

Hemorheological study and treatment with enema retention of Li Chong Tang combined with moxibustion in women suffering from chronic pelvic inflammatory diseases

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Abstract: The study was undertaken to investigate the blood stasis of chronic pelvic inflammatory disease (PID) with scientific method, hemorheology. The whole blood viscosities of chronic PID increased significantly compared with normal level, which was consistent with the blood stasis of Traditional Chinese Medicine (TCM) theory. Moreover, sixty women suffering from chronic PID were treated with Enema Retention of Li Chong Tang Combined with Moxibustion (ERM) for 6 weeks. The chronic PID score and the whole blood viscosity were evaluated before and after the ERM. The parameters of whole blood viscosities at low, median and high shear rate of chronic PID group decreased from 12.32 ± 0.31 , 6.66 ± 0.13 and 5.15 ± 0.52 , to the normal levels, 9.19 ± 0.13 , 5.42 ± 0.56 and 4.34 ± 0.43 ($p < 0.05$) after therapy of ERM and the symptoms score decreased from 13.73 ± 3.7 to 3.8 ± 1.4 ($p < 0.05$), which shows that the ERM is an effective therapy method to treat chronic PID.

Keywords: Blood stasis; Chronic PID; Enema retention; Hemorheology; Li Chong Tang; Moxibustion.

INTRODUCTION

Pelvic inflammatory disease (PID) is a spectrum of upper genital tract infections, which happens frequently among women of reproductive age (Burstein and Workowski, 2003; Haggerty and Ness, 2008; Paavonen, 1998; Scholes *et al.*, 1996; Smith *et al.*, 2007; Sutton *et al.*, 2005; Workowski and Berman, 2010). PID is considered as serious disease burden, which need healthcare issue worldwide. Moreover, PID cause 94% women disease associated with sexually infections (including HIV) in developed countries (Rein *et al.*, 2000; Stephen and Chandra, 2006). The PID causes more serious burden of disability than the burden of HIV among men (Delia *et al.*, 1996; Jorma, 1998; Simms and Stephenson, 2000). According to its progress and clinical manifestations, PID is classified as acute or chronic types. It is reported that cases of chronic PID are nine times than acute ones by the National Centre of Health Statistics in the early 1990s (Cates *et al.*, 1990; Washington and Katz, 1991).

Treatment for the acute infection consists of antibiotics, analgesics and rest. Response to antibiotics treatment is usually rapid and effective, while the signs and symptoms often subside within a few days. However, management of chronic PID, when antibiotics have failed to alleviate the symptoms, is often a difficult problem. The antibiotic resistant and dysbacteriosis induced by antibiotics from long time treatment often make the patients suffered from recurrent, long standing chronic disease (Jaiyeoba *et al.*,

2011; Jorma, 1998; Simms and Stephenson, 2000). Different therapeutic options should be proposed in order to cure PID worldwide (Judlin, 2010).

Traditional Chinese Medicine (TCM) attracts more and more attention as an alternative treatment to cure chronic diseases, including prostatitis, diabetes, nephropathy and PID these years (Chen and Hu, 2006; Gao *et al.*, 2005; Liang *et al.*, 2006; Zhang *et al.*, 2004). It is reported in some papers that acupuncture and moxibustion were effective in the therapy of chronic PID (Wang, 1989; Woźniak and Stachowiak, 2003; Zhen, 2008).

From the view of TCM, the chronic diseases is caused by "blood stasis", which come from poor blood circulation or blood stagnation inside vessels. Therefore, the treatment principle is activating blood circulation and removing blood stasis (Lu *et al.*, 2008; Yun *et al.*, 2001; Zheng *et al.*, 2007). Chronic PID is also caused by blood stasis from the viewpoint of TCM (Cao, 2004). For the treatment of chronic PID, general treatment principles are often to expel blood stasis. TCM, which could promote blood circulation and remove stagnation in the vessels are widely studied recently (Liu *et al.*, 2007; Shen *et al.*, 2005; Zhang *et al.*, 2004). Li Chong Tang is a formula coming from a well known Chinese medicine book, Yi Xue Zhong Zhong Can Xi Lu (Records of Heart-felt Experiences in Medicine with Reference to the West) written by Zhang XiChun, which could expel blood stasis and promote blood circulation (Li, 2000; Peng and Niu, 2008).

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In this study, we investigate hemorheology of chronic PID women to elucidate the blood stasis of chronic PID in TCM with scientific methods. Moreover, an effective therapeutic method, which combined the Enema retention of Li Chong Tang with moxibustion (ERM) were applied to treat the chronic PID. Enema is thought to be efficient way to cure certain gynecological diseases though it is not a traditional TCM way. Rapid rectal assimilation of medicine, as well as the rectum closing to the site of reproductive organs, makes enema therapy as efficient way to cure uterine fibroids and chronic PID.

MATERIALS AND METHODS

Subjects

The Ethics Committee of The Affiliated Hospital to Changchun University of Chinese Medicine approved the protocol of the present study, and informed written consent was obtained from all patients. The study was conducted at The Affiliated Hospital to Changchun University of Chinese Medicine in 2014.

Sixty women at the reproductive age (21-45 years) with the diagnosis of chronic PID participated in the study. The other sixty healthy women were as normal group. The participants had undergone no antibiotic therapy or other medication that could interfere with hemorheology during the 90 day period prior to this study. Exclusion criteria were a history or presence of coronary heart diseases, renal failure, blood coagulation disorders, hypertension, stroke, thromboembolic disorders, allergic disease of unknown cause, or estrogen-dependent neoplasia. Individuals with abnormal genital bleeding of unknown cause were also excluded from the study.

The main criteria about the chronic PID were as follow:

- 1) In all cases, the diagnosis of chronic adnexitis was made by a gynecologist (gynecological examination and transvaginal ultrasonography).
- 2) All of the women have more than two years of ineffective pharmacotherapy, such as antibiotics, in their medical history.
- 3) Manifestations: Distention and cold pain in the lower abdomen during menstruation.

A system to score the severity of the disease was awarded on the basis of the signs and symptoms shown as table 1.

Composition and preparation of drug

Li Chong Tang is composed of 9 herbal or animal drugs. A mixture of these drugs was listed in table 2. The drugs were extracted with 0.5L hot water. After the extraction was condensed to 0.1L by boiling, it was filtered.

Protocol

The patients were given the extract by retention enema. The participants receiving retention enema were instructed to retain the enema for at least 2 hours and remain in the left lateral decubitus position while the

enema was retained. At the same time of enema, the moxibustion of point cv8 was conducted. Each patient was treated with above method per day (except menstrual period) for 6 weeks.

Determination of hemorheological parameters

Whole blood viscosity was measured by hemorheology auto-analyzing system. The 5.0mL blood sample per women was put into test tube with heparin (0.2mg/mL) as an anticoagulant. Whole blood viscosity at the shear rates of 200 s^{-1} , 100 s^{-1} , 30 s^{-1} and plasma viscosity (PV) were tested by MVIS-2035 hemorheology auto-analyzing system.

STATISTICAL ANALYSIS

Data were analyzed with the SPSS package (Version 11.5, SPSS Inc., US). ANOVA was employed to compare the experimental and normal groups. Paired t-test was employed to compare pre- and post-treatment of experimental group with ERM. A value of $p < 0.05$ was used as indicating statistical significance.

RESULTS

The hemorheology of chronic PID

The results of the variables of hemorheology were shown in fig.1. Compared with the normal group (9.15 ± 0.15 , 5.44 ± 0.52 and 4.33 ± 0.44), the whole blood viscosities of chronic PID at low, median and high shear rate (12.32 ± 0.31 , 6.66 ± 0.13 and 5.15 ± 0.52 , $p < 0.05$) were markedly larger. At the same time, the plasma viscosity (PV) increased from normal 1.51 ± 0.26 to 1.85 ± 0.31 ($p < 0.05$).

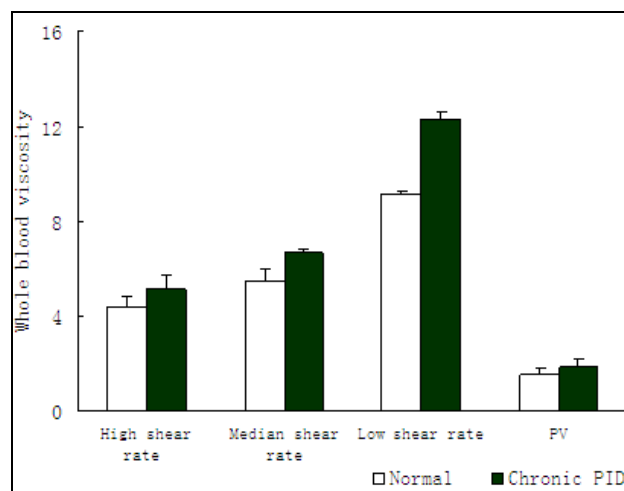


Fig. 1: The whole blood viscosities of chronic PID and normal at different shear rate ($p < 0.05$).

Effect of ERM on hemorheological parameter

After the treatment of ERM, the whole blood viscosities at low, median and high shear rate of chronic PID group

Table 1: The System to score the severity of chronic PID

Symptoms	Score
Limited movement of the uterus with tenderness	5
Cord-like oviduct and tenderness	5
Patchy thickening on one side or both sides of the uterus and tenderness	5
Falling pain in the lower abdomen and waist	3
Leucorrhagia	1
Low grade fever and fatigue	1
Abdominal pain during menstrual period	1
One additional year of illness course	0.5

Table 2: Composition of Li Chong Tang

Components Pinyin Name	Linnean Classification	Amount
Dang shen	Codonopsis Radix	6g
Huang qi	Astragali Radix	9g
Bai zhu	Atractylodis Macrocephalae Rhizoma	6g
Shan yao	Dioscoreae Rhizoma	15g
San leng	Sparganii Rhizoma	15g
E zhu	Curcumae Rhizoma	15g
Tian hua fen	Trichosanthis Radix	12g
Zhi mu	Anemarrhenae Rhizoma	12g
Ji nei jin	Endothelium Corneum Gigeriae Galli	9g

decreased from 12.32 ± 0.31 , 6.66 ± 0.13 and 5.15 ± 0.52 to the normal levels, 9.19 ± 0.13 , 5.42 ± 0.56 and 4.34 ± 0.43 ($p < 0.05$) (fig. 2). The plasma viscosity also decreased from 1.85 ± 0.31 to 1.52 ± 0.18 ($p < 0.05$).

Efficacy of ERM to treat chronic PID

The patients exhibited a significant decrease in mean score from 13.73 ± 3.7 to 3.8 ± 1.4 ($p < 0.05$) after 6 weeks therapy (fig. 3), which shows the symptoms were alleviated in an extent.

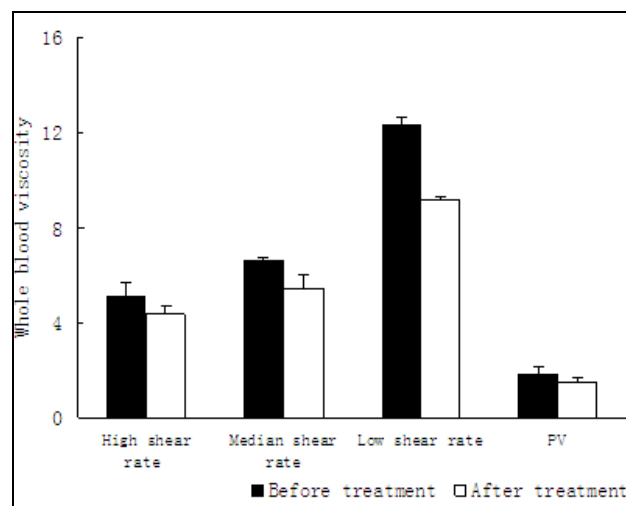


Fig. 2: The whole blood viscosities of chronic PID before and after treatment at different shear rate ($p < 0.05$).

DISCUSSION

TCM, which basic frame of theoretical system had been established more than two thousand years ago, has developed together with Chinese ancient culture. The major superiority of TCM lies in its theoretical system, literature data and clinical effect. TCM has successively improved and enriched together with scientific and technical achievements (Ma, 2006). According to theory of TCM, the chronic PID is caused by blood stasis. In this work, we tried to elucidate the blood stasis of chronic PID with modern scientific method, hemorheology. The relation of blood flow to pressure, flow volume, and blood viscosity could be revealed by hemorheology (Lu, 2008). From our work, it is shown that the chronic PID had rheological consequences in terms of the appearance of whole blood viscosities. The whole blood viscosities of chronic PID women significantly increased, which was consistent with the TCM theory, blood stasis. There is few quantity index to illustrate blood stasis in the past TCM. Through this work, it is shown that the increase of whole blood viscosities could elucidate blood stasis of chronic PID.

The treatment principle of chronic PID in TCM is to activate blood flow and remove blood stasis. Many Chinese herbal formulas with the action of promoting blood circulation and removing blood stasis have been used successfully in the past. In this study, Li Chong Tang

combined with moxibustion was applied to treat the chronic PID. The whole blood viscosity is parameter-reflecting hemorheology, which could evaluate the therapeutic efficacy in activating blood circulation and removing blood stasis. From the results, it is shown that the parameters of whole blood viscosities decreased to the normal level after therapy of ERM. At the same time of whole blood viscosities decreasing, the symptoms scores, which is a normal standard for estimation of chronic PID, decreased significantly too. The decrease of whole blood viscosities and symptoms scores shows an internal consistency as a result of alleviated chronic PID.

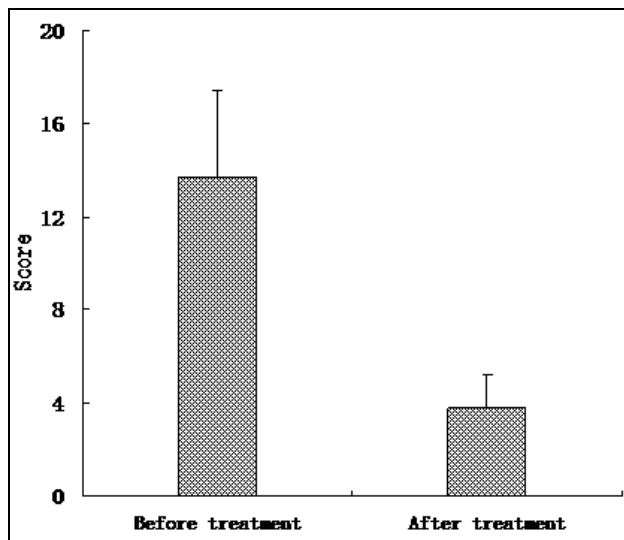


Fig. 3: Changes of scores before and after treatment with ERM ($p < 0.05$).

CONCLUSIONS

This study provides strong evidence that the blood stasis of chronic PID could be elucidated with scientific method, hemorheology. It also demonstrated that ERM is an effective therapy method to treat the chronic PID while it removes blood stasis.

REFERENCES

Burstein GR and Workowski KA (2003). Sexually transmitted diseases treatment guidelines. *Curr. Opin. Pediatr.*, **15**(4): 391-397.

Cao DN (2004). Clinical application of the empirical prescriptions for chronic pelvic inflammation. *J. Tradit. Chin. Med.*, **24**: 112-115.

Cates W, Rolfs RT and ARAL SO (1990). Sexually transmitted diseases, pelvic inflammatory disease and infertility: an epidemiologic update. *Epidemiol. Rev.*, **12**(1): 199-220.

Chen JX and Hu LS (2006). Traditional Chinese medicine for the treatment of chronic prostatitis in China: A systematic review and meta-analysis. *J. Altern.*

Complem. Med., **12**(8): 763-769.

Delia S, Andy S, Fred EH, Holly A, King KH and Walter ES (1996). Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *New Engl. J. Med.*, **334**: 1362-1366.

Gao ZQ, Deng YY, Wang L and Chen YP (2005). Researches on the establishment of chronic nephropathy models and the effect of TCM on these models. *Zhongguo Zhong. Xi. Yi. Jie. He. Za. Zhi.*, **25**(2): 186-189.

Haggerty CL and Ness RB (2008). Diagnosis and treatment of pelvic inflammatory disease. *Women's Health*, **4**: 383-397.

Jaiyeoba O, Lazenby G and Soper DE (2011). Recommendations and rationale for the treatment of pelvic inflammatory disease. *Expert Rev. Anti-Infe.*, **9**(1): 61-70.

Jorma P (1998). Pelvic inflammatory disease: From diagnosis to prevention. *Dermatol. Clin.*, **16**: 747-756.

Judlin P (2010). Current concepts in managing pelvic inflammatory disease. *Curr. Opin. Infect Dis.*, **23**(1): 83-87.

Li YD (2000). Three cases report of treatment of ovarian cyst with Li Chong Tang. *Forum on traditional Chinese medicine*, **15**: 37.

Liang XC, Guo SS and Hagino N (2006). Current status of clinical and experimental researches on cognitive impairment in diabetes. *Chin. J. Integr. Med.*, **12**(1): 68-74.

Liu RF and Yang XN (2007). Effect of Penqiangyan Granule on the immune function of patients with chronic pelvic inflammatory disease of blood-stasis and Shen-deficiency syndrome type. *Zhongguo Zhong. xi. Yi. Jie. He. Za. Zhi.*, **27**(9): 841-843.

Lu Y, Hu YL, Kong XF and Wang DY (2008). Selection of component drug in activating blood flow and removing blood stasis of Chinese herbal medicinal formula for dairy cow mastitis by hemorheological method. *J. Ethnopharmacol.*, **116**(2): 313-317.

Ma J (2006). Modern scientific technique and inheritance and innovation of TCM. *Chinese Archives of TCM.*, **24**: 5-7.

Paavonen J (1998). Pelvic inflammatory disease: from diagnosis to prevention. *Dermatol. Clin.*, **16**(4): 747-756.

Peng ZQ and Niu ZB (2008). The recent study about gynaecology theory of Zhang xi chun. *Hebei. J. TCM.*, **30**: 1221-1224.

Rein DB, Kassler W J, Irwin KL and Rabiee L (2000). Direct medical cost of pelvic inflammatory disease and its sequelae: Decreasing, but still substantial. *Obstet. Gynecol.*, **95**(3): 397-402.

Scholes D, Stergachis A, Heidrich FE, Andrilla H, Holmes KK and Stamm WE (1996). Prevention of pelvic inflammatory disease by screening for cervical chlamydial infection. *New Engl. J. Med.*, **334**(21): 1362-1366.

- Shen BQ, Situ Y, Huang JL, Su XM, He WT, Zhang MW and Chen QB (2005). A clinical study on the treatment of chronic pelvic inflammation of Qi-stagnation with blood stasis syndrome by Penyanqing capsule. *Chin. J. Integr. Med.*, **11**(4): 249-254.
- Simms I and Stephenson JM (2000). Pelvic inflammatory disease epidemiology: What do we know and what do we need to know? *Sex. Transm. Infect.*, **76**(2): 80-87.
- Smith KJ, Ness RB, Wiesenfeld HC and Roberts MS (2007). Cost-effectiveness of alternative outpatient pelvic inflammatory disease treatment strategies. *Sex. Transm. Dis.*, **34**(12): 960-966.
- Stephen EH and Chandra A (2006). Declining estimates of infertility in the United States: 1982-2002. *Fertil. Steril.*, **86**(3): 516-523.
- Sutton MY, Sternberg M, Zaidi A, Louis MES and Markowitz LE (2005). Trends in pelvic inflammatory disease hospital discharges and ambulatory visits, United States, 1985-2001. *Sex. Transm. Dis.*, **32**(12): 778-784.
- Wang XM (1989). On the therapeutic efficacy of electric acupuncture with moxibustion in 95 cases of chronic pelvic infectious disease (PID). *J. Tradit. Chin. Med.*, **9**(1): 21-24.
- Washington AE and Katz P (1991). Cost of and payment source for pelvic inflammatory disease: Trends and projections, 1983 through 2000. *Jama. J. Am. Med. Assoc.*, **266**(18): 2565-2569.
- Woźniak PR, Stachowiak GP, Pięta-Dolińska AK and Oszukowski PJ (2003). Anti-phlogistic and immunocompetent effects of acupuncture treatment in women suffering from chronic pelvic inflammatory diseases. *Am. J. Chinese Med.*, **31**(2): 315-320.
- Yun, YP, Do JH, Ko SR, Ryu SY, Kim JH, Song HC and Kim SH (2001). Effects of Korean red ginseng and its mixed prescription on the high molecular weight dextran-induced blood stasis in rats and human platelet aggregation. *J. Ethnopharmacol.*, **77**(2): 259-264.
- Zhang Q, He J, He S and Xu P (2004). Clinical observation in 102 cases of chronic pelvic inflammation treated with qi jie granules. *J. Tradit. Chin. Med.*, **24**(1): 3-6.
- Zhen HL, Wang Y and Liu XJ (2008). Observation on therapeutic effect of warming needle moxibustion on chronic pelvic inflammation of cold-damp stagnation type. *Zhongguo zhen. Jiu.*, **28**(10): 736-738.
- Zheng X, Zhao X, Wang S, Luo K, Wei Y and Zheng J (2007). Co-administration of *dalbergia odorifera* increased Bioavailability of *salvia miltiorrhizae* in Rabbits. *Am. J. Chinese Med.*, **35**(5): 831-840.