

灵芝对应激性溃疡的影响和抗乙酰胆碱作用

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摘要 灵芝浸膏给小鼠灌胃, 每日1.0g/kg和2.0g/kg, 连续3d, 末次给药后1h, 用束缚水浸法造成应激性溃疡。结果表明, 灵芝能显著降低溃疡的发生率及减少胃粘膜出血。灵芝拮抗乙酰胆碱对离体肠肌的收缩, IC_{50} 为 8.5×10^{-4} g/ml。灵芝抑制应激性溃疡的形成, 可认为是其对外周副交感神经的阻断作用。

关键词 灵芝 应激性溃疡 抗胆碱药

灵芝对中枢神经有抑制作用, 减少动物的自发活动, 加强催眠药的作用, 提高痛阈等^[1]。临床也观察到可改善病人的睡眠。本文通过灵芝对应激性溃疡的作用, 来观察灵芝对副交感神经功能的影响。

1 材料

动物: 昆明种小鼠, 雄性, 体重20~22g, 由上海医科大学实验动物部提供。豚鼠, 体重300~400g, 雌雄不拘, 市场采购。

药物: 灵芝水浸膏, 棕黄色干燥粉末, 由日本和汉生药研究所提供。每1g浸膏相当于原生药25g。灵芝混悬液用0.5%CMC研磨配制。硫酸阿托品, 上海第十制药厂产品。

2 方法和结果

2.1 应激性溃疡: 每组10只小鼠, 灵芝剂量分别为0.4、1.0、2.0g/kg, 硫酸阿托品0.04g/kg, 对照CMC 0.2g/kg。各组小鼠灌胃药液容积相同, 0.4ml/10g体重, 1次/d, 连续3d。应激实验前小鼠禁食不禁水24h, 末次给药后1h, 将小鼠置于金属网制小笼中, 浸于23℃水槽中, 液面保持在胸骨剑突水平。水浸22h后断椎处死。先结扎贲门, 取出全胃, 挤出胃液, 用红细胞稀释液稀释10倍, 在显微镜下计数红细胞。然后从十二指肠向胃内注入约2ml 1%甲醛, 结扎幽门, 将全胃置于1%甲醛液中。1h后沿大弯剪开, 用生理盐水略作冲洗, 解剖镜下检查胃粘膜病变。

稀释后胃液在血细胞计数板上计数红细胞, 算出红细胞数/mm³。结果表明, 灵芝大、中剂量和阿托品能明显减少红细胞数, 也即有减少溃疡出血的作用(表1)。镜检胃粘膜处可见咖啡色的出血点及局灶性粘膜缺损。粘膜缺损小于1mm或出血性糜烂小点, 称为点状溃疡。粘膜缺损达1mm长度就作为1个溃疡, 并按3个点状溃疡算作1个溃疡。实验表明, 灵芝大、中剂量及阿托品与对照组相比, 显著减少粘膜溃疡病变(表2)。

表1 灵芝对水浸应激性溃疡出血的影响
($\bar{x} \pm SD$)

组别	剂量 (g/kg·d)	红细胞数 万/mm ³	减少百分 率(%)
灵芝	0.4	44.71 ± 30.72*	20.8
灵芝	1.0	8.32 ± 11.26***	85.2
灵芝	2.0	4.11 ± 1.81***	92.7
对照阿托品	0.04	11.01 ± 14.03**	80.5
CMC	0.2	56.43 ± 50.61	—

P值和减少百分率均与对照组比较, * $P > 0.05$

** $P < 0.05$ *** $P < 0.01$ (下同)

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表2 灵芝对水浸应激性溃疡的作用 ($\bar{x} \pm SD$)

组别	剂量 (g/kg·d)	点状溃疡数	减少百分 率(%)	溃疡数	减少百分 率(%)
灵芝	0.4	31.4 ± 8.7*	6.5	20.2 ± 5.4*	4.3
灵芝	1.0	13.7 ± 7.7***	59.2	8.1 ± 5.8***	61.6
灵芝	2.0	13.7 ± 7.1**	59.2	6.8 ± 4.1***	67.8
对照阿托品	0.04	4.5 ± 3.9**	86.6	1.8 ± 2.0***	91.5
CMC	0.2	33.6 ± 13.1	—	21.1 ± 8.8	—

* $P > 0.05$ *** $P < 0.01$

2.2 拮抗乙酰胆碱对离体肠的作用：取出豚鼠回肠，置于20ml器官浴槽内，恒温通气，通过弹力换能器描记肠肌收缩曲线。测定浴槽内不同浓度的灵芝对抗乙酰胆碱对肠肌的收缩作用。当灵芝浓度为 2.5×10^{-4} 、 5.0×10^{-4} 、 1.0×10^{-3} 和 2.0×10^{-3} g/ml时，抑制乙酰胆碱收缩的百分率分别为8%、34%、58%和83%。每一抑制百分率为5次实验的均值。算得灵芝 IC_{50} 为 81.5×10^{-4} g/ml。

3 讨论

束缚水浸造成应激性溃疡。此溃疡形成机制被认为是精神和躯体在应激情况下，中枢内下丘脑和副交感神经系统过度兴奋所致，特别是迷走神经由过度活动起了重要的作用[2, 3]。当迷走神经功能亢进时，胃壁肌神经性痉挛，压迫粘膜血管，粘膜发生贫血性坏死，再受到过多胃液分泌的作用而形成溃疡[4]。抗胆碱药在外周阻断乙酰胆碱对腺体、胃肌和血管的作用，可使处在异常状态的分泌、肌痉挛和血流障碍得到缓解或消除。因此阿托品对应激性溃疡有明显的防治作用[5]。本实验表明，灵芝口服剂量1.0g/kg和2.0g/kg时，如同阿托品一样有明显的抗应激性溃疡作用。某些中枢抑制药如氯丙嗪、眠尔通对应性溃疡也有一定抑制作用[2]。林春等报道，当灵芝口服剂量超过2g/kg时，才呈现对中枢神经系统的抑制作用，小鼠自发活动减少或加强催眠药的作用[1]。因此本实验灵芝抗应激性溃疡的有效剂量范围内，很少有中枢作用的参与，主要表现为外周作用。

从灵芝抗应激性溃疡效应在离体肠拮抗乙酰胆碱的作用，可以认为灵芝在外周具有阻断副交感神经系统功能的作用。

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Fubida Granule is a new Chinese herbal preparation. It consists of Rizoma Chuanxiong, Fructus Forsythiae and Herba Asari. It is used for the treatment of acute and subacute paranasal sinusitis. This work reports a new HPLC method for the determination of tetramethylpyrazine in the chinese herbal preparation. A reverse phase column C_{18} was used for the separation with methanol-water (52:48) at 1.0ml/min as eluent and measured by UV detector at 292nm. The extraction recovery was 99.2%, RSD was 1.1% (n=4) and the sensitivity limit of quantitative analysis was 0.5 μ g/ml. The assay is simple, rapid and sensitive with good reproduction.

(Original article on page 459)

Experimental Studies on the Effect of "Liver-Softening Anti-Fibrotic Decoction" on Active and Inactive Fibrotic Rats

Jing Shugen, Wang Lingtai, Ren Jiawei, et al

"Liver-Softening Anti-Fibrotic Decoction", a preparation consisted mainly of medicinal herbs with tonifying "Qi", flourishing "Yin", activating blood and eliminating stasis, was given by gavage to Dimethyl nitrosamine (DMN) induced fibrotic rat to assess its effect on active and inactive liver fibrosis. It was found that this preparation, besides its promoting growth and protein metabolism activities, can also lower serum alkaline phosphatase, decrease serum hyaluronate and liver hydroxy proline, with a better curative effect on experimental liver fibrosis in rats than its prophylactic effect.

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Effect of Lingzhi (*Ganoderma lucidum*) on Water-Immersion Stress Ulcer in Mice and Its Antagonism to Acetylcholine in Vitro

Cheng Zhanghua, Masao Mori, et al

Mice were pretreated po with 0.4g/kg, 1.0g/kg, 2.0g/kg Lingzhi aqueous extract once daily for 3 days respectively. 1h after the last dose, they were kept under restraint plus water-immersion stress for 22h. Lingzhi 1.0g/kg, 2.0g/kg, and atropine 0.04g/kg markedly decreased ulcer formation and hemorrhage incidences compared with control ($P < 0.01$). Lingzhi in different dosages could produced by acetylcholine. Its IC_{50} was found to be 8.5×10^{-4} g/ml. Ulcer formation under stress condition is due to stimulation of the excessive central hypothalamus and parasympathetic nervous system; especially vagal overactivity plays an important role. The results suggest that Lingzhi possesses a blocking effects on peripheral para-sympathetic nervous system.

(Original article on page 472)

Effect of Ginseng and Angelica Sinensis Decoction (GASD) on Learning and Memory of Dementia Rat with Hippocampal Lesions Induced by Quinolinic Acid

Song Qianliu, Zong Ruiyi and Xie Xianglin