

益智灵冲剂对实验性老年痴呆病理模型的作用

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内容提要 选用60只LACA小白鼠,口服氯化铝造成老年痴呆模型,用中药益智灵冲剂进行治疗,观察脑记忆功能及脑组织重量(脑重)变化。结果表明:益智灵冲剂可使痴呆小白鼠的记忆功能改善,脑重恢复正常水平。说明益智灵冲剂对老年痴呆具有一定的疗效。

关键词 益智灵冲剂 脑复康 记忆障碍 脑重 老年痴呆病理模型 避暗法

中药益智灵冲剂是以益智健脑、养心安神为主要作用,临床用以治疗老年痴呆等智力减退的验方。为探索本方的疗效机理,我们模拟造成更接近老年痴呆的动物病理模型。在此基础上,观察本方对受试动物记忆能力及脑重的变化,进而阐明其原理。为今后研究老年痴呆的病理变化和有效方药提供参考资料。

材料与方药

一、药物来源

益智灵冲剂是以益智仁、红参须等中药组成的水溶性冲剂,由株州中药厂生产(批号:910601)。氯化铝($AlCl_3$)由广东台山化工厂生产(批号:890302)。乙酰吡咯烷酮(Pyrrolidoni)由熊岳制药厂生产(批号:901123)。

二、模型制作与分组

选择LACA小白鼠(湖南医科大学动物试验中心提供)60只,雌雄各半,体重22~28g,3~4月龄。随机分为5组,即正常组(I)、痴呆模型组(II)、模型加脑复康组(III)、模型加益智灵冲剂I剂量组(IV)、模型加益智灵冲剂II剂量组(V)。模型鼠每只投以氯化铝4mg/d,共饲养90天。II组每鼠加投脑复康5mg/d;IV组每鼠加投益智灵冲剂52mg/d;V组每鼠加投益智灵冲剂76mg/d;I组每鼠给予同等量冷水。

三、观察方法

饲养90天后,用反射箱(浙江鄞县生产)进行避暗法(Step through test)试验。其箱分为明、暗两室。明室14×15×30cm,上方20cm处悬一10W电灯;暗室18×5×30cm。两室之间有一直径为3cm大小的圆孔。两室底部均铺以铜栅。暗室底部铜栅可以通

电,选用40V电压。暗室与一计时器相连,计时器可自动记录潜伏期的时间(s)。实验时将鼠面部背向洞口放入明室,同时启动计时器。小鼠穿过洞口进入暗室受到电击,计时器自动停止。取出小鼠,记录每鼠从放入明室至进入暗室遇到电击所需时间,此即潜伏期。24h后重新测验,记录进入暗室的动物数、潜伏期和5min内的电击次数。测试毕,断颈解剖取出大脑,用NT托盘扭力天平称取脑湿重。

结 果

一次性被动回避(One trial passive avoidance responses)试验结果表明:II组与I组相比,有非常显著性差异($P<0.01$);III组与II组比较,有统计学意义($P<0.05$);IV、V组与II组比较,有非常显著性差异($P<0.01$)。见表1。

表1 益智灵冲剂对小鼠记忆功能障碍的影响

组 别	n	5min内错误次数 ($\bar{x} \pm S$)	潜伏期(s) ($\bar{x} \pm S$)
对照(I)	12	0.97±0.58	221.23±29.8
模型(II)	12	3.74±0.69 $\Delta\Delta$	42.74±19.32 $\Delta\Delta$
脑复康(III)	12	2.26±0.54*	87.44±26.70
I剂量YZL(IV)	12	1.63±0.62**	188.46±45.34**
II剂量YZL(V)	12	1.58±0.56**	179.64±37.20**

注:YZL=益智灵冲剂;n=动物数,I与II比; $\Delta\Delta P>0.01$;III、IV、V与II比,* $P<0.05$,** $P<0.01$ 。

解剖称重的大脑,采用脑重/体重×100系数进行统计处理,结果显示:V组与I、II组比较,有统计学意义($P<0.05$);IV组与I、II组比较,有非常显

著性差异 ($P < 0.05$); II 组与 I、III 组相比, 有统计学意义 ($P < 0.01$)。见表 2。

表 2 益智灵冲剂对小鼠脑湿重的影响

组 别	n	脑 湿 重 ($\bar{x} \pm S, g$)
正常(I)	12	1.35 ± 0.15
模型(II)	12	1.20 ± 0.26
脑康复(III)	12	$1.46 \pm 0.34^*$
I 剂量 YZL(IV)	12	$1.49 \pm 0.29^{**}$
II 剂量 YZL(V)	12	$1.10 \pm 0.35^{**}$

注: YZL=益智灵冲剂; n=动物数; III、IV、V 与 I、II 比, $^*P < 0.01$, $^{**}P < 0.05$

讨 论

老年痴呆是由于人随着年龄(60 岁以上)增大, 而成熟的智能因脑实质的变化而引起的严重伤害, 进而影响工作及生活。当大脑受到原发性和直接侵袭, 以及有继发性和间接病变时, 有可能形成痴呆, 但其机制是复杂的。记忆障碍, 特别是近记忆力障碍, 是老年痴呆病的特征之一。在记忆内容障碍即回忆障碍中, 作为量的障碍, 有记忆增进和记忆减退及健忘; 而作为质的障碍, 有记忆错误。这些都将妨碍社会记忆^[1]。大脑的一切功能活动皆依赖于脑的物质基础。老年痴呆脑重(1300~1400g)平均比正常减少 7~10%(90~100g)^[2]。据间接推算, 神经细胞减少更显著^[2]。国外资料报道, 老年痴呆引起脑体积缩小(包括脑组织容量减少, 脑室扩大, 脑回增宽)^[3]。大脑萎缩(额叶与颞叶显著, 脑重 1000g 以下)^[4]。尸验证实, 脑重量减轻^[5]。

老年痴呆脑内出现无定型硅酸铝, 铝对形成老年痴呆有直接作用^[6]。经解剖表明, 正常人脑组织铝含量 $< 4 \mu g/g$ (干重), 而老年痴呆者脑铝含量为正常人

的 1.5~3 倍, 最高可达 $107 \mu g/g$ (干重)^[7]。由于铝被摄入脑组织(其转运机制尚不明), 引起痴呆病理变化为弥漫性大脑皮层萎缩, 脑重量多在 1000g 以下^[7]。李文彬^[8]用 $AlCl_3$ 造成大白鼠中毒痴呆模型, 用脑复康治疗, 可以改善中毒。本组用益智灵冲剂作对照, 从实验结果看, 益智灵冲剂疗效较脑复康为优。

益智灵冲剂是长期临床总结出来的以益智健脑、养心安神为目的的经验方, 主要针对弱智儿童、儿童多动症、老年呆症、文痴、善忘、痴呆及包括西医老年性痴呆、脑血管性痴呆(多发性梗塞痴呆及脑出血、脑血栓形成、脑栓塞后痴呆等)及混合性痴呆、脑叶萎缩症(Pick 病)等病症。从临床观察来看(另文报道), 本方药可明显地改善以上病证的临床症状。本研究为益智灵冲剂的疗效机制提供了初步的实验依据。但脑的记忆功能改善和脑重增加的机理还待进一步研究。

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JPYQLSD was to regulate the energy metabolism of rats.

Key Words Chinese herbs, Jian-Pi Yi-Qi Li-Shui Tang, nephrotoxicity, cisplatin

(Original article on page 614)

Anti-tumour Study of Combined Therapy of Yi Kang Ling (益康灵) with Chemotherapeutic Agents

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Result of animal experiment proved that Yi Kang Ling, a TCM compound preparation, could markedly inhibit the growth of implanted tumour in mice. The inhibiting effect to the experimental tumour of combined therapy of Yi Kang Ling and the chemotherapeutic agents-CTX or MMC was better than that using singly. The Yi Kang Ling could alleviate toxicity of chemotherapy which caused the weight loss of mice. It could markedly increase the immune organs' weight, raise the phagocytosis of abdominal macrophage and promote the formation of serum hemolysin inhibited by CTX. The experimental result revealed that the combined therapy of Yi Kang Ling and the chemotherapeutical agents could enhance anti-tumour effect and lower the toxicity of chemotherapy. Toxicological experiment showed that the Yi Kang Ling did not have any toxic effect against organism.

Key Words Yi Kang Ling, anti-tumour effect, immune regulation

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Experimental Study on Tea in Inhibiting Mutational Specificity of 6 Antineoplastic Drugs

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According to the principles of SOS response, the authors tested the mutational specificity of tea and its inhibitory effects to the mutational specificity of 6 antineoplastic drugs by using the method of mutational and anti-mutational synchronous test. The results revealed that the tea had no mutational toxicity but anti-mutation effect. It also had the inhibitory effect on mutational toxicity of 6 antineoplastic drugs, including Mitomycin C, Bleomycin, Fluorouracil, Cis-diaminodichloroplatinum, Arabinosylcytosin and Mustargen. These results have provided referential basis for further study on anti-cancer effect and clinical use of tea.

Key Words tea, antineoplastic drugs, SOS test, anti-mutational

(Original article on page 620)

Effect of Yizhiling Granule(益智灵冲剂) on Experimental Pathological Model of Alzheimer's Disease

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Alzheimer's disease is an important problem of gerontology which manifested as serious loss of memory, especially of recent memory, decrease of brain weight. The pathological model of the disease in mice was made with administration of $AlCl_3$ and then Yizhiling Granule was given to treat it. Results: In the experiment of one trial passive avoidance response there were significant difference between the normal group and the model group ($P < 0.01$) and significant difference between the treated group and the model group ($P < 0.05-0.01$); as for fresh brain weight, the treated group was significantly different from the normal group ($P < 0.01$) and model group ($P < 0.05$). They indicate that Yizhiling Granule could improve memory and increase brain weight. This research seems to provide experimental basis for treatment of the disease.

Key Words Yizhiling Granule, brain weight, pathological model of Alzheimer's disease

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