

阳明腑实证患者肠粘膜屏障功能的改变及复方大承气汤干预作用的临床观察

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摘要 目的:探讨阳明腑实时肠粘膜屏障功能改变的机制及复方大承气汤对肠粘膜屏障功能的防护作用。方法:20例阳明腑实证患者随机分为两组,一组给予常规治疗,另一组在常规治疗基础上给予中药复方大承气汤,连续5天。采血检测二胺氧化酶(DAO)和内毒素(ET)含量及尿中乳果糖与甘露醇排泄率比值(M/L)以观察肠粘膜通透性。另以10名健康志愿者作为正常对照组。结果:与对照组相比较,阳明腑实证患者尿中M/L比值明显升高;血中ET和DAO含量显著增加。应用复方大承气汤后,上述指标均明显降低($P<0.01$)。结论:阳明腑实证患者肠粘膜屏障受损,肠粘膜通透性增高,中药复方大承气汤可降低肠粘膜通透性,保护肠粘膜屏障功能,并能有效降低血内毒素含量。

主题词 阳明实证/中医药疗法 复方大承气汤/治疗应用

阳明腑实证是张仲景《伤寒论》中的一个主要证型,是临床常见症候群,具有发病急、病情重、变化快、并发症多的特点。如不及时诊治,常可引起休克、成人呼吸窘迫综合征(ARDS)、多器官功能不全综合征(MODS)而危及生命。我们以前的研究发现^[1],肠源性内毒素血症很可能就是阳明腑实证发生发展的病理基础,推测可能与阳明腑实证时肠道屏障损伤有关,但一直没有直接的证据。本研究应用双糖探针法测定阳明腑实证患者肠粘膜通透性,作为肠粘膜屏障功能的重要指标,观察阳明腑实证患者肠粘膜屏障损伤及其所引起内毒素血症的变化,并观察复方大承气汤的影响。

1 临床资料

1.1 观察对象:选择临床上具有阳明腑实证表现的腹部外科感染患者共20例,包括急性胰腺炎、急性胆系感染、急性肠梗阻、腹部手术后腹腔感染等。其中男11例,女9例。年龄15~81(54.45 ± 15.64)岁。入选条件:临床表现为腹痛、腹胀、不大便或大便秘结、发热、体温高于 37.6°C 、脉率 >100 次/分。腹部有压痛、反跳痛及不同程度的肌紧张。无糖尿病、肾病病史。

1.2 分组及处理:阳明腑实证患者随机分为常规治疗组及中药治疗组两组,同时设立非阳明腑实证对照组。对照组为非肠道、肿瘤、感染性疾病的患者及健康者共

10例;常规治疗组为阳明腑实证患者10例,男6例,女4例,平均年龄 57.52 ± 14.20 岁;中药治疗组为阳明腑实证患者10例,男5例,女5例,平均年龄 52.41 ± 16.79 岁。

2 治疗及观察方法

2.1 治疗方法:常规治疗组采用常规治疗方法,包括饮食控制、胃肠减压、抗生素以及静脉输液等。中药治疗组在常规治疗基础上给予中药复方大承气汤。方剂由大黄、芒硝、枳实、厚朴、金银花、连翘等组成(其中大黄后下,芒硝冲用),制成水煎剂,每剂200ml,每日1剂,早晚分服,不能口服者则从胃管注入或经肛管保留灌肠。以每日排便2~3次为宜,大便次数超过3次则减少药量。一般情况下中药见效后再用2日,不超过5日,如需连续用药,则根据病情辨证加减,或选用健脾和胃,益气养血之品。

2.2 主要仪器、试剂:高效液相色谱分析仪为ESA公司产品,乳果糖、甘露醇、阴阳离子树脂均为Fluca公司产品,尸胺氧化酶、二胺氧化酶、过氧化物酶、抗坏血酸氧化酶、DA-67均为Wako公司产品。

2.3 观察指标和方法:血浆内毒素(ET)用鲎试剂偶氮基质显色法定量检测,结果用EU/ml表示;血清二胺氧化酶(DAO)用比色法^[2],结果用U/L表示;尿中乳果糖与甘露醇排泄率比值(L/M)用带特殊电化学检测器的高效液相色谱法(HPLC-PED)^[3,4]。

2.4 统计学处理:数据均用均数 $\pm$ 标准差($\bar{x}\pm s$)表示,结果以SPSS10.0统计软件进行方差分析及 t 检验,以 $P<0.05$ 为检验显著性标准,或进行多元相关分析。

3 治疗结果

3.1 两组大便次数变化比较:附表示,两组患者治疗前大便次数均减少,经治疗后大便次数增加($P<0.01$),尤以中药治疗组增加更为显著($P<0.01$)。

3.2 肠粘膜通透性变化比较:附表示,与对照组相比,治疗前阳明腑实证患者尿中L/M比值显著增高($P<0.01$),表明阳明腑实证患者肠粘膜通透性增高。经过治疗后,其比值均明显降低($P<0.01$)。中药治疗组与常规治疗组相比,其比值下降的水平更为显著($P<0.05$),但尚未达到对照组水平。

基金项目:国家自然科学基金资助项目(39700194)

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收稿日期:2002-11-01;修回日期:2003-03-03

附表 各组大便次数、L/M 比值、血 DAO 和血 ET 含量变化比较($\bar{x} \pm s$)

组别	例数	大便次数(次/24h)	L/M	DAO(U/L)	ET(EU/ml)
对照组	10	1.0 $\pm$ 0.4	0.0248 $\pm$ 0.0084	4.803 $\pm$ 1.132	0.034 $\pm$ 0.008
常规治疗组	治疗前	0.0 $\pm$ 0.4 $\blacktriangle$	0.0962 $\pm$ 0.0231 $\blacktriangle$	7.494 $\pm$ 2.412 $\blacktriangle$	0.372 $\pm$ 0.077 $\blacktriangle$
	治疗后	1.0 $\pm$ 0.2*	0.0691 $\pm$ 0.0181*	4.347 $\pm$ 1.085*	0.225 $\pm$ 0.052*
中药治疗组	治疗前	0.0 $\pm$ 0.3 $\blacktriangle$	0.1055 $\pm$ 0.0125 $\blacktriangle$	8.106 $\pm$ 2.265 $\blacktriangle$	0.381 $\pm$ 0.071 $\blacktriangle$
	治疗后	2.0 $\pm$ 0.4* $\triangle\triangle\triangle$	0.0489 $\pm$ 0.0152* $\triangle\triangle$	4.143 $\pm$ 1.252*	0.147 $\pm$ 0.036* $\triangle\triangle\triangle$

与本组治疗前比较,* $P<0.01$;与对照组比较, $\blacktriangle P<0.01$;与常规治疗组治疗后比较, $\triangle P<0.05$, $\triangle\triangle P<0.01$

3.3 血清 DAO 含量变化比较:附表示,与对照组相比,阳明腑实证患者血清中 DAO 含量显著增高($P<0.01$)。经过治疗后,其含量均明显降低($P<0.01$)。两治疗组间比较,差异无显著性($P>0.05$)。

3.4 血浆 ET 含量变化比较:附表示,与对照组相比,阳明腑实证患者的血浆 ET 水平显著增高($P<0.01$)。经治疗后,两组均有明显降低($P<0.01$),中药治疗组较常规治疗组 ET 水平下降更为显著($P<0.01$),但尚未达到对照组水平。

3.5 相关性分析:在阳明腑实证患者中,血中 ET 与 DAO 的含量与肠粘膜通透性(以尿中 L/M 比值表示)呈正相关。

4 讨论

肠道屏障在 MODS 发生发展中的作用越来越引起研究人员的注意^[8,9]。因此,研究肠道屏障损伤的机制和防护措施具有重要意义。以前的研究发现,阳明腑实证和内毒素血症互为因果,形成恶性循环。内毒素血症很可能就是阳明腑实证的主要病理基础,内毒素血症又能反过来进一步提高肠粘膜通透性,促使肠道中的细菌和内毒素不断侵入体内形成恶性循环^[7]。此外,内毒素能够激活体内多种炎症介质,如肿瘤坏死因子、一氧化氮,通过后者的作用加重肠粘膜的损伤,肠粘膜屏障功能进一步削弱,肠粘膜通透性进一步增高。

肠粘膜和外周血中 DAO 的活性能可靠地反映肠上皮细胞成熟度和完整性,其变化可反映肠粘膜屏障的功能状态^[8]。肠组织缺氧、缺血或营养障碍会引起肠粘膜 DAO 活性下降,继而导致血中 DAO 活性下降。肠粘膜受到严重损伤时,由于上皮破坏致大量 DAO 入血反而引起血中 DAO 一过性增高。本研究证明,阳明腑实证患者发病初期血清 DAO 升高,并与血中内毒素及肿瘤坏死因子水平呈正相关,后两者均可破坏肠粘膜。表明患者正处于肠粘膜破坏期,为大量 DAO 入血所致。经治疗后,血中 DAO 含量逐渐下降,肠粘膜通透性与 DAO 含量呈正相关。

复方大承气汤主要用枳实、厚朴、芒硝、大黄 4 味,枳实消痞散结,厚朴除满行气,芒硝软坚润燥,大黄清热泻下,辅以金银花、蒲公英、栀子、牡丹皮清热、泻火、

解毒。用复方大承气汤攻下后,大便解,热结去,腹满除,津液回,胃气和,阴阳平,则病愈人安。本研究证实,应用复方大承气汤治疗的阳明腑实证患者肠粘膜通透性和血中内毒素水平较用药前均显著降低。结合陈海龙^[9]及李新宇^[10]以往的实验,复方大承气汤保护肠粘膜屏障、防治肠源性内毒素血症的可能机制为:(1)增强胃肠道运动功能,增加肠血流量,降低肠粘膜通透性;(2)抑制革兰阴性细菌生长和繁殖,排出肠道积滞,使肠道内细菌和内毒素排出体外,减少肠源性内毒素的产生和吸收,减少细菌移位,达到菌毒兼治的目的;(3)降低巨噬细胞活性,减少肿瘤坏死因子 α 、一氧化氮等炎症细胞因子的产生和释放;(4)增强网状内皮系统的吞噬能力和提高机体免疫力,保护肠粘膜屏障等作用。因此,临床上可应用通里攻下法对阳明腑实证及其造成的肠源性内毒素血症进行有效防治。

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ABSTRACTS FROM ORIGINAL ARTICLES

Changes of Intestinal Mucosal Barrier Function and Interference Action of Compound Dachengqi Decoction in the Patient of Excess Syndrome of Yangming Fu-Organs

Chen Hailong, Feng Limin, Guan Fenglin

Objective: To explore the mechanism of changes of intestinal mucosal barrier function and protective action of Compound Dachengqi Decoction on intestinal mucosal barrier function in the patient of excess syndrome of Yangming Fu-organs. **Methods:** 20 cases of excess syndrome of Yangming Fu-organs were randomly divided into 2 groups. One group was treated by routine method, and another was treated by Chinese herbs Compound Dachengqi Decoction on the basis of routine treatment, for 5 consecutive days. Blood diamine oxidase (DAO) activity and endotoxin (ET) content, the ratio of urine excretion rates of milk fructose and mannitol (M/L) and intestinal mucosal permeability were investigated. Additionally, 10 healthy subjects were used as normal control group. **Results:** As compared with the control group, M/L ratio in urine, blood DAO activity and ET content in the patient of excess syndrome of Yangming Fu-organs significantly increased. After treatment by Compound Dachengqi Decoction, all the above mentioned indexes significantly decreased ($P < 0.01$). **Conclusion:** In the patient of excess syndrome of Yangming Fu-organs, intestinal mucosa is injured and the intestinal mucosal permeability increases, and Compound Dachengqi Decoction can decrease the intestinal mucosal permeability, protect intestinal mucosal barrier function and effectively decrease blood endotoxin content.

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Key Words: Excess syndrome of Yangming/TCM therapy, Compound Dachengqi Decoction/treatment application

(Original article on page 672)

Effects of Xinglou Chengqi Decoction on Serum Tumor Necrosis Factor and Nitric Oxide Contents in the Patient of Acute Cerebral Infarction

Ma Yunzhi, Wu Jitao

Objective: To explore further the mechanism of Xinglou Chengqi Decoction for treatment of cerebral infarction. **Methods:** Serum tumor necrosis factor (TNF) and nitric oxide (NO) contents were determined in 65 cases of acute cerebral infarction (ACI) who took Xinglou Chengqi Decoction, 45 cases of acute cerebral infarction and 20 healthy subjects. **Results:** Serum TNF and NO

contents in the patient of ACI were significantly higher than those in healthy subjects. One week later, serum TNF and NO contents in two groups of ACI patients decreased, and in treatment group it is reduced more obviously, with a significantly difference as compared with control group ($P < 0.01$). **Conclusion:** Xinglou Chengqi Decoction can decrease serum TNF and NO level in the patient of ACI, which might be one of the mechanisms of Xinglou Chengqi Decoction for treatment of acute cerebral infarction.

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Key Words: Cerebral infarction/TCM therapy, TNF/metabolism, @Xinglou Chengqi Decoction

(Original article on page 674)

Experimental Study on Correlativity of Damp-heat Quantification in Damp-Heat Syndrome of Epidemic Febrile Disease

Wu Shijiu, Liao Libing, Wen Xiaomin, et al.

Objective: To explore experimental methods for damp-heat quantification in damp-heat syndrome of epidemic febrile disease and scan highly correlative quantification indexes. **Methods:** AQP2, endothelin (ET), calcitonin-gene related peptide (CGRP) and granulocyte colony stimulating factor (G-CSF), middle molecular substance (MMS) and hydrosulfide substances (R-SH) were determined in the damp-heat animal model. **Results:** AQP2 level in damp-heat model group was significantly lower than that in normal control group, and after treatment by Qingxiang Powder it was restored basically to the normal level. ET level in damp-heat model group was higher and CGRP was lower than that in normal group ($P < 0.01$). Blood G-CSF and MMS increased and R-SH level decreased in the damp-heat rats. After treatment of one week by Qingxiang Powder, blood G-CSF, MMS and R-SH basically restored to normal, and G-CSF positive rate increased in model control group. **Conclusion:** AQP2, ET, CGRP, G-CSF, R-SH and MMS can be respectively used as correlative quantification indexes for the patient with "more dampness", "more heat" and "the cause of disease of damp-heat".

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Key Words: Dampness-heat/diagnosis, Epidemic febrile disease/diagnosis, @Quantification of damp-heat

(Original article on page 688)