

doi: 10.13241/j.cnki.pmb.2017.14.015

## 丹葵片治疗老年性主动脉瓣狭窄的临床疗效分析\*

陈芳<sup>1</sup> 孙洁<sup>1</sup> 司春婴<sup>2</sup> 高爱社<sup>1</sup> 孙续鹏<sup>1</sup> 朱中玉<sup>3Δ</sup>

(1 河南中医药大学基础医学院病理与病理生理教研室 河南 郑州 450016;

2 河南中医药大学第一附属医院心内科 河南 郑州 450000; 3 河南省人民医院心内科 河南 郑州 450007)

**摘要 目的:**探讨丹葵片对老年性主动脉瓣狭窄患者临床疗效及血清炎症因子水平的影响。**方法:**选取老年性主动脉瓣钙化患者共34例,将其随机分为丹葵片治疗组(22例)及对照组(12例)。根据西雅图心绞痛问卷中文版、SF-36生活质量量表、中医临床证候评分比较两组的治疗效果,ELISA检测治疗前后患者血清肿瘤坏死因子 $\alpha$ (TNF- $\alpha$ )、白介素6(IL-6)及同型半胱氨酸(HCY)的水平。**结果:**丹葵片治疗组患者心绞痛程度及治疗满意度较常规治疗组均有明显统计学差异,丹葵片可提高病人生活质量,改善中医部分证候,减轻血清炎症因子表达。**结论:**丹葵片或可减缓主动脉瓣钙化进展,其原因可能和炎症反应减轻有关。

**关键词:**丹葵片;老年性主动脉瓣狭窄;炎症因子

**中图分类号:**R542.52;R242 **文献标识码:**A **文章编号:**1673-6273(2017)14-2666-05

## Analysis of the Therapeutic Effect of Dan Lou Tablet on the Degenerative Aortic Calcification in Elderly Patients\*

CHEN Fang<sup>1</sup>, SUN Jie<sup>1</sup>, SI Chun-ying<sup>2</sup>, GAO Ai-she<sup>1</sup>, SUN Xu-peng<sup>1</sup>, ZHU Zhong-yu<sup>3Δ</sup>

(1 Department of pathology and pathophysiology, Henan University of TCM, Zhengzhou, Henan, 450016, China;

2 Department of cardiology, First Affiliated Hospital of Henan University of TCM, Zhengzhou, Henan, 450000, China;

3 Department of cardiology, Henan Provincial Peoples' Hospital, Zhengzhou, Henan, 450007, China)

**ABSTRACT Objective:** To investigate the effect of Dan Lou tablet on the efficacy and expression of serum inflammatory factors in elderly patients with degenerative aortic calcification. **Methods:** A total of 34 cases of aortic valve calcification patients were randomly divided into two groups, the treatment group and the control group, 22 patients in Dan Lou tablet group, 12 patients in the control group. The efficacy was compared between two groups according to the Seattle angina questionnaire in Chinese version, SF-36 scale of quality of life, TCM clinical syndrome score. The serum TNF- $\alpha$ , IL-6 and HCY levels were detected by ELISA before and after treatment. **Results:** The improvement of angina pectoris degree and the degree of satisfaction were superior in the treatment group than those of the control group, Dan Lou Tablet could enhance the quality of life, improve syndrome and reduce serum inflammatory factors levels of patients. **Conclusions:** Dan Lou tablet could slow down the progression of aortic valve calcification, which might be related to attenuate the inflammation.

**Key words:** Dan Lou Tablet; Degenerative aortic valve stenosis; Inflammatory cytokines

**Chinese Library Classification(CLC):** R542.52; R242 **Document code:** A

**Article ID:** 1673-6273(2017)14-2666-05

### 前言

老年性主动脉瓣狭窄属老年退行性心脏瓣膜病,是老年心血管疾病致死和致残的重要原因之一<sup>[1]</sup>。目前认为该病是一种与年龄相关的主动脉瓣结缔组织退行性变、纤维化或钙化引起的瓣膜及支架的功能异常性疾病,其发病机制同动脉粥样硬化高度类似,亦是一个慢性炎症过程<sup>[2-3]</sup>。目前该病仍以外科手术治疗为主,手术治疗创伤大、风险较高,且对有明确手术禁忌症患者,现代医学暂无有效药物治疗手段<sup>[4]</sup>,故深入研究中医药对老年性主动脉瓣狭窄患者的作用具有积极意义<sup>[5]</sup>。丹葵片是广泛应用于临床的一类中成药,其作用不仅局限于冠心病的预防

及治疗,还被广泛应用于心、脑、肺等多相关学科<sup>[4,5]</sup>。本研究根据老年性主动脉瓣疾病病理变化特点及瓣膜病性心绞痛的临床特征,观察丹葵片对老年性主动脉瓣狭窄患者疗效及血清炎症因子表达的影响。

### 1 材料与方法

#### 1.1 研究对象

选取2015年7月至2016年7月在河南中医药大学第一附属医院心内科及河南省人民医院心内科住院老年性主动脉瓣钙化病人共34例。随机分为丹葵片治疗组及对照组,丹葵片治疗组22例,对照组12例,病人详细资料及用药情况见表1,

\* 基金项目:河南省高等学校重点科研项目(16A310027);河南中医药大学博士启动基金项目(BSJJ 2015-01)

作者简介:陈芳,女,讲师,从事中医药防治心血管疾病研究,电话:15238353068, E-mail: lotusflake2004@163.com

Δ 通讯作者:朱中玉, E-mail: zhongyuzhu@live.cn

(收稿日期:2016-09-26 接受日期:2016-11-08)

所有病人入组前均签署知情同意书,请心外科会诊后病人本人要求暂使用药物保守治疗,丹莪片治疗组给予常规治疗药物及丹莪片(吉林康奈尔公司,1.5 g/次,每日2次)口服治疗,对照组仅使用常规治疗药物。入组患者常规询问病史后进行临床资料

统计,结果显示两组患者的性别、年龄、危险因素、心脏功能及主动脉瓣口狭窄程度等各个指标均未见明显差异 ( $P>0.05$ ),具有可比性(见表1)。

表1 两组患者基本临床资料比较( $\bar{x}\pm s$ )

Table 1 Comparison of the clinical characteristics of patients with calcific aortic valve between two groups

|                                     | CAVS patients with Dan Lou Tablet | Control subjects | P value |
|-------------------------------------|-----------------------------------|------------------|---------|
| Patients (n)                        | 22                                | 12               |         |
| Age(years)                          | 65± 2.2                           | 63± 4.5          | >0.05   |
| Male gender                         | 14                                | 7                | >0.05   |
| Risk factors                        |                                   |                  |         |
| Hypertension                        | 5                                 | 2                | >0.05   |
| Diabetes mellitus                   | 1                                 |                  | >0.05   |
| Renal disease                       | 0                                 | 0                | >0.05   |
| Tobacco use                         | 7                                 | 4                | >0.05   |
| Laboratory parameters               |                                   |                  |         |
| Total Cholesterol (mg/dl)           | 162± 15.2                         | 157± 16.5        | >0.05   |
| HDL (mg/dl)                         | 42± 3.7                           | 40± 4.1          | >0.05   |
| LDL(mg/dl)                          | 110± 12.5                         | 108± 11.6        | >0.05   |
| Medications                         |                                   |                  |         |
| Statins                             | 22                                | 12               | >0.05   |
| ACEi/ARB                            | 20                                | 11               | >0.05   |
| β-blocker                           | 20                                | 11               | >0.05   |
| Echocardiographic parameters        |                                   |                  |         |
| LVEF(%)                             | 58± 10.3                          | 60± 11.5         | >0.05   |
| Transvalvular gradient(mmHg)        | 48± 6.5                           | 46± 5.0          | >0.05   |
| Aortic valve area(cm <sup>2</sup> ) | 1.2± 0.5                          | 1.4± 0.3         | >0.05   |

## 1.2 诊断标准及排除标准

老年性主动脉瓣狭窄超声诊断标准依据2012年ESC《心脏瓣膜疾病治疗指南》纳入:根据主动脉瓣射流速度、平均跨瓣压差、有效瓣口面积、速度比等进行评价<sup>[6,7]</sup>,选取中、重度主动脉瓣狭窄的60岁以上人群分组进行,具体评价标准:主动脉射流速度:3.0-4.0或>4.0 m/s;平均跨瓣压差30-50或>50 mmHg;速度比0.25-0.5或<0.25;有效瓣口面积1.0-1.5或<1.0 cm<sup>2</sup><sup>[7]</sup>。

排除标准:风湿性心脏病、先天性心脏病、肺源性心脏病、胶原病、梅毒及感染性心内膜炎<sup>[7]</sup>等所致的瓣膜病变;贫血、甲状腺及甲状旁腺功能异常等代谢性的疾病<sup>[7]</sup>;自身免疫性疾病病史;近3月内有感染及抗生素使用史<sup>[7]</sup>。

## 1.3 临床疗效评价

1.3.1 心绞痛发作情况临床评估 两组患者均于治疗开始及治疗4周后对心绞痛发作的诱因,持续时间,发作频率等进行评估。结合西雅图心绞痛问卷中文版(Seattle Angina Questionnaire)从体力活动受限程度、心绞痛稳定性、心绞痛发作频率、治疗满意度及主观感受等5个方面对心绞痛严重程度进行临

床评估,总分为100分,评分越高,心绞痛控制情况越好。

1.3.2 生活质量评估 治疗前后采用中文版36条目简明健康调查量表(36 items short form health survey, SF-36)评定患者生活质量,从躯体功能、社会功能、角色受限程度、心理健康、角色心理、躯体疼痛感、精力、及综合健康等8个领域综合评估,总分100分,评分越高,生活质量越好。

1.3.3 中医临床证候评分 参照《现代中医临床诊断学》比较两组治疗前后中医临床证候评分,中医证候包括:胸闷、胸痛、持续时间、发作频率及气短、疲乏、心悸、自汗、证候等<sup>[6]</sup>的总评分,每单项满分5分<sup>[6]</sup>。

1.3.4 血脂及炎症指标检测 对所有入选患者入院时抽取空腹肘静脉血,由医院检验科进行血脂检测,详见表1,治疗开始及治疗4周后采取清晨空腹肘静脉采血,测定患者血清炎症因子,所抽出血液注入抗凝管混合后离心3000 rpm,15 min。离心后取上清液血清应用ELISA法检测炎症指标,包括人肿瘤坏死因子α(TNF-α),同型半胱氨酸(HCY)及白介素-6(IL-6)等。TNF-α, IL-6试剂盒购自武汉博士德公司,HCY试剂盒购自美

国 R&D 公司,操作依据说明书进行。

#### 1.4 统计学分析

所有统计分析资料均采用 SPSS13.0 软件进行,所有计量数据采用  $\bar{x} \pm s$  表示,组间分析应用 student-t 检验,所有计数资料采用卡方检验,以  $P < 0.05$  为差异有统计学意义。

## 2 结果

### 2.1 两组心绞痛发作情况临床评估的比较

应用西雅图心绞痛评分标准对两组患者的心绞痛程度进行评估,结果显示两组患者活动受限程度、心绞痛稳定性、心绞痛发作频率、治疗满意度及主观感受评分均较对照组明显升高,且丹莪片治疗组以上指标明显高于对照组,差异均具有统计学意义( $P < 0.05$ ),提示丹莪片可有效缓解老年性主动脉瓣狭窄患者的心绞痛症状,提升患者的治疗满意度。

表 2 两组患者治疗前后西雅图心绞痛评分比较( $\bar{x} \pm s$ )

Table 2 Comparison of the Score of Seattle angina pectoris between two groups before and after treatment

| Indexes                | CAVS patients with Dan Lou Tablet |                          | Control subjects |                 |
|------------------------|-----------------------------------|--------------------------|------------------|-----------------|
|                        | Before treatment                  | After treatment          | Before treatment | After treatment |
| Physical limitations   | 30.2± 5.8                         | 71.4± 6.3*               | 30.5± 6.5        | 68.4± 7.1*      |
| Stablility of AP       | 45.3± 4.1                         | 74.6± 2.5** <sup>#</sup> | 44.5± 3.0        | 73.1± 6.3*      |
| Frequency of AP        | 43.3± 2.8                         | 69.8± 5.2*               | 40.4± 3.3        | 61.0± 2.8       |
| Treatment satisfaction | 29.8± 4.5                         | 58.8± 4.3** <sup>#</sup> | 30.5± 1.7        | 49.6± 6.2*      |
| Subjective feeling     | 35.0± 5.2                         | 72.5± 3.5** <sup>#</sup> | 35.5± 2.8        | 55.6± 4.8*      |

Note: \* $p < 0.05$ , \*\* $p < 0.01$  vs. before treatment; <sup>#</sup> $P < 0.05$  vs. control group subjects; AP=angina pectoris.

### 2.2 两组治疗前后生活质量比较

应用 SF-36 量表进行治疗前后两组的生活质量评估,结果显示两组患者治疗后躯体功能、社会功能、角色受限程度、心理健康、角色心理、躯体疼痛感、精力及综合健康评分均明显高于

治疗前,且丹莪片治疗组以上指标明显高于对照组,差异均具有统计学意义( $P < 0.05$ ),提示丹莪片可有效提高老年性主动脉瓣狭窄患者的生活质量,改善患者体力活动受限程度及减轻躯体痛苦。

表 3 两组治疗前后生活质量 SF-36 评分量表结果比较( $\bar{x} \pm s$ )

Table 3 Comparison of the SF-36 sale score bewteen two groups before and after treatment ( $\bar{x} \pm s$ )

| Indexes              | CAVS patients with Dan Lou Tablet |                          | Control subjects |                 |
|----------------------|-----------------------------------|--------------------------|------------------|-----------------|
|                      | Before treatment                  | After treatment          | Before treatment | After treatment |
| Physical function    | 61.2± 1.8                         | 73.2± 3.4*               | 62.2± 1.8        | 71.2± 3.4       |
| Role Limitation      | 46.3± 2.1                         | 51.2± 6.6                | 46.3± 2.2        | 50.2± 2.6       |
| Social Function      | 71.2± 3.5                         | 71.8± 5.3                | 71.2± 3.4        | 71.8± 4.2       |
| Mental healthness    | 66.2± 3.5                         | 70.2± 4.1                | 64.2± 5.1        | 66.2± 7.0       |
| Body Pain            | 42.5± 8.6                         | 77.3± 6.5** <sup>#</sup> | 40.1± 5.6        | 55.3± 2.1*      |
| Vigour               | 63.0± 2.5                         | 75.4± 3.8*               | 66.0± 2.5        | 72.6± 4.5*      |
| Psychological status | 67.5± 3.5                         | 72.5± 4.5                | 68.5± 3.5        | 69.5± 5.6       |
| Total heathness      | 63.5± 2.6                         | 73.1± 4.5** <sup>#</sup> | 61.0± 2.6        | 66.1± 4.5*      |

Note:\* $P < 0.05$  vs. before treatment; <sup>#</sup> $P < 0.05$  vs. control group subjects.

### 2.3 两组治疗前后中医临床证候评分比较

根据胸闷痛程度、时间及有无气短、疲乏等伴随症状对两组患者治疗前后评分进行对比,结果显示两组患者治疗后胸闷、胸痛、持续时间、发作频率及气短、疲乏、心悸、自汗、证候评分均较治疗前显著降低,且丹莪片治疗组以上指标明显低于对照组,差异均具有统计学意义( $P < 0.05$ ),提示丹莪片在改善老年性主动脉瓣狭窄患者心悸、乏力、自汗等症状上更有优势,明显改善证候总评分<sup>[6]</sup>。

### 2.4 两组治疗前后血清 TNF- $\alpha$ 、IL-6 及 HCY 水平比较

两组患者经过治疗后血清 TNF- $\alpha$ 、IL-6 及 HCY 水平均较治疗前不同程度下降,但对照组改变无明显统计学意义,而丹莪片治疗组血清 TNF- $\alpha$ 、HCY 水平较治疗前显著降低,且血清 HCY 水平显著低于对照组,差异具有统计学意义( $P < 0.05$ )。

## 3 讨论

老年性主动脉瓣狭窄是一类退行性瓣膜病变<sup>[1]</sup>,随年龄增长,病程延长,主动脉瓣狭窄逐步加剧,引起左室肥厚,出现冠脉血流量相对减少所致对应心肌供氧不足,从而导致心内膜下

表 4 两组治疗前后中医临床症状评分比较( $\bar{x} \pm s$ )Table 4 Comparison of the score of clinical symptoms of traditional chinese medicine before and after treatment( $\bar{x} \pm s$ )

| Indexes                 | CAVS patients with Dan Lou Tablet |                 | Control subjects |                 |
|-------------------------|-----------------------------------|-----------------|------------------|-----------------|
|                         | Before treatment                  | After treatment | Before treatment | After treatment |
| Chest tightness         | 4.1± 0.5                          | 3.3± 0.4        | 4.2± 0.4         | 3.5± 0.4        |
| Chest pain              | 4.1± 0.3                          | 3.6± 0.4        | 4.1± 0.3         | 3.7± 0.3        |
| Duration of Chest pain  | 3.1± 1.0                          | 2.0± 0.3*       | 3.2± 0.8         | 2.1± 0.3*       |
| Frequency of Chest pain | 2.5± 0.3                          | 2.0± 0.4        | 2.3± 0.3         | 2.1± 0.4        |
| Breathless              | 2.1± 0.4                          | 1.1± 0.1*       | 2.4± 0.9         | 1.7± 0.1        |
| Tiredness               | 2.4± 0.2                          | 1.1± 0.2**      | 2.3± 0.4         | 1.8± 0.2        |
| Heart palpitation       | 1.6± 0.3                          | 0.4± 0.2**      | 1.8± 0.5         | 1.4± 0.3        |
| Sweating                | 1.7± 0.2                          | 0.5± 0.2**      | 1.7± 0.2         | 1.5± 0.2        |
| Total Score             | 21.6± 0.3                         | 14.1± 0.2**     | 22.3± 0.6        | 15.8± 0.3*      |

Note: \*P<0.05 vs. before treatment; \*\*P<0.05 vs. control group subjects.

表 5 两组治疗前后血清 TNF- $\alpha$ 、IL-6 及 HCY 水平比较( $\bar{x} \pm s$ )Table 5 Comparison of the serum TNF- $\alpha$ , IL-6 and HCY levels between two groups before and after treatment( $\bar{x} \pm s$ )

| Indexes                | CAVS patients with Dan Lou Tablet |                 | Control subjects |                 |
|------------------------|-----------------------------------|-----------------|------------------|-----------------|
|                        | Before treatment                  | After treatment | Before treatment | After treatment |
| TNF- $\alpha$ (pmol/L) | 38.2± 4.8                         | 31.4± 3.2*      | 37.2± 4.5        | 34.4± 8.2       |
| IL-6(ng/L)             | 28.3± 4.1                         | 29.6± 1.5       | 30.5± 2.3        | 31.4± 3.3       |
| HCY(umol/L)            | 19.3± 2.6                         | 16.2± 1.1**     | 20.4± 2.1        | 19.0± 3.8       |

\*P<0.05 vs. before treatment; \*\*P<0.05 vs. control group subjects.

缺血和心绞痛的发生<sup>[1]</sup>。而该心绞痛使用硝酸酯类制剂可能会出现晕厥及恶性心律失常、甚至心源性猝死,目前尚无较好的控制方法<sup>[7-9]</sup>。导致出现心绞痛主要病因是因为主动脉瓣狭窄导致的一系列病理生理变化。现代医学研究普遍认为老年性退行性钙化性主动脉瓣膜疾病也是慢性、积极的炎症反应过程,从病理组织学特征角度该病与动脉粥样硬化具有诸多相似之处,推测其发生机制可能和瓣膜损伤及继发炎症反应有关。病理组织学观察结果显示正常主动脉瓣几乎无炎性细胞存在,而狭窄瓣膜早期可观察到以巨细胞、致粥样硬化特征性的泡沫样巨噬细胞及淋巴细胞浸润,进展期可观察到大量的淋巴细胞、肥大细胞浸润等病理特征。而上述细胞均可分泌大量细胞因子及炎症因子,因此血清炎症因子、血栓因子等细胞因子在病变的发展中起重要作用,这些指标升高是主动脉瓣狭窄进行性加重的表现<sup>[10-13]</sup>。

丹菱片是临床常用成药,主要用于胸痹心痛因痰瘀互结而起等病症。丹菱片方剂主要由瓜蒌皮、薤白、丹参、黄芪、葛根、川芎、赤芍、泽泻、骨碎补、郁金等构成<sup>[14]</sup>,其方中瓜蒌化痰理气,薤白豁痰通阳;丹参、赤芍、葛根和川芎等活血化瘀,通络止痛<sup>[15-17]</sup>;黄芪可益气温阳<sup>[17]</sup>;泽泻健脾渗湿;郁金、骨碎补取由肾补心之要<sup>[17]</sup>,以上诸药共奏宽胸通阳、化痰散结、活血化瘀之奇效。因老年性主动脉瓣狭窄导致心绞痛发病机与动脉粥样硬化类似,故应用丹菱片治疗老年性主动脉瓣狭窄具有一定的中医理论根据<sup>[15-17]</sup>。

现代药理学研究表明瓜蒌提取物能够提高心肌耐缺氧能力、发挥清除氧自由基等作用,黄芪、薤白、葛根、川芎、丹参可以扩张冠状动脉周围血管增加冠脉血流量、降低心肌耗氧量,减轻心绞痛症状,减轻炎症反应<sup>[18-20]</sup>。本研究中,应用丹菱片治疗的老年性主动脉瓣狭窄病人心绞痛症状发作情况、中医症候评分、生活质量均显著提高;同时,患者血清炎症因子水平也分别是 Hcy、TNF- $\alpha$  水平在使用丹菱片后均下降,提示丹菱片或可减缓主动脉瓣钙化进展,其原因可能和炎症反应减轻有关,具体机制仍有待进一步研究。

#### 参考文献(References)

- [1] Somers P, Knaapen M, Mistiaen W. Histopathology of calcific aortic valve stenosis[J]. Acta cardiologica, 2006, 61(5): 557-562
- [2] Rajamannan N M, Subramaniam M, Rickard D, et al. Human aortic valve calcification is associated with an osteoblast phenotype [J]. Circulation, 2003, 107(17): 2181-2184
- [3] Schoen F J, Levy R J. Calcification of tissue heart valve substitutes: progress toward understanding and prevention [J]. The Annals of thoracic surgery, 2005, 79(3): 1072-1080
- [4] Dougherty C M, Dewhurst T, Nichol W P, et al. Comparison of three quality of life instruments in stable angina pectoris: Seattle angina questionnaire, short form health survey (SF-36), and quality of life index-cardiac version III [J]. Journal of clinical epidemiology, 1998, 51(7): 569-575
- [5] Wang G, Wang L, Xiong Z Y, et al. Compound salvia pellet, a

- traditional Chinese medicine, for the treatment of chronic stable angina pectoris compared with nitrates: a meta-analysis [J]. Medical Science Monitor, 2005, 12(1): SR1-SR7
- [6] He Q, Wang J, Zhang Y, et al. Effect of Yiqi Yangyin Decoction on the quality of life of patients with unstable angina pectoris[J]. Chinese journal of integrative medicine, 2010, 16: 13-18
- [7] Venardos N, Nadlonek N A, Zhan Q, et al. Aortic valve calcification is mediated by a differential response of aortic valve interstitial cells to inflammation[J]. journal of surgical research, 2014, 190(1): 1-8
- [8] Weiss R M, Lund D D, Chu Y, et al. Osteoprotegerin inhibits aortic valve calcification and preserves valve function in hypercholesterolemic mice[J]. PLoS One, 2013, 8(6): e65201
- [9] Cai Z, Li F, Gong W, et al. Endoplasmic reticulum stress participates in aortic valve calcification in hypercholesterolemic animals [J]. Arteriosclerosis, thrombosis, and vascular biology, 2013, 33 (10): 2345-2354
- [10] Mahler G J, Farrar E J, Butcher J T. Inflammatory cytokines promote mesenchymal transformation in embryonic and adult valve endothelial cells [J]. Arteriosclerosis, thrombosis, and vascular biology, 2013, 33(1): 121-130
- [11] Leopold J A. Cellular mechanisms of aortic valve calcification[J]. Circulation: Cardiovascular Interventions, 2012, 5(4): 605-614
- [12] Afsar C U, Uzun H, Yurdakul S, et al. Association of serum fetuin-A levels with heart valve calcification and other biomarkers of inflammation among persons with acute coronary syndrome [J]. Clinical & Investigative Medicine, 2012, 35(4): 206-215
- [13] Chen Y, Zhang M, Mao S, et al. GW26-e2219 Danlou Tablet Decreases Cytokine IFN- $\gamma$  and Attenuates the Progression of Atherosclerosis [J]. Journal of the American College of Cardiology, 2015, 66(16\_S)
- [14] Chen J, Cai H W, Miao J, et al. Danlou Tablet Fought against Inflammatory Reaction in Atherosclerosis Rats with Intermingled Phlegm and Blood Stasis Syndrome and Its Mechanism Study [J]. Zhongguo Zhong xi yi jie he za zhi, 2016, 36(6): 703
- [15] Wang L, Mao S, Qi J, et al. Effect of Danlou Tablet on periprocedural myocardial injury among patients undergoing percutaneous coronary intervention for non-ST elevation acute coronary syndrome: A study protocol of a multicenter, randomized, controlled trial [J]. Chinese journal of integrative medicine, 2015, 21: 662-666
- [16] Ruizhen J, Chenghong Y, Zhiqing H, et al. GW24-e1008 the hypolipidaemic activity of danlou tablet extract in triton WR-1339 induced hyperlipidaemic rats: a comparison with rosuvastatin [J]. Heart, 2013, 99(Suppl 3): A90-A91
- [17] Guo L L, Wang J, Lin F, et al. Effect of danlou tablet on arrhythmia model rats induced by transient myocardial ischemia/reperfusion[J]. Zhongguo Zhong xi yi jie he za zhi Zhongguo Zhongxiyi jiehe zazhi, 2014, 34(9): 1125-1129
- [18] Wang S H, Wang J, Li J. Efficacy assessment of treating patients with coronary heart disease angina of phlegm and stasis mutual obstruction syndrome by Danlou tablet [J]. Zhongguo Zhong xi yi jie he za zhi, 2012, 32(8): 1051-1055
- [19] Liu J X, Lin C R, Ren J X, et al. Experimental study on pathogenetic involvement regularity of phlegm, toxin and blood-stasis syndromes in Chinese miniswine with phlegm-stasis cementation syndrome of coronary heart disease [J]. Zhongguo Zhong yao za zhi, 2013, 38(23): 4138-4143
- [20] Dong J, Zhu Y, Gao X, et al. Qualitative and quantitative analysis of the major constituents in Chinese medicinal preparation Dan-Lou tablet by ultra high performance liquid chromatography/diode-array detector/quadrupole time-of-flight tandem mass spectrometry [J]. Journal of pharmaceutical and biomedical analysis, 2013, 80: 50-62

(上接第 2634 页)

- [13] Perez CA, Samudra N, Aiyagari V. Cognitive and Functional Consequence of Cardiac Arrest[J]. Curr Neurol Neurosci, 2016, 16(8)
- [14] Fink EL, Berger RP, Clark RSB, et al. Serum Biomarkers of Brain Injury to Classify Outcome After Pediatric Cardiac Arrest [J]. Crit Care Med, 2014, 42(3): 664-674
- [15] Dell Anna AM, Scolletta S, Donadello K, et al. Early neuroprotection after cardiac arrest[J]. Curr Opin Crit Care, 2014, 20(3): 250-258
- [16] Bro-Jeppesen J, Kjaergaard J, Wanscher M et al. Systemic Inflammatory Response and Potential Prognostic Implications After Out-of-Hospital Cardiac Arrest [J]. Crit Care Med, 2015, 43 (6): 1223-1232
- [17] Bhalala US, Koehler RC, Kannan S. Neuroinflammation and Neuroimmune Dysregulation after Acute Hypoxic-Ischemic Injury of Developing Brain[J]. Frontiers in Pediatrics, 2015, 2
- [18] Madathil RJ, Hira RS, Stoeckl M, et al. Ischemia reperfusion injury as a modifiable therapeutic target for cardioprotection or neuroprotection in patients undergoing cardiopulmonary resuscitation [J]. Resuscitation, 2016, 105: 85-91
- [19] Hess DC, Hoda MN, Khan MB. Humoral Mediators of Remote Ischemic Conditioning: Important Role of eNOS/NO/Nitrite [J]. Acta Neurochir Suppl, 2016, 121: 45-48
- [20] Anrather J, Hallenbeck JM. Biological networks in ischemic tolerance - rethinking the approach to clinical conditioning[J]. Transl Stroke Res, 2013, 4(1): 114-129
- [21] Nance DM, Sanders VM. Autonomic innervation and regulation of the immune system (1987-2007)[J]. Brain Behav Immun, 2007, 21 (6): 736-745
- [22] Mastitskaya S, Marina N, Gourine A, et al. Cardioprotection evoked by remote ischaemic preconditioning is critically dependent on the activity of vagal pre-ganglionic neurones[J]. Cardiovasc Res, 2012, 95 (4): 487-494
- [23] Hiraki T, Baker W, Greenberg JH. Effect of vagus nerve stimulation during transient focal cerebral ischemia on chronic outcome in rats[J]. J Neurosci Res, 2012, 90(4): 887-894
- [24] Basalay M, Barsukevich V, Mastitskaya S, et al. Remote ischaemic pre- and delayed postconditioning - similar degree of cardioprotection but distinct mechanisms[J]. Exp Physiol, 2012, 97(8): 908-917