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# 氯沙坦联合环磷腺苷葡胺对肺心病患者心肺及免疫功能的影响 *

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**摘要 目的：**探讨氯沙坦联合环磷腺苷葡胺对肺心病患者心肺功能和免疫功能的影响。**方法：**选择 2010 年 9 月至 2015 年 9 月我院接诊的 94 例肺心病患者并按随机数表法分为观察组和对照组，每组各 47 例。对照组给予常规肺心病治疗，观察组在对照组的基础上给予氯沙坦联合环磷腺苷葡胺进行治疗。比较两组治疗前后 CO、LVEF、SV、FEV1 及 FEV1/FV、IgG、IgA、补体 C3、血清白细胞介素 -2 (interleukin-2，IL-2)、可溶性白细胞介素 2 受体 (soluble interleukin-2 receptor，sIL-2R)、8- 异前列腺素 (8-ISO prostaglandin，8-iso-PG) 水平的变化以及治疗后的临床疗效。**结果：**治疗后，观察组 CO、LVEF、SV、FEV1 及 FEV1/FVC 水平均显著高于对照组[(5.21± 0.27) vs (4.15± 0.46)，(63.42± 6.17) vs (52.37± 5.76)，(74.68± 9.24) vs (64.56± 11.73)，(1.75± 0.27) vs (1.32± 0.31)，(75.68± 10.62) vs (65.49± 10.05)](P<0.05)，血清补体 C3 高于对照组[(1.34± 0.12) g/L vs(1.16± 0.10) g/L] (P<0.05)；血清 sIL-2R、8-iso-PG 水平显著低于对照组 [(371.46± 161.06) U/ml vs (435.75± 152.43) U/ml,(23.58± 11.72) ng/L vs (31.08± 11.39) ng/L] (均 P<0.05)；观察组总有效率高于对照组[(95.74)% vs(78.72)%] (P<0.05)。**结论：**氯沙坦联合环磷腺苷葡胺可有效提高肺心病患者心、肺及免疫功能。

**关键词：**氯沙坦；环磷腺苷葡胺；肺心病；心肺功能；疗效

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# Effect of Losartan Combined with Cyclic Adenosine Monophosphate on the Heart, Lung and Immune Functions of Patients with Pulmonary Heart Disease*

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**ABSTRACT Objective:** To study the curative efficacy of losartan combined with cyclic adenosine monophosphate in the treatment of pulmonary heart disease and the serum levels of IL-2, sIL-2R and 8-iso-PG. **Methods:** 94 patients with pulmonary heart disease who were treated from September 2010 to September 2015 were selected and randomly divided into the observation group and the control group with 47 cases in each group. The control group was treated with conventional treatment of pulmonary heart disease, while the observation group was treated with losartan and cyclic adenosine monophosphate on the basis of control group. Then the cardiac function, pulmonary function, immune function, serum levels of IL-2, sIL-2R and 8-iso-PG and curative effect in the two groups were observed and compared before and after the treatment. **Results:** After treatment, the cardiac function improved in both groups (P<0.05); The levels of CO, LVEF, SV, FEV1 and FEV1 / FVC in the observation group were higher than those of the control group [(5.21± 0.27) vs (4.15± 0.46), (63.42± 6.17) vs (52.37± 5.76), (74.68± 9.24) vs (64.56± 11.73), (1.75± 0.27) vs (1.32± 0.31), (75.68± 10.62) vs (65.49± 10.05)] (P<0.05); The complement C3 level of observation group was higher than that of the control group[(1.34± 0.12) g/L vs(1.16± 0.10) g/L] (P<0.05); The levels of sIL-2R and 8-iso-PG of observation group were lower than those of the control group [(371.46± 161.06) U/ml vs(435.75± 152.43) U/ml, (23.58± 11.72) ng/L vs(31.08± 11.39) ng/L] (P<0.05). The total effective rate of observation group was higher than that of the control group [95.74% vs78.72%] (P<0.05). **Conclusion:** Losartan combined with adenosine cyclophosphamide could improve the heart, lung and immune function, enhance the level of complement C3, and improve the symptoms of ischemia and hypoxia.

**Key words:** Losartan; Cyclic adenosine monophosphate; Pulmonary heart disease; Heart and lung function; Effect

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## 前言

肺心病是由肺血管系统、肺组织及胸廓等发生病变，从而

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增大肺循环阻力及肺动脉高压,增大右心室,最终导致心、肺衰竭的心脏病,又称慢性肺源性心脏病。该病症在我国属于常见病、多发病,患病率高达 15%~50%,且占住院心脏病比例高达 38%~46%[7-9]。根据患者起病急缓及病程分为慢性和急性,以慢性肺心病为主。肺动脉血管及慢性支气管等发生病变不断增加肺循环的阻力,临床症状多为慢性咳嗽、气急、乏力及咳痰等,若未及时治疗,则会逐步损伤心、肺功能,最终形成心、肺功能衰竭[1-3]。近年来,肺心病患者多采用镇咳、祛痰、平喘和抗感染等常规治疗,然而由于患者机体已经有不同程度的损伤,故该治疗方式效果并不理想。

氯沙坦是血管紧张素 II 受体拮抗剂(AIIA)类的抗高血压药物,能够阻断血管紧张素 II。环磷腺苷葡胺可有效改善心肌缺血缺氧状态,二者联合治疗肺心病可有效改善患者心、肺功能,效果明显[4,5]。为进一步探讨氯沙坦联合环磷腺苷葡胺治疗肺心病的应用价值,我院选取了 94 例肺心病患者,在常规治疗基础上采用氯沙坦联合环磷腺苷葡胺进行治疗,探讨了其疗效及对患者血清白细胞介素 -2(interleukin-2,IL-2)、可溶性白细胞介素 2 受体(soluble interleukin-2 receptor,sIL-2R)、8- 异前列腺素(8-ISO prostaglandin,8-iso-PG)水平的影响,现报道如下。

## 1 资料与方法

### 1.1 一般资料

选取 2010 年 9 月至 2015 年 9 月我院接诊的 94 例肺心病患者。排除标准[6]:① 具有语言、认知类障碍;② 患有肝、肾等严重耗损性疾病;③ 近期进行手术或者患有恶性肿瘤、感染、高血压等其他心脏类病变;④ 近期使用过抗凝或纤溶药物。将所有患者随机分为观察组和对照组,每组各 47 例。观察组患者年龄 40~74 岁,平均(57.63± 2.48)岁;男 22 例,女 25 例;病程 6~24 年,平均(12.06± 3.48)年;支气管哮喘 10 例,慢性支气管炎 27 例,肺气肿 10 例。对照组患者年龄 42~73 岁,平均 (56.94± 2.57)岁;男性 20 例,女性 27 例;病程 5~25 年,平均(12.68± 3.71)年;其中支气管哮喘 9 例,慢性支气管炎 26 例,肺气肿 12 例。整个研究在患者知情同意并签署知情同意书的情况下进行,且通过我院伦理委员会批准。两组患者的性别、年龄等情况比较差异均无统计学意义,具有可比性(P>0.05)。

### 1.2 治疗方法

对照组患者按照 " 慢性肺源性心脏病诊疗规范 " 进行常规治疗,主要治疗包括:纠正电解质紊乱、化痰、平喘、利尿、强心及抗炎等。观察组在对照组基础上以氯沙坦联合环磷腺苷葡胺治疗。氯沙坦钾片 (科素亚,规格 50 mg× 7 s,国药准字 H20000371,厂家:杭州默沙东制药有限公司),口服 50 mg,1 次 /1 d,联合环磷腺苷葡胺(凯缇,厂家:无锡凯夫制药有限公司,规格:30 mg,国药准字 H20050864),经稀释后静脉滴注 120 mg,1 次 /1 d。两组疗程均为 2 周,一疗程后对比两组患者疗效。

### 1.3 观察指标

1.3.1 **心功能** 检测患者治疗前后心功能指标:心输出量(CO)、左室射血分数(LVEF)及每搏量(SV)。

1.3.2 **肺功能** 检测患者治疗前后肺功能:用力肺活量(FVC)及一秒用力呼气容积(FEV1)。

1.3.3 **免疫功能** 检测患者治疗前后免疫功能:免疫球蛋白 A(IgA)、免疫球蛋白 G(IgG)以及补体 C3 含量。

1.3.4 **血清 IL-2、sIL-2R、8-iso-PG 水平** 分别取患者治疗前后早晨空腹静脉血,以双抗体夹心 ELISA 法检测 sIL-2R 及 8-iso-PG 水平 (试剂盒由上海恒远生物科技有限公司提供),采用多抗体夹心 ELISA 法检测 IL-2 水平 (试剂盒由上海沪宇生物科技有限公司提供)。

1.3.5 **治疗疗效评价** ① 显效:患者心悸、咳喘等心衰症状明显改善,基本未闻肺部湿啰音,肝脏有效缩小至少 2 cm,心功能分级降低 2 级;② 患者临床症状有所改善,可略闻肺部湿啰音,肝脏有所缩小,心功能分级降低 1 级;③ 患者治疗后无任何变化或反而加重病情。

### 1.4 统计学分析

数据用 SPSS18.0 软件包处理,计量资料用均数± 标准差($\bar{x}$± s) 表示,并采用 t 检验,计数资料的比较采用 $\chi^2$ 检验,以 P<0.05 表示差异具有统计学意义。

## 2 结果

### 2.1 两组患者治疗前后的心功能比较

治疗前,两组患者 CO、LVEF、SV 水平比较差异无统计学意义(P>0.05);治疗后,两组患者 CO、LVEF、SV 水平均较治疗前显著提高(P<0.05),且观察组的 CO、LVEF、SV 水平均显著高于对照组(P<0.05)。详见表 1。

**表 1 两组患者治疗前后心功能的比较($\bar{x}$± s)**

Table 1 Comparison of the heart function between the two groups before and after treatment($\bar{x}$± s)

| Groups | CO(L/min) | | LVEF(%) | | SV( mL/times) | |
|---|---|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Observation group(n=47) | 3.42± 0.29 | 5.21± 0.27*# | 44.32± 4.88 | 63.42± 6.17*# | 50.43± 10.64 | 74.68± 9.24*# |
| Control group(n=47) | 3.38± 0.31 | 4.15± 0.46* | 44.29± 4.91 | 52.37± 5.76* | 50.07± 10.98 | 64.56± 11.73* |

Note: Compared with before treatment, *P＜0.05; compared with the control group, #P＜0.05.

### 2.2 两组患者治疗前后的肺功能比较

治疗前,两组患者的 FEV1 及 FEV1/FVC 水平比较差异无统计学意义(P>0.05);治疗后,两组患者 FEV1 及 FEV1/FVC 水平均较治疗前显著提高 (P<0.05),且观察组患者 FEV1 及 FEV1/FVC 水平显著高于对照组(P<0.05)。见表 2。

### 2.3 两组患者治疗前后的免疫功能比较

治疗前,两组患者血清 IgG、IgA 及 C3 水平比较差异无统计学意义(P>0.05);治疗后,两组患者血清 IgG 及 IgA 水平较治疗前无明显变化(P>0.05),观察组患者 C3 水平与治疗前相比明显提高,且明显高于对照组(P<0.05)。详见表 3。

### 2.4 两组患者治疗前后血清 IL-2、sIL-2R、8-iso-PG 水平的比较

治疗前,两组患者血清 IL-2、sIL-2R、8-iso-PG 水平比较差

异无统计学意义(P>0.05);治疗后,两组患者的血清 IL-2 水平及对照组患者的 sIL-2R、8-iso-PG 水平均较治疗前无明显变化(P>0.05),观察组患者的血清 8-iso-PG 及 sIL-2R 水平较治疗前明显下降,且明显低于对照组(P<0.05)。详见表 4。

**表 2 两组患者治疗前后肺功能的比较($\bar{x}\pm s$)**

Table 2 Comparison of the lung function between the two groups before and after treatment ($\bar{x}\pm s$)

| Groups | FEV1(L) | | FEV1/FVC(%) | |
|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment |
| Observation group(n=47) | 1.18± 0.33 | 1.75± 0.27*# | 60.47± 10.65 | 75.68± 10.62*# |
| Control group(n=47) | 1.17± 0.34 | 1.32± 0.31* | 61.06± 10.47 | 65.49± 10.05* |

Note: Compared with before treatment, *P＜0.05; compared with the control group, #P＜0.05.

**表 3 两组患者治疗前后的血清 IgG、IgA 及 C3 水平比较($\bar{x}\pm s$,g/L)**

Table 3 Comparison of the serum IgG, IgA and C3 levels between the two groups before and after treatment ($\bar{x}\pm s$,g/L)

| Groups | IgG | | C3 | | IgA | |
|---|---|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Observation group(n=47) | 11.88± 2.06 | 12.02± 1.98 | 1.14± 0.11 | 1.34± 0.12*# | 1.53± 0.22 | 1.52± 0.20 |
| Control group(n=47) | 11.72± 2.04 | 11.93± 2.01 | 1.13± 0.14 | 1.16± 0.10 | 1.55± 0.19 | 1.56± 0.21 |

Note: Compared with before treatment, *P＜0.05; compared with the control group, #P＜0.05.

**表 4 两组患者治疗前后血清 IL-2、sIL-2R、8-iso-PG 水平的比较($\bar{x}\pm s$)**

Table 4 Comparison of the serum levels of IL-2, sIL-2R, 8-iso-PG between the two groups before and after treatment ($\bar{x}\pm s$)

| Groups | IL-2(pg/mL) | | sIL-2R(U/mL) | | 8-iso-PG(ng/L) | |
|---|---|---|---|---|---|---|
| | Before treatment | After treatment | Before treatment | After treatment | Before treatment | After treatment |
| Observation group(n=47) | 1375.11± 420.45 | 1490.15± 402.45 | 508.58± 162.42 | 371.46± 161.06*# | 41.58± 9.56 | 23.58± 11.72*# |
| Control group(n=47) | 1368.97± 417.88 | 1421.34± 441.28 | 503.43± 163.02 | 435.75± 152.43 | 41.84± 9.35 | 31.08± 11.39 |

Note: Compared with before treatment, *P＜0.05; compared with the control group, #P＜0.05.

### 2.5 两组患者的疗效比较

观察组总有效率为 95.74%,显著高于对照组(78.72%,P<0.05)。详见表 5。

**表 5 两组患者的疗效比较[例(%)]**

Table 5 Comparison of the clinical efficacy between the two groups [n(%)]

| Groups | Markedly | Effective | Invalid | Total effective rate |
|---|---|---|---|---|
| Observation group(n=47) | 20(42.55) | 25(53.19) | 2(4.26) | 45(95.74) |
| Control group(n=47) | 14(29.79) | 23(48.94) | 10(21.28) | 37(78.72) |

## 3 讨论

肺心病进展分为代偿和失代偿期。患者代偿期多呈现慢性咳嗽、哮喘等症状,逐步变化成乏力、呼吸困难等;当患者处于失代偿期时,肺组织已经开始逐步损伤,交感神经及肾素 - 血管紧张素 - 醛固酮系统的活性提高,从而引起体液潴留、血管收缩以及重塑心脏血管等,临床症状由心悸、胸闷等逐步衍变成头痛、烦躁、精神错乱等严重缺氧状态,呼吸道感染后,通常呈现呼吸衰竭症状,严重者易发生休克以致死亡[10,11]。目前,肺心病患者的治疗多采用常规治疗法[12,13],主要通过抗炎、强心、平喘等对病情进行控制,但由于肺心病患者心肌及肺组织已受到损伤,处于缺氧状态,特别是高龄患者心肺代偿功能逐步减退,且耐受性逐步降低,治疗效果并不理想。

血管紧张素Ⅱ可抑制一氧化氮的有效合成,同时对氧化应激起诱发和强化作用,氧化应激的产物自由基则会加强分解一氧化氮,最终损伤肺部血管内皮细胞,由于血管紧张素Ⅱ会增加白细胞相互黏附的作用,进一步加重损伤肺组织[14,15]。氯沙坦是一种抗高压药物,直接作用于肾素 - 血管紧张素系统,属于血管紧张素Ⅱ受体的拮抗剂,通过有效抑制血管紧张素Ⅱ中的 1 型受体使血管紧张素Ⅱ水平下降,阻断体液潴留、血管收缩以及重塑心脏血管等病理作用,达到改善右心室增大且有效提高心脏舒张及收缩功能的作用[16-18]。环磷腺苷葡胺属于非洋地黄类强心剂,是环磷酸腺苷的一种衍生物,且其作用机制也与洋地黄类不同,该药物亲水亲脂性较强,可直接提高环磷酸腺苷的溶脂性,从而增强心肌收缩力,并对心脏泵血功能进行有效改善,同时对外周血管起扩张作用,有效降低心脏负荷及耗氧量,提高心排血量,从而对缺血缺氧的心肌细胞进行有效保护[19,20]。有研究表明氯沙坦联合环磷腺苷葡胺可有效改善患者心、肺及免疫功能。本研究结果也表明氯沙坦和环磷腺苷葡胺联合治疗的患者肺功能及心功能水平均优于常规治疗。

IL-2 属于 T 细胞生长因子,可有助于 T 细胞的分泌,当 IL-2 受体释放至血清中时则变为 sIL-2R,肺心病患者的心肌及

肺组织损伤会导致膜 IL-2R 水平增高，与 sIL-2R 竞相结合 IL-2，从而使 IL-2 的免疫监视功能发挥抑制作用[21,22]。本研究中，联合治疗患者 sIL-2R 水平有效降低，可能使膜 IL-2R 可有效与 IL-2 相结合，从而增强患者的免疫功能。研究表明氧自由基对细胞膜脂质的花生四烯酸起过氧化作用，产物为 8-iso-PG，其结构较为稳定，属于前列腺素的异构体，并且不因食物脂质的含量和药物影响而产生变化，一般被用来反映机体氧化应激的强度，由于环磷腺苷葡胺和氯沙坦联合可有效抑制患者的炎症反应，降低机体肺组织损伤及肺血管平滑肌细胞增生，最终降低机体肺动脉高压状态，其氧化应激强度也逐渐降低[23-25]。本研究中，沙坦联合环磷腺苷葡胺治疗患者 8-iso-PG 水平有效降低，且与常规治疗患者相比降低程度更加明显。补体 C3 属于反映免疫功能的血清含量最高的成分，当机体出现组织损伤时，C3 会呈明显提升状态，并逐步降低。据研究，C3 可有效反映患者的病情，当病情有所缓解时，C3 含量则会逐步恢复正常。慢性肺心病患者由于肺组织等机体的损伤，其 C3 含量会显著低于正常值[26,27]。本研究中，氯沙坦联合环磷腺苷葡胺治疗患者血清 sIL-2R 水平有效降低至(371.46± 161.06)U/mL，且补体 C3 含量提升至(1.34± 0.12)g/L，逐步偏向正常。经联合治疗，肺心病患者的临床症状如平喘、心悸及肺部湿啰音等均得到改善，患者的不适感逐步降低，本研究中，总有效率高达 95.74%，表明氯沙坦联合环磷腺苷葡胺治疗与常规治疗相比，效果更为显著。

综上所述，氯沙坦联合环磷腺苷葡胺可有效提高患者心、肺及免疫功能，增强患者补体 C3 水平，并改善缺血缺氧症状。

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