

# “咳痰敏”治疗慢性气管炎 316 例临床观察及药理实验

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我们在防治慢性气管炎的临床观察和研究过程中,逐步筛选几种有效药物,固定处方,配制成新的成药——“咳痰敏”。于1978年12月至1979年3月应用于临床,通过对316例的治疗观察获得较好的疗效。现将临床观察和药理实验报告如下:

## 临床资料

一、药物组成及用法:鱼腥草 31.25g 七叶一枝花 31.25g 桔梗 12.5g 法半夏 9.375g 罂粟壳 7.8125g 氨茶碱 0.25g 苯海拉明 25mg。

按以上药物用量比例,先将五味中药(其中半夏用量80%)加水煎煮两次,药液合并过滤、浓缩,加入95%乙醇至含醇量为75%,沉淀24小时,过滤,回收乙醇,得浸膏。再加入预先粉碎的法半夏(20%),拌制颗粒,烘干。然后加入粉碎的氨茶碱、苯海拉明细粉及适量润滑剂,混匀,压片,包糖衣,即得“咳痰敏”片剂。每片含药0.3克。服法:每日3次,每次3片。

二、观察方法:本组病例来自观察组各医院专科门诊和住院病例。全部病例均按全国慢支统一诊断和疗效判断标准。于治疗前、中、后分别填写观察表,并行随访。10天为1疗程,服药3疗程为统计对象。治疗期间停用其它药物。除住院病例外,不改变患者原来生活习惯和工作环境。

三、一般资料:男191例,女125例。年龄21~75岁,51岁以上168例。职业包括工人、农民、财贸职工、干部和家庭妇女等。病程最短3年,最长34年。316例中属单纯型182例,喘息型134例。急性发作期122例,慢性迁延期194例。有87例伴肺气肿。

四、治疗结果:316例中临床控制60例(19.0%),显效88例(27.85%),好转107例(33.85%),无效61例(19.3%)。总有效率80.7%,控显率达46.85%。

治疗前后主症变化:咳嗽由310例减为188例,消除116例(38.15%)。咯痰由310例减为176例,消除134例(43.22%)。气喘由194例减为110例,消除84例(43.29%)。表明咳痰敏对慢支的咳、痰、喘等主要症状均有效。

从分型分期的疗效看,单纯型182例,有效146例(80.2%),喘息型134例,有效109例(81.3%),二者无显著差异( $P>0.05$ )。属急性发作期122例,有效101例(82.7%),慢性迁延期194例,有效154例(79.4%),二者亦无显著差异( $P>0.05$ )。显示咳痰敏适应范围广,对慢支的发作期和迁延期,单纯型或喘息型均有治疗效用。

87例合并肺气肿者,45例无效(51.7%),表明对合并肺气肿的慢支患者疗效较差。48例作周围血象白细胞计数及分类检查,9例 $>10,000$ ,治疗后8例降至正常范围。58例胸部X线透视,治疗前后无显著变化。29例痰菌培养仅发现1例生长金葡菌落,治疗后转阴。

起效时间:半数以上在6天之内起效(62.3%),1~3天起效91例,占总例数28.8%,4~6天起效106例,占总例数33.5%。

临床观察无明显毒付作用,个别病例稍感口干,不影响治疗,无须处理。

## 药理实验

一、镇咳试验:采用沸腾水氨刺激法。取体重18~25g正常小白鼠20只一组,分给药、对照两组。分别口服咳痰敏及等量CMC 1小时后,用氨蒸气刺激小鼠45秒,记录每组动物在5分钟内的咳嗽只数和咳嗽次数。结果见表1。

表1 咳痰敏对小鼠镇咳作用观察

组别	剂 量	咳嗽只数	咳嗽次数	P 值
给药组	30mg/只	8.5	35	<0.05
对照组	等量CMC	15.5	96	

结果表明:咳痰敏具有明显镇咳作用。

二、祛痰试验:采用小白鼠酚红排泄法。取体重18~25g正常小白鼠20只,分为给药、对照两组。将咳痰敏灌胃给药,半小时后腹腔注射酚红,半小时后处死。用5%碳酸氢钠液灌洗呼吸道,测定两组灌洗

液中酚红含量, 见表2。结果表明: 小白鼠口服40mg咳痰敏后, 有明显的祛痰作用。

表2 咳痰敏对小鼠呼吸道酚红排泄影响

组别	剂量	动物数	酚红排出量	P值
给药组	40mg/只	10	0.41 $\mu$ g	<0.05
对照组	等量CMC	10	0.25 $\mu$ g	

三、平喘试验: 1. 豚鼠离体气管试验: 取正常豚鼠气管连接在毛细管上, 然后放入有台氏液的保温浴槽中, 浴槽体积为50ml, 加入药物体积为0.5~1ml, 观察毛细管液柱面的升或降, 作为反映气管平滑肌的收缩或扩张。

试验时先在浴槽中加入 $1 \times 10^{-5}$ g的组织胺, 毛细管液面即上升, 3分钟后再加入咳痰敏, 浴槽内药物浓度分别为0.8mg/ml、1.6mg/ml。然后观察5分钟, 并计算液面下降的百分数。结果见表3。

表3 咳痰敏对豚鼠离体气管平滑肌收缩影响

药物浓度	液面下降百分率(%)
0.8mg/ml	80
0.16mg/ml	143

结果初步显示咳痰敏浓度分别为0.8mg/ml和1.6mg/ml时, 对组织胺引起的气管平滑肌收缩有明显对抗作用, 且有浓度加大效果增强的趋向。

2. 整体豚鼠平喘试验: 取健康豚鼠置喷雾罩内, 先进行一次预试验。凡接受0.3%组织胺喷雾30秒钟后, 在6分钟内出现喘息抽搐反应的为合格。2天后分别口服给药, 1小时后再按预试验时的条件喷雾1次, 观察6分钟内豚鼠出现喘息抽搐的潜伏期和发生数。用药前后自身比较。结果见表4。

表4 咳痰敏对豚鼠组织胺致喘的影响

动物数	给药量	致喘潜伏期(秒)		抽搐动物数		P值
		给药前	给药后	给药前	给药后	
4	1.6g/kg	14.5	>360	4/4	0/4	<0.01

注: 6分钟内没有发生抽搐的豚鼠致喘潜伏期按>360秒计算。

结果表明: 豚鼠口服咳痰敏后有明显的对抗组织胺引起的喘息抽搐作用。

四、毒性试验(LD<sub>50</sub>测定): 选用体重18~20g健康小白鼠, 随机分5组, 每组10只。按1:0.75的

剂量比例分别灌胃给药, 观察3天内小鼠死亡只数。按机率单位法计算, LD<sub>50</sub>为2,775.5 $\pm$ 3.8mg/kg, 表明安全度大。小鼠中毒死亡前呈现轻度中枢兴奋现象。

## 讨 论

慢性气管炎是一种严重危害人民健康的常见病, 多发病。我们既往应用中医辨证施治原则进行辨证治疗, 获得一定疗效。但是感到辨证用药灵活性较大, 不便于总结, 而且中药煎剂服药不便, 亦不利于高发季节大量病例的防治。为此, 我们在以往工作的基础上, 通过临床用药筛选和总结, 并针对慢支临床表现的感染、咳嗽、咯痰、气喘等主症, 选用具有消炎、祛痰、镇咳、平喘作用的有效药物, 逐步固定处方, 组成了“咳痰敏”的配方。在消炎方面, 根据中药清热解毒类药普遍具有抗菌抗病毒及消炎作用的特点以及临床经验, 选用鱼腥草、七叶一枝花。鱼腥草清热解毒, 临床主用于清肺热。所含鱼腥草素对流感杆菌、金黄色葡萄球菌等有抑制作用, 并能增强白细胞吞噬能力, 为临床治疗气管炎、肺炎及肺脓肿的主要药物。七叶一枝花(*Chrysanthemum indicum*, L.)又名蚤休, 系百合科植物七叶一枝花的根茎, 清热解毒作用较强, 并对G<sup>+</sup>及G<sup>-</sup>细菌有抑制作用, 且能平喘、止咳, 二药配伍用作抗感染、消炎。桔梗、半夏用于祛痰。桔梗宣肺化痰, 且能宣利肺气, 半夏燥湿化痰并能止咳, 二药配伍功擅祛痰, 且宣肺止咳。罂粟壳镇咳, 且能收敛肺气, 与消炎、祛痰药配伍, 用于慢支既治久咳, 又不致肺气耗损, 且无敛肺滞痰之弊。在此基础上, 选用西药氨茶碱平喘, 苯海拉明抗过敏, 且能止咳。这样, 诸药配伍, 共奏消炎、祛痰、镇咳、平喘之功。通过对冬季慢支高发季节316例的治疗观察, 有效率80.7%, 控显率46.85%。并适用于单纯型或喘息型的急性发作或慢性迁延阶段。药理实验初步表明其镇咳、祛痰、平喘作用显著, 因而临床疗效是可以肯定的。

咳痰敏以中药为主, 辅以西药, 各取所长, 也是中西药结合应用的一种尝试。制剂通过浓缩提取, 用量小, 服用方便。临床应用无明显毒付作用。对于防治慢支的中西医结合研究及探索有效药物和配方来说, 具有一定意义。但由于系初步工作, 还存在一些缺点, 且治疗中未设对照组, 因之实验设计不够完善, 有待于进一步改进、提高。

参加本项工作的协作单位: 南京药物研究所药理室、徐州中医院、徐州市立三院、徐州商业医院、徐州铁路医院、南京铁道医学院附院等。

## A Clinical and Experimental Study on Anti-platelet Aggregation Effect of d-Catechin (赤芍精)

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d-Catechin (赤芍精) is extracted from Chi-shao (赤芍, *Paeonia lactiflora*), one of the active components of a TCM in common use Huo Xue Hua Yu herb (活血化瘀药). In animal experiments, a TXA<sub>2</sub>-like substance was produced through the incubation of arachidonic acid and rabbit PRP. After adding d-catechin or aspirin into PRP separately (terminal concentration is 0.1% each), the inhibition rates of biosynthesis of the TXA<sub>2</sub>-like substance were 39.5% and 37.2% respectively. The inhibition rate of the biological activity of the TXA<sub>2</sub>-like substance that contracted rabbit's aortic strips was 54.4% following the addition of d-catechin into the bath.

In clinical study, the single blind randomized control method was employed to observe the clinical effects in 22 patients with angina pectoris due to coronary heart disease. The patients were treated with d-catechin on surface activation and aggregation of blood platelet under electronmicroscope following the modified Schatz method. The results showed that the patients spread type platelets decreased from  $41 \pm 2.3\%$  to  $25 \pm 1.6\%$ , and the aggregation number decreased from  $117 \pm 10$  to  $48 \pm 10.9$  after one course treatment (200–250 mg/day) with intravenous infusion of d-catechin. No significant influence on spread type platelets and aggregation number was found while the patients were treated with normal saline as control (20 ml/day, intravenously).

The cAMP level within the patient's platelets determined by radioimmunoassay tended to rise (from  $10 \pm 1$  to  $13 \pm 2$  Pmol/ $130 \times 10^4$  platelet,  $P > 0.05$ ) following a single dose (250 mg) of intravenous d-catechin. The anti-anginal attack efficacy of d-catechin was 16/21, and the ECG improvement 7/22.

(Original article on page 15)

## The Relation between Serum Gastrin Level and the Syndrome of Deficiency in the Spleen

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Taking the serum gastrin level as an index, the patients with spleen-deficiency symptoms were observed and compared with the normal.

The serum gastrin mean level of 31 normal cases was  $130.0 \pm 44.0$  pg/ml, whereas the level of 14 cases of deficiency patients who had spleen-deficiency symptoms was  $73.2 \pm 33.7$  pg/ml. The latter is significantly lower than the normal ( $P < 0.001$ ). There is no significant difference between other groups of differentiation of symptom-complexes in TCM and the normal ( $P > 0.05$ ).

20 normal mice were observed. Their serum gastrin mean level was  $451 \pm 74$  pg/ml. The corresponding figure for 18 spleen-deficiency mice was  $344 \pm 68$  pg/ml, which is significantly lower than the normal ( $P < 0.05$ ). After the treatment with decoction of four noble ingredients (四君子汤), it seems that there is a rise in the serum gastrin mean level.

A preliminary discussion with regard to the above-mentioned results suggests that the decrease of the serum gastrin level might be one of the pathologic mechanisms leading to spleen-deficiency. Clinically, it might serve as an index of observation of the dysfunction of the spleen in transporting and distributing nutrients and water (脾失健运).

(Original article on page 25)

## The Treatment of Chronic Bronchitis with Ketanmin (咳痰敏)—— A Clinical Study of 316 Cases and Pharmacological Experiments

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On the basis of past experiences from combining TCM and WM in the treatment and prophylaxis of chronic bronchitis, a new preparation, "Ketanmin" (咳痰敏) in form of tablets, has been prescribed after some steps of screening and summing-up for potent medicinal elements. Ketanmin contains extracts of *Houttuynia cordata* Thunb. (鱼腥草), *Chrysanthemum indicum* (七叶一枝花), *Radix platycodon* (桔梗), *Rhizoma Pinelliae* (半夏) and *Pericarpium Papaveris* (罂粟壳) with Aminophylline and Benadryl. 316 patients were treated with Ketanmin, each subject taking 3 tablets three times a day during the season with high incidence from December 1978 to March 1979. The patients treated with this new preparation had an over-all effective rate of 80.7% with a prominent improvement rate of 46.85%. Ketanmin has evident effects against cough, expectoration and dyspnea.