

中药前列腺汤对实验性前列腺炎病理模型的影响

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内容提要 本文采用消痔灵注射液成功地创建了大鼠前列腺纤维增生性炎症病理模型, 观察中药前列腺汤对其影响。光学显微镜显示: 给药组大鼠前列腺间质炎细胞浸润及纤维母细胞增生程度均轻于给水组。透射电镜结果表明: 给药组的腺细胞表面分泌颗粒及腺腔内金属颗粒样物质(包括 Zn)均明显增加, 胞浆内容酶体增多。实验从细胞和亚细胞水平的结构变化为前列腺汤减轻炎症反应和纤维组织增生提供了客观依据。

关键词 前列腺汤 实验性前列腺炎

中药前列腺汤是以活血化瘀治则为主组方治疗慢性前列腺炎的有效方剂^[1]。为进一步探索本方药的疗效机理, 我们用我院研制治疗内痔的消痔灵注射液, 成功地创建了模拟人的前列腺纤维增生性炎症病理模型, 为今后研究慢性前列腺炎的病理变化找到一条途径。在病理模型基础上, 观察本方药治疗慢性前列腺炎的病理形态学改变, 进而说明其作用原理。

材料和方法

一、药物制备: 前列腺汤由丹参、泽兰、赤芍、红花、白芷、穿山甲、败酱草、蒲公英等药味组成。煎煮后过滤去渣, 水浴浓缩滤液, 使每毫升药液含生药3g。

二、模型制作和分组: 选择雄性 Wistar 大鼠 34 只, 体重350~400g, 3~4 月龄。异戊巴比妥钠按 100mg/kg 腹腔注射。麻醉成功后, 无菌条件下取下腹正中切口, 直达腹腔, 提出膀胱及两侧精囊, 暴露附于精囊内侧的前列腺背叶, 分别注入25%消痔灵注射液0.2ml, 缝合肌肉、皮肤。

消痔灵的药理作用分为两个阶段, 一是纤维增生性炎症, 二是纤维瘢痕硬化。此外, 根据两批预实验的观察结果, 我们选用术后第七天, 即纤维增生性炎症阶段, 将大鼠随机分为给药组(17只)和给水组(17只)。给药组每只大鼠每次按10ml/kg量灌胃给药, 给水组予等容量自来水灌胃, 均每日一次。30天后断脊处死大鼠, 取前列腺组织标本观察。

另外, 取两只正常大鼠的前列腺组织标本, 作为正常对照观察。

三、观察方法

1. 解剖观察: 前列腺形状, 色泽及与周围粘连情

况。

2. 显微镜观察: 10%福尔马林液固定标本, 乙醇系列脱水, 二甲苯透明, 石蜡包埋。切片厚度4~5 μm, HE染色, 普通光学显微镜观察前列腺组织形态学变化。

3. 透射电镜观察: 标本取自前列腺组织中央部位 2×2 mm大小, 1%锇酸-25%戊二醛双固定, 乙醇系列脱水, EPON812环氧树脂包埋, LKB-IV型超薄切片机切片, 日立H-600型透射电镜观察。

结 果

一、解剖所见

正常前列腺组织柔软, 红润, 有光泽。给水组有58.8%(10只)的腺组织与周围有不同程度粘连, 组织表面缺少光泽。17.6%(3只)的腺组织表面有灰白色点状结节。给药组只有23.5%(4只)的腺组织与周围粘连, 粘连程度也轻, 组织表面光泽多正常, 未见到灰白色结节。

二、显微镜观察

正常前列腺上皮细胞多为立方或柱状, 腺腔形态不一, 皱壁多, 内含许多分泌物, 间质有少量平滑肌细胞、成纤维细胞。

给水组有52.9%(9只)的间质内充满多量单核细胞, 淋巴细胞及巨噬细胞浸润, 炎细胞呈团簇状, 41.3%(7只)的间质增宽, 纤维母细胞大量增生, 少数腺腔变窄, 腺细胞破坏, 腺腔内分泌物减少或无。

给药组有11.8%(2只)的间质内有多量炎细胞浸润, 89.2%(15只)炎细胞浸润轻微, 并且局限。纤维母细胞增生也轻, 腺上皮多呈立方形, 腺腔增大, 分泌物较多。

我们将炎细胞浸润及纤维母细胞增生程度制定分级标准,判定结果见附表。给药组大鼠前列腺炎细胞浸润及纤维母细胞增生程度与给水组比较,均明显减轻。统计学处理均有显著差异。

附表 两组大鼠前列腺炎细胞浸润及纤维母细胞增生程度比较

组别	n	炎细胞浸润			纤维母细胞增生		
		重度	轻度	基本正常	重度	轻度	基本正常
给水	例数 17 % 100	9 52.9	8 47.1	0 0	7 41.3	6 35.2	4 23.5
给药	例数 17 % 100	2 11.8	11 64.7	4 23.5	2 11.8	4 23.5	11 64.7
P值		<0.025			<0.05		

注: n为动物只数。炎细胞浸润程度分级标准: 重度: 炎细胞浸润呈灶簇状; 轻度: 炎细胞散在; 基本正常: 炎细胞偶见或无。纤维组织增生程度分级标准: 重度: 纤维母细胞呈束状; 轻度: 纤维母细胞散在; 基本正常: 偶见增生或无。

三、透射电镜观察

正常前列腺腺细胞内含少量溶酶体, 线粒体小而少, 胞质内有分泌颗粒, 通过顶浆分泌入腺腔。给水组腺细胞瘦长, 细胞表面分泌颗粒极少, 腺腔内金属颗粒少, 溶酶体少。给药组可见腺细胞增殖, 细胞体积肥大, 细胞之间膜分界不清, 腺细胞表面分泌颗粒较多, 腺腔内布满金属颗粒样物质, 溶酶体增多增大。

讨 论

经考察国内文献, 尚未见到有慢性前列腺炎动物模型的报道。本模型为增生性炎症病理变化。我们设计本模型的主要思路是: (1) 临床上前列腺局部触诊多以硬化硬结为主。(2) 病理改变主要以腺泡内炎细胞浸润, 腺腔梗阻, 间质纤维化为其特点。因此, 我们采用消痔灵注射液, 应用其药理特性, 造成腺体炎症及纤维增生性改变, 并获得成功。

大鼠前列腺分为腹叶及背叶, 腹叶较大且饱满, 位于精囊及尿道下方。在预实验中, 我们发现腹叶形

态结构简单, 腺泡腔较大, 间质少, 制作模型时不易造成炎症性改变。可能是药物注入后极易排泄之故。我们认为腹叶相当于McNeal⁽²⁾所称人的前列腺中央区。大鼠之背叶附于精囊内侧, 长条形, 体积较腹叶小。形态学观察, 腺腔较小, 皱壁多而复杂, 间质较宽, 制作模型时极易形成炎症及增生性改变, 因此选择背叶制作模型。我们认为背叶相当于人的前列腺外周区。因管腔狭小, 腺液引流不畅, 较易形成炎症, 与McNeal提出的人的前列腺炎主要是发生在外周区较为符合。

前列腺汤是以活血化瘀治则为主组方, 主要是针对慢性前列腺炎临床上多表现的血瘀证候, 如腰骶部、少腹部固定不移的疼痛, 尿频尿痛及触诊前列腺多呈硬化硬结改变。符合《内经》“结者散之”“留者攻之”的治疗原则。二十余年的临床观察表明, 本方药可明显的改善临床症状, 降低前列腺液白细胞数, 并可促进前列腺质地变软, 使临床治愈率显著提高。大量的实验研究已证明, 本方药中的丹参、泽兰、红花、穿山甲等活血化瘀药对改善微循环, 减轻炎症反应及抑制纤维组织增生均具有肯定作用。从本实验的结果看, 给药组大鼠前列腺间质炎细胞浸润及纤维母细胞增生程度均明显轻于给水组, P值分别小于0.025、0.05。腺腔内分泌物也明显的多。透射电镜见腺细胞增殖, 体积肥大, 胞浆内溶酶体增多, 腺细胞表面分泌颗粒及腺腔内金属颗粒样物质 (包括Zn-前列腺抗菌因子⁽³⁾) 均明显增加。说明前列腺汤有减轻消痔灵注射液引起的大鼠前列腺炎细胞浸润及纤维组织增生作用, 并可使病理模型的前列腺上皮细胞的分泌功能恢复, 增加Zn含量, 增强前列腺的抗炎及损伤组织的修复能力。本研究为中药前列腺汤的疗效机制提供了一定的实验依据。

参 考 文 献

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lower than the normal subjects and senile subjects ($P < 0.01$), and showed that serum Zn was positively interrelated with SOD-1 ($r = 0.34$). Integrating SOD-1 and the function of serum Zn, Cu in senile especially the relations between Zn, Cu and SOD-1, the authors have made a preliminary probe into the mechanism of senile Yang deficiency's occurrence.

Key Words senile patients with Yang deficiency, superoxide dismutases, serum zinc, serum copper (Original article on page 473)

The TCM-WM Treatment of Severe Renal Failure in Patients with Epidemic Hemorrhagic Fever

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This article reports the treatment of 23 cases (with the control group 20 cases) of severe renal failure in patients with epidemic hemorrhagic fever (EHF) by integrated traditional Chinese medicine and western medicine (TCM-WM), i. e., the renal protective decoction and modern medical treatment during the period of 1988~1989. The effects were as follows: (1) The curative rate was elevated and the morbidity was dropped ($P < 0.01 \sim 0.05$). (2) Both the period of oliguria and albuminuria were shortened ($P < 0.01 \sim 0.05$). (3) The severity of the complication, e. g., massive gastro-intestinal hemorrhage, etc., was much reduced ($P < 0.05$). (4) The degree of azotemia was getting milder. And the renal function was much improved ($P < 0.05$). The mode of action of the renal protective decoction is based on the point of view of the TCM in the treatment of infectious disease.

Key Words hemorrhagic fever, epidemic, renal failure, acute, treatment

(Original article on page 475)

Experimental Research on the Cold-Constitution and the Heat-Constitution (I)

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This paper reports the experimental research on the cold-constitution (CC) and the heat-constitution (HC). The authors have selected the CC and HC in Wistar rats, and have determined adenylate kinase (ADK) activities: energy charge and $\text{Na}^+\text{-K}^+\text{-ATPase}$ activities in liver, the amounts of T_3 , T_4 , progesterone, testosterone and estradiol in serum, 17-KS in urine. The ADK activities were markedly different between the HC group and the CC group ($P < 0.01$). The $\text{Na}^+\text{-K}^+\text{-ATPase}$ activities were obvious different between the HC group and the CC group ($P < 0.05$). The energy charge of the HC group has increased by 16.1% as compared with the CC group in cells. The contents of T_3 , T_4 of the HC group were higher than the CC group ($P < 0.01$). The content of progesterone of the HC group was higher than the CC group as well ($P < 0.01$). The contents of E_2 and 17-KS had no differences. These results indicated that differences between the CC and the HC were based on the basic metabolism and its regulators.

Key Words constitution, adenylate kinase, energy charge, $\text{Na}^+\text{-K}^+\text{-ATPase}$, thyroxine, progesterone, testosterone (Original article on page 477)

Effect of Herbal Prostatitis Decoction on Experimental Prostatitis in Rats

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Herbal prostatitis decoction is a great effective prescription to treat chronic prostatitis in promoting the blood circulation and relieving the stasis. The authors had succeeded in making rats experimental fibrous proliferation type prostatitis models by using Xiaozhiling(消痔灵) injection method. Rats were divided into two groups: the decoction-given group (DG) and the water-given group (WG). Microscopically, both inflammatory cell infiltration and fibroblast proliferation of interstitial tissue in the DG were slight than the WG ($P < 0.025$, $P < 0.05$). Transmission electron microscopic observations showed both the secretary particles and metal-granule-like substances