

滋阴、助阳药对“高甲”、“低甲”大鼠模型 肝细胞核甲状腺激素受体的影响

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内容提要 本实验用已建立的肝细胞核甲状腺激素受体(T_3R)测定法,观察 3 组中药对“高甲”和“低甲”模型大鼠 T_3R 和甲状腺激素的影响。结果发现滋阴药(生地、玉竹)能降低“高甲”模型血清甲状腺激素水平,同时也降低肝细胞核已升高的 T_3R 的最大结合量(B_{max}),使之接近正常。助阳药 I(附子、肉桂)能升高“低甲”模型血清甲状腺激素水平,但反而降低 T_3R 的 B_{max} 。助阳药 II(仙灵脾、苁蓉)也升高血清甲状腺激素水平,但对 T_3R 的 B_{max} 无显著影响。这 3 组中药对 T_3R 的 K_d 均无影响。

关键词 肝细胞核 甲状腺激素 甲状腺激素受体 滋阴药 助阳药

甲状腺功能亢进症(甲亢)和甲状腺功能减退症(甲减)国内早已有人用中药治疗,而且证明能恢复血清甲状腺激素的水平^①。邝氏^②还从实验研究了中药对促甲状腺素释放激素(TRH)的影响。但中药对动物肝细胞核甲状腺激素受体(T_3R)的影响尚未见报告。本文就 3 组中药各对高甲状腺素血症(高甲)及低甲状腺素血症(低甲)模型的 T_3R 影响报告如下。

材料和方法

Wistar 雌性大白鼠,体重 160~200g,本校动物中心供应。“高甲”及“低甲”模型制作按邝氏^②法。将动物随机分成 6 组:(1)“高甲”组:每鼠每日喂甲状腺片混悬液 2ml,约含甲状腺片 160mg,连续 1 周。(2)“高甲”+滋阴药组:已造型动物每日除喂甲状腺片外,再喂滋阴药液 2ml,连续半月。(3)“低甲”组:腹腔戊巴比妥麻醉,作双侧甲状腺切除术,1 周后造型完成。(4)“低甲”+助阳药 I 组:已造型大鼠每日喂助阳药 I 液 2ml,连续半月。(5)“低甲”+助阳药 II 组:同(4),但改助阳药 II 液。(6)正常对照大鼠不作处理。每组 8 只,但造型成功者为 6~7 只。

滋阴药液:生地、玉竹(本实验所用中药均由上海市杨浦区药材公司供应,杨浦区药检所鉴定)各 100g,加水煎 1 h 后,浓缩至 100ml,每 ml 药液含生药各 1g。

助阳药 I 液:熟附子、肉桂,同上法浓缩至相同浓度。助阳药 II 液:苁蓉、仙灵脾,同上法浓缩至相

同浓度。

所有模型或加中药组大鼠均于造型或喂药半月后断头取血和肝脏,血清用于测定甲状腺激素,用上海放射免疫技术研究所提供的药盒。肝脏用于测定 T_3R ,最大结合量(B_{max})反映受体数目,解离常数(K_d)反映受体的亲和力。测定方法用放射配体结合法,参照 DeGroot 法^③改良而成,简述如下。肝脏剪碎,加冷 Tris 蔗糖缓冲液制成匀浆,置 0°C,4000rpm,离心 15min,沉渣用高渗蔗糖液 0°C,40000rpm 30min 超速离心分离出肝细胞核。每份标本作 5 点,每点 2 管,一管为总结合管,另一管为非特异结合管¹²⁵I- T_3 浓度梯度为 $1\sim5\times10^{-10}M$,肝细胞核浓度为 1×10^6 核/管,非特异管中 T_3 浓度为 $1\times10^{-8}M$,反应温度为 37°C,反应 50min,然后 0°C 1200rpm,15min 离心。洗去游离的¹²⁵I- T_3 。测定每管沉渣中 cpm 数,用 Scatchard 作图法计算 T_3R 的 B_{max} 和 K_d 。

DNA 测定用改良的二苯胺法^④。

结 果

以上实验结果,见附表。

讨 论

在中医辨证中,甲亢属于阴虚范畴,甲减属于阳虚范畴。一般认为阳虚的病理生理改变和甲状腺激素有关,而助阳药可改善甲减阳虚患者的症状和 T_3 、 T_4 水平^①,外周血淋巴细胞核 T_3R 的 B_{max} 也相应降低,接近正常^⑤。甲亢肝肾阴虚患者用滋阴药也能改善患者症状和降低血清甲状腺激素^⑥。在动物实验中,邝氏^②报告党参、黄芪、仙灵脾、苁蓉、附子、肉桂能

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附表 滋阴、助阳药各对“高甲”、“低甲”模型大鼠血TT₃、TT₄及肝细胞核T₃R的作用 ($\bar{x} \pm S$)

组别	鼠数	TT ₃ (nmol/L)	TT ₄ (nmol/L)	T ₃ R	
				Bmax (fmol/100μgDNA)	Kd ($\times 10^{-10}$ mol/L)
正常对照	8	1.23±0.25	76.69±15.28	87.45±10.33	2.48±0.47
“高甲”	6	5.74±3.82***	163.15±23.89*	167.14±25.62*	2.31±0.28
“高甲”+滋阴药	7	0.94±0.49△△	102.38±20.84*△	98.98±15.24△△	2.46±0.49
“低甲”	6	0.59±0.19***	19.13±4.88**	69.56±8.82*	2.36±0.32
“低甲”+助阳I	6	1.12±0.26△	44.18±13.61*△	24.89±10.86**△	2.22±0.21
“低甲”+助阳II	7	1.26±0.29△	42.37±11.04*△	52.94±9.83*	2.20±0.69

注：与正常对照组比，* $P > 0.05$ ，** $P < 0.01$ ，*** $P < 0.001$ ；与未用药模型组比，△ $P < 0.01$ ，△△ $P < 0.001$

提高“低甲”模型鼠血清T₄水平，TRH和垂体重下降，但对T₃无影响。本实验观察到“低甲”模型大鼠的表现及血T₃、T₄低下，和文献报告一致，助阳药也能改善这些变化，而且使T₃接近正常，T₄虽仍低于正常，但与模型组相比已明显升高。本实验助阳药对T₃的影响与邱氏⁽²⁾的结果不同，可能因本组单味中药的剂量较大所致。

我们发现助阳药I和II虽都能回升血清甲状腺激素水平，但不能使T₃R的Bmax升高，此与患者不同⁽⁵⁾。甲减患者淋巴细胞T₃R较正常值升高2倍以上，助阳药可使之降低接近正常。而本实验则“低甲”模型的肝细胞核T₃R的Bmax原来就比正常值低，助阳药虽也是使之降低，却比正常值更低。这可能因大鼠和人不同，也可能因肝细胞和血淋巴细胞不同。

我们还发现不同助阳药对T₃R影响不完全一样。助阳药I不但不能回升T₃R的Bmax，反而使之下降更甚。而助阳药II虽也使之下降，但与模型组无统计学差异。助阳药I的附子、肉桂属辛温、大热，而苁蓉、仙灵脾则性甘酸，以补肾壮阳为主。我们⁽⁷⁾曾观察到这两组药物对“阳虚”模型小鼠肝脾DNA更新率作用不同，附、桂无明显作用，而苁蓉、仙灵脾则能提高DNA更新率。因此，苁蓉、仙灵脾似乎较附、桂更适应甲减的治疗。从本实验来看，两组助阳药的T₃、T₄基本相同，而T₃R的Bmax则不同，故T₃R的改变不能用激素的升降调节来解释。

“高甲”模型大鼠的症状和血TT₄水平可用龙胆草、党参、石斛、黄连、生地、黄芩来改善，但对TT₃作用不明显⁽²⁾。我们仅用二味生地和玉竹，也能改善“高甲”大鼠表现，使血TT₃降至正常，而TT₄仍略高于正常。这结果似乎比上方更好一些。本组动物用生地、玉竹后使原来增高的T₃R的Bmax也明显下降，与正常对照组相比已无显著差异。国外有人⁽⁸⁾

测定甲亢患者用他巴唑治疗前后外周血淋巴细胞核T₃R情况，发现用药后T₃R的Bmax轻度下降，与我们的动物实验用中药结果一致，不过程度不同。国内有人⁽⁹⁾研究生地、龟板对“高甲”模型大鼠β-肾上腺素能受体的影响，喂6天中药后血甲状腺激素仍高于正常，但症状改善，而肾组织中β-受体恢复正常。我们认为滋阴药的作用在早期可能是降低β-受体的Bmax，以后通过降低甲状腺激素和T₃R的Bmax发挥治疗作用。这和他巴唑的治疗机理不一样。

本结果显示滋阴药、助阳药可能从分子水平调节T₃R的Bmax，但对其Kd均无影响，而不仅仅是作用于激素本身，这方面还值得进一步探索。

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Key Words chronoacupuncture, Na Ja Fa, gastric acid secretion, gastrin, prostaglandin E₁
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Clinical Research and Mechanical Inquiry into the Treatment of Chronic Superficial Gastritis Using Ziwuliuzhu(子午流注) Day-Prescription of Acupoint

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According to the day-prescription of acupoint mentioned by Xu Feng(徐风) in Encyclopaedia of Acupuncture and Moxibustion, the authors used opening acupoints to treat 31 chronic superficial gastritis patients (young male) and closing points to treat 15 patients for comparison. Besides, the authors observed the changes of hydrochloric acid of gastric juice, volume of juice and serum gastrin of the patients before and after the acupuncture. Results of clinical treatment: In the opening acupoint group, 13 were cured, 12 effected, 4 improved and 2 ineffective. The total effective rate was 93.55%. There was no significant difference between the results of the two groups. Results of experiment: to the hyperacidity patients of the two groups, the content of hydrochloric acid tended to fall after acupuncture while to the hypoacidity patients the content tended to rise after acupuncture. The changes of the gastric juice volume were different in the two groups. In the opening group, we could also see that the low volume rose and high volume fell after acupuncture. However, the closing group showed that the low volume fell after acupuncture. There was not any significant difference. The changes of serum gastrin indicated that, after acupuncture, all the serum gastrin in the two groups went up. But the peak value in the opening group appeared at 30 minutes after acupuncture while in the closing group it appeared at one hour. In both groups, there were significant differences between those results before and after acupuncture.

Key Words Ziwuliuzhu, chronic superficial gastritis, gastric juice, serum gastrin
(Original article on page 94)

Study on Protective Mechanism of *Salvia miltiorrhiza* and *Paeonia lactiflora* for Experimental Liver Damage

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Experimental model of acute liver damage with D-galactosamine was made. Thereafter, *Salvia miltiorrhiza* (SM) and *Paeonia lactiflora* (PL) were given to the rats. Survival rate of rats and liver coefficient (liver weight/body weight) were observed. Changes of ALT and bilirubin in serum were detected. Level of plasma fibronectin (PFN) was determined at various times. Changes of pathological histology under microscope and electron-microscope were observed. The results showed that SM and PL could increase plasma fibronectin levels in rats, and improve the reticuloendothelial system function and plasma opsonic activity. Aggregation of microaggregated albumin, collagen fragment and immune complexes were markedly reduced. Liver immune damage and microcirculation disorder were avoided. Meanwhile, PFN could cause increase of phagocytosis of Kupffer cell to endotoxin. It is concluded that SM and PL play an important role in protective hepatocyte.

Key Words *Salvia miltiorrhiza*, *Paeonia lactiflora*, fibronectin
(Original article on page 102)

Effects of Yin(阴)-Tonics and Yang(阳)-Tonics on Serum Thyroid Hormone Levels and Thyroid Hormone Receptors of Hepatic Cell Nucleus in Hyperthyroxinemic and Hypothyroxinemic Rats

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Hyperthyroxinemia model was made by giving thyroid tablet suspension to Wistar rats and hypothyroxinemia model was made by thyroidectomy. We measured serum thyroid hormone levels