A Clinical Study on the Treatment of Chronic Pelvic Inflammation of Qi-stagnation with Blood Stasis Syndrome by Penyanqing Capsule (盆炎清胶囊)*

SHEN Bi-qiong (沈碧琼), SITU Yi (司徒仪), HUANG Jian-ling (黄健玲), SU Xiao-mei (苏晓梅), HE Wei-tang (何伟棠), ZHANG Mao-wei (张茂威), and CHEN Qu-bo (陈曲波)

ABSTRACT **Objective:** To observe the clinical efficacy of Penyanqing Capsule (盆炎清胶囊, PYQC) in treating pelvic inflammation of Qi-stagnation with blood stasis syndrome. **Methods:** The randomized, single blinded, parallel positive drug controlled method was adopted, with 82 patients assigned into two groups by envelop method. The 42 patients in the treated group received PYQC 3 times a day, 4 capsules each time taken orally; the 40 patients in the control group were given orally Fuyankang tablets (妇炎康片, FYKT) 3 times a day, 6 tablets each time. The therapeutic course for both groups was 2 months, and 2 courses of treatment were given successively to observe the comprehensive effect, changes of symptoms and signs before and after treatment. The effects of PYQC on hemorrheological character in part of the patients and on the pathogenetic chlamydia and mycoplasma were also observed. **Results:** The total effective rate in the treated group was 83.3%, which was insignificantly different from that in the control group (77.5%, $P>0.05$). However, PYQC could significantly lower the hemorrheologic indexes in patients and showed definite influence on the pathogenetic chlamydia and mycoplasma. **Conclusion:** PYQC has good therapeutic effect in treating chronic pelvic inflammation of Qi-stagnation with blood stasis syndrome, and showed definite effect on chlamydia and mycoplasma.

KEY WORDS chronic pelvic inflammation, Qi-stagnation with blood stasis syndrome, Penyanqing Capsule, therapeutic efficacy evaluation

Chronic pelvic inflammation (CPI), is an often encountered disease in gynecologic clinics, is characterized by protracted course and hard to be cured. Qi-stagnation with blood stasis syndrome (QSBSS) is one of the syndrome types of CPI[1]. According to the TCM therapeutic principle of regulating Qi to dispel stagnancy and dissolving blood stasis to relieve pain, Penyanqing Capsule (盆炎清胶囊, PYQC), a Chinese herbal preparation worked out on the basis of the experienced prescription of Prof. SITU Yi to treat CPI, was used to treat patients with CPI of QSBSS from Dec. 1997 to Dec. 2000, and good efficacy was obtained. The results of the study is reported as follows.

METHODS

Diagnostic Standards

In reference to the diagnostic standard for CPI in "Guiding Principle of Clinical Research on New Drugs of TCM"[2], patients were diagnosed as CPI if they had such symptoms as pain and tenesmic distension in lower abdomen, and soreness in lumbosacral region, which would be aggravated after labor, sexual intercourse and defecation. And around the menstrual period, it might be accompanied with low fever, hypermenorrhea and leukorrhagia. And through gynecological examination, such signs would be found as uterus postposition, limited motion or even fixed motion due to adhesion; when there exists salpingitis, funicular stick in uni- or bi-laterals of uterus with mild tenderness is palpable, and when there is inflammation of pelvic connective tissues, there would appear tenderness thickening or enclosed mass in one or both sides of pelvic cavity.

The condition of the disease was classified and scored according to the standard of scoring on CPI in the afore-said guidance[2]: limited motion of uterus with tenderness was scored as 5 points; funicular stick like oviduct with tenderness as 5;

* Supported by the Foundation of Guangdong Provincial Administration of TCM (No. 97206)

Department of Gynecology, the Second Hospital Affiliated to Guangdong University of TCM, Guangzhou (510120)
Correspondence to: Dr. SHEN Bi-qiong
Tel: 020—81887233; Fax: 020—81867705
E-mail: shbiq@126.com

sheet thickening in uni- or bi-laterals of uterus as 5; soreness in lower abdomen and lumbar region as 3, leukorrhagia as 1, low fever as 1, and abdominal pain in menstrual period as 1, with every increased year of the course of CPI counted as 0.5 points. Patients with the accumulated scores up to over 15 points were regarded as in severe condition, 10—14 points as in moderate condition and 5—9 points as in mild condition.

The diagnosis of QSBSS was made in reference to the same guidance mentioned above[2], i. e. patients mainly manifested dull pain or distension in lower abdomen, soreness in lumbo-sacral region, which got aggravated during menstrual period or after labor; with yellow or white colored leukorrhagia, or having mammary distended pain before menstrual period; pale tongue with thin white or thin yellow fur, pulse stringy or small-stringy.

General Materials

All the patients enrolled were out-patients of the gynecological clinics of authors' hospital, having sexual life, and conforming to the diagnostic standard of CPI with TCM syndrome type of QSBSS, accompanied with dampness-heat or Pi-deficiency syndrome in some individuals due to their different constitutions.

The 82 patients were randomly assigned into two groups in ratio of 1 : 1 according to the sequence of hospitalization by the randomized number produced by cyber-software PEMS 3.1 packaged in envelop. The 42 patients in the treated group were aged 18—54 years, 32.5±7.3 years on average; with the course of disease 5 days — 10 years, 3.8±2.0 years on average. Among them 23 patients had fertility history, 8 had been undergone abdominal surgical operation, and 8 complicated with infertility. Gynecological examination found unshaped inflammatory mass in one side of accessory area in 5 patients. Ultrasonic examination showed the mass was in an irregularly shaped mixed area, 3.0—5.0 cm in size. By TCM syndrome typing, 39 belonged to QSBSS, 2 were QSBSS accompanied with dampness-heat, 1 accompanied with Pi-deficiency. Eleven patients were in severe condition, 25 moderate and 6 mild.

The 40 patients in the control group were aged 18—56 years, 33.2±7.9 years on mean; with the course of disease 3 days — 9.5 years, 3.6±2.0 years on mean. Among them 15 patients had fertility history, 7 had been undergone abdominal surgical operation, and 5 complicated with infertility. Gynecological examination found unshaped inflammatory mass in one side of accessory area in 3 patients. Ultrasonic examination showed the mass was an irregularly shaped mixed area, 3.0—4.8 cm in size. By TCM syndrome typing, 38 belonged to QSBSS, 1 was QSBSS accompanied with dampness-heat and 1 accompanied with Pi-deficiency. Ten patients were in severe condition, 22 moderate and 8 mild.

Comparison of the general materials between the two groups showed insignificant difference ($P>0.05$), and so they were comparable.

At the same time, 50 healthy women with no blood stasis syndrome, who visited the gynecological clinics of the authors' hospital for physical checks, were selected to set up the healthy control group, their age ranging between 20—55 years, 34.0±7.6 years on mean, with no significant difference as compared with the age in the two patients' groups ($P>0.05$).

Treatment

PYQC consisting of such kinds of Chinese herbs as red sage root, red peony root, immature bitter orange, pubescent holly root, etc. was provided by the Preparation Department of Guangdong Provincial Hospital of TCM, each capsule containing 1.85 g of crude drugs. It was used to treat the patients in the treated group, with 4 capsules taken each time, three times a day.

Patients in the control group were treated with Fuyankang tablets (妇炎康片, FYKT), a product of Jieshou Pharmaceutical Factory, Anhui Province, consisting of red peony root, Chinese angelica root, smilax glabra rhizome, burreed tuber, szechwan chinaberry, tumeric rhizome, yanhusuo rhizome, gordon euryale seed, flavescent sophora root, yellow cocktree bark, red sage root and cyperus tuber, each tablet containing 0.25 g of crude drug. It was given to the patients in the control group three times a day, 6 tablets each time.

One course of treatment lasted two months for either group, and two courses were given successively. The medication would be stopped in the menstrual period, and other drugs which could influence the effect of the treatment were forbidden.

The therapeutic efficacy was evaluated at the end of therapeutic course. Follow-up study was

carried out on the cured patients to know the long-term therapeutic efficacy. For the patients of infertility, the treatment would be stopped when they got pregnant in the therapeutic course, and the case was evaluated as cured.

Items of observation

Symptoms and signs (by gynecologic examination) were observed and scored by an appointed specialist in the corresponding time of the menstrual cycles before and after treatment.

Hemorrheologic indexes, including high and low shear whole blood viscosity, plasma viscosity, erythrocyte aggregation index, hematocrit and erythrocyte sedimentation rate (ESR), were measured before and after treatment using the hemorrheometer type LING-100 produced by the Instrument Plant of Shanghai Medical University.

Cervical exudate was collected for detection of chlamydia trachoma (CT) antigen and cultivation of ureaplasma urealyticum (UU) and human mycoplasm (Mh) in the following way: Cervix was exposed by vaginoscope and the exudate attached to the external orifice was cleaned with a dry sterilized cotton swab. A sterilized cotton swab was inserted into the cervical canal for 1.5—2.0 cm, rotated 2 circles to collect the exudate, which was placed in an aseptic test tube for use. The immunological detection on CT antigen was conducted using the test kit of Unipath Co., UK. The cultivation of UU and Mh was carried out using the special culture solution and tested with the kit provided by Black Horse Biotech Institute, Zhuhai, Guangdong Province. All patients who showed positive outcome in the detection or culture were disallowed to have sexual intercourse in the therapeutic period, and their sexual partner would receive the treatment simultaneously.

Standard for Efficacy Evaluation

Referring to the standard in the "Guiding Principle of Clinical Research on New Drugs of TCM"[2], the efficacy of treatment was evaluated depending on the changes of symptoms, signs and gynecological examination findings (S1) and scores of condition (S2). It was evaluated as cured when patients after treatment had their S1 normalized, or patients of infertility get pregnant and S2 lowered to zero; as markedly effective when S1 obviously improved and S2 reduced by over 2/3; as effective when S1 improved, and S2 reduced by over 1/3; and as ineffective when no improvement was shown after treatment in either S1 or S2.

Statistical Analysis

Variance analysis was used for analyzing measurement data, Chi-square test was used for analyzing enumeration data, rank-sum test was used for analyzing ranked material. The α value was set on 0.05. The analysis was carried out using software SPSS 11.0.

RESULTS

Comprehensive Effects

In the treated group, the effect was evaluated as cured in 10 patients (23.8%, among them, one infertility patient got pregnant and so was regarded as cured), as markedly effective in 12 (28.6%), as effective in 13 (30.9%) and as ineffective in 7 (16.7%), the total effective rate being 83.3%. While in the control group, it was respectively cured in 8 (20.0%), markedly effective in 11 (27.5%), effective in 12 (30.0%) and ineffective in 9 (22.5%, among them, 2 patients had their connection with doctor interrupted, and so they were regarded as ineffective), the total effective rate being 77.5%. Comparison of the total effective rate between the two groups showed no significant difference ($P>0.05$).

One of the two patients in the treated group who were accompanied with dampness-heat syndrome was cured and the other proved the treatment markedly effective, while the patient accompanied with Pi-deficiency was treated effectively. While in the control group, the treatment of the two patients with the two accompanying syndromes proved to be markedly effective in both patients. The 5 patients with inflammatory enclosed mass in the treated group had their mass disappeared completely in 3, the mass size reduced by 2/3 in 1 and by 1/3 in 1. While those (3 patients) in the control group, the mass disappeared completely in 2 and the size reduced by 1/3 in 1. The statistical analysis on the patients with accompanying syndromes or enclosed mass was not conducted due to the few case numbers.

Chin J Integr Med 2005 Dec; 11(4): 249—254

Relationship between the Condition of Disease and the Therapeutic Effects

As shown in Table 1, the therapeutic effect showed itself in patients of various conditions in both groups, but the total effective rate in patients in the mild condition in the treated group were significantly superior to that in the severe condition, showing significant statistical difference ($P<0.05$), while comparison of that in mild vs moderate and moderate vs severe cases showed insignificant difference ($P>0.05$).

In the control group, the total effective rate in patients in the moderate condition was markedly higher than that in patients in severe condition, showing significant difference ($P<0.05$), but the difference was insignificant in comparison of the total effective rate in patients in mild condition with either that of moderate or that of severe condition ($P>0.05$). Differences between the two groups in therapeutic effect in patients in the same condition were insignificant ($P>0.05$).

Changes of Clinical Symptoms

As shown in Table 2, in the treated group after treatment, excepting that the reduction of low fever was insignificant, obvious improvement was shown in symptoms of lower abdominal tenesmic distention and pain, lumbosacral pain, leukorrhagia, menstrual disorder and dysmenorrhea ($P<0.05$ or $P<0.01$). All the above-mentioned symptoms, except dysmenorrhea, were significantly improved in the control group ($P<0.05$ or $P<0.01$). Comparison of the improvement in corresponding symptoms between the two groups showed no significant difference ($P>0.05$).

Changes of Hemorrheologic Characters in the Treated Group

As shown in Table 3, all the hemorrheologic parameters, including high shear blood viscosity, low shear blood viscosity, plasma viscosity, erythrocyte aggregation Index, hematocrit and ESR, measured in 29 patients of the treated group, were higher than those in the healthy control group, and all the differences, except that for ESR, had statistical significance ($P<0.01$), indicating the existence of high blood viscosity in patients with CPI. All the parameters, except ESR, were lowered to some extent, and

Table 1. Relationship of the Condition of Disease with Therapeutic Effect [Cases (%)]

Group	*n*	Condition	Therapeutic Effect				
			Cured	Markedly Effective	Effective	Ineffective	Total Effective
Treated	6	Mild	3(50.0)	2(33.3)	1(16.7)	0	6(100.0) *
	25	Moderate	6(24.0)	7 (28.0)	9(36.0)	3(12.0)	22(88.0)
	11	Severe	1 (9.1)	3 (27.3)	3(27.3)	4(36.4)	7(63.6)
Control	8	Mild	3 (37.5)	1(12.5)	1(12.5)	3 (37.5)	5(62.5)
	22	Moderate	4 (24.0)	8(28.0)	9(36.0)	1(12.0)	21(95.5)*
	10	Severe	1 (9.1)	2(27.3)	2(27.3)	5(36.4)	5(50.0)

Note: * $P<0.05$, compared with the severe condition in the same group

Table 2. Changes of Symptoms before and after Treatment (Cases)

Group	*n*	Time	Lower Abdominal Pain	Lumbosacral Pain	Lower Abdominal Tenesmic Distention	Leukorrhagia	Menstrual Disorder	Dysmenorrhea	Low Fever
Treated	42	BT	33	21	23	19	16	10	5
		AT	6**	4**	5**	7**	4 **	3 *	2
Control	40	BT	34	19	20	17	16	9	6
		AT	6**	4**	4**	5**	4**	6	0*

Notes: BT: before treatment, AT: after treatment; * $P<0.05$, ** $P<0.01$, compared with BT in the same group

Table 3. Changes of Hemorrheologic Parameters before and after Treatment ($\bar{x}\pm s$)

Group	n	Time	Whole Blood Viscosity(mPa/s)		Plasma Viscosity(mPa/s)	Erythrocyte Aggregation Index	Hematocrit (%)	ESR (mm/h)
			High Shear	Low Shear				
Treated	29	BT	6.38±1.33*	10.02±2.76*	1.86±0.25*	1.66±0.26*	46.25±3.99*	16.37±10.02
		AT	5.52±0.98△	8.02±2.55△	1.73±0.19△	1.49±0.24△	41.39±3.70△	16.06±9.99
Healthy control	50		5.30±0.85	6.6±1.63	1.71±0.10	1.31±0.23	38.00±2.83	14.30±9.48

Notes: * $P<0.01$, compared with the healthy control group; △$P<0.01$, compared with before treatment in the same group; BT means before treatment, AT means after treatment

showed significant difference as compared with those before treatment respectively ($P<0.05$ or $P<0.01$), suggesting the blood viscosity manner was significantly improved after PYQC treatment.

Changes of CT in Cervical Exudate and Outcome of UU and Mh Culture

CT detection and UU, Mh culture were conducted in 38 patients in the treated group. Results showed that before treatment, the cervical culture showed positive of UU in 12 patients (31.6%) and positive of Mh in 7 (18.4%); immunological detection showed CT antigen positive in 10 patients (26.3%), 4 patients (10.5%) were positive both to UU and CT.

After PYQC treatment, 3 of the 12 patients with UU infection, 1 of the 7 with Mh, and 2 of the 10 with CT were cured, suggesting that PYQC had a definite therapeutic effect in treating CT, UU and Mh, but statistical analysis could not be conducted due to the small number of samples.

Outcome of Follow-up Study

The follow-up study was carried out three months after the treatment came to an end. The outcome showed that relapse occurred in 2 patients (1 in each group) 2 months after the withdrawal of medication. Follow-up on cured patients with CT, UU, and Mh infection showed that only one patient had UU returned to positive, with all other tests proved to be negative. And inquiry of the recurrence one showed that she was not disengaged from sexual life during the treatment and her sexual partner didn't receive synchronous treatment.

DISCUSSION

CPI is an often encountered inflammatory disease of the productive organ in women in fertilizable period, which is characterized by various protracted and relapsed symptoms hard to be cured and could result in such sequelae as infertility, ectopic gestation, chronic pelvic pain and adhesion, and is therefore considered as a stubborn disease in gynecologic department.

There has been no large sample epidemiological research reported so far. Statistical material of the authors' hospital in recent 10 years showed that CPI occur mainly in women in sexual maturation period, and many patients could be harassed by infertility, chronic pelvic pain, and ectopic gestation for a long time. Its incidence rate could be severely influenced by such sexual pathophorous diseases as infections of CT, UU and Mh[3].

Treatment to activate blood circulation to remove blood stasis of TCM could improve the blood circulation in tissues to ameliorate its nutrition, increase the metabolism of the body, and promote the absorption, soften and resolve the inflammation and hyperplastic tissues. It has been proved by pharmacodynamic study that PYQC, which possesses the effects of regulating Qi to drive stagnancy off, resolving blood stasis to relieve pain, could improve such inflammation induced symptoms as reddened swelling, hot sensation and pain, and also improve the microcirculation to increase the local blood supply, accelerate the absorption of inflammation and elevate the immunity of

organism[4]. Modern pharmacologic study showed that red sage root and red peony root have anti-blood coagulation action, could promote blood circulation in tissues, and improve the hemorrheologic manner of organism[5]. Ilexonin A, the effective ingredient of pubescent holly root has the action of dredging blood vessels, improving microcirculation and promoting absorption of hematoma. Also it could antagonize inflammation, relieve pain and inhibit the infiltration of inflammatory cells. Bacteriostasis test showed that it has an obvious inhibitory effect on the pathogens of CPI as staphylococcus aureus and bacillus coli[6].

PYQC is used in clinical practice to treat patients with CPI of QSBSS, and results of this observation showed that its effective rate reached 83.3%, very close to that of FYKT (77.5%), and that PYQC could effectively relieve various clinical symptoms of CPI, such as pain in lower abdomen and lumbosacral region, tenesmic distention, leukorrhagia, menstrual disorder and dysmenorrhea.

It has been found that QSBSS in CPI is closely related with blood viscosity manner, which is revealed in patients with CPI as compared with healthy persons, and therefore it is considered that increased blood viscosity is one of the pathologic characters of CPI with QSBSS. PYQC showed marked effects in improving the abnormality of hemorrheologic manner and could cure such patients effectively. It has also been illustrated that PYQC could inhibit the pathogens of CPI such as mycoplasma and chlamydia, though this needs to be further confirmed by randomized, double blinded trials.

REFERENCES

1. Huang JL, Shen BQ, Li YP, et al. The exploration of differentiation syndrome and treatment on pelvic inflammatory disease. Chin J Inform Tradit Chin Med 2000; 7 (6) : 10, 37.
2. Ministry of Health, People's Republic of China. Guiding principle of clinical research on new drugs of TCM. Beijing: China Medico-Pharmaceutical Sciences and Technology Publishing House, 1993 : 252—254.
3. Huang JL, Shen BQ, Chen QB, et al. The analysis of the results on 168 cases of pelvis infected by CT and UU taken on cervix uteri. Chin J Dermatovenereol 2000; 14 (4) : 253—254.
4. Shen BQ, Situ Y, OU YQ. A pharmacodynamic study of Penyan Qing Capsule. J Guangzhou Univ Tradit Chin Med 2001; 18(2) : 159—162.
5. Wang YS, Deng WL, Xue CS, editors. Pharmacology and clinics of Chinese materia medica. Beijing: People's Medical Publishing House, 1998 : 190—192, 528—531.
6. Wang BX, editor. Modernistic pharmacology and clinics of Chinese materia medica. Tianjin: Tianjing Sciences and Technology Translation Press, 2004 : 331—333.

(Received January 10, 2005)