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大承气汤辅助治疗 ARDS 患者对其 pH、PaO₂/FiO₂ 和氧化应激状态的影响 *

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摘要 目的:观察大承气汤辅助治疗 ARDS 患者对其 pH、氧合指数(PaO₂/FiO₂)及氧化应激状态的影响。**方法:**选择 2014 年 8 月~2016 年 8 月于成都中医药大学临床医学院就诊的 82 例 ARDS 患者,按治疗方式的不同随机分为对照组与实验组,对照组接受常规治疗,实验组在对照组的基础上联合大承气汤治疗,两组均持续用药 7 天。观察两组 ICU 住院时间、机械通气时间、不良反应的发生情况、治疗前后 pH、PaO₂/FiO₂、血气超氧化物歧化酶(SOD)、谷胱甘肽过氧化物酶(GSH-Px)、丙二醇(MDA)水平的变化。**结果:**实验组 ICU 住院时间、机械通气时间及不良反应的发生率均显著短于或低于对照组(P<0.05)。治疗前,两组 pH、PaO₂/FiO₂、血清 SOD、GSH-Px、MDA 水平比较差异无统计学意义(P>0.05);治疗后,两组 pH、PaO₂/FiO₂、血清 SOD、GSH-Px 水平均较治疗前显著上升,且实验组 PaO₂/FiO₂、血清 SOD、GSH-Px 水平明显高于对照组,两组血清 MDA 水平均较治疗前明显降低,且实验组血清 MDA 水平显著低于对照组(P<0.05)。**结论:**大承气汤辅助治疗 ARDS 能够有效改善患者 pH、PaO₂/FiO₂,缓解氧化应激状态,利于患者恢复。

关键词:急性呼吸窘迫综合征(ARDS);大承气汤;动脉血气分析;氧化应激

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Influence of Dachengqi Decoction Adjuvant Therapy on pH, PaO₂/FiO₂ and Oxidative Stress Status of Patients with ARDS*

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ABSTRACT Objective: To observe the influence of dachengqi decoction adjuvant therapy on the pH, PaO₂/FiO₂ and oxidative stress status of patients with ARDS. **Methods:** 82 patients with ARDS admitted in Chengdu university of traditional Chinese medicine clinical medicine from August 2014 to August 2016 were selected and randomly divided into the control group and the experimental group according to different treatment methods, the control group was treated by conventional methods, while the experimental group was treated by Dachengqi Decoction based on the control group, both groups were continuously treated for 7 days. The mechanical ventilation, length of ICU hospitalization time, and incidence of adverse reactions, changes of pH, Pa O₂/Fi O₂, superoxide disproportionation alcohol (SOD), glutathione peroxidase (GSH-Px), propylene glycol (MDA) levels before and after treatment were compared between two groups. **Results:** The ICU hospitalization time, mechanical ventilation time and incidence rate of adverse reactions in the experimental group were significantly shorter or less than those of the control group (P<0.05). After treatment, the pH, PaO₂/FiO₂, serum levels of SOD, GSH-Px of both groups were all risen than those before treatment, the PaO₂/FiO₂, serum levels of SOD, GSH-Px of experimental group were obviously higher than those of the control group, the serum levels of MDA of both groups were significantly decreased than those before the treatment, which was lower in the experimental group than that of the control group(P<0.05). **Conclusion:** Dachengqi Decoction auxiliary treatment of patients with ARDS could effectively improve the pH, PaO₂/FiO₂, relieve the oxidative stress status.

Key words: Acute respiratory distress syndrome (ARDS); Dachengqi decoction; Arterial blood gas analysis; Oxidative stress

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前言

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急性呼吸窘迫综合征(ARDS)是由气胸、血胸、肺挫伤等严重肺内外病变引起肺部毛细血管出现弥漫性的受损,导致其通透性增加、肺部的顺应性下降,进而引起动脉血气改变。其中,肺不张、肺水肿是 ARDS 的主要病理改变,难治性低氧血症及进行性呼吸窘迫是其主要临床特征^[1,2]。ARDS 的发病突然,进

展快速,预后较差,尽管目前器官功能支持手段可进行肺开放、肺保护通气等治疗方式,但仍存在较高的病死率^[3,4]。近年来,中药治疗动物急性肺损伤已取得了较好的效果^[5,6]。ARDS 属中医阳明腑实证,应以泻火通便、凉膈泻热以治之,大承气汤为中医阳明腑实证的代表方剂,可通里攻下,但其作用机制仍未完全明确^[7]。有研究表明氧化应激在 ARDS 发生发展期中发挥了重要作用,能够增强机体过氧化,协同局部炎症反应,导致组织损伤加剧^[8]。本研究主要探讨了大承气汤辅助治疗 ARDS 患者对其 pH、氧合指数(PaO₂/FiO₂)及氧化应激状态的影响,从而为 ARDS 的临床治疗提供参考依据。

1 资料与方法

1.1 一般资料

选择 2014 年 8 月~2016 年 8 月于成都中医药大学临床医学院就诊的 82 例 ARDS 患者,纳入标准:符合 ARDS 相关诊断标准^[9](伴 ARDS 高危诱因,发病急骤、呼吸窘迫或者呼吸频数,低氧血症,胸部平片提示双侧肺部可见浸润阴影,排除除肺静脉受压、肾病综合征、肝硬化等非心源性肺水肿);属中医阳明腑实证(脘腹胀满、大便干结、呼吸急促、苔黄燥、舌红绛等症状);无肺性脑病、肝性脑病、肝肾综合征等并发症;受伤至入院时间在 6h 以内;意识异常。排除心功能严重不全;呼吸系统慢性病变;近期接受过干扰素、免疫抑制剂、激素等治疗;免疫功能低下或者重度贫血;过敏体质。对照组中,17 例女性,24 例男性;年龄 25~71 岁,平均(47.69±6.82)岁;病因:6 例重症胰腺炎,14 例脓毒症,12 例肺部感染,9 例其他。实验组中,19 例女性,22 例男性;年龄 23~72 岁,平均(47.12±6.75)岁;病因:5 例重症胰腺炎,16 例脓毒症,11 例肺部感染,9 例其他。两组一般

临床资料比较差异均无统计学意义(P>0.05),具有可比性。

1.2 治疗方法

对照组选用常规治疗,积极处理患者原发病,予以敏感抗生素、补液等基础治疗,并接通呼吸机进行辅助通气,同时实施常规心电图监测。实验组于对照组基础上联合大承气汤治疗,将生大黄 30 g(需后下)、黄连 6 g、芒硝 18 g(冲服)、厚朴 24 g、枳实 12 g 等加适量清水并浸泡 20 min,大火煮沸 5 min 后取文火煎煮 10 min,去渣留汁,予以真空包装,200 mL/袋,单剂为 2 袋,予以患者早晚经缓慢胃管给药,两组均持续用药 7 d。记录两组 ICU 住院时间、机械通气时间及不良反应的发生情况。

1.3 观察指标

于治疗前及治疗结束时抽取患者 2 mL 空腹动脉脉血,常规处理后保存待检。pH、PaO₂/FiO₂ 选用血气分析仪进行。超氧化物歧化酶(SOD)及谷胱甘肽过氧化物酶(GSH-Px)按黄嘌呤氧化酶法进行,试剂盒:广西康迪药业有限公司、山西普德药业有限公司,丙二醇(MDA)按硫代巴比妥比色法进行,试剂盒:河北长天药业有限公司。

1.4 统计学分析

数据处理选用 SPSS18.0 软件进行,用($\bar{x} \pm s$)表示计量资料,组间比较选用 t 检验,用[(例)%]表示计数资料,组间比较用 χ^2 检验,以 P<0.05 为差异有统计学意义。

2 结果

2.1 两组 ICU 住院时间及机械通气时间比较

实验组 ICU 住院时间及机械通气时间均明显短于对照组,差异具有统计学意义(P<0.05),见表 1。

表 1 两组 ICU 住院时间及机械通气时间的比较($\bar{x} \pm s$)

Table 1 Comparison of the ICU hospitalization time and mechanical ventilation time between two group($\bar{x} \pm s$)

Groups	ICU hospitalization time(d)	Mechanical ventilation time(d)
Control group(n=41)	11.20±1.45	6.97±0.87
Experimental group(n=41)	9.45±1.12 ^a	5.23±0.65 ^a

Note: Compared with control group ^aP<0.05.

2.2 两组治疗前后 pH、PaO₂/FiO₂ 比较

两组治疗前 pH、PaO₂/FiO₂ 比较差异无统计学意义(P>0.05);两组治疗后 pH、PaO₂/FiO₂ 均较治疗前上升,但组间 pH 比

较差异无统计学意义(P>0.05),而实验组 PaO₂/FiO₂ 显著高于对照组(P<0.05),见表 2。

表 2 两组治疗前后 pH、PaO₂/FiO₂ 的比较($\bar{x} \pm s$)

Table 2 Comparison of the pH and PaO₂/FiO₂ between two group before and after treatment ($\bar{x} \pm s$)

Groups	Time	pH	PaO ₂ /FiO ₂
Control group(n=41)	Before treatment	7.01±1.16	156.90±19.52
	After treatment	7.39±0.40 ^b	215.88±26.97 ^b
Experimental group(n=41)	Before treatment	7.02±1.09	155.78±20.23
	After treatment	7.46±0.76	260.12±32.51 ^{ab}

Note: Compared with the control group ^aP<0.05; Compared with before treatment ^bP<0.05.

2.3 两组治疗前后氧化应激状态的比较

两组治疗前血清 GSH-Px、SOD、MDA 水平比较差异无统

计学意义(P>0.05);两组治疗后血清 GSH-Px、SOD 水平均较治疗前显著上升,且实验组明显高于对照组(<0.05),两组治疗后

血清 MDA 水平均较治疗前明显降低,且实验组显著低于对照组($P<0.05$),见表 3。

表 3 两组治疗前后氧化应激状态的比较($\bar{x}\pm s$)

Table 3 Comparison of the oxidative stress status between two group before and after treatment ($\bar{x}\pm s$)

Groups	Time	GSH-Px(mg/L)	SOD(U/L)	MDA(μ mol/L)
Control group(n=41)	Before treatment	135.79 $\pm$ 16.90	597.36 $\pm$ 74.73	11.32 $\pm$ 1.42
	After treatment	156.03 $\pm$ 19.52 ^b	731.06 $\pm$ 91.32 ^b	9.11 $\pm$ 1.13 ^b
Experimental group(n=41)	Before treatment	136.24 $\pm$ 15.03	598.20 $\pm$ 75.80	11.60 $\pm$ 1.32
	After treatment	189.21 $\pm$ 23.61 ^{ab}	811.35 $\pm$ 101.23 ^{ab}	7.28 $\pm$ 0.90 ^{ab}

Note: Compared with control group ^a $P<0.05$; Compared with before treatment ^b $P<0.05$.

2.4 两组治疗前后 APACHE II 评分的比较

两组治疗前 APACHE II 评分比较差异无统计学意义($P>0.05$);

两组治疗后 APACHE II 评分均较治疗前明显下降,且实验组显著低于对照组($P<0.05$),见表 4。

表 4 两组治疗前后 APACHE II 评分的比较($\bar{x}\pm s$)

Table 4 Comparison of the APACHE II score between two group before and after treatment($\bar{x}\pm s$)

Groups	Time	APACHE II score(points)
Control group(n=41)	Before treatment	27.89 $\pm$ 3.45
	After treatment	23.15 $\pm$ 2.91 ^b
Experimental group(n=41)	Before treatment	28.06 $\pm$ 3.21
	After treatment	19.12 $\pm$ 2.36 ^{ab}

Note: Compared with control group ^a $P<0.05$; Compared with before treatment ^b $P<0.05$

2.5 两组不良反应发生情况的比较

两组均有气道水样分泌物、呼吸机肺炎、腹胀发生,实验组

不良反应的发生率(26.828%)较对照组明显降低(63.41%)($P<0.05$),见表 5。

表 5 两组不良反应发生情况的比较[(例)%]

Table 5 Comparison of the incidence of adverse reactions between two group[(n)%]

Groups	Airway watery discharge	Breathing machine pneumonia	Abdominal distension	Adverse reaction rate
Control group(n=41)	9(21.95)	10(24.39)	7(17.07)	26(63.41)
Experimental group(n=41)	4(9.75)	4(9.75)	3(7.31)	11(26.82) ^a

Note: Compared with control group ^a $P<0.05$.

3 讨论

ARDS 是临床常见危重症之一,为急性肺损伤进展至后期的主要表现,能够出现焦虑、烦躁、发绀、呼吸性碱中毒等症状,甚者可导致多个器官衰竭^[10,11]。临床治疗应积极处理创伤、尽快纠正患者缺氧状态、明确感染病灶,避免严重并发症的产生,但抗氧化剂、糖皮质激素、血液净化等常规手段对病死率的改善无显著作用^[12]。

中医学认为 ARDS 属阳明腑实证,大肠与肺互为表里,肺热邪气可传入大肠并移于阳明,同肠道糟粕互结,致肺气堵塞,浊气内陷,引痞胀腹满、浊气上逆,致肺气雍塞;阳明腑实,可使大便干结,引肺脏宣泄所失,致肺脏受损,喘促气逆,无权肃降,大肠与肺脏互为因果,可恶性循环^[13]。中医予以通里攻下法,可治阳明防肺受损,大承气汤方是伤寒论的经典方剂,由生大黄、黄连、芒硝、厚朴、枳实等合成,可起到攻下热结、行血祛瘀、通

体护脏等功效^[14]。生大黄性寒、苦,入大肠、胃经,可通里攻下、清热祛火;黄连入大肠、脾胃经,可泻火清热;芒硝可通便泻火、解毒;厚朴可消积行气;枳实可除痞解气,增强生大黄通腑理气之功^[15-17]。药理学目前研究认为,大承气汤能够清除毒素、杀菌,保护肠粘膜屏障,缓解炎症反应,同时可缓解肺水肿,保护肠、肺等功能^[18,19]。临床研究显示大承气汤治疗 ARDS 患者可取得良好的临床效果,本研究结果也显示大黄承气汤治疗的患者住院时间及机械通气时间均明显少于常规治疗者。

ARDS 患者由于肺部严重损伤,导致呼吸功能比较差,肺部换气及通气功能受阻,引起机体氧供出现影响,使血气分析及氧代谢指标产生相应的异常变化^[20]。其中, pH 能够客观反映机体的酸碱平衡程度,其水平增加可提示代谢性或者呼吸性碱中毒,水平降低说明机体处于肺心病、肺水肿或呼吸衰竭状态。细胞内氧合状态难以直接测定, PaO₂/FiO₂ 能够有效提示机体的氧合,判断机体是否缺氧。本研究结果显示所有喊着治疗前

pH、PaO₂/FiO₂ 均相对较低,治疗后均有一定上升,但大黄承气汤治疗后 PaO₂/FiO₂ 上升更为明显,表明大承气汤治疗能更有效促进动脉血气的改善,利于二氧化碳的排出。有研究表明肺脏正常状态下能够保持抗氧化及氧化平衡,肺部损伤时能够诱导氧自由基的过度发生,引起明显的氧化应激反应,导致肺泡损伤,参与 ARDS 进展^[21]。MDA 水平能够直接反映机体的过氧化程度,并能间接提示氧自由基的生成情况及其对于组织细胞造成的损伤程度。SOD 能够减少氧自由基对于细胞产生的损伤,并可使受损细胞得到及时修复。GSH-Px 作为机体一种抗氧化酶,能够清除脂质过氧化物,缓解自由基诱导的损伤。本研究结果显示患者治疗后 GSH-Px、SOD 均较治疗前上升,且 MDA 有明显下降,且大承气汤的改善作用更明显,提示其更有利于氧化应激的缓解,避免其对机体形成的进一步损伤。同时,本研究结果显示大黄承气汤治疗后 APACHE II 评分下降更明显,进一步说明其有利于病情程度缓解,促进患者的恢复。此外,两组治疗后均有气道水样分泌物、呼吸机肺炎、腹胀发生,但大承气汤组并发症率明显较低,说明其安全性更佳。

综上所述,大承气汤辅助治疗 ARDS 能够有效改善患者 pH、PaO₂/FiO₂,缓解氧化应激状态,利于患者恢复。

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