

四藤饮治疗类风湿性关节炎 123 例临床观察

许 峰* 戴小明* 章光华* 刘冠英*

摘要 目的:以清热利湿解毒、活血通络止痛为治疗原则,观察中药四藤饮治疗类风湿性关节炎(RA)的临床疗效。方法:采用中药四藤饮治疗 RA123 例,并与西药甲氨喋呤加尼美舒利治疗 67 例对照,对主要症状、体征及相关实验室检测指标治疗前后变化进行比较。结果:治疗组显效率 72.36%,总有效率 95.94%,对照组分别为 65.67%和 86.57%,两组疗效有显著性差异($P<0.05$)。两组主要临床症状、体征和实验室检测指标治疗前后变化比较,治疗组改善较对照组更为显著,且不良反应少,说明治疗组疗效优于对照组。结论:四藤饮治疗类风湿性关节炎疗效确切,不良反应少,有较好的应用与开发价值。

主题词 关节炎,类风湿/中医药疗法 @ 四藤饮

类风湿性关节炎(RA)是以慢性进行性对称性关节肿痛为主要临床表现,以关节的滑膜炎、细胞浸润、滑膜及关节骨血管翳形成,最终导致关节结构破坏,引起关节功能障碍为主要病理变化的一种常见自身免疫性疾病。因其病因未明,迄今尚无根治的方法。我们在总结多年临床经验的基础上选择以中药雷公藤、青风藤为主配方组成的四藤饮治疗 RA,并与同期采用西药甲氨喋呤(MTX)加尼美舒利(Nimesulide)治疗的病例作对照,以前瞻随机法对照进行临床观察,现将结果总结如下。

1 临床资料

1.1 病例选择:病例来源均为本院 1998~2002 年 10 月风湿病专科的门诊或住院病人。西医诊断标准参照 1987 年美国风湿病学会修正的标准^[1],中医诊断标准参照 1993 年国家卫生部《中药新药临床研究指导原则》^[2]。同时排除下列情况:18 岁以下或 65 岁以上者;合并有心、脑、血管、肝、肾和造血系统等严重原发性疾病者;持续服用激素治疗 3 个月以上者;晚期严重关节毁损、畸形、丧失劳动力者。

1.2 一般资料:190 例 RA 患者随机分为两组,治疗组 123 例,男 19 例,女 104 例,年龄 18~64 岁,平均 45.48±11.67 岁;病程 69±46 个月。对照组 67 例,男 11 例,女 56 例,年龄 18~64 岁,平均 43.16±13.36 岁,病程 58~49 个月。两组之间性别、年龄、病程经统计学处理差异均无显著性($P>0.05$),具有可比性。

2 治疗及观察方法

2.1 治疗方法:治疗组给予四藤饮(药物组成:雷公藤 15g,青风藤 20g,忍冬藤 20g,鸡血藤 30g,桑枝 30g,白芍 30g,知母 8g,露蜂房 12g,淫羊藿 15g,川芎 15g,地龙 12g,全蝎 10g,桑寄生 15g)水煎服,1 日 2 次。对照组给予甲氨喋呤 15mgd(上海信谊药业有限公司生产,批号 020701),每周 1 次加尼美舒利 0.1g(海南中瑞康芝制药有限公司生产,批号 020802)。每日 2 次。2 个月为 1 个疗程,连续治疗观察 2 个疗程。

2.2 观察指标

主要症状、体征:包括晨僵时间(min)、关节疼痛(按关节疼痛个数计数)、关节压痛(Ritchie 指数)、关节肿胀(Lansbury 指数)、关节功能(Steinbroker 分级),双手平均握力(kPa),15 米步行时间(s),以上 7 项每 10 天作 1 次观察记录。

实验室检测:血沉(ESR)、C 反应蛋白(CRP)、类风湿因子(RF)、血常规、肝功能、肾功能于治疗前及治疗后每 2 个月各查 1 次。

2.3 统计学方法:计量资料用 t 检验,组间计数资料比较采用 χ^2 检验,疗效比较用 $Ridit$ 检验。

3 治疗结果

3.1 疗效标准:参照美国风湿病学会类风湿关节炎临床缓解标准^[3],需具有下列至少 5 项,持续至少 2 个月。(1)晨僵时间不超过 15 分钟;(2)无疲乏感;(3)无关节压痛;(4)无关节痛、关节活动时痛;(5)关节或腱鞘无软组织肿胀;(6)血沉低于 30mm/h(女性)或 20mm/h(男性);有活动性血管炎表现、心包炎、胸膜炎、肌炎和(或)近期无原因的体重下降或发热者不能视为缓解。据此达 5 项及以上者为显效,达 3 项及以上者为有效,未达 3 项以下者为无效。

表 1 两组临床疗效比较[例(%)]

组别	例数	显效	有效	无效	总有效
治疗组	123	89(72.36)	29(23.58)	5(4.06)	118(95.94)
对照组	67	44(65.67)	14(20.90)	9(13.43)	58(86.57)

3.2 治疗结果

3.2.1 两组疗效比较:表 1 示,治疗组显效率 72.36%,总有效率 95.94%,而对照组分别为 65.67%和 86.57%,经 χ^2 检验两组疗效差异有显著

* 广东省江门市五邑中医院,江门市华园东路 30 号(529030)

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表 2 两组治疗前后主要症状及体征变化比较($\bar{x} \pm s$)

组别	例数	晨僵(min)	关节疼痛(个)	关节压痛(级)	关节肿胀(分)	关节功能(级)	双手平均握力(kPa)	15 米步行时间(s)
治疗组	123	97.06 ± 57.49	6.89 ± 1.46	2.01 ± 0.67	19.67 ± 9.35	2.19 ± 0.88	6.90 ± 1.56	21.93 ± 6.93
疗后	123	45.85 ± 37.97** Δ	2.08 ± 1.43**	0.95 ± 0.64** Δ	2.35 ± 6.45** Δ	0.84 ± 0.50**	14.01 ± 3.72** Δ	16.79 ± 4.15**
对照组	67	92.33 ± 46.53	6.99 ± 1.55	2.18 ± 0.6	17.22 ± 7.33	1.88 ± 0.52	6.78 ± 1.51	21.96 ± 6.26
疗后	67	57.13 ± 34.53**	2.11 ± 1.42**	1.35 ± 0.77**	8.99 ± 7.76**	1.46 ± 0.68	11.38 ± 3.39**	18.31 ± 11.73*

与本组治疗前比较, * $P < 0.05$, ** $P < 0.01$; 与对照组治疗后比较, $\Delta P < 0.05$, $\Delta\Delta P < 0.01$ 。下表同

表 3 两组治疗前后实验室检测指标变化比较($\bar{x} \pm s$)

组别	例数	RF(log)	ESR(mm/h)	CRP(mg/L)
治疗组	123	2.4 ± 0.4	56.03 ± 14.16	27.51 ± 13.16
疗后	123	1.6 ± 0.4** Δ	20.67 ± 3.14** Δ	10.70 ± 5.16** Δ
对照组	67	2.4 ± 0.3	53.60 ± 15.42	26.67 ± 14.07
疗后	67	1.8 ± 0.6**	28.65 ± 3.52**	18.87 ± 6.40**

性($P < 0.05$),说明中药四藤饮方药治疗 RA 疗效优于西药甲氨喋呤加尼美舒利。

3.2.2 两组主要临床症状、体征和实验室检测指标治疗前后变化比较:表 2 示,治疗组 7 项主要症状、体征治疗后均较治疗前有改善(P 均 < 0.01),对照组除关节功能分级改善不显著,其余症状体征也有明显改善($P < 0.05$ 或 $P < 0.01$),但治疗后两组比较,除关节疼痛和 15 米步行时间外,其余差异均有显著性($P < 0.05$ 或 $P < 0.01$),治疗组优于对照组。表 3 示,两组治疗后 RF、ESR、CRP 均显著下降(P 均 < 0.01),但治疗组明显优于对照组($P < 0.01$)。

3.2.3 不良反应:治疗组有 20 例出现厌食和消化不良,无转氨酶升高和白细胞减少发生,不良反应发生率为 16.3%,而对照组有 27 例分别出现厌食、腹胀、腹痛、转氨酶升高,白细胞减少,其中转氨酶升高 8 例(11.9%),白细胞减少 4 例(5.9%),不良反应发生率为 40.3%,说明治疗组安全性明显优于对照组($P < 0.01$)。

4 讨论

RA 属中医“痹证”范畴,历代医家又有称为“历节病”、“顽痹”、“骨痹”等,当代著名中医风湿病专家焦树德教授根据其发病及临床特征,引经据典,定中医病名为“尪痹”。其病因病机多为先天禀赋不足,正气亏虚或后天失养,腠理不固,“风、寒、湿三气杂至,合而为痹”。本虚标实是本病的病机特点,本虚为气血、阴阳、脏腑亏损,标实为外受风寒湿热之邪,内生痰浊瘀血之患。尤其是岭南之地,临海多山,气候潮湿、闷热,风湿之邪多从热化,风湿热毒乘虚而入,痹阻于肌肉、筋骨、经络之间,湿遏热阻,气血不畅,日久则成痰瘀互结,深入骨髓而发为“尪痹”。所以在治疗上我们以清热利湿解毒、活血通络止痛为主,重用雷公藤清热解毒、通络止痛,

青风藤祛风除湿、镇痛消肿,合忍冬藤、桑枝清热利湿、通经活络以缓解关节红肿热痛;配伍川芎、鸡血藤、地龙、全蝎、露蜂房活血逐瘀、通络止痛以改善关节晨僵、屈伸不利;桑寄生、淫羊藿、白芍、知母补益肝肾,养筋壮骨以防止关节骨蚀筋萎。上肢痛为主酌加羌活、片姜黄;湿甚、四肢困重加苍术、防己、土茯苓、威灵仙;久痛不缓加白芥子、制乳香、没药、土鳖虫;脾虚纳差加砂仁、白术、党参。其中雷公藤作为抗风湿主要药物,其免疫抑制作用已被许多研究证实^[4]。它既可活化 CD₃ 细胞促其增生,又可抑制 CD₄ 细胞及 B 细胞的功能,使 CD₄/CD₈ 比值降低。雷公藤还能激活 NK 细胞、巨噬细胞及促使干扰素分泌,所以其抗炎作用表现在对炎性细胞趋化、血小板聚集、前列腺素生成和其他炎症介质释放及纤维组织增生均有不同程度抑制作用。对 RA 患者关节疼痛、晨僵、抑制关节血管翳形成,骨质破坏都有较好的治疗效果。雷公藤的主要不良反应表现在胃肠道不适、抑制骨髓生长和生殖腺分泌,这可能与单纯使用雷公藤提取物或药物剂量、配伍有关。我们采用复方配伍治疗 123 例 RA,除少量胃肠道不适外,未出现造血和生殖系统的不良反应。青风藤主要含青藤碱,为吗啡结构类药物,具有吗啡类药物所具有的药理作用^[5],镇痛作用明显,但无成瘾性,此外还具有抗炎、降压等作用。西医目前治疗 RA 主要以消炎镇痛和免疫抑制剂类药物合用,有一定的治疗效果^[6],我们在辨证施治的基础上选用四藤饮组方治疗 RA 疗效明显优于西药,而且不良反应少,说明中医药治疗 RA 疗效确切,值得进一步研究,推广使用。

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ABSTRACTS FROM ORIGINAL ARTICLES

Clinical observation on 102 cases of alcoholic fatty liver treated with Juge Yigan Decoction

Jia Jingpeng, Jiang Sen

Objective: To explore the ideal method to treat alcoholic fatty liver. **Methods:** 102 cases of alcoholic fatty liver were treated with Juge Yigan Decoction as treatment group, and the effect was compared with control group. **Results:** Effect of treatment group was superior to that of control group. Clinically cured rate, effective rate and ineffective rate in treatment group were 74.5%, 21.6% and 3.9% respectively, superior to 31.6%, 56.1% and 12.3% in control group. There was significant difference between two groups ($P < 0.01$). **Conclusion:** Juge Yigan Decoction is an ideal choice for treatment of alcoholic fatty liver.

Author's address: First People's Hospital of Yaodu District, Linfen City, Shanxi Province, Shanxi 041000

Key Words: Fatty liver, alcoholic/TCM therapy

(Original article on page 750)

Clinical observation on 123 cases of rheumatoid arthritis treated with Sitengyin

Xu Feng, Dai Xiaoming, Zhang Guanghua, et al.

Objective: To observe the effect of Sitengyin on rheumatoid arthritis (RA). **Methods:** 123 cases of RA were treated with Sitengyin, and 67 cases were given Methotrexate and Nimesulide as control. Main symptoms, signs and results of related laboratory tests were compared between two groups before and after treatment. **Results:** Markedly effective rate and total effective rate of treatment group were 72.36% and 95.94% respectively, and those of control group were 65.67% and 86.57%. There was significant difference in efficacy between the two groups ($P < 0.05$). Compared with control group, improvement of main symptoms, signs and results of laboratory tests of treatment group was more remarkable with less side-effect, indicating that efficacy of treatment group was superior to that of control group. **Conclusion:** Sitengyin is definitely effective in treatment of RA, with less side-effect. It is of great value of application and development.

Author's address: Wuyi TCM Hospital of Jiangmen City, Guangdong Province, Guangdong 529030

Key Words: Arthritis, rheumatoid/TCM therapy

(Original article on page 760)

Experimental study on fluorescence histochemistry and ultra-microstructure changes of cardiac muscle of model rats with heart deficiency syndrome

Liu Liqing, Zhou Shengnian

Objective: To observe the effect of heart deficiency syndrome on microstructure and ultra-microstructure of cardiac muscle cells.

Methods: Healthy rats were randomly divided into model group and control group. For model group, cardiac muscle was taken respectively after 48 hours and 72 hours to make frozen slices and ultra-filmy slices. Fluorescence and electric microscope were used to observe changes of distribution, content and ultra-microstructure of heparin and DNA within cardiac muscle cells. **Results:** After 48 hours, fluorescence PAS reaction of cardiac muscle cells of model group reduced significantly, and after 72 hours, electropositive matters in DAN fluorescence reaction was much less than that of control group. Based on tridimensional and quantificational analysis, there was significant difference in chondriosome density between two groups ($P < 0.01$). **Conclusion:** Syndrome of heart deficiency could result in injury of cardiac muscle cells and affect metabolism of cardiac muscle and structure of cardiac muscle cells.

Author's address: Teaching and Research Department of Histology and Embryology, Shandong University of TCM, Jinan 250014

Key Words: Heart deficiency syndrome/pathology, cardiac muscle/ultra-microstructure

(Original article on page 775)

Effect of Xianqi Decoction on bone mass density, IL-6 and plasma acid phosphatase in experimental osteoporosis rats

Zhang Lijun, Zhang Yan, Xu Qian, et al.

Objective: To investigate the effect of Xianqi Decoction on experimental osteoporosis of rats and its mechanism. **Methods:** 72 female SD rats aged 7 months were randomly divided into two groups, i. e. 60 for operation group, 12 for sham-operation group. Bilateral ovariectomy was performed on operation group. 2 months later, postmenopausal osteoporosis model rats were successfully established. Rats in operation group were randomly divided into model group, western medicine group, Xianqi Decoction low dose group, middle dose group and high dose group. Total six groups were given corresponding medicine by intragastric perfusion. 60 days later, rats were sacrificed after taking blood sample. Serum IL-6, plasma acid phosphatase (ACP) and bone mass density of vertebra and femur were determined. **Results:** Compared with model group, IL-6 and ACP level in three Xianqi Decoction groups was significantly reduced ($P < 0.05$ or $P < 0.01$), and there was no significant difference among Xianqi Decoction groups and western medicine group. Bone mass density in all drug-administered groups was increased ($P < 0.05$).

Author's address: Out Clinic of Hubei College of TCM, Wuhan 430061

Key Words: Osteoporosis/TCM therapy, Bone mass density/drug effect

(Original article on page 780)