

实验研究

补中益气汤对气虚邪侵发热动物体温的影响

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摘要 在探讨甘温除热理论源流的基础上,以甘温所除之“热”为“气虚夹邪”所致为研究思路,初步建立了家兔“气虚邪侵”发热动物模型,以模型动物的体温、症、征动态变化为观测指标,观察了甘温除热代表方剂补中益气汤及其拆方的退热效应。结果表明,补中益气汤全方对“气虚邪侵”发热动物的降温作用最佳。

主题词 发热/中医药疗法 补中益气汤/治疗应用 甘温清热

甘温除热理论是由金元时代李东垣受《素问·调经论》等经旨启发,结合其实践经验所创,临床实践证明,甘温除热法确为治疗某些发热性病证的有效方法之一。建国以来,尤其自1961年《中医杂志》开展甘温除热法的讨论至今,国内发表了数百篇有关探讨甘温除热法理论和临床验案的文章,对甘温除热的涵义、作用机理、临床应用指征及其代表方剂等进行了较深入的研究,但尚未见到有关实验研究的报道。通过对古今研究甘温除热文献的梳理,我们认为探讨甘温除热机理应从“气虚夹邪”立论,甘温所除之“热”为气虚无力抗邪,邪毒入侵,或邪毒内生,或毒伤正虚,正邪相争而致,甘温除热的关键在于益气扶正祛邪^[1]。本实验以此为据,建立了“气虚邪侵”发热动物模型,用甘温除热代表方剂补中益气汤进行治疗,为进一步研究甘温除热机理提供依据。

1 实验材料

选用白色健康中国本兔,雌雄各半,体重 2.0 ± 0.2 kg,由西安医科大学实验动物中心提供。实验药物补中益气汤及其拆方生药均由陕西中医学院附属医院中药房提供,经该院药用植物教研室鉴定符合《中国药典》1995年版各生药品种。汤液制备按文献报道^[2]。浓缩成100%溶液。

对照用药为陕西中医学院制剂室提供的同批蒸馏

水。伤寒、副伤寒三联菌苗由卫生部兰州生物制品研究所提供(批号为960412)。

2 实验方法

2.1 动物分组、造模及处理:筛选体温在正常范围($38.5 \sim 39.5^{\circ}\text{C}$)动物48只,称重后随机分为6组。除空白组外,其余5组动物均禁食7天,不禁水^[3],造成气虚,再给除气虚组外的其余4组动物经耳缘静脉注射伤寒、副伤寒三联菌苗 0.5ml/kg ,造成“气虚邪侵”发热模型,并重新随机分为模型组、全方组(模型+补中益气汤)、拆方I组(模型+补中益气汤去升麻、柴胡)、拆方II组(模型+升麻、柴胡)。

造模动物出现发热(体温上升 1°C 以上)等症后,各治疗组动物按文献方法^[2]给予相应的实验药液,每日3次,各对照组给等量蒸馏水,共给药48小时。

2.2 观测指标与方法:以李东垣《脾胃论》中所列发热、气高而喘、肢体沉重、怠惰嗜卧、气短精神少等“热中”证的辨证要点为依据,筛选出能于兔身上观察到的身热、耳廓潮红、灼热、喘促气急、蜷卧懒动、舌质淡等征象为客观指标。在室温 $18 \sim 20^{\circ}\text{C}$ 的条件下,用普通肛表插入兔直肠5cm,持续3分钟,测量体温。实验前,间隔1小时测肛温2次,取均值作为基础体温值。造模后0.5小时,每1小时测体温1次,测24小时内动态体温变化,参照文献^[4]选用平均体温曲线、发热峰值(ΔT)均数、发热指数(TRI)为衡量体温动态变化指标。

3 实验结果

3.1 实验动物主要症状、体征的动态变化:造模后1.5小时开始,各组动物均有不同程度的发热,至4小时后,模型组动物发热更为明显,呼吸急促,眼结膜充血,耳廓潮红,根部灼热,蜷卧懒动,并伴消瘦,体重下降(与造模前比较 $P < 0.01$),毛发疏散,干枯无泽,易脱落,食量减少,舌质淡等症。至6小时后体温继续上升,出现气喘、鼻煽、不食、精神委顿等症,而各治疗组发热诸症较轻,其中全方组与模型组相比,差异最为显著。至24小时,治疗各组动物发热症状基本消失,模型组动物仍有发热反应。气虚组动物始终表现出四肢蜷卧、

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表 1 造模后各组动物(各 8 只)体温(℃)均值比较($\bar{X} \pm S$)

造模后时间	全方组	拆方 I 组	拆方 II 组	模型组	气虚组	空白组
基础体温	38.70±0.24	38.78±0.23	38.68±0.23	38.78±0.24	38.72±0.21	38.70±0.34
2 小时	39.40±0.43	39.35±0.23*	39.20±0.30**	39.65±0.29	38.30±0.22*****	39.0±0.25**
4 小时	38.95±0.24***	39.45±0.43**△	39.20±0.31**	40.40±0.42	38.20±0.24*****	39.20±0.36**
6 小时	39.50±0.43**	39.90±0.58△△	39.60±0.29**△	40.38±0.54	38.40±0.34*****	38.80±0.33**
8 小时	39.70±0.42**	41.0±0.77△△	40.15±0.35△	41.0±0.75	38.50±0.20*****	39.10±0.26**
10 小时	38.85±0.22***	40.50±0.46**△△	39.85±0.42**△△	40.85±0.79	38.55±0.21*****	39.30±0.31**
12 小时	39.25±0.45**	39.95±0.51△△	39.60±0.43**△△	40.25±0.54	38.30±0.32*****	39.0±0.31**
14 小时	38.95±0.23***	39.70±0.58**△△	39.50±0.35**△△	40.0±0.58	38.25±0.22*****	39.50±0.30**
16 小时	39.05±0.31***	39.50±0.21*△	39.40±0.31**△	39.95±0.22	38.40±0.21*****	38.80±0.27
18 小时	39.0±0.32*	39.30±0.73	39.0±0.32*	39.65±0.73	38.35±0.20*****	38.90±0.27**
20 小时	39.08±0.33*	39.35±0.67	38.85±0.22**	39.52±0.32	38.20±0.23*****	39.0±0.31**
22 小时	38.70±0.24**	39.25±0.31*	38.80±0.21**	39.50±0.30	38.40±0.22*****	38.80±0.24**
24 小时	38.68±0.23	39.28±0.24	38.75±0.22	39.48±0.23	38.30±0.24	38.90±0.22

与模型组比较 * $P<0.05$, ** $P<0.01$, *** $P<0.001$;与全方组比较 $\Delta P<0.05$, $\Delta\Delta P<0.01$;与空白组比较 # $P<0.05$, ## $P<0.01$

表 2 各组解热效应指标比较($\bar{X} \pm S$)

组别	动物数	发热峰值(ΔT) (℃)	发热指数(TRI) (cm^2)
全方组	8	0.92±0.26	6.15±0.47
拆方 I 组	8	2.30±0.59*	11.0±1.08△☆
拆方 II 组	8	1.35±0.37*	7.85±1.37△△
模型组	8	2.10±0.56*	12.58±0.96△☆
气虚组	8	0.05±0.015	0.30±0.02
空白组	8	0.60±0.19	1.40±0.12

与全方组 ΔT 比较 * $P<0.01$;与全方组 TRI 比较 $\Delta P<0.001$, $\Delta\Delta P<0.01$;与拆方 II 组 TRI 比较 ☆ $P<0.01$

喜挤堆、毛枯易脱、纳差、大便不调、舌质淡等症。空白组无任何症、征。

3.2 造模后 24 小时内各组动物体温均值变化比较:从表 1 可以看出,在整个动态观测过程中,全方组动物体温变化较缓慢,与模型组及拆方 I 组相比差异均有极显著性差异($P<0.01$),与拆方 II 组在 8~16 小时也显示出一定的差异($P<0.05$),与空白组相比,差异无显著性($P>0.05$)。气虚组动物体温与各组相比差异均有显著性($P<0.01$),尤其与模型组相比,差异性非常显著($P<0.001$)。

3.3 各组动物解热效应指标比较:由表 2 结果来看,全方组 ΔT 显著低于模型组、拆方 I 组及拆方 II 组($P<0.01$)。全方组 TRI 值与模型组、拆方 I 组相比,差异有非常显著性($P<0.001$),与拆方 II 组相比,差异有极显著性($P<0.01$)。拆方 II 组与模型组、拆方 I 组相比差异亦有极显著性($P<0.01$)。

4 讨论

本实验以甘温除热法所除之“热”为气虚无力抗邪,邪毒入侵所致为主导思路,建立“气虚邪侵”发热动物模型。造模分两步进行:先造成气虚,然后在气虚的基础上施加符合“感邪”因素的致热原,即造成“气虚邪侵”发热模型。

针对单纯气虚是否出现发热(有体温升高)的问题,在气虚造模过程中,每日观测动物体温变化,结果表明,随着禁食时间的延长,动物体温渐趋下降,有的甚至降至正常范围以下,与正常动物相比,差异有极显著性($P<0.01$),且蜷卧、少动、喜挤堆取暖等,与其他同类研究报道一致^[3]。造模后,又特设气虚组,继续观测体温变化,与模型组差异有非常显著性。此与《素问·刺志论》“气虚者,寒也”的论点吻合。

由于模型的建立是将两种较为成熟的方法结合而成,并且有“热中”证症状及体征的出现及客观检测指标的佐证,又有方药治疗效果作为反证,因此,可以认为本模型是成功的。

微生物及其产生的内毒素是常见的产生内生致热原细胞的激活物。本实验采用给气虚动物注射菌苗的方法造成“气虚邪侵”发热模型,以显示各组动物最大发热高值的 ΔT ,以及反映各组动物发热速度、整个发热过程变化趋势的 TRI 作为客观指标。就 24 小时各组动物体温动态变化而言,模型组始终趋于高水平,而且发热速度快,与治疗组中的全方组形成鲜明对比。全方组体温在用药后 2 小时即开始下降,尽管在发热后 6 小时内有波动,但变动幅度未超过 1℃,24 小时时,体温完全恢复到基础体温水平。拆方 I 组体温变化高于全方组和

ABSTRACTS OF ORIGINAL ARTICLES

An Assessment on Cerebral Hemorrhage Treated by Injection of Radix Acanthopanax Senticosi

Wu Yuezhou, Cai Hong, Yu Na, et al.

Thirty cases of cerebral hemorrhage were treated by regular therapy plus hemotherapy with ultraviolet radiation as control, with another 30 such cases treated by the same method plus injection of Radix A. Senticosi. Results showed that the marked effect of treatment group was 96.7% and total effective rate 100%, while that of the control group were 60.0% and 83.3% respectively, ($P < 0.01$), the former being obviously superior to the latter. This demonstrated that the herbal injection can be applied not only for cerebral infarction, but also for cerebral hemorrhage with a bleeding amount below 30 ml.

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Key words: Cerebral hemorrhage/TCM therapy Radix A. Senticosi/therapeutic application

(Original article on page 213)

Influence of Treatment of Nephropathy by Integrated Medicine on Growth and Sex Development

Jiang Shu'ai, Yu Jianer

Fifty cases of nephrosis in children were treated by combined use of the methods of nourishing — yin — decreasing — fire, invigorating — Qi — benefiting — kidney, and activating — circulation — removing — stasis and hormone — immune depressor. The patients' body height, exams of secondary sex characters were examined at the OPD and follow-up at home, and the age of their first appearance of seminal emission or menstruation, the bone — age measurement of left wrist bone by X-ray film and were compared with another 31 cases of children treated by the same remedy but without TCM therapies. The retardation of sexual development in the treatment group was greatly decreased.

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Key words: nephrosis/therapy by integrated Chinese and Western medicine

(Original article on page 215)

Effect of Buzhongyiqi Decoction on Temperature in Animal with Fever due to Deficiency of Qi

Zhang Liping

When exploring the theory of removal of heat by herbs of sweet — warm nature, by applying the way of thinking that the "heat" removed by this way is caused by "deficient Qi complicated with evil pathogens", a rabbit model of fever caused by "evil pathogens with deficient Qi" was established. The dynamic changes of the temperature, manifestations were used as indices to observe the antipyretic effects of Buzhongyiqi decoction, a representative recipe of such treating principle, and its individual ingredients. Result revealed that the whole recipe yielded the best antipyretic effect in this study.

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Key words: fever/TCM therapy Buzhongyiqi Decoction/therapeutic application

(Original article on page 236)

Experimental Study of Effect of Acupuncture on Behaviors of Mice Model of Rapid Senilized Dementia

Han Jingxian, Li Ping, Liu Qingzhong, et al.

By adopting scoring method on the degree of senilization and methods of high cross frame labyrinthine experiment and shuttle box on the basis of systematic observation on behavior characteristics of rapid senilized dementia in SAM — P/8 model, the effect of acupuncture method for wakening the consciousness and opening of orifices was observed. Results showed SAM — P/8 revealed apparent senilized characteristics of brain, being in a low intelligent condition, which is a rather ideal model for the study of natural dementia in the elderly. The acupuncture methods revealed an action of delaying senility process, improving the condition of frightening and increasing the ability of learning and memory.

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Key words: Dementia, senile/acupuncture therapy behavior, animal

(Original article on page 239)