidentatae Radix	6.0
陳　皮	Citri Pericarpium	4.0
當　歸	Angelicae gigantis Radix	4.0
補骨脂 鹽水炒	Psoraleae Fructus	4.0
遠　志	Polygalae Radix	3.0
五味子	Schizandrae Fructus	3.0
砂　仁	Amomi Fructus	3.0
	Total amount	113.0

4. Outcomes

The NIH-Chronic Prostatitis Symptom Index (NIH-CPSI) was developed for use in clinical trials. It measurse the three most important domains in CP/CPPS; pain, voiding symptoms and quality of life. The sensitivity and specificity of the CPSI has been confirmed in a number of randomised placebo-controlled trials[29].

The primary endpoint was a decrease in NIH-CPSI total score from baseline to week 6. The secondary outcomes included decrease in NIH-CPSI subscale score, response rate of CPSI total score or subscale score, International Prostate Symptom Index, cytokines like β-endorphin and prostaglandin E2 in prostatic fluid.

5. Tests to detect side effects

To detect side effect, even though no specific side effect is known, we observed participants' unspecific complaint and any progression of CP/CPPS symptoms at every visit. Furthermore, at prior and after treatment, blood samples were collected for complete blood count, differential count(CBC&DC) and biochemistry test to evaluate any abnormalities of liver and kidney function, or other unknown side effects.

6. Statistical Analyses

Because no trial is performed with BSGYT, this trial is based on a trial with finasteride, which targets CP/CPPS like BSGYT. According to this assumption, setting significance at 0.05 with 80% power, each group needs at least 7 participants[28]. We used Mann-Whitney test to compare NIH-CPSI total scores, Fisher's exact test to compare responders of each group, Wilcoxon's signed-ranks test to compare cytokine level. (the GraphPad Prism for Windows, Version 5.01 (GraphPad Software, Inc.)

Ⅲ. Results

1. Participants

Between October 18, 2007 and December 22, 2007, 34 patients were screened and 27 participants were enrolled. Participants were assigned to Placebo or BSGYT group equally, with a computer generated, random, double blinded design. Two of these participants were dropped because they have stopped medication, one for Bell's palsy the other for food poisoning. Three more participants withdrew their agreements for personal reasons like move(Fig. 1). Between the two groups, baseline demographic & clinical characteristics such as age, BMI, duration of symptoms, treatment history, CPSI-total score and subscale score, IPSS, cytokine levels were similar(Table 2).

2. Primary Outcome

After 6 weeks, the BSGYT group improved 5.7 points more than the placebo group on average. The mean decrease in NIH-CPSI total score was 11.0 among BSGYT participants, compared with 5.3 among the placebo participants. (Mann Whitney test P=0.038) (Fig. 1) No demographic or clinical characteristic was associated with the results.

Table 2. Baseline Demographic and Clinical Characteristics*

Characteristic (SD)	Case(N=12)	Control(n=10)	P value†
Age,mean years	41.8(5.2)‡	39.6(8)	0.46
Duration of symptoms, months	49.5(26.8)	62.8(68.3)	0.54
Height	171.1(11.6)	173.2(4.9)	0.31
Weight	68 (11.6)	68.2(9.6)	0.97
BMI	23.14(3.1)	22.67(2.6)	0.71
Treatment history§			1.0
0 Treatment	1	0	
1 or more treatment	11	10	
NIH-CPSI score ¶			
Total	23.5(3.7)	24.3(3.8)	0.67
Pain subscale	9.8(2.9)	11.2(2.7)	0.25
Urinary subscale	5.8(2.2)	4.8(1.7)	0.28
QoL subscale	8(2.2)	8.3(1.4)	0.71
IPSS ¶	19.4(7.7)	14.9(5.5)	0.13
Cytokines ¶			
Prostaglandin E2	67.12	30.08	0.06
β-endorphin	0.13	0.17	0.25

* Apply Per Protocol analysis. † P value were based two-tailed, and significance was set at $p < 0.05$. ‡ mean(standard deviation) § Fisher's Exact Test was used. ¶ Mann-Whitney test was used.

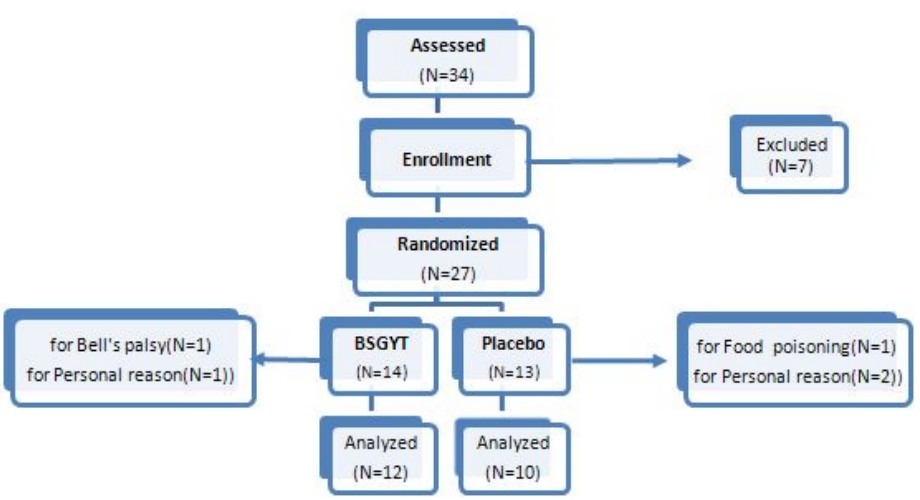

Fig. 1. Clinical trial comparing BSGYT and Placebo for CP/CPPS. Of the 27 participants, 22(81%) completed treatment sessions of 6 weeks.

Withdrawal was five, two for stopping medicine because of chance disease, three for personal reason like move away. No participants complained significant and severe side effects, or showed lab abnormality.

3. Secondary Outcomes

Of the 12 BSGYT participants, 10(83.3%) responded (defined as 〉 25% improvement in NIH-CPSI[10]), compared with 4 (66.7%) placebo participants(relative risk[RR] 2.08, Confidence interval[CI] 0.9-4.6 Fisher's exact test P=0.07), including 4 BSGYT and 1 placebo group participants reporting more than 50% improvement. (non-significant). In NIH-CPSI pain score, 10 participants of BSGYT responded (defined as decline of one third) compared to 3 participants of placebo group(relative risk[RR] 2.78, Confidence interval[CI] 1.04-7.40 Fisher's exact test P=0.027 (Fig. 2).

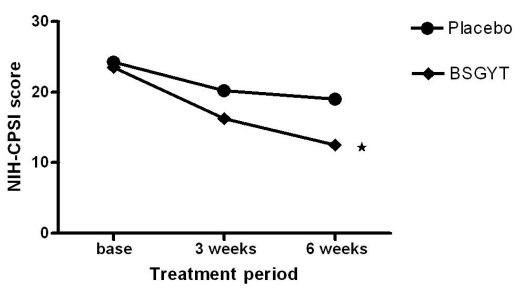

Fig. 2. After 6 weeks, NIH-CPSI total score of BSGYT group improved more than 5 points compared with placebo group.

The mean decrease in NIH-CPSI total score was 11.0 among BSGYT participants(★ Mann Whitney test P=0.038).

In the CP/CPPS patients, PGE2 concentrations in prostatic fluid are higher than in asymptomatic controls, and high PGE2 might inhibit β-endorphin release[11]. In this study, PGE2 was decrease by 20.73pg/dl in BSGYT group, 3.12pg/dl in placebo group. PGE2 decrease was significant in the participants whose CPSI-pain score improved. (defined as decline of one third, Wilcoxon's signed-ranks test P=0.037, (Fig.3). Change of β-endorphin was insignificant.

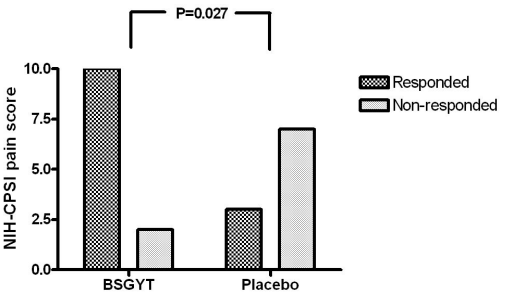

Fig. 3. In NIH-CPSI pain score, almost three times of BSGYT group responded compared with placebo group.(Fisher's exact test P=0.027)

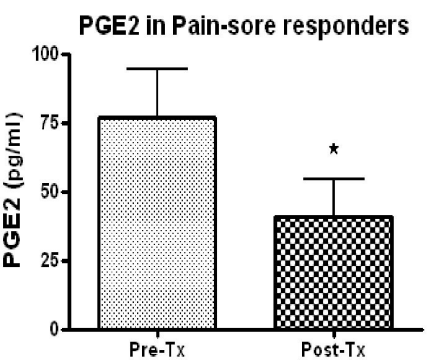

Fig. 4. In NIH-CPSI pain-score responders, we can observe a meaningful decrease in PGE2(★ Wilcoxon's signed-ranks test P=0.037), which induces pain in CP/CPPS patients.

4. Side effects

CP/CPPS is a chronic disease, and prostate blood supply is poor. Therefor medicines for CP/CPPS might be used in long term or in large dosage, so they are required to be tested for side effects. There was no specific complaint except for a placebo participants who complained mild dyspepsia. No significant adverse change in biochemistry, CBC&DC was observed in both group.

Ⅳ. Discussion

It has been suggested that many urological conditions such as benign prostatic hyperplasia (BPH), chronic prostatitis, voiding or erectile dysfunction might be amended by complementary and alternative medicine treatment strategies. Biofeedback, acupuncture, high frequency electrostimulation, hyperthermia, and herbal medicine has been used for CP/CPPS but more evidence is needed for herbal medicine[12,25]. This double-blinded placebo-controlled randomized clinical trial with *Bosingunyang-tang*(BSGYT) revealed marked improvement of total NIH-CPSI score and high response rate in CPSI-pain score with a decrease in PGE2.

Pain decrease is a clinically important improvement in individual patients even if improvement of urinary symptoms is not sufficient[13]. Pain is not only thought to be the primary symptom, but also a central feature in QoL[14]. This central and/or peripheral pain sensitization in the pelvis may result from tenderness of prostate and pelvis, so acupuncture was regarded as an important complementary and alternative therapy to treat painful and chronic conditions[15,16]. But it is also important to note that half of the CP/CPPS patients suffering from pain has no sites of tenderness whatsoever. This heterogeneity shows there is a need for a pain control therapy that is not based on muscle tenderness.

Bosingunyang-tang(BSGYT) consists of fifteen medical herbs, based on Yukmijihang-tang (YMJHT). YMJHT is used for teating Yin deficiency of liver and kidney, hectic fever, dizziness, inflammation and gynecological diseases. Also, it is a cardiac tonic & diuretic, and these actions are probably effected by vasodilation[17]. Based on YMJHT, BSGYT was made for "deficiency of Yang in Yin" because tendon and muscle is strengthened by Yang in Traditional Korean Medical theory. Additional medicines is for "Deficiency of Yang." Theses medicines have anti-inflammatory or antioxidant effects. For example, Angelicae gigantis Radix inhibit inflammatory mediators and Lycii Fructus, Morindae officinalis Radix have antioxidant effect[18,19]. As a result, BSGYT treats CP/CPPS, which reflects "deficient qi"(energy of life) with focal inflammation and urinary symptoms in Traditional Korean Medical theory, and it improved the total NIH-CPSI score and showed high response rate of CPSI-pain subscale score[20]. This is more significant than traditional Chinese formulae reported before 2003, and as effective as Quercetin[21,25]. (improvement from 21.0 to 13.1, in NIH-CPSI total score)

BSGYT may have some effects on immune reaction. In men with CP/CPPS, the action between the immune, endocrine and nervous systems is involved in producing symptoms like pain. Inflammatory marker prostaglandin E2(PGE2) is synthesized from the expression of Cyclo-oxygenase-type-2(Cox-2), and results in pain.[22] PGE2 is also known to inhibit β-endorphin, an endogenous opioid produced by immune cells, and treatments with antibiotics decrease PGE2 and increase β-endorphin therefor relieve pain[23,26]. In this trial, BSGYT decreased PGE2 level, especially in participants whose CPSI-pain subscale score decreased.

This study has some limitations. In this trial, NIH-CPSI total score was the most valid

measure, but the score is subjective to the participant's personal attention in both group. Also, the number of participant was small(N=22), and the duration of the trial was short(6 weeks). Selecting BSGYT might be seemed inadequate by some Traditional Korean Medical doctors.

Ⅴ. Conclusion

In summary, the BSGYT group improved 11 points, 5.7 points more on average than the placebo group. And the BSGYT group showed three times higher response rate than the placebo group. These effects might have resulted from PGE2 decrease in prostatic fluid. Clinical trials with longer treatment period are indicated to reveal more effects on endocrine and nervous system.

Reference

1. Roberts RO, Lieber MM, Bostwick DG, Jacobsen SJ. A review of clinical and pathological prostatitis syndromes. Urology. 1997;49(6):809-21.
2. Schaeffer AJ. Etiology and management of chronic pelvic pain syndrome in men. Urology. 2004;63(3 Suppl 1):75-84.
3. Alexander RB, Propert KJ, Schaeffer AJ, Landis JR, Nickel JC, O'Leary MP 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):581-9.
4. Krieger JN, Nyberg L, Nickel JC. NIH consensus definition and classification of prostatitis. JAMA. 1999;282(3):236-7.
5. Collins MM, Stafford RS, O'Leary MP, Barry MJ. Distinguishing chronic prostatitis and benign prostatic hyperplasia symptoms: results of a national survey of physician visits. Urology. 1999;53(5):921-5.
6. Krieger JN, Egan KJ, Ross SO, Jacobs R, Berger RE. Chronic pelvic pains represent the most prominent urogenital symptoms of "chronic prostatitis". Urology. 1996;48(5):715-21; discussion 721-2.
7. Wenninger K, Heiman JR, Rothman I, Berghuis JP, Berger RE. Sickness impact of chronic nonbacterial prostatitis and its correlates. J Urol. 1996;155(3):965-8.
8. Schaeffer AJ. Clinical practice. Chronic prostatitis and the chronic pelvic pain syndrome. N Engl J Med. 2006;355(16):1690-8.
9. Ku JH, Paick JS, Kim SW. Chronic prostatitis in Korea: a nationwide postal survey of practicing urologists in 2004. Asian J Androl. 2005;7(4):427-32.
10. Mehik A, Alas P, Nickel JC, Sarpola A, Helström PJ. Alfuzosin treatment for chronic prostatitis/chronic pelvic pain syndrome: a prospective, randomized, double-blind, placebo-controlled, pilot study. Urology. 2003;62(3):425-9.
11. Pontari MA, Ruggieri MR. Mechanisms in prostatitis/chronic pelvic pain syndrome. J Urol. 2008;179(5 Suppl):S61-7.
12. Capodice JL, Bemis DL, Buttyan R, Kaplan SA, Katz AE. Complementary and alternative medicine for chronic prostatitis/chronic pelvic pain syndrome. Evid Based Complement Alternat Med. 2005;2(4):495-501.
13. Propert KJ, Litwin MS, Wang Y, et al. Responsiveness of the National Institutes of

Health Chronic Prostatitis Symptom Index (NIH-CPSI). Qual Life Res. 2006;15(2):299-305.
14. Nickel JC, Tripp DA, Chuai S, Litwin MS, Landis JR, Alexander R, et al. Psychosocial variables affect the quality of life of men diagnosed with chronic prostatitis/chronic pelvic pain syndrome. BJU Int. 2008;101(1):59-64.
15. Berger RE, Ciol MA, Rothman I, Turner JA. Pelvic tenderness is not limited to the prostate in chronic prostatitis/chronic pelvic pain syndrome (CPPS) type IIIA and IIIB: comparison of men with and without CP/CPPS. BMC Urol. 2007;7:17.
16. Capodice JL, Jin Z, Bemis DL, Samadi D, Stone BA, Kapan S, et al. A pilot study on acupuncture for lower urinary tract symptoms related to chronic prostatitis/chronic pelvic pain. Chin Med. 2007;2:1.
17. Jin UH, Kim DI, Lee TK, Lee DN, Kim JK, Lee IS et al. Herbal formulation, Yukmi-jihang-tang-Jahage, regulates bone resorption by inhibition of phosphorylation mediated by tyrosine kinase Src and cyclooxygenase expression. J Ethnopharmacol. 2006;106(3):333-43.
18. Kim JH, Jeong JH, Jeon ST, Kim H, Ock JY, Suk KH et al. Decursin inhibits induction of inflammatory mediators by blocking nuclear factor-kappaB activation in macrophages. Mol Pharmacol. 2006;69(6):1783-90.
19. Lin RD, Hou WC, Yen KY, Lee MH. Inhibition of monoamine oxidase B (MAO-B) by Chinese herbal medicines. Phytomedicine. 2003;10(8):650-6.
20. Lee SWH, Liong ML, Yuen KH, Leong WS, Chee PY, Choong WP et al. Acupuncture versus sham acupuncture for chronic prostatitis/chronic pelvic pain. Am J Med. 2008;121(1):79.e1-7.
21. Shoskes DA, Zeitlin SI, Shahed A, Rajfer J. Quercetin in men with category III chronic prostatitis: a preliminary prospective, double-blind, placebo-controlled trial. Urology. 1999;54(6):960-3.
22. Jang TL, Schaeffer AJ. The role of cytokines in prostatitis. World J Urol. 2003;21(2):95-9.
23. Vlaskovska M, Hertting G, Knepel W. Adrenocorticotropin and beta-endorphin release from rat adenohypophysis in vitro: inhibition by prostaglandin E2 formed locally in response to vasopressin and corticotropin-releasing factor. Endocrinology. 1984;115(3):895-903.
24. Nickel JC, Shoskes D, Wang Y, et al. How does the pre-massage and post-massage 2-glass test compare to the Meares-Stamey 4-glass test in men with chronic prostatitis/chronic pelvic pain syndrome? J. Urol. 2006;176(1):119-24.
25. Chen JX, Hu LS. Traditional chinese medicine for the treatment of chronic prostatitis in China: a systematic review and meta-analysis. Journal of Alternative and Complementary Medicine (New York, N.Y.). 2006;12(8):763-9.
26. Nickel JC. Inflammation and benign prostatic hyperplasia. Urol. Clin. North Am. 2008;35(1):109-15; vii.
27. Chong CH, Ryu DS, Oh TH: The Korean version of NIH-Chronic Prostatitis Symptom Index (NIH-CPSI): validation study and characteristics on chronic prostatitis. Korean J Urol. 2001;42:511-20.
28. Nickel JC, Downey J, Pontari MA, Shoskes DA, Zeitlin SI. A randomized placebo-controlled multicentre study to evaluate the safety and efficacy of finasteride for male chronic pelvic

pain syndrome (category IIIA chronic nonbacterial prostatitis). BJU Int. 2004;93(7):991-5.
29. Schaeffer AJ, Anthony J. NIDDK-sponsored chronic prostatitis collaborative research network (CPCRN) 5-year data and treatment guidelines for bacterial prostatitis. Int J Antimicrob Agents. 2004;24 Suppl 1:S49-52.