

doi: 10.13241/j.cnki.pmb.2015.09.032

大黄蛰虫胶囊联合维生素 C 钠治疗黄褐斑的疗效及对血清和血液流变学的影响

丁香玉 林碧雯 解方 朱文巍 王文娟 张昕[△]

(中国人民解放军总医院皮肤科 北京 100853)

摘要 目的:研究大黄蛰虫胶囊联合维生素 C 钠治疗黄褐斑的临床疗效及对血清和血液流变学的影响。**方法:**选取 2012 年 8 月到 2013 年 8 月我院收治的黄褐斑患者 140 例,按照随机数字表法平均分成研究组和对照组,每组 70 例,研究组给予大黄蛰虫胶囊联合维生素 C 钠治疗,对照组给予大黄蛰虫胶囊治疗,两组均治疗 1 个月。3 个月后比较两组临床疗效,并检测两组患者的血清睾酮(T)、雌二醇(E2)、孕酮(P)、过氧化脂质分解产物丙二醛(MDA)、超氧化物歧化酶(SOD)以及血液流变学水平的变化。**结果:**研究组总有效率 85.7% (60/70) 显著高于对照组的 57.1% (40/70),两组比较差异具有统计学意义($P < 0.05$);与治疗前和对照组相比,治疗后研究组 SOD、E2 显著升高,MDA、T 显著降低,差异均具有统计学意义($P < 0.05$);两组 P 水平均无明显变化;治疗后研究组血液流变学各指标较治疗前和对照组显著下降,差异均有统计学意义(均 $P < 0.05$)。**结论:**大黄蛰虫胶囊联合维生素 C 钠治疗黄褐斑具有较好的临床疗效,可以调节患者的性激素水平,改善患者的血流变学。

关键词:大黄蛰虫胶囊; 维生素 C 钠; 黄褐斑; 疗效; 血液流变学**中图分类号:**R758.42 **文献标识码:**A **文章编号:**1673-6273(2015)09-1721-04

Clinical Effect of Dahuang Zhechong Capsule Combined with Vitamin C Sodium in the Treatment of Chloasma and its Effect on Serum and Blood Rheology

DING Xiang-yu, LIN Bi-wen, XIE Fang, ZHU Wen-wei, WANG Wen-juan, ZHANG Xin[△]

(Department of Dermatology, General Hospital of PLA, Beijing, 100853, China)

ABSTRACT Objective: To study the clinical effect of Dahuang Zhechong capsule combined with vitamin C sodium in the treatment of chloasma and its effect on serum and blood rheology. **Methods:** 140 cases of chloasma patients from August 2012 to August 2013 in our hospital were divided into study group and control group according to the random number table method, with 70 cases in each group. The study group were treated by Dahuang Zhechong capsule combined with vitamin C, and the control group was given Dahuang Zhechong capsule treatment, all patients were treated for 1 months. The clinical efficacy was compared and the serum testosterone(T), estradiol(E2), progesterone(P) malondialdehyde(MDA), superoxide dismutase (SOD) and the changes of hemorheologic level of two groups were detected after 3 months of treatment. **Results:** The total effective rate of the study group was 85.7% (60/70), significantly higher than 57.1% (40/70) of the control group, the difference was statistically significant($P < 0.05$); Compared with before treatment and with the control group, SOD, E2 levels of the study group significantly increased, MDA, T level significantly reduced after treatment, the difference was statistically significant ($P < 0.05$); P levels of the two groups presented no obvious change; After treatment, hemorheological indexes of the study group significantly decreased compared with before treatment and with those of the control group, the difference was statistically significant (all $P < 0.05$). **Conclusion:** Dahuang Zhechong capsule combined with vitamin Csodium presents good curative effect in the treatment of chloasma, can regulate the level of sex hormone and improve hemorheological.

Key words: Dahuang Zhechong capsule; Vitamin C sodium; Chloasma; Effect; Hemorheological**Chinese Library Classification(CLC):** R758.42 **Document code:** A**Article ID:** 1673-6273(2015)09-1721-04

前言

黄褐斑是生长于面部的一种色素代谢失常, 多呈对称分

作者简介: 丁香玉(1980-), 女, 本科, 主治医师, 从事色素性疾病方面的研究, E-mail: dingxiangyu8899@126.com

△通讯作者: 张昕(1976-), 女, 硕士, 副主任医师, 从事皮肤美容、变态反应方面的研究

(收稿日期: 2014-10-23 接受日期: 2014-11-19)

布, 表现为蝶形, 多分布在面颊部^[1]。血中的雌激素水平高是该病的主要原因^[2,3]。中医上称为“肝斑”、“面尘”, 黄褐斑多发于青年女性, 疾病缓慢, 病势绵延, 给患者带来很大的心理负担^[4,5]。黄褐斑治疗较难, 应用中医药来治疗黄褐斑具有较好的效果且前景乐观。本文选取 2012 年 8 月到 2013 年 8 月我院收治的 140 例黄褐斑患者, 分别给予大黄蛰虫胶囊联合维生素 C 钠和大黄蛰虫胶囊治疗旨在探究其临床疗及对血清和血液流变学的影响, 现将结果报道如下。

1 资料与方法

1.1 一般资料

选取 2012 年 8 月到 2013 年 8 月我院收治的黄褐斑患者 140 例,所有患者均符合黄褐斑临床诊断标准^[6],均为女性。排除标准^[7]:(1)过敏体质者或者对药物成分存在过敏者;(2)存在严重心、肝肾等原发疾病患者;(3)合并心血管和脑血管等疾病;(4)妊娠和哺乳期的妇女。在患者知情同意下按照随机数字表法平均分成研究组和对照组,每组 70 例。其中研究组年龄 18-45 岁,平均(38.3±1.2)岁;病程 0.3-15 年,平均病程(5.8±1.3)年。对照组年龄 19-45 岁,平均(38.2±1.2)岁;病程 0.3-15 年,平均病程(5.7±0.9)年。两组患者年龄、病程均无显著差异($P>0.05$),具有可比性。

1.2 治疗方法

研究组给予患者大黄蛰虫胶囊(生产厂家:江苏颐海药业有限责任公司,批准文号:国药准字 Z20054026),4 粒/次,2 次/天。同时给予患者维生素 C 钠胶囊(生产厂家:广西圣保堂药业有限公司,批准文号:国药准字 H20052413)200 mg/ 次,每天 3 次。对照组仅给予大黄蛰虫胶囊治疗,用量与研究组一样。两组治疗时间均为 1 个月。

1.3 观察指标

3 个月后观察两组患者的临床疗效,并于治疗前后和药物治疗 3 个月后采集空腹静脉血液 5 mL,放置在试管中,离心分

离血清来检测两组患者的血清睾酮(T)、雌二醇(E2)、孕酮(P)、过氧化脂质分解产物丙二醛(MDA)、超氧化物歧化酶(SOD),应用 GW2007-097 锥板式的血流变仪器来检测血液流变学变化。

1.4 疗效评价

根据中国中西医结合学会皮肤性病专业委员会色素病学组对于 2003 年修订黄褐斑的疗效标准^[8]:痊愈:观察患者的色斑的面积消退 90%以上,其颜色基本上消失,治疗后下降指数 ≥ 0.8 ;显效:观察患者的色斑的面积 $>60\%$,其颜色明显的变浅,下降指数 ≥ 0.5 ;有效:观察患者的色斑的面积消退 $>30\%$,颜色变浅,治疗以后下降指数 ≥ 0.3 ;无效:观察患者色斑的面积消退 $<30\%$,治疗以后下降指数 ≤ 0 。(总有效率=基本治愈率+显效率+有效率)。下降指数评定参考赵敏办法^[9]。

1.5 统计学方法

全部数据均在 SPSS17.0 软件上统计,其中计量资料用($\bar{x}\pm s$)表示,应用 t 检验,计数的资料应用 χ^2 检验,检验标准以 $P<0.05$ 表示有统计学意义。

2 结果

2.1 两组临床疗效比较

由表 1 可知,研究组的总有效率 85.7%(60/70)显著高于对照组的 57.1%(40/70),两组比较差异具有统计学意义($\chi^2=12.052, P<0.05$)。

表 1 两组临床疗效比较[n(%)]

Table 1 Comparison of clinical efficacy between two groups [n(%)]

组别 Groups	例数 Cases	痊愈 Recovery	显效 excellence	有效 Effective	无效 Invalid	总有效率 Total effective rate
研究组 Study group	70	18(25.7)	23(32.9)	19(27.1)	10(14.3)	60(85.7) [▲]
对照组 Control group	70	13(18.6)	15(21.4)	12(17.1)	30(42.9)	40(57.1)

注:与对照组比较, $\chi^2=12.052$,[▲] $P<0.05$ 。

Note: compared with control group, $\chi^2=12.052$,[▲] $P<0.05$.

2.2 两组血清指标比较

由表 2 可知,两组治疗前各指标比较差异均无统计学意义(均 $P>0.05$),与治疗前和对照组相比,治疗后研究组 SOD、E2

显著升高,MDA、T 显著降低,差异均具有统计学意义($P<0.05$);两组 P 水平均无明显变化。

表 2 两组治疗前后血清指标比较($\bar{x}\pm s$)

Table 2 Comparison of serum indexes before and after treatment in two groups($\bar{x}\pm s$)

组别 Groups	治疗时间 Treatment time	E ₂ (Pg/ml)	T(ng/ml)	P(mg/ml)	SOD(U/ml)	MDA(nmol/ml)
研究组 Study group	治疗前 Before treatment	19.2±2.1	0.6±0.1	0.9±0.2	96.2±1.1	8.5±0.9
	治疗后 After treatment	19.5±2.3	0.6±0.2	0.9±0.1	98.1±0.9	7.8±2.1
对照组 Control group	治疗前 Before treatment	19.2±1.9	0.6±0.3	0.9±0.3	97.2±0.1	9.2±0.8
	治疗后 After treatment	31.3±2.8 ^{△▲}	0.3±0.1 ^{△▲}	0.9±0.2	107.1±0.2 ^{△▲}	7.2±0.3 ^{△▲}

注:与治疗前比较, $\triangle P<0.05$;与对照组治疗后比较,[▲] $P<0.05$ 。

Note: compared with before treatment, $\triangle P<0.05$; compared with the control group after treatment,[▲] $P<0.05$.

2.3 两组血流变学比较

由表 3 可知,两组治疗前全血粘度值和血浆粘度值比较差异均无统计学意义(均 $P>0.05$);治疗后两组全血粘度值和血浆

粘度值较治疗前均有下降,差异有统计学意义(均 $P<0.05$);治疗后研究组全血粘度值和血浆粘度值较对照组下降更明显,差异具有统计学意义($P<0.05$)。

表 3 两组治疗前后血液流变学比较($\bar{x} \pm s$)
Tabel 3 Comparison of hemorheology before and after treatment between groups($\bar{x} \pm s$)

组别 Groups	治疗时间 Treatment time	全血粘度值 Whole blood viscosity(ma/s)	血浆粘度值 Plasma viscosity(ma/s)
研究组 Study group	治疗前 Before treatment	21.02± 0.23	1.66± 0.36
	治疗后 After treatment	19.32± 0.71 ^{△▲}	1.65± 0.21 ^{△▲}
对照组 Control group	治疗前 Before treatment	21.32± 0.14	1.59± 0.24
	治疗后 After treatment	15.14± 0.23 [△]	1.52± 0.27 [△]

注:与治疗前比较,△P<0.05;与对照组治疗后比较;▲P<0.05

Note: compared with before treatment, △P<0.05 ;compared with control group after treatment, ▲P<0.05

3 讨论

最新研究发现人体内的黄褐斑和人体内的氧自由基发生有很大的关系,人体内的氧化反应速度增加,抗氧化的活性降低,氧化以及抗氧化平衡失调是导致黄褐斑产生的重要因素^[10]。正常体内氧自由基可以清除体内的氧化性损伤物质,是体内的氧化和抗氧化处于动态平衡中^[11]。黄褐斑的发生则是调节氧化和抗氧化的机制发生障碍,使体内不能及时清除生理条件下产生的过氧化脂酶^[12]。本文研究发现,治疗后研究组MDA下降,而SOD升高,说明应用大黄蛰虫胶囊联合维生素C钠治疗黄褐斑可以改善患者氧化和抗氧化机制。

黄褐斑的发生和血流动力学指标异常也存在一定的关系,一般患者存在血液粘度增加,与中医上所述的气滞血瘀和脉络阻滞相关,血液流变学出现异常会引起血液循环发生障碍,是患者末梢组织出现缺血缺氧,引起代谢功能失调^[13]。据研究发现,雌激素可以刺激黑色素细胞分泌黑色素颗粒,孕激素则能增加黑色素体的转运,增加黑色素的含量^[14-16]。本文研究发现,研究组治疗后E₂显著升高,T显著降低,两组患者P水平均无明显变化。进一步证明大黄蛰虫胶囊联合维生素C钠治疗黄褐斑可以改善患者血清激素水平,对黄褐斑的治疗具有一定疗效。黄褐斑在中医学中称之为黑斑和蝴蝶斑,发于皮,气血瘀滞,经络不通,气血不能上荣于面,是黄褐斑的主要病机^[17]。大黄蛰虫胶囊有调节内分泌之功效,祛除刺激黑素细胞分泌物功能,它富含阿魏酸,维生素A、维生素E、维生素B12、叶酸等物质,能扩张外周血管,增加面部血流量,改善面部营养,从而达到祛斑的作用,其中阿魏酸可抑制垂体分泌黄体生成素和催产素,拮抗促性腺激素释放,抑制酪氨酸酶活性,防止酪氨酸氧化形成黑色素,抑制黑色素形成^[18,19]。本研究结果显示,研究组总有效率85.7%显著高于对照组的57.1%,可以证明大黄蛰虫胶囊联合维生素C钠治疗黄褐斑具有较好的临床疗效。维生素C钠胶囊在临床应用中的优点在于其不良反应少,可与多种药物配合使用,扩大临床适用范围,还解决了维生素C保存的问题,使得维生素C在用于药物时的质量和中性特征,长期使用安全有效^[20]。

综上所述,黄褐斑是一种慢性疾病,给患者带来很大的负担,应用大黄蛰虫胶囊联合维生素C钠治疗黄褐斑取得较好的治疗效果,能显著改善患者血清性激素的水平,改善患者的血流变学。

参 考 文 献(References)

- [1] 郭静,张伟,丁黎,等.熊果苷制剂对豚鼠皮肤安全性及脱色作用的研究[J].宁夏医科大学学报,2012,34(6): 592-595,封4
Guo Jing, Zhang Wei, Ding Li, et al. Safety and Decoloration of the Arbutin Preparations on the Skin of Guinea Pigs [J]. Journal of Ningxia Medical University, 2012, 34(6): 592-595, 4
- [2] Shi HF, Xu B. Clinical Observation on the Treatment of Chloasma by Chinese Herbs Combined with Acupuncture [J]. Chin J Integr Med, 2007, 13(3): 219-23
- [3] Adela Avila S, Peñaloza J, González F, et al. Dysphagia, melanosis, gastrointestinal stromal tumors and a germline mutation of the KIT gene in an Argentine family [J]. Acta Gastroenterol Latinoam, 2014, 44(1): 9-15
- [4] Fields K, Milikowski C, Jewell T, et al. Localized diffuse melanosis associated with melanoma successfully treated with imiquimod cream 5%: a case report and review of the literature [J]. Cutis, 2014, 93(3): 145-150
- [5] 石红乔.黄褐斑膏方调治体会[J].中医杂志,2011,52(11): 972-973
Shi Hong-qiao. Experience of chloasma herbal paste [J]. Journal of Traditional Chinese Medicine, 2011, 52(11): 972-973
- [6] 黎宁,陈彦伟,磨思慧,等.强脉冲光(IPL)技术治疗皮肤色素性及血管性疾病临床疗效观察[J].广西医学,2006,28(3):366-367
Li Ning, Chen Yan-wei, Mo Si-hui, et al. Clinical effect observation of intense pulsed light (IPL) technique in the treatment of skin pigmented and vascular diseases [J]. Guangxi Medical Journal, 2006, 28(3): 366-367
- [7] 王丽丽,张金虎,朱胜君,等.化浊解毒熏蒸法对黄褐斑不同证型的选择性研究[J].时珍国医国药,2013,24(3): 3-4
Wang Li-li, Zhang Jin-hu, Zhu Sheng-jun, et al. Selective study on Huazhuo Jiedu fumigation for different syndromes of chloasma [J]. Lishizhen medicine and Materia Medica Research, 2013, 24(3):3-4
- [8] 余士根,郑敏,方红,等.天然维生素E胶丸治疗黄褐斑有效性与安全性的多中心随机开放临床观察 [J].中国皮肤性病学杂志,2012,26(04): 367-368
Yu Shi-gen, Zhen Min, Fang Hong, et al. Efficacy and Safety of Vitamin E Capsules in the Treatment of Chloasma: A Multi-Center, Randomized and Open Clinical Trial [J]. The Chinese Journal of Dermatovenereology, 2012, 26(04): 367-368
- [9] 赵敏.大黄蛰虫丸治疗气滞血瘀型黄褐斑临床观察 [D].辽宁中医药大学,2012

- Zhao Min. Clinical observation of Dahuang Zhechong Pill in the treatment of qi stagnation and blood stasis type of chloasma [D]. Liaoning University of Traditional Chinese Medicine, 2012
- [10] Qian YF, Xie J, Yang SP, et al. In vivo study of spoilage bacteria on polyphenoloxidase activity and melanosis of modified atmosphere packaged Pacific white shrimp[J]. Food Chem, 2014, 155: 126-131
- [11] 吴小红, 王煜明, 刘瓦利. 女性黄褐斑 130 例临床资料分析 [J]. 中国皮肤性病学杂志, 2011, 25(11): 863-864, 873
Wu Xiao-hong, Wang Yu-ming, Liu Wa-li. Clinical Analysis of 130 Female Patients with Chloasma [J]. The Chinese Journal of Dermatovenereology, 2011, 25(11): 863-864, 873
- [12] 郑彩慧, 杨晓娜, 李艳玲, 等. 桃红四物合六味地黄汤加减治疗黄褐斑[J]. 中国实验方剂学杂志, 2012, 18(2): 222-224
Zheng Cai-hui, Yang Xiao-na, Li Yan-ling, et al. Taohong Siwu and Liuwei Dihuang Decoction Combined Treatment of Melasma Case[J]. Chinese Journal of Experimental Traditional Medical Formulae, 2012, 18(2): 222-224
- [13] 陈红, 郭渝南, 吴元胜, 等. 祛斑胶囊治疗黄褐斑的临床观察及抗氧化作用研究[J]. 中草药, 2003, 34(2): 160-162
Chen Hong, Guo Yu-nan, Wu Yuan-sheng, et al. Clinical observation and anti-oxidation in treating chloasma with Queban Capsule [J]. Chinese traditional and herbal drugs, 2003, 34(2): 160-162
- [14] 史红斐, 徐兵, 郭希超, 等. 调肝脾针法治疗黄褐斑的疗效及女性激素、促黑激素、超氧化物歧化酶、过氧化脂质的观察[J]. 浙江中医杂志, 2009, 44(1): 52-54
Shi Hong-fei, Xu Bing, Guo Xi-chao, et al. Therapeutic Effects of Acupuncture of Attempering the Liver and the Spleen on Chloasma and Its Effect on Female Sex Hormone, Melanophore Stimulating Hormone, Superoxide Dismutase and Lipid Peroxide [J]. Zhejiang Journal of Traditional Chinese Medicine, 2009, 44(1): 52-54
- [15] Huang HY, Wang XL, Wei YL. Acupuncture combined with acupoint injection with syndrome differentiation for 49 cases of chloasma [J]. Chinese Acupuncture, 2013, 33(9): 797-798
- [16] 张璐, 林孝华, 唐东阳, 等. 红宝石点阵激光联合氨甲环酸治疗黄褐斑临床观察[J]. 中国皮肤性病学杂志, 2012, 26(12): 1139-1141
Zhang Lu, Lin Xiao-hua, Tang Dong-yang, et al. Efficacy of Ruby Dot Matrix Laser Combined with Tranexamic Acid Tablets in the Treatment of Melasma [J]. The Chinese Journal of Dermatovenereology, 2012, 26(12): 1139-1141
- [17] 黄恺飞, 王梅兰, 杨辉, 等. 清斑胶囊对 ICR 鼠皮肤色素生成及抗氧化作用的实验研究[J]. 中国美容医学, 2011, 20(10): 1569-1571
Huang Kai-fei, Wang Mei-lan, Yang Hui, et al. Experimental research of Qing-ban capsule on the pigment formation of ICR mouse and the ability of anti-oxidation [J]. Chinese Journal of Aesthetic Medicine, 2011, 20(10): 1569-1571
- [18] 柯友辉, 陈浩波, 苏文婷, 等. 疏肝化斑汤加情志干预治疗黄褐斑的临床观察及其对血清 α -MSH 的影响 [J]. 中国中西医结合杂志, 2012, 32(12): 1701-1703
Ke You-hui, Chen Hao-bo, Su Wen-ting, et al. Clinical observation of Shugan huaban decoction combined with mental intervention in treatment of chloasma and its effect on serum α -MSH [J]. Chinese Journal of Integrated Traditional and Western Medicine, 2012, 32(12): 1701-1703
- [19] Zhang X, Liang Y, Wang HY. Invasive ductal carcinoma of the breast associated with extensive melanin melanosis: a case report and review of the literature[J]. Int J Clin Exp Pathol, 2014, 7(3): 1218-1223
- [20] Armienta SR, Camacho NM, Hernández GM, et al. Panenteric melanosis secondary to melanoma of the rectum: a case report[J]. Rev Gastroenterol Mex, 2014, 79(1): 60-62

(上接第 1717 页)

- depression[J]. Archives of general psychiatry, 2006, 63(8): 856-864
- [7] Zarate CA Jr, Mathews D, Ibrahim L, et al. A randomized trial of a low-trapping nonselective N-methyl-D-aspartate channel blocker in major depression[J]. Biol Psychiatry, 2013, 74(4): 257-264
- [8] Loo CK, Katalinic N, Garfield JB, et al. Neuropsychological and mood effects of ketamine in electroconvulsive therapy: a randomised controlled trial[J]. J Affect Disord, 2012, 142(1-3): 233-240
- [9] Abdullah CG, Fasula M, Kelmendi B, et al. Rapid antidepressant effect of ketamine in the electroconvulsive therapy setting [J]. J ECT, 2012, 28(3): 157-161
- [10] Covvey J R, A N Crawford, D K Lowe. Intravenous ketamine for treatment-resistant major depressive disorder [J]. Ann Pharmacother, 2012, 46(1): 117-123
- [11] Martínez-Amorós E, Cardoner N, Soria V, et al. Long-term treatment strategies in major depression: a 2-year prospective naturalistic follow-up after successful electroconvulsive therapy[J]. J ECT, 2012, 28(2): 92-97
- [12] Yamano M, Akamatsu N, Tsuji S. Cognitive function related to temporal lobe epilepsy: advances in research on new cognitive function [J]. Brain Nerve, 2013, 65(5): 551-559
- [13] Papazacharias A, Nardini M. The relationship between depression and cognitive deficits [J]. Psychiatr Danub, 2012, 24 (Suppl 1): 179-182
- [14] Sackeim HA, Prudic J, Fuller R, et al. The cognitive effects of electroconvulsive therapy in community settings [J]. Neuropsychopharmacology, 2007, 32(1): 244-254
- [15] Donahue A. B. Electroconvulsive therapy and memory loss: a personal journey[J]. The journal of ECT, 2000, 16(2): 133-143
- [16] Prudic J, Pester S, Sackeim H D. Subjective memory complaints: a review of patient self-assessment of memory after electroconvulsive therapy[J]. The Journal of ECT, 2000, 16(2): 121-132
- [17] Murrough JW, Perez AM, Pillemier S, et al. Rapid and Longer-Term Antidepressant Effects of Repeated Ketamine Infusions in Treatment-Resistant Major Depression [J]. Biol Psychiatry, 2012, 12(2): 45-47
- [18] Krystal AD, Weiner RD, Dean MD. Comparison of seizure duration, ictal EEG, and cognitive effects of ketamine and methohexitol anesthesia with ECT [J]. J Neuropsychiatry Clin Neurosci, 2003, 15(1): 27-34
- [19] Beall EB, Malone DA, Dale RM, et al. Effects of electroconvulsive therapy on brain functional activation and connectivity in depression [J]. J ECT, 2012, 28(4): 234-241
- [20] Husain MM, Rush AJ, Fink M, et al. Speed of response and remission in major depressive disorder with acute electroconvulsive therapy (ECT): a Consortium for Research in ECT (CORE) report [J]. J Clin Psychiatry, 2004, 65(4): 485-491