

克糖灵对 II 型糖尿病患者胰岛 A、B 细胞功能的影响

天津市第二医院心脏内分泌研究室(300141)

王执礼 张 志 高双荣 黄建伟 王崇义 王班凤
阎兆鹏 高淑珍 宋淑香 邵戴珍 张国英 王冠清

河北省沧州市中西医结合医院

殷志远 于生龙 阎凤祥 苏秀海 瑞新智 张淑芬 郝秀兰 赵齐雄
王洪生 冯秀河 李文东 王瑞章 马金奇* 杨 欢 王凤岭

内容提要 本文报告了应用克糖灵治疗 II 型糖尿病 38 例, 通过对服用该药患者治疗前后血中葡萄糖、胰岛素、C 肽、胰高糖素等的观察, 探讨克糖灵对 II 型糖尿病胰岛 A、B 细胞功能的影响。结果表明: 克糖灵对 II 型糖尿病不仅可明显地降低血糖, 而且有显著改善糖耐量作用。对于肥胖 II 型糖尿病可促进胰岛 B 细胞分泌胰岛素增加, 同时可能抑制胰岛 A 细胞分泌胰高糖素或改善了 A 细胞对血糖感受能力等一系列作用来实现糖尿病的治疗作用。认为克糖灵在目前 II 型糖尿病治疗领域中不失为一有效且较理想的药物。

关键词 克糖灵 II 型糖尿病 胰岛 A、B 细胞 血糖 胰岛素 C 肽 胰高糖素

我们对服用克糖灵的 II 型糖尿病患者治疗前后血中葡萄糖、胰岛素、C 肽、胰高糖素的变化进行了测定, 以观察克糖灵对胰岛 A、B 细胞功能的影响, 结果报告于下。

例)。所有患者于本次检查前一周停用一切降糖药物。上述两组患者根据病史、口服糖耐量试验(OGTT), 胰岛素(IRI)、C 肽(IRCP)释放试验确立 II 型糖尿病的诊断。

临 床 资 料

方 法

一、健康人对照组 33 例, 男 15 例, 女 18 例, 年龄 34~48, 平均 41.5 ± 6.8 岁。均无糖尿病家族史, 心、肺、肝、肾均无异常, 无影响糖代谢的内分泌代谢疾病, 体重指数为 1.03 ± 0.06 。

一、治疗方法: 克糖灵组方: 西洋参 0.3g 黄芪 6g 丹参 6g 熟地 6g 王不留行 6g 大黄 0.6g, 加优降糖 2.5mg(一片) 共粉为一袋, 每日一袋, 分 3 次口服, 3 个月为 1 个疗程。

二、非胰岛素依赖型糖尿病(II 型糖尿病) 38 例, 均系单纯饮食治疗不能控制者。其中男 16 例, 女 22 例, 年龄 36~69 岁, 平均 53.53 ± 9.60 岁。病程 0.5~20 年。按照体重指数分为肥胖组和非肥胖组。体重指数大于 1.20 为肥胖组(14 例), 体重指数小于 1.20 为非肥胖组(24

二、实验室检查方法: 正常人和 II 型糖尿病患者均在试验前一天晚餐后开始禁食, 试验当天清晨空腹取静脉血后立即口服 100g 面粉的馒头, 随后在 60、120、180 分钟分别取血测血糖(G)、IRI、IRCP 和胰高糖素(IG)。

1. 胰岛素、C 肽、胰高糖素的标准品、标记抗原和抗血清均由海军总医院放免检验中心提供。

* 现在秦皇岛市中医院

2. 去激素人血清, 本室自备。

3. 血糖用葡萄糖氧化酶法测定。

4. 胰岛素、C肽和胰高糖素: 用改进的海军总医院放免分析法测定。(1)用SEP—PAK C_{18} Cartridge 对胰岛素、C肽和胰高糖素 ^{125}I 标记物进行再纯化。(2)胰岛素、C肽和胰高糖素的标准品, 由用缓冲液稀释改为用去激素人血清稀释。

结 果

一、33例健康人 OGTT 的血清中G、IRI、IRCP 和 IRG 测定值: 见表1。将所测值用APPLE-II 微机做正态性D检验, $P>0.2$ 。故认为本实验法采用的33例健康人血清中G、IRI、IRCP和IRG含量的总体均属正态分布。

二、克糖灵治疗前后 OGTT 的G、IRI、IRCP 和 IRG 及其曲线下面积的变化: 见表1、2。

1. 血糖变化: 克糖灵治疗3个月后, 两组

II型糖尿病(肥胖组和非肥胖组)OGTT 各时相的G和G面积较治疗前显著降低($P<0.01$), 表明克糖灵对II型糖尿病不仅有明显的降低血糖作用, 而且有改善糖耐量的作用。

2. 胰岛素和C肽的变化: 从表1、2可知, 非肥胖组治疗后 OGTT 中120min与空腹IRI浓度的比值较治疗前显著增加 $P(<0.01)$, 而空腹IRI浓度、空腹IRCP浓度无显著差异($P>0.05$)。进馒头餐后IRI、IRCP各时相所测值均显著增加, IRI和IRCP峰值在120min出现, 分别为治疗前的1.19和1.25倍($P<0.01$)。治疗后的IRI和IRCP面积分别为治疗前的1.12和1.16倍($P<0.01$)。治疗后的IRI/G比值为治疗前的1.2倍($P<0.05$)。表明克糖灵可促进非肥胖糖尿病患者胰岛B细胞分泌胰岛素。

肥胖II型糖尿病不同于非肥胖II型糖尿病, 其治疗前 OGTT 中多时相IRI和IRCP所测值及IRI、IRCP面积均高于健康对照组和非肥胖II型糖尿病组。用克糖灵治疗后, 空腹进

表1 健康人及糖尿病两组治疗前后G、IRI等值比较 ($\bar{x}\pm S$)

组 别	时间 (min)		G (mg/dl)	IRI ($\mu u/ml$)	IRCP (pmol/ml)	IRG (pg/ml)
健康人对照 (33例)	0		87.36 $\pm$ 19.19	14.03 $\pm$ 5.75	0.34 $\pm$ 0.10	88.51 $\pm$ 23.72
	60		120.90 $\pm$ 28.69	87.72 $\pm$ 25.64	0.86 $\pm$ 0.11	67.78 $\pm$ 16.46
	120		101.10 $\pm$ 16.15	70.18 $\pm$ 25.35	1.07 $\pm$ 0.11	56.01 $\pm$ 12.43
	180		77.77 $\pm$ 12.46	24.73 $\pm$ 13.97	0.51 $\pm$ 0.14	80.33 $\pm$ 20.76
非肥胖型 糖尿病 (24例)	0	治前	211.67 $\pm$ 74.00	18.93 $\pm$ 13.91	0.37 $\pm$ 0.12	139.60 $\pm$ 36.43
		治后	135.33 $\pm$ 37.12**	15.50 $\pm$ 7.31	0.37 $\pm$ 0.12	75.39 $\pm$ 36.24**
	60	治前	336.13 $\pm$ 111.62	27.38 $\pm$ 19.71	0.55 $\pm$ 0.34	117.01 $\pm$ 30.12
		治后	245.79 $\pm$ 67.47**	30.29 $\pm$ 13.93*	0.64 $\pm$ 0.25*	60.03 $\pm$ 36.74**
	120	治前	370.25 $\pm$ 106.65	37.14 $\pm$ 30.18	0.69 $\pm$ 0.55	109.13 $\pm$ 34.71
		治后	248.88 $\pm$ 81.51**	44.35 $\pm$ 17.93**	0.86 $\pm$ 0.43**	51.12 $\pm$ 28.11**
	180	治前	305.54 $\pm$ 113.68	48.03 $\pm$ 39.65	0.97 $\pm$ 1.24	108.07 $\pm$ 37.78
		治后	205.46 $\pm$ 88.63**	53.75 $\pm$ 23.87*	1.12 $\pm$ 1.12*	57.90 $\pm$ 38.88**
肥胖型 糖尿病 (14例)	0	治前	200.43 $\pm$ 75.20	23.62 $\pm$ 15.72	0.49 $\pm$ 0.13	115.51 $\pm$ 45.95
		治后	135.43 $\pm$ 49.03**	16.24 $\pm$ 6.95**	0.37 $\pm$ 0.09*	66.02 $\pm$ 33.98**
	60	治前	291.86 $\pm$ 96.42	34.99 $\pm$ 21.10	0.75 $\pm$ 0.35	97.89 $\pm$ 41.49
		治后	227.50 $\pm$ 48.47**	33.70 $\pm$ 14.05	0.73 $\pm$ 0.24	55.71 $\pm$ 31.70**
	120	治前	321.00 $\pm$ 107.77	49.94 $\pm$ 30.70	1.08 $\pm$ 0.61	89.44 $\pm$ 38.54
		治后	231.79 $\pm$ 67.80**	47.14 $\pm$ 15.91	1.01 $\pm$ 0.40	48.73 $\pm$ 28.43**
	180	治前	264.71 $\pm$ 120.20	65.60 $\pm$ 38.71	1.28 $\pm$ 0.77	88.96 $\pm$ 37.29
		治后	192.71 $\pm$ 72.06**	59.80 $\pm$ 17.42*	1.05 $\pm$ 0.37	55.52 $\pm$ 36.69*

注: 与治疗前比较, * $P<0.05$, ** $P<0.01$

表2 健康对照及糖尿病两组治疗前后 G、IRI 等面积及面积比值比较 ($\bar{x} \pm S$)

组别		G 面积 (mg·h/dl)	IRI 面积 (μ u·h/ml)	IRCP 面积 (pmol·h/ml)	IRG 面积 (pg·h/ml)	IRI/G	IRCP/G	IRI/IRG	IRCP/IRG
健康对照 (33例)		304.57 ± 56.24	177.28 ± 60.85	2.38 ± 1.12	208.21 ± 51.13				
非肥胖型 (24例)	治前	964.69 ± 286.01	98.25 ± 75.25	1.86 ± 1.49	350.42 ± 96.48	0.15 ± 0.12	2.22 ± 2.10	0.33 ± 0.28	6.92 ± 7.90
	治后	657.06** ± 183.49	110.48** ± 35.45	2.16** ± 1.12	175.46* ± 99.79	0.18* ± 0.08	3.51* ± 1.97	0.81** ± 0.57	16.30** ± 11.34
肥胖型 (14例)	治前	845.43 ± 272.48	130.94 ± 75.66	2.69 ± 1.40	289.93 ± 121.11	0.17 ± 0.10	3.43 ± 1.96	0.58 ± 0.42	12.80 ± 11.30
	治后	632.29** ± 180.00	120.03** ± 34.69	2.46 ± 0.83	165.22* ± 94.75	0.21 ± 0.08	4.18 ± 1.75	0.93* ± 0.43	20.93* ± 14.75

注: 与治疗前比较, * $P < 0.05$, ** $P < 0.01$

馒头餐后 60、120 和 180min 的 IRI、IRCP 以及它们的面积与治疗前比较非但不增加, 反而有不同程度的降低, 尤以 IRI、IRCP 空腹值和 IRI 面积为显著 ($P < 0.01$)。IRI/G、IRCP/G 虽较前增加, 但无显著性 ($P > 0.05$)。提示, 肥胖 II 型糖尿病存有明显的胰岛素抵抗, 表明克糖灵对此组患者胰岛 B 细胞无促进其分泌作用。

3. 胰高糖素的变化: 用克糖灵治疗后, 非肥胖 II 型糖尿病组的 OGTT 空腹及 60、120min 的 IRG 值和 IRG 面积均明显下降。表明克糖灵可抑制非肥胖 II 型糖尿病患者的胰岛 A 细胞分泌胰高糖素。另一方面, 治疗后 IRI/IRG 和 IRCP/IRG 比值分别是治疗前的 2.45 和 2.36 倍, 这可能是由于治疗后胰岛素分泌增加而胰高糖素分泌减少所致。

讨 论

一、胰岛 B 细胞功能的变化: 本组结果显示非肥胖 II 型糖尿病治疗前空腹血糖和曲线下面积均显著高于健康对照组 ($P < 0.01$), 空腹胰岛素及 C 肽虽高于对照组, 但由于同时相血糖增高, 故 IRI/G、IRCP/G 均显著低于对照组 ($P < 0.01$)。这表明体内胰岛素相对不足。治疗前 OGTT 的胰岛素和 C 肽释放曲线低平, 各时相的 IRI/G、IRCP/G 均低于对照组 ($P <$

0.01), 显示非肥胖的 II 型糖尿病患者胰岛 B 细胞对糖负荷刺激的反应能力和贮备功能均降低。

应用克糖灵治疗后, 空腹血糖明显降低, 糖耐量改善, 空腹胰岛素、C 肽虽然无明显增加 ($P > 0.05$), 但由于同时相血糖明显降低, 所以 IRI/G、IRCP/G 显著高于治疗前水平, 表明胰岛素相对增多, OGTT 的胰岛素及 C 肽释放曲线较前明显改善, 胰岛素和 C 肽面积较前显著增加 ($P < 0.01$)。表明本方剂对本组非肥胖 II 型糖尿病的主要降糖作用是促进胰岛 B 细胞分泌增多。

有人通过研究证实, II 型糖尿病中肥胖者对内生胰岛素有抵抗^[4~6]。其中一些空腹血糖高于 200mg/dl 的患者其空腹 IRCP 和 IRI 略高于正常, 但刺激试验所引起的 IRCP 和 IRI 分泌低于正常。提示这类糖尿病患者的 B 细胞贮备功能不良^[5,6]。

Garcia 等人对 928 例正常及糖尿病患者按体重指数与 IRCP 浓度进行了分组研究^[7], 结果表明肥胖的 II 型糖尿病患者血胰岛素浓度高于正常人。本组肥胖 II 型糖尿病治疗前空腹血糖、血糖面积均高于对照组, 空腹 IRI、IRCP 和 IRI、IRCP/G 面积及 IRI/G、IRCP/G 比值均明显高于健康对照组。糖刺激下 IRI 和 IRCP 释放曲线呈高反应型, 表明肥胖组并非胰岛素

分泌不足所致,而是存在胰岛素抵抗^(10~12)。

目前认为可能与下列因素有关:(1)胰岛素结构异常,与受体结合力降低。(2)胰岛素原不能完全转化为胰岛素。(3)胰岛素受体或受体后缺陷等⁽⁶⁾。用克糖灵治疗可使空腹血糖下降。血糖面积减少,糖耐量明显改善,空腹IRI、IRCP较前降低,IRI、IRCP面积亦较前减少,但IRI/G、IRCP/G比值却无明显改变。上述结果表明,克糖灵对肥胖II型糖尿病有明显降糖作用,但IRI、IRCP不但不增加反而较前减少,说明克糖灵能降低有胰岛素抵抗的肥胖II型糖尿病患者的血糖并改善糖耐量,但不促进胰岛B细胞分泌胰岛素⁽¹⁾。其机制可能与胰外作用有关^(10~12)。

二、胰岛A细胞功能变化:本组的II型糖尿病治疗前空腹血IRG及其面积明显高于正常($P<0.01$),糖负荷后其分泌亦未受到明显抑制。我们认为II型糖尿病胰岛A细胞存有分泌功能异常,非肥胖II型糖尿病胰岛B细胞功能减退,胰岛素相对不足,间接地影响A细胞功能,使其失去对血糖的感受能力。A细胞对高糖的抑制和对低糖的刺激反应异常致胰高糖素分泌过多。肥胖II型糖尿病的胰岛素不降低和胰高糖素增高的原因似与B细胞功能无关,而是A细胞原发性功能缺陷所致^(1~6)。这一点有待于进一步证实。

克糖灵治疗上述两组II型糖尿病IRG均较治疗前显著降低,表明克糖灵可能抑制II型糖尿病胰岛A细胞分泌胰高糖素或改善了A细胞对血糖的感受能力。

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(上接第136页)

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Abstracts of Original Articles

Clinical Analysis of 418 Patients with Wilson's Disease in TCM-WM Treatment

Yang Renmin(杨任民), et al

Department of Neurology, Affiliated Hospital of Anhui College of TCM, Hefei (230061)

From 1974 to 1988, 418 cases of Wilson's disease were treated with TCM-WM in our hospital. 147 cases were of Wilson's type; 149 cases were of pseudosclerosis type; 40 cases were of abdominal and hepatocerebral type; 21 cases were of choreoathetosis type and 21 cases of other types. After a course of treatment for 3 to 6 months, 103 patients showed marked improvement and 286 made some improvement, but no effect was found in 22 patients and 7 deaths were observed. The results were as follows: (1) The mortality in the severe and moderate groups were significantly higher than the mild ($P < 0.05$) and the marked effective rate was less than the latter ($P < 0.01$). (2) The marked effective rate was lower in abdominal and hepatocerebral type, and no significant difference was found in recovery rate between Wilson's type and pseudosclerosis type.

(Original article on page 134)

Effect of Ke-Tang-Ling(克糖灵) Administration on Pancrease Islets Cells Function in Non-Insulin-Dependent Diabetes Mellitus

Wang Zhili(王执礼), Yin Zhiyuan(殷志远)*, et al

Department of Cardio-Endocrinology, Tianjin No2 Hospital, Tianjin (300141)

*Cangzhou TCM-WM Hospital, Hebei

Radioimmunoassay methods were modified for insulin(IRI), C-peptide (IRCP) and glucagon (IRG) in the clinical investigation on normal subjects and 38 patients with non-insulin-dependent diabetes mellitus (NIDDM). In the control group, the peaks of glucose and IRI appeared 1 hour after glucose was taken. IRCP peak, however, appeared 1 hour later. IRG showed its maximum value on fasting and then reached its lowest point at the second hour after glucose loading. The authors' interests were focused on the changes of blood glucose, IRI, IRCP, and IRG in oral glucose tolerance test (OGTT) before and after Ke-Tang-Ling (KTL) was administered in NIDDM. The results demonstrate that the glucose levels and undercurve areas at various phases in OGTT were significantly decreased ($P < 0.01$) in comparison of before and after the treatment with KTL in NIDDM (including obese and non-obese groups). In non-obese group, however, IRI, IRCP, and their undercurve were remarkably increased ($P < 0.01$). In obese group their values were decreased. It suggests that KTL plays a therapeutic role in decreasing blood glucose in non-obese NIDDM. The mechanism involved in this process may be related to its stimulating effect. IRG levels were decreased also ($P < 0.01$) after the treatment with KTL in both obese and non-obese NIDDM, suggesting an inhibitory effect on glucagon secretion from α cells in pancrease.

(Original article on page 137)

A Study on Relation Between Changes of Plasma TXB_2 , $PGF_{1\alpha}$ and Differentiation of Symptoms and Signs of TCM in Severe Icteric Hepatitis

Wang Chenbai(汪承柏), He Jiangping(贺江平), Xu Jianhua(许建华), et al

Department of TCM-WM, 302 Hospital of PLA, Beijing (100039)

Clinical observations and experimental studies were made in 52 cases of chronic cholestatic hepatitis, 30 cases of chronic severe hepatitis, 30 healthy control persons, and 30 animals with experimental intrahepatic cholestasis. The results were as follows: Plasma TXB_2 and $PGF_{1\alpha}$ were higher than their normal values both in cases of chronic cholestatic hepatitis and in cases of chronic severe hepatitis ($P < 0.01$), the ratio of TXB_2 and $PGF_{1\alpha}$ was normal in cases of chronic severe hepatitis and lower than normal value in cases of chronic cholestatic hepatitis ($P < 0.01$). The cases were divided into 4 types (hepatitis due to blood stasis and blood heat, blood stasis and blood heat accompanying symptoms of fluid retention in the epigastrium, damp-heat, and composite factors) according to differentiation of symptoms and signs on the basic theories of TCM. Significant difference was found in TXB_2 , $PGF_{1\alpha}$, $PGF_{1\alpha}/TXB_2$ and bilirubin when compared with each other in the 4 types of hepatitis patients ($P < 0.01$). Bilirubin, TXB_2 , $PGF_{1\alpha}$ and $PGF_{1\alpha}/TXB_2$ in the survivors became normal or close to normal after they were treated with blood-cooling and circulation-promoting Chinese herbal medicine and prescriptions by changing their dosages according to