

• 临床论著 •

黄连素治疗Ⅱ型糖尿病60例 疗效观察及实验研究

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内容提要 本文报告应用黄连素治疗Ⅱ型糖尿病60例的临床疗效及动物实验研究。结果表明黄连素对Ⅱ型糖尿病患者及实验性糖尿病动物均有明显降低血糖效果，患者临床症状基本消失，血清胰岛素水平上升，临床总有效率可达90%，无明显副作用。通过实验动物病理检查胰岛β细胞的观察表明黄连素有促进β细胞修复的作用。

我们对糖尿病住院患者用黄连素治疗腹泻时，偶然发现黄连素有降糖疗效，故于1983~1987年应用黄连素治疗Ⅱ型糖尿病，并取得较好效果，现报道如下。

临床 研究

一、对象

按1982年2月北京召开的全国糖尿病研究协作组扩大会议确定国内暂行的两个诊断标准，即WHO糖尿病诊断标准、国内诊断标准及1980年WHO采纳的分类方案^①。本组60例均诊断为非胰岛素依赖型(Ⅱ型)糖尿病，男性36例，女性24例；年龄37~69岁，平均54岁；病程2个月~5年。全部病例营养状况佳，肥胖者18例，超重者8例，标准体重者34例。本组患者均未用过胰岛素治疗，亦未发生过酮症。60例中重度糖尿病(空腹血糖 $>250\text{mg/dl}$)12例，中度(空腹血糖 $150\sim250\text{mg/dl}$)38例，轻度(空腹血糖 $<150\text{mg/dl}$)10例；合并高血压者12例，冠心病者2例，肺心病者1例，无明显合并症者45例。另取60例血糖正常者进行对照观察，以了解黄连素是否有双向调整作用及低血糖副作用。

二、方法

1. 治疗方法：60例患者采用自身对照法，首先单纯饮食疗法一个月以上，如疗效不明显(血糖、尿糖测定4次无改善)则加用黄连素，每次 $0.3\sim0.5\text{g}$ ，1日3次口服。每次服量可根据三餐前血糖水平定期适当调正。空腹血糖 $<8.33\text{mmol/L}$ (150mg/dl)每次服 0.3g ，血糖

$8.33\sim13.9\text{mmol/L}$ 者 0.4g ，血糖 $>13.9\text{mmol/L}$ (250mg/dl)者 0.5g 。此期活动量与单纯饮食疗法时相同。疗程为1~3个月，少数(5例)40天后见效者疗程延至3个月以上。60例血糖正常者疗法与疗程同上。

2. 观察方法：治疗前后每周记录1次症状、体征，测空腹及餐后2小时血糖(氧化酶法)、尿糖。每2周测24小时尿糖定量、血脂、血清胰岛素测定(30例门诊患者)。合并高血压者每周测血压1次。统计学处理采用t检验法。

三、结果

1. 疗效判定标准：按临床疾病治愈好转标准^②。

2. 降糖疗效：60例患者治疗后(饮食疗法加黄连素)空腹血糖为 $117.19\pm25.98\text{mg/dl}$ ($6.6\pm1.4\text{mmol/L}$)，较治疗前(单纯饮食疗法) $208.65\pm51.68\text{mg/dl}$ ($11.6\pm2.9\text{mmol/L}$)明显下降($P<0.01$)。

30例患者治疗后血清胰岛素为 $21.93\pm3.46\mu\text{u/ml}$ 较治疗前 $16.1\pm2.68\mu\text{u/ml}$ 上升显著($P<0.01$)。

60例中治疗后空腹血糖 $<6.105\text{mmol/L}$ (110mg/dl)36例(理想控制标准)； $6.105\sim7.215\text{mmol/L}$ ($110\sim130\text{mg/dl}$)14例(较好控制)； $7.215\sim8.325\text{mmol/L}$ ($130\sim150\text{mg/dl}$)4例(一般控制)； $>8.325\sim11.1\text{mmol/L}$ (200mg/dl)6例。空腹血糖达一般控制以上者54例，总有效率为90%。餐后2小时血糖达理想控制标准(130mg/dl 以下)12例，较好控制

(150mg/dl以下)16例,一般控制(180mg/dl即9.99mmol/L以下)12例,其余20例除2例未查外,有16例餐后血糖虽未达到上述标准,但较治疗前平均下降5.988mmol/L(107.9~mg/dl),2例血糖下降不足3.33mmol/L。空腹尿糖除8例(±)、8例(+)外,余均为(-)。24小时尿糖定量达理想控制标准(5g以下)36例,达正常量(<100mg)4例,较好控制(<10g)8例,一般控制(<15g)4例,余8例平均较治疗前下降39.25g。60例中血胆固醇明显降低,平均下降76mg/dl,β-脂蛋白及甘油三酯也有下降趋势。

服药后血糖下降时间:2周后开始下降者30例,3周后者14例,1个月后者14例(其中5例40天后血糖开始下降)。36例空腹血糖在2个月后达理想控制标准。

60例血糖正常者(对照组),治疗前空腹血糖 $\bar{X}=4.8\text{mmol/L}(86.35\text{mg/dl})$,治疗后 $\bar{X}=4.9\text{mmol/L}(88\text{mg/dl})$,二者比较差异无统计学意义。

2. 症状疗效:全部病例多饮、多尿、易饥症状消失,平均每日饮水量减少2352ml,尿量减少1370ml,58例口渴消失,2例口渴明显减轻。治疗后患者体力普遍增强,12例合并高血压者,血压基本恢复正常。症状好转时间与血糖下降时间基本一致。

4. 远期效果:随访观察17例,随访3年2例,2年10例,半年5例。结果11例维持治疗结束时疗效,6例停药或吃水果后血糖又复上升,再服黄连素仍有疗效。

实验研究

一、方法

1. 动物:实验用大白鼠由我院医学动物室供给,体重120~140g,雌雄各半,分笼饲养,共42只。

2. 造型:新鲜配制的4%四氧嘧啶生理盐水溶液,每只大白鼠按12mg/100g剂量,每日腹腔注射1次,连续注射2天^[3]。于注射后第5天测血糖,其造型成功率为76%。又重复同样剂量注射1次,造型成功率达100%。

3. 分组治疗:模型复制成功后,根据血糖高低进行分组。正常大白鼠血糖为120mg/dl,造型后血糖最高达1320mg/dl,最低220mg/dl,取其中间值(300~500mg/dl)25只,高或低于此值一律淘汰。中间值25只依血糖高低划分为二个等级,即300~400mg/dl;401~500mg/dl,以此等级随机分成对照组及黄连素组。对照组大白鼠10只(血糖 $400\pm85\text{mg/dl}$),每天给予生理盐水0.1ml,肌肉注射28天。黄连素组大白鼠15只(血糖 $409\pm96.32\text{mg/dl}$),每天给黄连素注射液0.1ml(含黄连素2mg),肌肉注射28天。

二、在疗程中,每周测定血糖、尿糖1次,治疗结束后10天,动物全部剖杀采血,测定血糖。结果:血糖测定:对照组治疗后7天血糖均值为183.66mg/dl,14天186.11mg/dl,21天为178.9mg/dl,28天为188.33mg/dl,38天(停药后10天)为191.67mg/dl。黄连素组治疗在上述相应天数测血糖均值分别为90.25mg/dl、109.04、85.71、92.40、98.35mg/dl。与对照组比较,黄连素组血糖明显降低,差异非常显著($P<0.01$)。病理检查:动物剖杀时取全胰,用Bouin氏苦味酸固定,石蜡包埋切片,醛复红胰岛β细胞染色。镜下观察均按一定顺序方向,从左到右每只观察10个胰岛,每个胰岛根据β细胞数量多少,采取评分方法统计记录。如胰岛β细胞不见或只见几个者为重度(无效),评3分;如见正常的1/2者为中度(好转),评2分;见2/3者为轻度(显效)评1分;接近正常者为极轻度(控制),评0.5分。然后将每只分数总和除以胰岛数,即得每只分数。再将每组分总和除以该组动物,即得每组分均值。对照组3分7只,2分3只,合计27分/10只,均值2.7;黄连素组3分2,2分3只,1分4只,0.5分6只,合计19分/15只,均值1.26。两组采用等级指数法统计处理。结果黄连素组与对照组比较,差异非常显著, $P<0.01$ 。说明黄连素有修复胰岛β细胞的作用。

讨论

一、对于Ⅱ型糖尿病的治疗,目前口服降

糖药物常有出现低血糖、明显的胃肠道反应、肝肾功能损害、过敏反应及高乳酸血症等副作用,对心血管损害则有争议。本组资料表明,黄连素对Ⅱ型糖尿病患者确有降低血糖作用,总有效率达90%,而对血糖正常者的血糖水平无明显影响($P<0.01$)。黄连素对实验性糖尿病动物亦有显著降糖效果($P<0.01$),停药后1周以上,仍维持疗效,与临床观察结果相一致。疗程中除2例在服药一个月后感轻度腹胀、食欲略减外,余均无显著不良副作用。经减量后(每次0.3g,1日3次)上述症状消失。全部患者治疗期间肝、肾功能及血象均无异常变化。对部分患者有降血压、降血脂作用。

二、据目前研究,黄连素除有抗菌、抑制病毒、抗原虫等作用外,动物实验证实有降低血压作用,主要是通过抗胆碱酯酶而增强乙酰胆碱作用及扩张血管所致。同时有降血脂及抗肾上腺素样作用^[4]。据本组实验动物胰岛 β 细胞

的观察,治疗组与对照组比较胰岛 β 细胞恢复及血糖下降明显($P<0.01$)。临床观察血糖下降而血清胰岛素水平上升,所以考虑黄连素降低血糖的机理除具有抗升糖激素作用外,还与促进胰岛素 β 细胞再生及功能恢复有关。至于对正常血糖水平无明显影响。动物实验也证明该药毒性很低,据报告1次口服小碱碱2.0或黄连粉100g未见任何副作用^[4]。本药同时有降血压、降血脂及其它抗感染等作用,对防止糖尿病的并发症亦有意义。

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慢性弓形体病诊治 1 例

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牟××, 男, 29岁。以慢性肾小球肾炎, 肝硬化精治疗效果差, 转入本院治疗(住院号080)。患者既往有食未熟牛肉和鼻蛆史, 否认肝炎、肾炎病史。体检: 面部及眼睑浮肿, 浅表淋巴结肿大, 可移动, 有压痛, 结膜充血, 鼻粘膜有溃疡及血块结痂, 肝肋下1.0cm, 质硬, 有触痛, 肝颈回流征(+), 脾肋下4.0cm, 质中, 边缘钝, 有压痛, 双肾区有压痛及叩击痛, 双下肢有轻度凹陷性水肿。其他(-)。实验室检查: 红细胞 $3.5 \times 10^{12}/L$, 血红蛋白108g/L, 血小板 $92 \times 10^9/L$, 白细胞 $2.9 \times 10^9/L$, 中性0.56, 淋巴0.33, 嗜酸细胞0.11, 血清总蛋白47.5g/L, 白蛋白27.5g/L, 球蛋白20g/L, IgG 32g/L, IgA 1.13g/L, IgM 0.48g/L, C₃ 0.25 g/L, HBsAg(-), 循环免疫复合物阳性; 尿蛋白(+++), 尿红细胞(++), 白细胞(++), 超声波检查: 肝肋下1.0cm, 厚10.5cm, 脾肋下4.0cm, 厚9.5cm, 胆囊呈“双边影”, 壁厚0.6cm, 双肾光点增强, 左肾受挤压变形。特殊检查: 血清弓形体间接血凝试验1:512, 皮下结节切片镜检发现弓形体。诊断: 慢性弓形体病。

治疗方法: (1) 特异治疗: 乙胺嘧啶 12.5mg, 每日

2次; 磺胺嘧啶、重碳酸钠各1g, 每日4次; TMP 0.1g, 每日3次。7天为1个疗程, 共3个疗程, 疗程间间歇5天~1个月。第四个疗程起服用螺旋霉素1g, 每日3次, 共2个疗程。治疗中配用酵母, 叶酸, 维生素C、B₁、B₆, 能量合剂, 肝太乐等。(2) 中药治疗: 西药治疗的前3个疗程煎服一贯煎加黄柏、茵陈、龙胆草、白花蛇舌草、垂盆草等滋肝补肾、清热利湿之品, 在疗程的间歇期服用一贯煎合四君子汤加白茅根、茵陈等益气养阴利湿等品, 后2个疗程煎服一贯煎合逍遥散加减, 重用黄芪。

患者经过半年多的治疗, 临床症状及体征显著好转, 出院前检查: 超声波: 肝肋下0.9cm, 脾肋下2.0cm, 厚度5.9cm。弓形体间接血凝1:64。血尿实验室检查均恢复正常。出院1个月后恢复健康与工作。

体会: 弓形体病在特异治疗的疗程间歇期, 按照中医辨证施治的原则, 配合应用中药治疗, 可收到调节机体功能, 增强免疫机制, 改善症状的效果, 有利于本病的早日康复。

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Abstracts of Original Articles

Therapeutic Effect of Berberine on 60 Patients with Type II Diabetes Mellitus and Experimental Research

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Since 1983, the authors have observed the therapeutic effect of berberine on 60 cases with type II diabetes mellitus. Among these cases the average age of 36 males and 24 females was 54. Of these patients, 18 were obese, 8 over-weighted and 34 standard weight. Among them, 12 patients were severe, 38 mediate and 10 mild. Self-comparison was taken. Therapeutic diet of diabetes was prescribed only one month. With the exception of effective cases, berberine was given 0.3~0.5g three times a day by oral administration for 1~3 months.

As the result of treatment, major symptoms of diabetes disappeared, the patients' strength enhanced, their blood pressure once complicated with hypertension turned to normal and blood lipid decreased. The fasting glycemic levels in 36 patients were controlled, 14 cases turned better, 4 cases effective, 6 cases ineffective. The total effective rate attained to 90% without serious adverse reaction to berberine during the treatment.

In experimental study the authors made close observation on modelled rats suffering from diabetes induced by alloxan and chosen rats of glycemic levels being 16.65~27.75 mmol/L (300~500mg/dL). These animals were divided into berberine group and control group. After a course of the treatment, all animals were dissected and their whole pancreas were taken out to be examined pathologically. The results showed that the animals of berberine group were healthier than those of the control group ($P < 0.01$). It is suggested that the mechanism of declining blood sugar by berberine may be associated with promoting regeneration and functional recovery of pancreas islet β cells.

(Original article on page 711)

Study of Relation Between Hormone Level and the Type Divided by Differentiation of Symptom and Signs in Diabetes

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The concentrations of serum insulin, cortisol, T_4 , T_3 (RIA) and urine VMA, 17-OH, 17-KS and serum glucose (colorimetric analysis) were measured in patients with diabetes divided into four groups by traditional Chinese medicine, i. e. (1) Lung-heat and impairment of body fluids. (2) excessiveness of the Stomach-heat. (3) deficiency of Kidney-Yin(阴). (4) deficiency of both Yin and Yang(阳) and 30 controls. The results showed that the glucose level was not different among all patients with diabetes. The insulin level in group (2) was lower than that in the controls ($P < 0.05$), and the level in group (4) was significantly higher than that in the other groups ($P < 0.05$). The mean cortisol level in the patients was higher than that in the controls ($P < 0.01$), and the level in group (3) was lower than that in both (1) and (2) ($P < 0.05$). The level of both 17-OH and 17-KS in (1) and (2) were higher than that in (3) ($P < 0.05$, $P < 0.01$, respectively). The correlation between cortisol concentration and 17-OH level was found in all groups. Urine VMA levels in (1), (2) and (4) were higher than in the controls, and that in (3) were lower than in (1) and (2) respectively. The difference of level of T_4 and T_3 among the patients was not to be found, and T_3 level in (2) and (4), and T_4 level in (3) and (4) were lower than those in the controls. The results suggest that the concentrations of insulin, cortisol, T_4 and T_3 , etc. were correlative with the types of the patients with diabetes divided by the differentiation of symptom and signs. This would be of a clinical value for diagnosis and treatment of diabetes in traditional Chinese medicine.

(Original article on page 714)

A Study on Abnormal Psychiatric State of Qi-Gong (气功) Deviation

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This paper has analyzed and studied the mental state of 129 cases (male 106, female 23, mean age 34.6) with Qi-Gong deviation by method of clinical psychology. They include 100 cases of self