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环磷腺苷葡胺联合培哚普利在慢性心力衰竭中的应用研究

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摘要 目的:分析环磷腺苷葡胺联合培哚普利在慢性心力衰竭患者的应用价值。**方法:**以2013年1月至2015年12月新疆医科大学第五附属医院心血管内科诊治的慢性心力衰竭患者90例为研究对象,将其按照就诊病历顺序号分对照组、培哚普利组和联合组,每组30例。对照组患者接受常规治疗,培哚普利组患者在对照组的基础之上加用培哚普利,联合组患者在培哚普利组的基础之上加用环磷腺苷葡胺,三组患者均连续治疗2周,比较三组临床疗效及治疗前后患者的左心室重塑情况(左心室收缩末期内径(LVESD)和舒张末期内径(LVEDD))及左心室功能(左心室射血分数(LVEF)),患者活动能力(6 min的步行距离)以及血浆脑钠利肽(BNP)、胰岛素样生长因子1(IGF-1)、胱抑素(Cys-C)水平。**结果:**经过2周的治疗,培哚普利组和联合组的治疗总有效率分别为86.67%和96.67%,均显著高于对照组的66.67%($P<0.05$),但培哚普利组和联合组比较差异无统计学意义($P>0.05$);三组患者的LVEDD、LVESD、血浆BNP水平均较治疗前显著降低,且培哚普利组和联合组均显著低于对照组($P<0.05$),联合组LVESD、血浆BNP水平显著低于培哚普利组;三组患者的LVEF和6 min步行距离、血浆IGF-1水平均较治疗前显著升高,且培哚普利组和联合组均显著高于对照组,联合组血浆IGF-1水平、LVEF和6 min步行距离显著高于培哚普利组($P<0.05$);联合组和培哚普利组治疗后的Cys-C水平治疗前显著降低,且联合组和培哚普利组显著低于对照组,联合组血Cys-C水平较培哚普利组更低($P<0.05$)。**结论:**环磷腺苷葡胺联合培哚普利治疗慢性心力衰竭临床疗效显著,可较单药治疗显著改善患者左心室重构情况、心室射血功能和活动能力,可能与协同调节患者血浆BNP、IGF-1、Cys-C水平有关。

关键词:慢性心力衰竭;环磷腺苷葡胺;培哚普利;脑钠利肽;胰岛素样生长因子1;胱抑素

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Application Research of Meglumine Cyclic Adenylate and Perindopril in Patients with Chronic Congestive Heart Failure

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ABSTRACT Objective: To investigate the application value of meglumine cyclic adenylate and perindopril in patients with chronic congestive heart failure (CCHF). **Methods:** 90 cases of patients with CCHF in our hospital from January 2013 to December 2015 were divided into control group, perindopril group and union group, 30 cases in each group. Patients in the control group were treated with conventional methods, patients in the perindopril group were treated with conventional methods and perindopril, and patients in the union group were treated with meglumine cyclic adenylate based on the treatment method of perindopril group. The treatment time of three groups were 2 weeks. Compared the clinical effect, LVEDD, LVESD, LVEF, 6-minute walk distance and plasma levels of BNP, IGF-1, Cys-C between three groups. **Results:** After treatment, the clinical effect of the perindopril group (86.67%) and union group (96.67%) were significantly higher than that of the control group (66.67%) ($P<0.05$); LVEDD, LVESD, and plasma levels of BNP and Cys-C of three groups after treatment were all significantly lower than before treatment ($P>0.05$), and the perindopril group and union group were all significantly lower than that of the control group ($P<0.05$); LVEDD and plasma levels of BNP of union group were significantly higher than that of the perindopril group ($P<0.05$), and the perindopril group were all significantly higher than that of the union group ($P<0.05$). **Conclusion:** The clinical effect of meglumine cyclic adenylate and perindopril in patients with CCHF are remarkable, and meglumine cyclic adenylate can improve the effect of perindopril on left ventricular remodeling situation, left ventricular function, and patients' activity, and those may be related with modify the plasma levels of BNP, IGF-1, Cys-C.

Key words: Chronic congestive heart failure; Meglumine cyclic adenylate; Perindopril; Brain natriuretic peptide; insulin like growth factor 1; Cys-C

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前言

慢性心力衰竭是指由任何心脏功能或结构异常引起的心室充盈或射血能力受损的复杂的临床综合征,是众多心血管疾病的严重和终末阶段,临床症状主要为活动耐量受限、呼吸困难、肺淤血、外周水肿等^[1]。据调查显示,目前我国成人中慢性心力衰竭的患病率约为 0.9%,且呈逐年上升趋势^[2]。临床对于慢性心力衰竭的药物目标主要是改善患者血流动力学及衰竭心脏的生物力学性质^[3]。环磷腺苷葡胺属于非洋地黄类强心剂,是一种人工合成的环磷酸核苷衍生物,具有正性肌力作用,可显著改善患者的左心功能和运动耐量^[4]。培哚普利是一种强效和长效的血管紧张素转换酶抑制剂,临床常用与各型高血压和心力衰竭的治疗^[5]。临床研究显示,环磷腺苷葡胺联合培哚普利改善慢性心力衰竭患者的左心功能、降低血浆氨基末端 B 型钠利尿酸前体(NT-proBNP)水平的效果要显著优于接受常规治疗^[6],但对于环磷腺苷葡胺协同提高培哚普利改善慢性心力衰竭患者的左心功能的效果,以及对胱抑素 C(Cys-C)、胰岛素样生长因子 1(IGF-1)水平的相关研究较少见。因此本研究拟进一步分析环磷腺苷葡胺联合培哚普利在慢性心力衰竭患者的应用价值,为慢性心力衰竭患者临床治疗方案的选择提供参考。

1 资料与方法

1.1 一般资料

以 2013 年 1 月至 2015 年 12 月新疆医科大学第五附属医院心血管内科诊治的慢性心力衰竭患者 90 例为研究对象,所有患者均符合纽约心脏病协会(NYHA)的心功能诊断和分级标准,经查体、病史、胸片、超声等检查确诊,3 个月内未接受过其他治疗;排除合并有严重的脑、肝、肾等器官功能障碍者,排除合并脑血管病及肿瘤者,排除收缩压低于 90 mmHg、血钾高于 5.5 mmol/L、血肌酐水平高于 252.2 mol/L 者;将 90 例患者根据就诊病历顺序号分对照组、培哚普利组和联合组,每组 30 例。对照组中男 17 例,女 13 例,年龄 35-75 岁,平均年龄(59.0±7.8)岁,病程 5-20 年,平均病程(7.2±3.5)年,基础疾病:高血压 15 例,冠心病 6 例,风湿性心脏病 5 例,扩张型心肌病 4 例;NYHA 分级:Ⅱ级 15 例,Ⅲ级 8 例,Ⅳ级 7 例。培哚普利组中男 16 例,女 14 例,年龄 35-75 岁,平均年龄(58.9±7.9)岁,病程 5-20 年,平均病程(7.0±3.1)年,基础疾病:高血压 15 例,冠心病 7 例,风湿性心脏病 5 例,扩张型心肌病 3 例;NYHA 分级:Ⅱ级 16 例,Ⅲ级 7 例,Ⅳ级 7 例。联合组中男 15 例,女 15 例,年龄 35-75 岁,平均年龄(59.6±7.2)岁,病程 5-20 年,平均病程(7.9±3.5)年,基础疾病:高血压 14 例,冠心病 7 例,风湿性心脏病 6 例,扩张型心肌病 3 例;NYHA 分级:Ⅱ级 14 例,Ⅲ级 9 例,Ⅳ级 7 例。三组的一般资料比较,差异无统计学意义(P>0.05)。

1.2 治疗方法

对照组:给予常规治疗:休息,限制水钠摄入,给予血管扩张药硝酸甘油(广东华南药业集团有限公司,国药准字 H44023987)0.5 mg/次,舌下含服,利尿剂呋塞米(山东圣鲁制药有限公司,国药准字 H37021208)20 mg/次、洋地黄类强心剂地高辛(上海禾丰制药有限公司,国药准字 H31021513)0.5 mg/次,溶于 20 mL 生理盐水中静脉推注,每天 1 次。

培哚普利组:在对照组治疗方法的基础之上加用培哚普利(施维雅(天津)制药有限公司,国药准字 H20034053)4 mg/次,每天 1 次,口服。

联合组:在培哚普利组治疗方法的基础之上加用环磷腺苷葡胺(江苏万邦生化医药股份有限公司,国药准字 H20003530),60-180 mg/次,溶于 200-500 mL 5%的葡萄糖溶液中静脉滴注,每天 1 次。

三组患者均连续治疗 2 周。

1.3 观察指标

(1)临床疗效:观察并记录治疗前和治疗后三组患者的临床症状(肺部啰音、呼吸及下肢肿胀情况)、心电图、NYHA 心功能分级,评价临床治疗效果,显效:治疗后患者的临床症状消失或显著改善,心电图正常,NYHA 心功能分级改善 2 级或以上,有效:临床症状减轻,心电图基本正常,NYHA 心功能分级改善 1 级,无效:临床症状、心电图 NYHA 心功能分级均为改善或加重^[7],总有效率=(显效例数+有效例数)/总例数×100%。(2)采用彩色多普勒超声测量患者治疗前后左心室重塑情况(左心室收缩末期内径(LVESD)和舒张末期内径(LVEDD))及左心室心功能(左心室射血分数(LVEF)),同时测定患者活动能力(6 min 的步行距离)。(3)分别于治疗前和治疗后采集患者清晨空腹外周静脉血 5 mL,采用酶联免疫吸附法检测血浆中脑钠利肽(BNP)、IGF-1、Cys-C 水平,试剂盒均购自南京建成生物工程研究所,所有操作严格按照试剂盒操作说明进行。

1.4 统计学方法

采用 SPSS17.0 统计学软件,计数资料(临床疗效等)以%表示,组间差异比较采用卡方检验,计量资料(左心室重塑情况和左心室心功能相关指标,NT-proBNP、IGF-1、Cys-C 等)以均值±标准差表示,组间差异比较采用 t 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 三组治疗后临床疗效比较

经过 2 周的治疗,培哚普利组和联合组的治疗总有效率分别为 86.67%和 96.67%,均显著高于对照组的 66.67%(P<0.05),但培哚普利组和联合组的总有效率比较差异无统计学意义(P>0.05)。

表 1 三组治疗后临床疗效比较

Table 1 Comparison of the clinical curative effect between three groups after treatment

Groups	Cases	Remarkable effect	Effect	Inefficacy	Total effective rate
Control group	30	9(30.00)	11(36.67)	10(33.33)	20(66.67)
Perindopril group	30	10(33.33)	16(53.33)	4(13.33)	26(86.67) [°]
Union group	30	16(53.33)	13(43.33)	1(3.33)	29(96.67) [°]

Note: Compared with control group, ° P<0.05.

2.2 三组治疗前后左心室重塑情况和左心功能比较

治疗前,三组患者的 LVEDD、LVESD、LVEF 和 6 min 步行距离比较,差异均无统计学意义($P>0.05$);治疗 2 周后,三组患者的 LVEDD、LVESD 较治疗前显著降低,且培哌普利组和联合组均显著低于对照组($P>0.05$);三组患者的 LVEF 和 6 min

步行距离较治疗前显著升高,且培哌普利组和联合组均显著高于对照组($P<0.05$);治疗后,联合组的 LVESD 显著低于培哌普利组,LVEF 和 6 min 步行距离显著高于培哌普利组($P<0.05$),但两组间 LVEDD 值比较差异无统计学意义($P>0.05$)。

表 2 三组治疗前后左心室重塑情况和左心功能比较

Table 2 Comparison of the left ventricular remodeling situation and left ventricular function between three groups before and after treatment

		Control group	Perindopril group	Union group
LVESD(mm)	Before treatment	51.63± 5.91	51.99± 5.88	51.02± 5.10
	After treatment	48.70± 5.22 [°]	41.61± 5.02 ^{° °}	37.35± 4.63 ^{° ° °}
LVEDD(mm)	Before treatment	60.68± 4.92	60.13± 4.51	59.97± 4.66
	After treatment	57.13± 3.55 [°]	53.07± 3.91 ^{° °}	52.17± 3.02 ^{° ° °}
LVEF(%)	Before treatment	35.83± 1.19	36.02± 1.66	35.67± 1.43
	After treatment	38.22± 1.35 [°]	41.13± 1.45 ^{° °}	46.25± 1.19 ^{° ° °}
6-minute walk distance (m)	Before treatment	302.26± 36.58	297.23± 38.99	299.18± 37.65
	After treatment	351.67± 42.69 [°]	442.39± 46.67 ^{° °}	502.31± 49.66 ^{° ° °}

Note: Compared with control group after treatment, [°] $P<0.05$; Compared with before treatment, [°] $P<0.05$; Compared with Perindopril group Perindopril group, [°] $P<0.05$.

2.3 三组治疗前后血浆 BNP、IGF-1、Cys-C 水平比较

治疗前,三组的 BNP、IGF-1、Cys-C 水平比较,差异均无统计学意义($P>0.05$);治疗 2 周后,三组的 BNP 水平均较治疗前显著降低,且联合组和培哌普利组显著低于对照组($P<0.05$),三组的 IGF-1 水平均较治疗前显著升高,且联合组和培哌普利组

显著高于对照组 ($P<0.05$),联合组和培哌普利组治疗后的 Cys-C 水平治疗前显著降低,且联合组和培哌普利组显著低于对照组($P<0.05$);治疗 2 周后联合组的 BNP、IGF-1、Cys-C 水平与培哌普利组比较,BNP、Cys-C 显著更低,IGF-1 显著更高 ($P<0.05$)。

表 3 三组治疗前后血浆 BNP、IGF-1、Cys-C 水平比较

Table 3 Comparison of the serum BNP, IGF-1, Cys-C levels between three groups before and after treatment

		Control group	Perindopril group	Union group
BNP(g/L)	Before treatment	1.220± 0.269	1.193± 0.297	1.201± 0.238
	After treatment	0.697± 0.166 [°]	0.432± 0.198 ^{° °}	0.309± 0.241 ^{° ° °}
IGF-1(g/L)	Before treatment	101.36± 16.62	102.57± 16.16	102.69± 16.09
	After treatment	110.45± 15.32 [°]	119.88± 15.97 ^{° °}	129.54± 15.77 ^{° ° °}
Cys-C(g/mL)	Before treatment	3.22± 0.69	3.14± 0.65	3.19± 0.59
	After treatment	2.99± 0.62	2.56± 0.56 ^{° °}	2.01± 0.51 ^{° ° °}

Note: Compared with control group after treatment, [°] $P<0.05$; Compared with before treatment, [°] $P<0.05$; Compared with Perindopril group Perindopril group, [°] $P<0.05$.

3 讨论

慢性心力衰竭是心血管内科常见疾病,呈慢性长期的进行性发展,5 年病死率达 50%^[8]。慢性心力衰竭的病因及发病机制较复杂,但目前临床普遍认为与心肌重塑、中枢神经系统和神经内分泌系统的过度激活有关^[9],其临床治疗方法包括药物治疗和非药物治疗,以药物治疗为主,而血管紧张素转换酶抑制剂是药物治疗的基石^[10]。

培哌普利一种强效和长效的血管紧张素转换酶抑制剂,其治疗慢性心力衰竭的机制主要是竞争性的阻断血管紧张素 I 转关为血管紧张素 II,从而降低组织和循环中的血管紧张素 II 水平,发挥抗增生和扩张血管的作用;其还可抑制缓激肽的降解,提高缓激肽水平,从而发挥保护心肌的有益作用^[11]。环磷腺

苷葡胺是非洋地黄类的正性肌力药物,亲脂性和亲水性均较高,可快速通过细胞膜,其发挥正性肌力作用的主要机制是抑制磷酸二酯酶的活性,抑制 cAMP 的分解,提高细胞内 cAMP 水平,从而促进 Ca^{2+} 内流,增强心肌收缩力,增强心脏泵血和射血能力;同时环磷腺苷葡胺还可抑制血管平滑肌与 Ca^{2+} 结合,从而扩张外周血管,降低心脏负荷,扩张冠脉血管,改善心肌缺血缺氧状态^[12]。大量临床研究已经证实培哌普利和环磷腺苷葡胺单独联合常规治疗方法用于慢性心理衰竭的治疗,可有效改善患者的心功能、心肌重塑、活动能力以及血浆 BNP 水平^[13,14]。环磷腺苷葡胺联合血管紧张素转换酶抑制剂及常规治疗是近年来治疗慢性心力衰竭的新趋势。彭静^[7]等研究显示:与单用常规治疗方法相比,环磷腺苷葡胺联合培哌普利及常规治疗用于慢性心力衰竭的治疗,不仅可显著改善患者的左心室重塑、心

室射血功能及血浆 NT-proBNP、IGF-1 和同型半胱氨酸的水平,但并未对培哚普利和常规治疗联合或不联合环磷腺苷葡胺治疗慢性心力衰竭的疗效差异进行比较。陈涛^[15]等比较了常规治疗、培哚普利和常规治疗、培哚普利和常规治疗联合环磷腺苷葡胺治疗慢性心力衰竭的疗效差异,但仅观察了 LVEDD、LVEF 和 NT-proBNP 的水平,因此,本研究在此基础上更加系统的评价了以上三种药物治疗方案的临床疗效差异,并且同时观察了患者血浆 BNP、IGF-1 和 Cys-C 水平的变化情况,以期探究联合用药提高临床疗效的机制,以及联合用药的临床评价提供参考。

本研究结果显示:经过 2 周的治疗,培哚普利组和联合组的治疗总有效率均显著高于对照组,但培哚普利组和联合组的总有效率比较差异无统计学意义,与陈涛^[15]等研究结果基本一致;本研究中,治疗 2 周后,三组患者的 LVEDD、LVESD 水平较治疗前显著降低,且培哚普利组和联合组均显著低于对照组;三组患者的 LVEF 和 6 min 步行距离较治疗前显著升高,且培哚普利组和联合组均显著高于对照组,说明在常规治疗的基础之上,单用培哚普利或联合环磷腺苷葡胺均可显著改善患者的心室重构和心功能及活动能力;治疗后,联合组的 LVESD 显著低于培哚普利组,LVEF 和 6 min 步行距离显著高于培哚普利组,但两组间 LVEDD 值比较差异无统计学意义,说明环磷腺苷葡胺联合培哚普利可显著提高培哚普利治疗慢性心力衰竭的临床效果,但对 LVEDD 的而改善不显著,但本研究结果中 LVEF 指标的变化情况与陈涛^[15]等的而研究结果存在差异,可能原因为本研究纳入病例数较少,或病理个体差异较大,造成一定的偏差。

BNP 是由心肌细胞分泌的多肽类神经激素,研究显示其在慢性心理衰竭患者血清中的水平与心衰的严重程度呈正相关,可预测慢性心理衰竭患者的心功能的预后情况^[16]。IGF-1 是一种抗心肌细胞凋亡因子,可促进心肌细胞和心肌纤维细胞的增殖及心肌修复和心肌侧支血管重建,改善心肌缺血^[17]。Cys-C 是一种非糖化碱性蛋白,又称半胱氨酸蛋白酶抑制剂 C,临床主要用于肾功能的检测^[18],但近年来相关研究显示慢性心力衰竭患者的血浆 Cys-C 与心衰严重程度及心功能有密切关系,心衰及心功能受损越严重,Cys-C 水平就越高,同时 Cys-C 还参与心肌重塑、炎症反应以及动脉粥样硬化等过程^[19,20]。因此,Cys-C 亦可用于预测和评价慢性心理衰竭患者的预后情况。本研究结果显示:治疗 2 周后,三组的 BNP 水平均较治疗前显著降低,且联合组和培哚普利组显著低于对照组,三组的 IGF-1 水平均较治疗前显著升高,且联合组和培哚普利组显著高于对照组,联合组和培哚普利组治疗后的 Cys-C 水平治疗前显著降低,且联合组和培哚普利组显著低于对照组;同时,联合组治疗后的 BNP、IGF-1、Cys-C 水平与培哚普利组比较,BNP、Cys-C 显著更低,IGF-1 显著更高,提示环磷腺苷葡胺协同提高培哚普利改善慢性心力衰竭患者的临床疗效,可能与协同改善患者血浆 BNP、IGF-1、Cys-C 水平有关。

综上所述,环磷腺苷葡胺联合培哚普利治疗慢性心力衰竭临床疗效显著,可较单药治疗显著改善患者左心室重构情况、心室射血功能和活动能力,可能与协同调节患者血浆 BNP、IGF-1、Cys-C 水平有关。

参考文献(References)

- [1] Schmaltz A A. Chronic congestive heart failure in infancy and childhood: new aspects of diagnosis and treatment [J]. *Klinische Pädiatrie*, 2015, 227(1): 3-9
- [2] Herlitz J. Effect of metoprolol CR/XL in chronic heart failure; Metoprolol CR/XL. Randomised Intervention Trial in Congestive Heart Failure[J]. *Lancet*, 2015, 353(9169): 2001-2007
- [3] Troughton R W, Frampton C M, Rocca B L, et al. Effect of B-type natriuretic peptide-guided treatment of chronic heart failure on total mortality and hospitalization: an individual patient meta-analysis[J]. *European Heart Journal*, 2014, 35(23): 1559-1567
- [4] Zhou R, Yao W, Yan-Hong L I, et al. Meglumine cyclic adenylate induces differentiation of bone marrow mesenchymal stem cells into cardiomyocytes in vitro [J]. *Chinese Journal of Tissue Engineering Research*, 2014, 18(1): 155-160
- [5] Sharma K, Kass D A. Heart failure with preserved ejection fraction: mechanisms, clinical features, and therapies[J]. *Circulation Research*, 2014, 115(1): 79-96
- [6] Hu Y, Peng D, Tang S, et al. To evaluate the clinical curative effect of meglumine adenosine cyclophosphate combined with Perindopril on patients with chronic congestive heart failure [J]. *Chinese Journal of Emergency Medicine*, 2014, 23(4): 439-442
- [7] 彭静, 陈俐, 马敏. 环磷腺苷葡胺联合培哚普利治疗慢性心力衰竭的效果[J]. *中国医药导报*, 2015, 12(34): 126-129
Peng Jing, Chen Li, Ma Min, et al. Effect of meglumine adenosine cyclophosphate combined with perindopril in treatment of chronic heart failure[J]. *China Medical Herald*, 2015, 12(34): 126-129
- [8] Ebner N, Elsner S, Steinbeck L, et al. Risk Factors of Anaemia-Development in Patients with Chronic Heart Failure: Results from the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF) [J]. *European Heart Journal*, 2014, 20(7): 38-39
- [9] Stewart S, Carrington M J, Horowitz J D, et al. Prolonged impact of home versus clinic-based management of chronic heart failure: Extended follow-up of a pragmatic, multicentre randomized trial cohort [J]. *International Journal of Cardiology*, 2014, 174(3): 600-610
- [10] Hirt M N, Muttardi A, Helms T M, et al. General practitioners' adherence to chronic heart failure guidelines regarding medication: the GP-HF study[J]. *Clinical Research in Cardiology*, 2015, 105(5): 1-10
- [11] Yao C Z, Huang X H, Li L. Perindopril Improves Cardiac Function but not Diaphragmatic Fatigue in Rats with Chronic Heart Failure[J]. *Latin American Journal of Pharmacy*, 2015, 34(1): 30-35
- [12] Hu Y, Peng D, Tang S, et al. To evaluate the clinical curative effect of meglumine adenosine cyclophosphate combined with Perindopril on patients with chronic congestive heart failure [J]. *Chinese Journal of Emergency Medicine*, 2014, 23(4): 439-442
- [13] Chang H Y, Jiang Y H, Yang G, et al. Effects of Different Dose of Perindopril on Cardiac Function in Patients with Congestive Heart Failure[J]. *China Pharmacy*, 2014, 25(20): 1850-1852
- [14] 张贵生, 张婷婷, 瞿玲玲. 环磷腺苷葡胺对老年慢性 CHF 病人心功能、血浆胱抑素 C 及脑钠肽的影响[J]. *中西医结合心脑血管病杂志*, 2014, 12(2): 137-138
Zhang Gui-sheng, Zhang Ting-ting, Qu Ling-ling, et al. Effects of Meglumine adenosine cyclophosphate on Cardiac Function, Cys-C and BNP levels of elderly patients with chronic CHF[J]. *Chinese Journal of Integrative Medicine on Cardio*, 2014, 12(2): 137-138

者的皮肤瘙痒症状,降低 BA 水平,改善肝功能,疗效显著且安全性高。但对于该联合用药方案的具体作用机制及有效性、安全性仍需更多前瞻性、多中心、大规模的临床研究证实。

参考文献(References)

- [1] Grymowicz M, Czajkowski K, Smolarczyk R. Pregnancy course in patients with intrahepatic cholestasis of pregnancy treated with very low doses of ursodeoxycholic acid[J]. Scand J Gastroenterol, 2016, 51(2): 78-85
- [2] Oztas E, Erkenekli K, Ozler S, et al. Can routine laboratory parameters predict adverse pregnancy outcomes in intrahepatic cholestasis of pregnancy?[J]. J Perinat Med, 2015, 43(6): 667-674
- [3] Xiang K, Yan K, Zhang F, et al. Evaluating the effectiveness and safety of ursodeoxycholic acid in treatment of intrahepatic cholestasis of pregnancy[J]. Medicine (Baltimore), 2016, 95(40): e4949
- [4] Ozkan S, Ceylan Y, Ozkan O V, et al. Review of a challenging clinical issue: Intrahepatic cholestasis of pregnancy[J]. World J Gastroenterol, 2015, 21(23): 7134-7141
- [5] Shemer E A W, Stephansson O, Thuresson M, et al. Intrahepatic cholestasis of pregnancy and cancer, immune-mediated and cardiovascular diseases: A population-based cohort study [J]. J Hepatol, 2015, 63(2): 456-461
- [6] Zhang Y, Hu L, Cui Y, et al. Roles of PPAR γ /NF- κ B signaling pathway in the pathogenesis of intrahepatic cholestasis of pregnancy[J]. PLoS One, 2014, 9(1): e87343
- [7] Ren X, Ma S, Wang J, et al. Comparative effects of dexamethasone and bergenin on chronic bronchitis and their anti-inflammatory mechanisms based on NMR metabolomics [J]. Mol Biosyst, 2016, 12(6): 1938-1947
- [8] Obstetrics Subgroup, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association. Guidelines for the management of intrahepatic cholestasis of pregnancy (2015)[J]. J Clin Hepatol, 2015, 31(7): 1575-1578
- [9] Ribalta J, Reyes H, Gonzalez M C, et al. S-adenosyl-L-methionine in the treatment of patients with intrahepatic cholestasis of pregnancy: a randomized, double-blind, placebo-controlled study with negative results[J]. Hepatology, 1991, 13(6): 1084-1089
- [10] Reyes H. What have we learned about Intrahepatic Cholestasis of Pregnancy?[J]. Hepatology, 2016, 63(1): 4-8
- [11] Reyes H. Sulfated progesterone metabolites in the pathogenesis of intrahepatic cholestasis of pregnancy: Another loop in the ascending spiral of medical knowledge[J]. Hepatology, 2016, 63(4): 1080-1082
- [12] Zhang Y, Lu L, Victor D W, et al. Ursodeoxycholic Acid and S-adenosylmethionine for the Treatment of Intrahepatic Cholestasis of Pregnancy: A Meta-analysis[J]. Hepat Mon, 2016, 16(8): e38558
- [13] Zhang W W, Liu Y S, Wang Y, et al. Research on Antidepressant Effects of S-adenosylmethionine in Patients with Liver Diseases[J]. Prog Mod Biom, 2015, 15(6): 1196-1197
- [14] Wang J, Zhang H, Su C, et al. Dexamethasone ameliorates H S-induced acute lung injury by alleviating matrix metalloproteinase-2 and -9 expression[J]. PLoS One, 2014, 9(4): e94701
- [15] Barbosa S J, Vieira L, Fernandescunha G M, et al. Anti-Inflammatory Effect of Dexamethasone Controlled Released From Anterior Suprachoroidal Polyurethane Implants on Endotoxin-Induced Uveitis in Rats[J]. Invest Ophthalmol Vis Sci, 2016, 57(4): 1671-1679
- [16] Wu Y Z, Banba C R, Li Y N. Dexamethasone for the Treatment of Rats with ANIT-induced Cholestasis [J]. J Clin Res, 2014, 31(1): 104-106
- [17] Glantz A, Marschall H U, Lammert F, et al. Intrahepatic cholestasis of pregnancy: a randomized controlled trial comparing dexamethasone and ursodeoxycholic acid[J]. Hepatology, 2005, 42(6): 1399-1405
- [18] Tan B J, Li Y M, Feng X P, et al. The Therapeutic Effect of Succinic Acid Adenosine Methionine Combined with Dexamethasone in Patients with Intrahepatic Cholestasis of Pregnancy and Its Influences on Immune Function[J]. J Int Obstet Gynecol, 2016, 43(5): 563-566
- [19] Cai A Q, Liu L Y, Zhang Y F, et al. Research progress of intrahepatic cholestasis of pregnancy [J]. Prog Obstet Gynecol, 2016, 25(11): 871-873
- [20] Xiang H, Zhang D H, Yi Y L, et al. Clinical value of the detection of serum IL-12 and TNF- α in patients with intrahepatic cholestasis of pregnancy[J]. Hainan Med J, 2016, 27(7): 1057-1059

(上接第 3710 页)

- [15] 陈涛, 陈丽华. 环磷腺苷葡胺联合培哚普利治疗慢性心力衰竭的疗效观察[J]. 安徽医药, 2015, 19(2): 384-386
Chen Tao, Chen Li-hua. Effects of Meglumine adenosine cyclophosphate combined with Perindopril on patients with chronic congestive heart failure[J]. Anhui Medical and Pharmaceutical Journal, 2015, 19(2): 384-386
- [16] Oremus M, Donwauchope A, Mckelvie R, et al. BNP and NT-proBNP as prognostic markers in persons with chronic stable heart failure[J]. Heart Failure Reviews, 2014, 19(4): 471-505
- [17] Arcopinto M, Isgaard J, Marra A M, et al. IGF-1 predicts survival in chronic heart failure. Insights from the T.O.S.C.A. (Trattamento Ormonale Nello Scompenso CArdiaco) registry[J]. International Journal of Cardiology, 2014, 176(3): 1006-1008
- [18] 李双海, 许放华, 王启林, 等. 慢性心力衰竭患者血清 hs-cTnT 及 galectin-3 水平及其临床意义[J]. 现代生物医学进展, 2016, 16(24): 4723-4726
Li Shuang-hai, Xu Fang-hua, Wang Qi-lin, et al. Clinical Significance of Galectin-3 and Hypersensitive Cardiac Troponin T Levels in Patients with Chronic Heart Failure [J]. Progress in Modern Biomedicine, 2016, 16(24): 4723-4726
- [19] Wang C, Chang Y, Zheng L, et al. A Correlation Study Between Serum Cystatin C and the Severity of Chronic Heart Failure [J]. Chinese Journal of Arteriosclerosis, 2014, 22(2): 181-185
- [20] Zhao F, Huang T, Cardiology D O, et al. The application of serum Cystatin C level in evaluation of cardiac function in patients with chronic heart failure[J]. Journal of Bengbu Medical College, 2014, 39(3): 324-325, 328