

大黄灌肠治疗慢性肾功能衰竭氮平衡研究

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内容提要 本文对大黄灌肠治疗慢性肾功能衰竭进行了氮平衡研究, 5 例患者治疗后, 血尿素氮下降; 平均粪氮含量增加; 尿尿素氮下降; 氮平衡和校正氮平衡有所降低, 维持氮有所增加, 但后三者变化均不显著。提示大黄灌肠有增加氮代谢产物排泄作用。

利用肠道排泄尿毒症“毒素”, 是慢性肾功能衰竭(CRF)非透析治疗的重要途径之一。口服氧化淀粉、甘露醇溶液等治疗CRF, 其主要机理就是通过此一途径^(1~3)。近年国内应用中药治疗CRF屡有报道, 其中有的中药是否具有增加肠道“毒素”排出的作用, 颇值得研究。

大黄是治疗CRF常用中药之一, 若干报道认为有较好疗效^(4~6), 为了认识该药对CRF的确切疗效和作用机理, 我们通过氮平衡测定的方法, 对大黄灌肠后肠道氮排泄情况和氮平衡作了初步研究, 现将有关结果和我们的看法报告如下。

资料与方法

一、一般资料和肾功能情况: CRF患者共 5 例, 男 3 例、女 2 例; 年龄 22~47 (平均 33.4) 岁。病因均为慢性肾小球肾炎。患者入院时肾功能情况: 内生肌酐清除率(Ccr) 8.7 ± 5.4 ml/min (2.8~18.4ml/min), 血清肌酐(Scr) 10.9 ± 6.9 (4.6~15.3 mg/dl), 血清尿素氮(BUN) 75.2 ± 41.5 (41~125mg/dl), 每日尿量 1593 ± 177 ml。

二、治疗方法: 所有病例均住院治疗观察。在住院期间, 患者每日蛋白摄入量平均值为 34.8g, 相当于每日摄入氮 5.438g, 每例患者每日蛋白摄入量相对恒定。每例患者均分两个阶段进行观察: (1) 对照期: 不应用大黄灌肠, 观察 14.2 ± 3.7 天; (2) 大黄治疗阶段: 每例用

大黄粉 10g, 加开水 500~700ml 浸泡, 去渣, 待温度降至 $38 \sim 37^\circ\text{C}$ 后, 行保留灌肠, 保留 10~15 分钟, 排便。每日灌肠一次。本阶段观察 12.4 ± 3.1 天。

在对照期和大黄灌肠阶段, 除维生素、降血压药维持应用外, 不用其它药物。

三、观察项目: 入院后, 除临床观察外, 大黄灌肠治疗前及治疗后, 均测定血、尿常规、BUN、Scr、Ccr、血清白蛋白(SA) 及总蛋白(STG)。

大黄灌肠前(对照期)和治疗期间, 均进行氮平衡测定。对照期氮平衡测定共观察 5.2 ± 1.3 天, 大黄治疗阶段观察 5.0 ± 1.2 天。饮食标本按每日全量的 1/4 留取, 置冰箱中, 以备定氮测定; 患者 24 小时尿液、粪便分别收集于置防腐剂的标本缸内。所有标本内氮含量测定均应用凯氏定氮法。

四、氮平衡计算方法

1. 氮平衡 = 氮总摄入量 g/日 - 氮总排出量 g/日 (尿氮 g/日 + 粪氮 g/日)

2. 校正氮平衡 = 氮平衡 g/日 - 总体液中尿素氮增加量 g/日

总体液量 = kg 体重 $\times 60\%$

总体液内尿素氮增加或减少量 = $\text{BUNf} - \text{BUNi}$ g/L $\times \text{BWf} \times 0.6\text{L} + (\text{BWf} - \text{BWf}) \text{kg} \times \text{BUNf}$

BUNf、BUNi 分别指观察期间结束时和开始时的 BUN; BWf、BWf 分别指结束时和开始时的体重。

3. 维持氮 = (总氮摄入量 g/日 - 氮平衡 g/日) / 体重

4. 统计学方法: 所有显著性比较均采用 t 测定。文中数据均以 $M \pm SD$ 表示。

结 果

一、临床观察: 所有 5 例病情均稳定。3 例患者恶心、呕吐消失或减轻, 2 例原来症状较轻, 变化不明显。

二、有关生化指标: 大黄治疗后 BUN 由治疗前 $62.80 \pm 35.50 \text{ mg/dl}$ 降为 $45.00 \pm 38.20 \text{ mg/dl}$ ($t=3.1515$, $P<0.05$), 平均下降幅度为 17.80 mg/dl , 比治疗前下降 28.3%, 而治疗后肌酐清除率、Scr、血红蛋白(Hgb)、血清白蛋白、总蛋白等均无显著变化(见表 1)。

表 1 大黄灌肠治疗前后有关生化指标的变化

| | BUN mg/dl | Scr mg/dl | Ccr ml/min | SA g/dl | STG g/dl | Hgb g/dl |
|-----|-------------------|------------------|-----------------|-----------------|-----------------|-----------------|
| 治疗前 | 62.80 ± 35.30 | 10.10 ± 6.90 | 8.80 ± 3.60 | 3.70 ± 0.80 | 5.90 ± 1.10 | 8.60 ± 0.80 |
| 治疗后 | 45.00 ± 38.20 | 10.00 ± 6.50 | 8.70 ± 3.40 | 3.50 ± 0.70 | 6.00 ± 1.10 | 7.90 ± 1.00 |
| P 值 | <0.05 | NS | NS | NS | NS | NS |

NS, 无统计学意义

三、氮排出量: 在大黄治疗阶段粪氮排出量由治疗前的 1.56 g/日 (平均值) 增加为 2.35 g/日 (平均值), 增加将近 0.80 g/日 ($t=3.4660$, $P<0.02$)。尿氮量有所减少, 约减少 0.30 g/日 , 总氮排出量仍有所增加(见表 2)。此外, 尿量也有显著减少。减少为 $1310 \pm 168 \text{ ml/日}$ (与治疗前比较, $t=3.4569$, $P<0.05$)。

表 2 大黄灌肠治疗前后氮排出量比较

| | 总氮摄入量 g/d | 粪 氮 g/d | 尿 氮 g/d | 总氮排出量 g/d |
|-----|-----------------|-----------------|-----------------|-----------------|
| 对照期 | 5.44 ± 1.30 | 1.56 ± 0.30 | 3.58 ± 0.49 | 5.14 ± 0.62 |
| 治疗期 | 5.47 ± 1.28 | 2.35 ± 0.60 | 3.32 ± 0.67 | 5.67 ± 1.18 |
| P 值 | >0.05 | <0.02 | >0.05 | >0.05 |

与对照期比较, 大黄治疗阶段的氮平衡和校正氮平衡均有所降低, 而维持氮则有所增加, 但尚不显著, 见表 3。

表 3 大黄治疗前后氮平衡的变化

| | 氮平衡 g/d | 校正氮平衡 g/d | 每日维持氮 g/kg |
|-----|------------------|------------------|-----------------|
| 对照期 | $+0.30 \pm 1.08$ | $+0.52 \pm 1.06$ | 0.08 ± 0.01 |
| 治疗期 | -0.19 ± 1.44 | $+0.14 \pm 0.85$ | 0.09 ± 0.01 |
| P 值 | >0.05 | >0.05 | >0.05 |

讨 论

一、关于大黄治疗 CRF 的机理: 从若干临床观察和动物实验结果看来, 应用大黄制剂口服、灌肠或腹腔注射等治疗 CRF, 确可使临床症状减轻及 BUN 下降, 但其确切机理尚不清楚。有人认为大黄的疗效可能与其“荡涤肠胃”即增加肠道排泄有关⁽⁴⁾, 也有认为可能是由于大黄使血浆、肝脏内的某些氨基酸水平下降, 尿素合成减少的结果⁽⁷⁾。其作用机理, 值得进一步研究。

Giodano 等应用氧化淀粉口服 (40 g/日) 治疗尿毒症患者, 可使粪便内氮排出量增加 $1 \sim 1.5 \text{ g/日}$ ^(1,2)。Friedman 等应用同法 (35 g/日), 可使患者粪便内氮排出量增加 0.9 g/日 , 但尿氮、尿量均减少, 氮平衡轻度降低或无变化⁽⁸⁾。我们应用大黄灌肠治疗 CRF, 可使患者粪便内氮排出量增加 0.8 g/日 , 提示大黄灌肠治疗后 BUN 下降可能与粪氮排出增多有关。

大黄治疗后粪氮排出增多, 是粪便内尿素氮增多, 还是粪便内未消化蛋白质增多, 目前尚不清楚。据认为, 大黄只对大肠有局部刺激作用, 促进大肠排便, 对小肠并无影响⁽⁹⁾, 由此看来, 大黄并不影响小肠的消化吸收⁽¹⁰⁾, 但尚无大黄能使小肠内蛋白质消化、吸收减少的根据。据此分析, 似以大便内氮代谢产物 (主要是尿素氮) 排泄增加的可能较大。

Ewe 报告, 大黄泻下的有效成份, 具有促进人体空肠、结肠内水和各种电解质的分泌之作用⁽¹¹⁾。这种促进作用很可能与抑制 $\text{Na}^+ - \text{K}^+ - \text{ATP}$ 酶活性有关。Goerg 等报道, 以含大黄酸 (20 mg/dl) 的等张碳酸氢钠液灌洗大鼠结肠后, 用扫描电镜进行观察, 可见粘膜细胞表面

突出,杯状细胞增多,由吸收状态转变为分泌状态,粘膜上皮漏出增加⁽¹²⁾。在水分、电解质分泌增加的情况下,是否也有尿素等物质的“漏出”(被动性扩散)、渗透作用增多,如果存在这种“漏出”,则在尿毒症时这种“漏出”的量要比正常人显著增加,因为尿毒症时体内尿素浓度比正常增加若干倍。此外,大黄有抑菌作用,如果使产生尿素酶的细菌受抑制,则粪便内尿素分解减少,这也是大黄增加粪氮排泄的可能机理之一。

二、关于大黄对氮平衡的影响:本文结果表明大黄灌肠治疗后氮平衡有所降低,维持氮有所增加,系何原因引起尚不明确。按照中医理论,大黄有致虚(脾虚、肾虚)作用。近年动物实验表明,大黄可使动物体重下降、血红蛋白下降及细胞免疫功能低下,提示大黄对蛋白质同化作用似有不利影响,虽有报道大黄有促进蛋白质同化作用,但从我们短期观察看来,大黄治疗后氮平衡变化并不显著,维持氮(达到氮平衡所需要的氮摄入量)只增加很少,按体重60kg计算,维持氮的增加只相当于2.79g蛋白质,患者营养状况也无明显变化。但是,长期应用大黄治疗后,营养状况下降、体重减少的可能还是存在的,我们也碰到过有这种情况的患者。由于这一原因,在治疗中须注意维持和改善患者的营养状况,如补充高生物价蛋白或必需氨基酸,对蛋白质摄入的限制也不应过严。据我们体会,大黄治疗合并应用必需氨基酸疗法者,则一般能维持较好营养状况。

应用大黄制剂治疗CRF,简便易行,费用低廉,适用于尿毒症前期和早期尿毒症患者。在治疗中根据患者情况单用或配合应用大黄制剂,值得提倡。关于大黄治疗CRF的机理,目前了解甚少,须进一步深入研究。

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· 简 讯 ·

▲中国中西医结合研究会儿科专业委员会成立大会暨第三次学术会议于1986年9月23~27日在苏州市召开。到会代表270人,卫生部崔月犁部长为大会题了词,题词写道:“中西医要互相学习,共同提高,为发展我国的医药卫生事业而奋斗”。大会收到学术论文262篇,分别在大会及分组会上交流。大会成立了中国中西医结合研究会儿科专业委员会,由21名专家组成。阎田玉主任医师任主任委员,叶孝礼、虞佩兰、时毓民任副主任委员,李贵任秘书。专业委员会挂靠

单位为北京友谊医院。大会对今后儿科专业委员会的工作提出了初步设想。(王 茜)

▲全国第二届中西医结合骨伤科学术会议于1986年10月11~15日在苏州市召开,与会代表共150人,大会收到论文325篇,有75篇论文在大会及小会交流。这些论文在质量上较上一届有所提高。大会还邀请了日本久留米大学的三位教授作了学术报告。代表们畅所欲言,讨论非常热烈。大会明确提出今后的工作和任务,并作了具体安排。

(刘玉兰)

marked increase in TXB_2 level in comparison with the normal control and the patients with BD syndrome ($P < 0.001$). The patients with both BD and BE syndrome showed a marked increase in TXB_2 level comparing with normal group and BD syndrome ($P < 0.001$). At the same time the patients with both BD and BE syndrome showed a marked decrease in 6-keto- $\text{PGF}_{1\alpha}$ level which is compared with normal persons and BE syndrome ($P < 0.01$). The group of BD syndrome, BE syndrome and both BD and BE syndrome showed a significant difference in $\text{TXB}_2/6\text{-keto-PGF}_{1\alpha}$ ratio in comparing with the normal control; and the $\text{TXB}_2/6\text{-keto-PGF}_{1\alpha}$ ratio showed a significant difference among the three groups. This result suggested that decrease in the level of 6-keto- $\text{PGF}_{1\alpha}$ in plasma might be a characteristic of the BD syndrome. The increase in level of TXB_2 in plasma might be a characteristic of the BE syndrome. However the increase in level of TXB_2 and the decrease in level of 6-keto- $\text{PGF}_{1\alpha}$ at the same time also showed that it might be a characteristic of both BD and BE syndrome. The levels of TXB_2 , 6-keto- PGF_1 and ratio of $\text{TXB}_2/6\text{-keto-PGF}_{1\alpha}$ in plasma might be one of the objective parameters for the syndrome differentiation of BD and BE in patients with IHD. The imbalance between TXB_2 and 6-keto- $\text{PGF}_{1\alpha}$ in plasma may be one of the basic pathological change in BD and BE syndrome in patients with IHD. To a certain extent, the change of balance regulating system of TXB_2 and 6-keto- $\text{PGF}_{1\alpha}$ levels may reflect the interdependence and mutual condition of the physiological function and pathological change of vital energy and blood. Therefore the TXA_2 and PGI_2 in plasma may be the material base of the vital energy and blood.

(Original article on page 15)

Clinical Observation on Treating Hypertensive Patients with Chrysanthemum Morifolium

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Among all the 54 patients suffering from hypertension, 31 were treated with Chrysanthemum morifolium glucoside and the remaining 23 as the control group, a placebo. The dosage was 0.5 g in capsule, three times a day. The course of treatment was 30 days. Hypertension was diagnosed according to the standard of WHO. Measurement of blood pressure and evaluation of therapeutic efficacy were determined by complying with unified national standards and levels. Results: 18 cases (58.1%) were marked effective, 8 cases (25.8%) effective, 5 cases (16.1%) non-effective. The total effectiveness was 83.9% and the control group 8.6%. The difference between these two groups was significant ($P < 0.01$). The effectiveness of the first stage hypertensives was more distinct than that of second and third stage. Before and after receiving treatment, the ECG of the patients showed no evident improvement or deterioration. As to blood lipids, the mean value of cholesterol and β -lipoprotein showed a slight reduction and no increase at all. Side-effects such as slight flatulence, acid regurgitation, nausea and headache appeared among a few patients. It was, however, unnecessary to stop medication or taking any other measures. They would disappear by themselves. The amount of urine was increased and the blood pressure decreased evidently one week after taking drugs. Possibly its hypotensive effect was relevant to the diuresis.

(Original article on page 18)

Nitrogen Balance in Uremic Patients Treated with Rhubarb Retention Enema

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It is known that uremic toxic substance can be excreted by GI tract. Recent reports suggested that blood urea nitrogen (BUN) of uremic patients was lowered by diarrhea with rhubarb. In order to evaluate the effectiveness and mechanism of rhubarb on uremia, the nitrogen balance (NB) in five uremic patients treated with rhubarb were studied. All these patients were in stable condition. Their Ccr was 8.70 ± 5.40 ml/min, Scr 10.90 ± 6.90 mg/dl, BUN 75.20 ± 41.50 mg/dl. The treatment was divided into two stages: (1) Control (14.20 ± 3.70 days): Average protein intake was 34.80 g/day. NB was studied for 5.2 ± 1.3 days. (2) Treatment with rhubarb (12.4 ± 3.1 days): Average protein intake was similar to that of control. Retention enema with 10 g/day of rhubarb powder added to 500~700 ml/day of water was used. NB was studied for 5.0 ± 1.2 days. Results: (1) After treatment with rhubarb, BUN was lowered from 62.80 ± 35.50 mg/dl to 45.00 ± 38.20 mg/dl ($P < 0.05$). No changes of Ccr and Scr were found. (2) Average feces nitrogen (FN) during treatment with rhubarb was increased from 1.56 g/day (control) to 2.35 g/day ($P < 0.02$). Urine nitrogen (UN) was decreased by 0.30 g/day (from 3.58 ± 0.49 g/day to 3.32 ± 0.67 g/day, $P < 0.05$). (3) NB during rhubarb treatment was lower than control ($+0.14 \pm 0.85$ g/day vs $+0.52 \pm 1.06$ g/day, $P < 0.05$). These results suggested that rhubarb retention enema on reduction of BUN was effective and this effectiveness might be related to decrease of FN by the drug. Because of NB change, the rhubarb treatment might exert harmful effect on the protein metabolism of uremic patients.

(Original article on page 21)

Effect of Herbal Mixture Jiang Qi Ding Chuan San (降气定喘散) on PEF, HR and BP in Asthmatics

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The folk herbal mixture Jiang Qi Ding Chuan San (JQDCS, 降气定喘散) which has been widely used for the treatment of chronic asthma in Guangzhou. It consists of Ephedra sinice, Semen Sinapis albae, dried