

水蛭防治初发期急性肾功能衰竭的实验研究

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内容提要 为了观察水蛭对初发期急性肾小管坏死(ATN)的防治作用,用禁水16h的成年雄性SD大鼠肌肉注射甘油引起ATN,在初发期给以不同药液,观察到水蛭组3、24、48h B_{cr} 升高值,24、48h BUN升高值均明显低于自来水组和单纯禁水组,而与纠正对照异搏停组相似;3、24h肾脏组织形态学损伤水蛭组亦较自来水组和单纯禁水组明显减轻。结果表明,水蛭有防治初发期ARF的作用。

关键词 急性肾功能衰竭 急性肾小管坏死 水蛭

文献^[1,2]指出,肾脏髓质和皮质瘀血在急性肾功能衰竭(ARF)的发生、维持和转归上起着重要作用。瘀血的程度与肾功能的变化存在相关性,故改善肾脏循环,防治瘀血当是防治ARF的重要措施之一。已证明丹参、川芎等植物性活血化瘀中药对实验性初发期ARF有良好的防治效果,有的已用于临床^[3]。本实验旨在观察水蛭对初发期ARF的防治作用。

材料与方法

成年、雄性Sprague-Dawley大鼠,体重180~250g,在室温18~22°C的实验室适应3天后,随机分为5组。(1)水蛭组(GH):动物禁水16h后肌肉注射50%的甘油1.0ml/100g体重,以引起急性肾小管坏死(ATN)。随后灌胃给予30%水蛭液1.5ml/100g体重,恢复饮水。6h后复给同剂量水蛭液1次。于注射甘油后第3、24、48h随机分批测动物动脉血尿素氮(BUN)、血肌酐(B_{cr}),并于注射后3、24h取肾脏标本做组织形态学检查。(2)自来水组(GW):灌注与水蛭液等容量的自来水。(3)异搏停组(GV):肌肉注射0.2mg/100g体重的异搏停。(4)单纯禁水组(GSDW):禁水并注射甘油后不予其他防治药液。(5)空白对照组(GVC)。后4组的其他处理同GH组。

BUN测定采用二乙酰一肟法, B_{cr} 采用苦味酸法。肾光镜观察用HE染色,超微结构使用透射电镜观察。统计学处理用组间均值t检验。

结 果

一、水蛭对BUN的影响,如表1所示。GH、GV、

表1 各组BUN变化 (mg/dl, $\bar{x} \pm S$)

组别	3h	24h	48h
GVC	19.2±2.0 (6)	19.2±2.0 (6)	19.0±2.0 (6)
GSDW	35.7±2.8* (6)	88.7±32.6* (7)	77.9±40.2* (6)
GW	36.7±2.8* (7)	69.4±28.6* (7)	90.7±50.6* (6)
GH	32.4±4.9* (7)	26.7±16.0* $\Delta\Delta$ (7)	31.6±12.1* $\Delta\Delta\Delta$ (6)
GV	35.5±5.6* (6)	17.6±1.4 $\Delta\Delta\Delta\Delta\Delta$ (5)	23.5±20.9* Δ (6)

注:()内为动物只数,与GVC组比,* $P<0.001$,与GSDW比, $\Delta P<0.05$, $\Delta\Delta P<0.01$, $\Delta\Delta\Delta P<0.001$;与GW组比, $\Delta P<0.05$, $\Delta\Delta P<0.01$;下同

GW和GSDW各时刻测定的BUN值除个别时组外,均明显高于GVC($P<0.001$)。但升高的幅度,GH于24、48h均明显低于GW和GSDW($P<0.05\sim 0.001$),而与GV近似。该两组间无统计学差异。

二、水蛭对 B_{cr} 的影响:如表2所示, B_{cr} 的改变规律与BUN相似,各时刻的测定值,诸注射甘油组皆明显高于GVC组($P<0.001$),然而升高幅度后,GH于3、24、48h皆明显低于GW和GSDW组($P<0.05\sim 0.01$),而与GV近似,两者间无统计学差异。

三、肾脏组织形态学改变:光镜所见,病变以近曲管最重。3h见近曲管上皮细胞呈颗粒性变,间杂以脂肪性变,偶见有坏死,肾小管腔扩张并有管型。包曼氏囊内有蛋白渗出物,肾间质偶见出血。24h的肾脏上述改变加重,出现广泛的肾小管上皮细胞坏死。不

表2 水蛭对 B_{Cr} 的影响 (mg/pl, $\bar{x} \pm S$)

组别	3h	24h	48h
GVC	1.1±0.2 (5)	1.1±0.2 (6)	1.1±0.2 (6)
GSDW	2.5±0.3* (6)	4.3±1.9* (7)	3.1±1.6* (6)
GW	2.5±0.3* (7)	3.2±1.0* (7)	3.5±1.6* (6)
GH	2.1±0.2*ΔΔ (7)	1.8±0.5*ΔΔ (7)	1.7±0.2*ΔΔ (6)
GV	1.9±0.2*ΔΔΔ (6)	1.7±0.1*ΔΔ (5)	1.9±0.7*ΔΔ (7)

论 3 h或24h, GH的肾脏病理程度较GW与GSDW组明显减轻后, 两组病变程度相近。

电镜所见, 3 h的GW、GSDW组可见近曲管上皮细胞胞质水肿, 内质网扩张, 部分线粒体肿胀, 嵴断裂, 溶酶体增多, 微绒毛有粘连、倒伏, 部分脱落, 管腔内有匀质样物。远曲管和集合管受损较轻, 肾小球无明显变化。GH的损伤明显减轻, 近曲管上皮细胞胞质轻度水肿, 内质网部分轻度扩张, 线粒体丰富, 基膜肿胀不明显, 嵴排列稍紊乱, 核及微绒毛无明显异常改变。24hGW、GSDW的近曲管上皮细胞高度水肿, 微绒毛肿胀明显, 数量减少, 乃至消失, 内质网及核周间隙不同程度地扩张, 线粒体肿胀, 嵴断裂或消失, 部分线粒体出现致密物沉积, 细胞核染色体边聚。GH改变较该两组明显减轻, 近曲管上皮细胞微绒毛基本正常, 部分近曲管上皮细胞胞质水肿, 内质网扩张, 线粒体较丰富, 部分线粒体水肿、嵴断裂。

讨 论

肌肉注射甘油引起ATN的动物模型为国内外学者研究ARF所常用^(3~6)。本实验注射甘油各组, 除24h的GV外, 各规定时刻测定的BUN、B_{Cr}值均明显高于GVC($P < 0.001$), 肾脏组织形态学也出现ATN的相应改变, 与国内外其他报道近似。结果表明本实验的ATN动物模型是可靠的。

文献^(3, 7)指出, ATN的初发期若予以理想药物的恰当治疗, 有可能使其不良病程进展逆转或明显减轻病情。本实验的结果, 不论从指示肾功能状态的BUN、B_{Cr}的定量分析, 还是对其肾脏进行的病理形态学定性分析, GH均明显优于GW和GSDW, 提示水蛭具有防治初发期ATN的作用。采用GV作纠正对照

是因为有报道钙拮抗剂异搏停对多种实验性ARF有防治作用^(8, 9), 并认为该作用与其扩张肾血管、利尿, 增加肾小球滤过率、抑制血小板聚集及血栓素(TXA₂)的形成以及抑制氧自由基的作用有关。本实验观察到的GV的良好效果提供了水蛭具有防治初发期ARF的一个强有力佐证。

根据在缺血性ARF动物模型上做的研究结果, 肾脏髓、皮质瘀血在ARF的发生和转归方面起着重要作用^(1, 2)。肌肉注射甘油引起ATN的原因, 认为兼有缺血和肾毒性。已证明该种模型的肾血管收缩, 球前动脉口径变窄, 血粘度增高⁽⁴⁾。水蛭是传统的活血化瘀中药, 对多种具有高凝状态的疾病疗效良好, 并证明它可降低红细胞压积、全血比粘度和红细胞电泳时间, 抑制大鼠由ADP诱导的血小板聚集, 延长凝血酶原时间⁽⁹⁾。故推想水蛭防治初发期ARF的主要机制之一, 可能是通过改善血液流变学和高凝状态, 从而改善肾血液循环, 防治肾脏、皮质的瘀血。王达平等⁽¹⁰⁾在高脂血症家兔中观察到, 水蛭明显地使6-酮-前列腺素F_{1α}升高、血栓素B₂降低, 从而改善了PGI₂/TXA₂的比值。如此认为, 使异常的前列腺素代谢得以改善, 可能是水蛭防治初发期ARF的又一重要机制。

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formation exceeded 30%), but immune-mediated AA (patient's PBMNC suppressed normal hematopoiesis) and stem cell-decreased AA (few of colony was formed) showed almost no expression for TSPG activity because of immunological suppression system and absence of progenitors.

Key Words total saponins of panax ginseng, hematopoietic progenitor cells, aplastic anemia

(Original article on page 285)

Mechanisms and Therapeutic Effect of Cordyceps Sinensis (CS) on Aminoglycoside Induced Acute Renal Failure (ARF) in Rats

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Nephrotoxic ARF model of rat was induced by IP injection of either Gentamycin or Kanamycin and treated with CS. The results of study showed that the simultaneous administration of CS with Gentamycin could protect the proximal tubular cells from Gentamycin toxicity and the use of CS after the establishment of Kanamycin nephrotoxic ARF could prompt an earlier recovery from ARF as compared with the control group.

The possible mechanisms of CS on ARF include: (1) protecting tubular cell sodium pump activity; (2) attenuating tubular cell lysosome overfunction stimulated by phagocytosis of aminoglycoside; (3) decreasing tubular cell lipoperoxidation in response to toxic injury.

Key Words Cordyceps sinensis, aminoglycoside, nephrotoxicity, acute renal failure, lipoperoxidation, lysosome

(Original article on page 288)

Study on the Granule of Shencao-Fuzheng Kangai (参草扶正抗癌冲剂)

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The clinical effect of the granule of Shencao Fuzheng Kangai had been proved and the animal experiment was carried out. The results showed that: (1) No toxic response was found in acute toxicity test. (2) The granule could prevent WBC from decreasing severely in chemotherapy experiment ($P < 0.01$). (3) It was indicated that the granule could improve the phagocytic function of macrophage in carbon clearance experiment ($P < 0.01$). (4) It was meant that the granule could inhibit the growing of some solid carcinoma in inoculation experimentants.

Key Words granule of Shencao Fuzheng Kangai, carbon clearance test

(Original article on Page 292)

Preventive and Therapeutic Effects of Hirudo on Incipient Acute Tubular Necrosis in Rats

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Male Sprague-Dawley rats, weighing 180-250 g and depleted with water for 16h, were injected with glycerol (im) to induce acute tubular necrosis, and then divided into groups given blood-activating and stasis-removing drug, Hirudo solution (GH), tap water (GW), verapamil (GV) and none (GSDW) in incipient stage separately. It was observed that levels of BUN increased at 24th and 48th h after administration of glycerol and levels of Bcr increased at 3rd, 24th and 48th h after injecting glycerol in GH were significantly lower than those increased in GW and GSDW ($P < 0.05$ — $P < 0.001$), but roughly similar to those in GV ($P > 0.05$ — $P > 0.5$). Renal histopathological damage under light microscope and electron-microscope in GH at 3rd and 24th h after administration of glycerol were also less severe than those in GW and GSDW. The results suggested that Hirudo could exert a preventive and therapeutic effects on incipient acute tubular necrosis induced by glycerol in rats.

Key Words acute renal failure, acute tubular necrosis, Hirudo

(Original article on page 295)