

• 实验研究 •

活血化瘀注射液对犬小肠血液动力学的影响

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内容提要 犬在体实验表明, 活血化瘀注射液静脉内注射可增加肠血流, 给药前平均值为 $181.56 \pm 62.38 \text{ ml} \cdot \text{min}^{-1}$, 给药后 20、40 及 60 分钟分别为 291.22 ± 98.12 、 307.56 ± 106.64 及 $283.33 \pm 96.84 \text{ ml} \cdot \text{min}^{-1}$, 差别非常显著。它还能增加肠组织氧耗, 给药前为 $4.85 \pm 2.23 \text{ ml} \cdot \text{min}^{-1}$, 给药后相应时间分别为 6.97 ± 3.62 、 6.97 ± 3.80 及 $7.11 \pm 3.04 \text{ ml} \cdot \text{min}^{-1}$, 差别显著或非常显著, $P < 0.05$ 或 $P < 0.01$ 。结果提示, 改善血流并增加组织氧耗可能是应用活血化瘀治则治疗急腹症的重要药理基础。

近年来组织氧供的研究已越来越受重视, 有充分的证据表明组织血流增加并不等于组织氧供实际增加, 因此组织氧供的研究较单纯血液循环的测定更加重要。活血化瘀药用于治疗急腹症已取得丰富经验, 实验也证明活血化瘀药能改善腹腔脏器血液循环, 究其是否确实能改善组织氧供则鲜为人知。我们以犬小肠为研究对象, 观察了活血化瘀注射液对肠血流及肠组织氧耗 (反映氧供的指标) 为主的血液动力学的影响。

材料及方法

一、实验标本制备: 取健康成年杂种狗, 雌雄不限。实验前禁食 24 小时, 不禁水。麻醉后, 先行气管插管以保持呼吸通畅。再向直肠内置温度传感器, 用继电器控制解剖台加热板以维持动物恒定体温。开腹后分离肠系膜上动脉 (SMA), 外套探头以电磁流量计测量肠血流。继之向肠系膜上静脉 (SMV) 内插管, 目的为取血标本以测静脉氧饱和度。最后分离一侧股动脉, 肝素化后作动脉插管, 自此可取得动脉血标本以测动脉氧饱和度并测量血压。测得肠血液动力学各指标基础值后, 用匀速注射器向狗前肢静脉内连续输入各试验用药, 观察血液动力学变化 1 小时, 每 20 分钟测定一次。

二、观察指标及计算方法: (1) 血压: 以水银检压计测量。(2) 肠血流: 以电磁流量计 (美国 Carolina 公司制) 测量。(3) 动-静脉氧差: 以血氧计 (美国 AO 公司制) 测得动、静脉血氧饱和度后按公式计算, 即动-静脉氧差 = (动脉氧饱和度 - 静脉氧饱和度) $\times 1.39 \times$ 血红蛋白浓度。(4) 肠氧耗: 按公式计算, 氧耗 = 血流 $\times$ 动-静脉氧差。(5) 肠血管阻力: 按公式计算, 血管阻力 = 血压 $\div$ 血流。(6) 血球比积: 取静脉血标本 1 ml, 用 Wintrob 管离心 36 分钟 (3000r/min)

后测量。

三、实验分组

1. 活血化瘀注射液组: 取狗 9 只, 活血化瘀注射液由本所药研室制备, 成分为丹皮、赤芍、桃仁、红花、元胡及当归。实验中应用 200% 浓度, 按每小时 3.75 ml/kg 体重投药 (临床试用剂量的 15 倍)。

2. 对照组: 取狗 8 只, 注射生理盐水, 剂量同活血化瘀注射液。

3. 已知药对照组: 取狗 8 只, 予低分子右旋糖酐 (山东淄川制药厂制), 每小时 10 ml/kg 体重给药。

结 果

一、各药物对犬小肠血液动力学的影响: 结果见附表。生理盐水对所测各指标均无影响。

低分子右旋糖酐可明显增加肠血流, 升高肠氧耗, 降低肠血管阻力, 并能升高血压和降低血球比积。活血化瘀注射液对血压、血球比积及肠动-静脉氧差无影响, 但可明显增加肠血流, 升高组织氧耗, 并降低血管阻力。

二、剂量相关实验: 应用成人临床试用剂量的 3.75、7.5、15 和 30 倍作上述同样实验, 取给药后 40 分钟 (药效峰值) 时各指标的变化作相关分析, 结果证明, 给药剂量与 SMA 血流、剂量及肠氧耗、剂量与肠血管阻力均不相关 ($P > 0.05$), r 值分别为 0.5476、-0.0359 和 -0.4010。

讨 论

一、组织氧供反映组织的氧利用情况, 它取决于血流的完善程度和组织氧提取 (动-静脉氧差) 的能力, 组织氧耗 (又称氧摄取) 正是表示血流与氧提取情况的综合指标, 即氧耗量 = 血流量 $\times$ 氧提取量, 因而组织氧耗可全面代表组织氧供^(1,2)。不同的血管扩张

附表 实验药物对犬小肠血液动力学的影响 (M±SD)

	组别	处 理 前	处 理 后		
			20min	40min	60min
血压(mmHg)	I	141.75±21.10	140.75±18.20	136.75±17.03	139.75±16.68
	II	122.75±7.02	127.50±7.35*	128.25±7.96	127.50±7.99
	III	122.89±11.49	120.00±11.31	121.33±13.19	119.56±13.26
肠血流量(ml·min ⁻¹)	I	197.13±58.43	174.88±58.80	177.38±79.09	176.75±73.91
	II	128.81±16.66	188.63±19.50**	199.50±22.15**	195.50±21.55**
	III	181.56±62.38	291.22±98.12**	307.56±106.64**	283.33±96.84**
肠氧耗量(ml·min ⁻¹)	I	4.34±3.31	4.10±3.47	4.13±2.95	4.43±3.36
	II	2.08±0.19	2.88±0.23*	2.45±0.26	2.66±0.47
	III	4.85±2.23	6.97±3.62*	6.97±3.80*	7.11±3.04**
肠血管阻力(mmHg·ml ⁻¹ ·min)	I	0.87±0.44	0.91±0.46	0.93±0.49	0.96±0.55
	II	1.86±0.25	1.69±0.28**	1.51±0.39**	1.69±0.42**
	III	0.75±0.27	0.44±0.13**	1.42±0.14**	0.45±0.15**
肠动-静脉氧差(ml·100 ⁻¹)	I	2.01±1.22	2.04±1.30	2.09±1.34	2.13±1.47
	II	1.86±0.25	1.69±0.28	1.51±0.39	1.69±0.42
	III	2.50±1.46	2.50±1.42	2.39±1.34	2.70±1.23
血球比积(%)	I	46.82±8.31	46.41±7.45	46.36±8.18	45.78±8.18
	II	46.20±2.34	44.03±2.64	42.89±2.58*	44.21±2.44*
	III	46.82±8.31	46.41±7.45	46.63±8.18	45.78±8.18

注: 与处理前比较*P<0.05,**P<0.01; I为生理盐水组, II为已知药对照组, III为活血化瘀注射液组

因子, 由于对组织氧提取的影响不同, 对组织氧耗的作用各异⁽¹⁾。异丙基肾上腺素降低氧提取能力, 因此虽增加肠血流, 并不改变氧耗量; 腺苷降低氧提取量的程度大于血流量, 故降低氧耗量; 2,4-二硝基苯酚能增加氧提取量, 因而增加血流量也增加氧耗量。

二、组织氧供的保证是绝对必需的, 临床或实验中总以氧耗代表组织氧供情况。心肌梗塞时, 心肌血流被阻断, 为保证心肌不再进一步坏死, 维持最低的氧供特别重要, 因此降低心肌组织代谢, 减少氧耗是正确的。肠血管阻塞所致的肠缺血时, 只要通过侧支循环维持最低氧供, 就不会发生肠粘膜坏死⁽²⁾。胰高血糖素能增加胰腺血流并抑制胰酶活性, 本应成为治疗出血性胰腺炎的理想药物, 只因其降低胰组织氧耗而有加重胰腺坏死之虞, 致使其治疗意义仍有争议⁽³⁾。外科伤口愈合及移植皮片成活也取决于组织血运的建立, 研究者常以皮下组织氧分压来判断术后伤口愈合的可能性^(4,5)。生理研究已从理论上证实, 机体器官有维持自身组织氧耗恒定的自动调节机制, 即当血流降低时, 以增加氧供能力使组织氧耗不致降低来补偿^(6,7)。以上均证明研究组织氧耗的必要性。

三、本实验证实, 活血化瘀注射液既能增加肠组织血流, 又能增加组织氧耗, 因此可认为是能增加组织氧供的血管扩张剂, 是应用来治疗急腹症的理想药物或辅助药物。与有类似作用的低分子右旋糖酐比较, 活血化瘀注射液具有下列优点: (1)用量低, 每小时3.75ml/kg体重即获得满意效果。(2)毒性小, 活血化瘀注射液为中药制剂, 全部由临床常用中药组成,

几乎没有毒性; 低分子右旋糖酐虽广泛应用, 但由于患者对其耐受性颇不相同, 因而有引起急性肾衰竭的病例报告⁽⁸⁾。(3)与低分子右旋糖酐比较, 活血化瘀注射液有持续地增加肠组织氧耗的作用。

四、活血化瘀药适用于各种急腹症的治疗, 因多种急腹症皆有气郁血瘀的共同病机。我们认为, 血液循环不良和组织氧耗降低很可能是气郁血瘀的病理生理基础, 因此应用活血化瘀注射液治疗可望起到治疗或辅助治疗的作用, 即增加组织血流和氧耗是有利的。

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灵芝对家兔血小板聚集作用的影响

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灵芝是担子菌纲多孔菌科灵芝属植物赤芝(*Ganoderma lucidum*)或紫芝(*G. japonicum*)的子实体, 是一类大型真菌, 具有广泛的药理作用。通过实验观察, 我们发现该药还具有较强的抗血小板聚集作用, 现将结果报告如下。

材料和方法 实验用大耳白家兔共44只。灵芝注射液由同济医院制药厂提供, 每毫升含相当于0.4g灵芝生药。自家兔心脏采血, 3.8%枸橼酸钠抗凝, 800 r/min离心10分钟, 分离富血小板血浆(PRP), 3000 r/min离心20分钟, 分离贫血小板血浆(PPP), 用PPP调整PRP, 使血小板计数在 20 ± 2 万/ mm^3 。实验分为体内和体外两部分。体外实验: 取200 μl 的PRP加10 μl 的灵芝液(终浓度分别为每毫升0.25mg、0.5mg和1.0mg), 以生理盐水作对照, 37 $^{\circ}\text{C}$ 温育5分钟, 然后持续搅拌下加ADP 10 μl (终浓度3 μM)或胶原10 μl (用兔跟腱自制, 0.1g兔跟腱剪碎, 加1 ml生理盐水磨成匀浆, 离心取上清液备用, 终浓度为贮藏液稀释2倍, 记录7分钟血小板聚集情况, 观察不同剂量的灵芝对ADP

或胶原诱导的血小板聚集作用的影响。体内实验: 将20只家兔(体重2~3 kg, 由同济医科大学动物实验中心提供, 随机分为两组, 给药组静脉注射灵芝液1.5g/kg, 对照组注射生理盐水3.75ml/kg。全部动物用戊巴比妥钠麻醉, 给药前和给药后10分钟自心脏采血, 分离PRP和PPP, 以同法测定血小板聚集性。血小板聚集仪为SPX-3型。

结果和分析 体外实验给0.25mg、0.5mg及1.0mg浓度的灵芝液后由ADP诱导的家兔血小板聚集表现不同程度的抑制, 最大聚集抑制率分别为21.16%、25.32%和44.75%, 与对照相比 $P < 0.01$; 上述浓度灵芝液对由胶原诱导的血小板聚集亦表现不同程度的抑制, 最大聚集抑制率分别为23.4%、29.06%和45.12%坡度减少为32.12%、40.15%和50.08%, 与对照组相比 P 值均 < 0.01 。体内实验结果表明, 生理盐水组对由ADP或胶原诱导的血小板最大聚集率无明显变化, 而灵芝组血小板聚集率明显被抑制(见附表)。

附表 灵芝对ADP和胶原诱导血小板聚集作用的影响 (M $\pm$ SE)

组别	血小板最大聚集率(%)		聚集抑制率(%)	坡度	
	处理前	处理后		处理前	处理后
ADP诱导	NS	39.40 $\pm$ 3.76	41.80 $\pm$ 3.68	-8.9	—
	灵芝	34.40 $\pm$ 3.56	24.50 $\pm$ 3.37*	30.78	—
胶原诱导	NS	64.30 $\pm$ 3.29	64.80 $\pm$ 3.16	0.27	1.90 $\pm$ 0.19
	灵芝	71.40 $\pm$ 3.65	42.60 $\pm$ 3.59*	45.28	2.15 $\pm$ 0.25
					1.21 $\pm$ 0.18*

注: NS为生理盐水组, 与NS组比, * $P < 0.01$

本文的实验结果表明, 家兔体内外给灵芝能明显抑制ADP和胶原诱导的血小板聚集作用, 抑制效应与剂量有关, 且在降低胶原诱导的血小板最大聚集率的同时, 还可使聚集速度变慢。本实验初步证明灵芝是

一种较强的血小板聚集抑制剂, 可用于预防动脉血栓形成, 阻止血小板活性增强所致心、脑血管疾病的发生和发展。其抗血小板聚集作用的有效成份和作用机制尚待研究。

drug to 79 patients (76%). 13 of them were on the mend with degree I consciousness. 4, 23, 24, 10 and 5 of the patients with degree II, III, IV, V and VI consciousness respectively. 25 patients failed to respond to medical treatment (24%). In 104 patients of Group B without ANP treatment, only 43 patients responded to other medical treatment (41%). 8, 4, 18, 9, and 4 patients took a turn for the better and got degree I, II, III, IV and V consciousness respectively. Inefficiency was observed among 61 patients (59%). Thus, there was a significant difference between the two groups statistically ($P < 0.005$).

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Observations of Daoyin-Tuna Qigong(导引吐纳气功)Short-Term Curative Effects on 103 Cases of Chronic Atrophic Gastritis

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Daoyin-Tuna Qigong therapy was applied to 103 cases with chronic atrophic gastritis (CAG). The average duration of disease was 7.8 years. Daoyin-Tuna Qigong exercises were done 4 times a day, 1 hour each time. 79 days made a course and no drug was given. 31 cases were checked with gastroscopy and biopsy, 30 cases with electrogastrogram and 34 cases with immunity detection before and after treatment course. Results: In clinical symptoms, the therapy appeared markedly effective in 72 cases (69.9%). The effective cases were 28 (27.2%). The total effective rate was 97.1%. The body weight of 95 cases (92.2%) increased by 2.4 ± 1.3 kg on the average at the end of the treatment course, and the capacity for eating was increased by 110 ± 70 g a day in 99 cases (96.1%). In gastroscopy and pathology examination, the rates of marked effectiveness were 51.5% and 48.4%, the effective 29.0% and 38.7%, the total effective 64.5% and 87.1% respectively. Electrogastragram check: the frequency and amplitude of the electrogastragram increased markedly ($P < 0.05$) in comparison with the pre-therapy. Immunology examination: E-rosette was $51.3 \pm 8.4\%$ before treatment and $55.3 \pm 7.7\%$ after treatment ($P < 0.05$). It is suggested that Daoyin-Tuna Qigong therapy would be a better and new treatment for CAG.

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Effect of Huoxue Huayu (活血化瘀) Injection on Hemodynamics of Canine Small Intestine

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The effect of Huoxue Huayu injection(HHI) on hemodynamics of canine small intestine was investigated in 25 healthy mongrel dogs. SMA was used for intestinal blood flow measurement with an electronic magnetic flowmeter. After measuring the arterial and venous oxygen saturation the intestinal oxygen consumption and vascular resistance were calculated. In the control group ($n=8$) the dog was infused with normal saline (NS) and in the experimental group ($n=9$) HHI was used with the same dosage of 3.75 ml per kg body weight per hour. Small molecular weight dextran (SMD) was administered in the third group as a known vasodilator agent. The results showed no effect of NS on intestinal hemodynamics. At the periods of 20, 40 and 60 minutes following HHI the mean values of intestinal blood flow were 291.22 ± 98.12 , 307.56 ± 106.64 and 283.33 ± 96.84 ml $\cdot$ min $^{-1}$ respectively. They were statistically different against the premedication values (181.56 ± 62.38 ml $\cdot$ min $^{-1}$). The values of intestinal oxygen consumption at the corresponding periods were 6.97 ± 3.62 , 6.97 ± 3.80 and 7.11 ± 3.04 ml $\cdot$ min $^{-1}$. They were markedly greater than those before HHI (4.35 ± 2.23 ml $\cdot$ min $^{-1}$). Analysis proved that blood flow and vascular resistance had a dependent relationship. HHI was marked by stronger effect than SMD when used in smaller dosage. It was believed that both the increase of blood flow and oxygen consumption might be an important pharmacological basis of the application of Huoxue Huayu principle in the treatment of acute abdominal diseases.

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