

口服棉酚者血清中睾丸酮、促黄体生成素 和卵泡素浓度的变化

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棉酚是一种作用于睾丸的抗精子发生药物、损伤变态过程的精子细胞和中晚期精母细胞^(1,2,3)，近期亦有人报道棉酚能进一步损伤精原细胞与间质细胞⁽⁴⁾，但棉酚对人垂体性腺轴系激素的影响报道不多。本文通过测定服用棉酚 1~79 个月的男子血中睾丸酮，LH 和 FSH 含量的变化，探讨棉酚对人垂体性腺轴系的影响、观察棉酚对睾丸间质细胞及生精上皮的损伤作用。

材 料 和 方 法

选择健康有生育力的男子、分为对照组和服药组。对照组年龄在 35 ± 4 岁，共 66 人。服药组 75 人，年龄在 34.3 ± 4 ，每人每日口服醋酸棉酚 15 mg，服至达到抗生育效果后，改服维持量，间日 15 mg。服药组按照服药时间再分为 6 组，并分别在停药的当天上午 9~11 时抽血，测定血清中睾丸酮，促黄体生成素 (LH) 及促卵泡素 (FSH) 含量。测定方法，均按世界卫生组织生殖生理放射免疫测定方法手册进行。¹²⁵I 标记的 LH、FSH 每月一次，³H-睾丸酮，每年一次，由 WHO 提供⁽⁵⁾。

实 验 结 果

正常男子与服棉酚者血清中睾丸酮、LH 和 FSH 含量的比较见表 1。对照组测得血清中睾丸酮的正常值是 18.6 ± 7.6 nmol/l，与各服药组均值间（按方差分析法， $P < 0.01$ ）有非常明显的差异。将各服药组各自与对照组相比，除第一组外，各服药组睾丸酮值有明显的增

Tab 1. Serum testosterone, LH and FSH levels in healthy and Gossypol-treated men ($\bar{X} \pm SD$)

Groups	No. of cases	Age	Duration of medication	Total dose (g/man)	Testosterone (nmol/l)	LH (Iu/l)	FSH (Iu/l)
Control	66	35 ± 4	0	0	18.6 ± 7.6	9.1 ± 5.3	7.2 ± 4.1
1	12	37 ± 4	12	1.7~1.2	24.8 ± 6.7	7.3 ± 2.5	8.9 ± 8.7
2	17	37 ± 6	13~24	4.2~0.73	$25.7 \pm 7.9^*$	8.2 ± 3.4	$15.2 \pm 7.4^{**}$
3	7	29 ± 4	25~36	7.3~0.94	$34.0 \pm 10.7^{**}$	9.1 ± 2.9	$12.4 \pm 5.0^*$
4	11	35 ± 3	37~48	10.2~0.24	$25.1 \pm 8.4^*$	8.8 ± 4.2	$18.2 \pm 12^{**}$
5	12	34 ± 3	49~60	11.8~1.1	$26.6 \pm 12.0^*$	9.7 ± 4.3	$11.0 \pm 5.0^*$
6	16	34 ± 3	61~79	15.8~10.2	$36.5 \pm 21.0^{**}$	9.8 ± 5.9	$12.0 \pm 6.0^*$

* $P < 0.05$; ** $P < 0.01$ (Compared with control)

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高 ($P < 0.05$)。正常对照组血清中 LH 值是 9.1 ± 5.2 IU/e, 与服药各组间相比, 无明显差别 ($P > 0.05$)。对照组血清中 FSH 值是 7.2 ± 4.1 IU/e, 按方差分析法与服药组相比有非常显著的差别 ($P < 0.01$)。将各服药组各自与对照组相比, 除第一组外, 血清中 FSH 值均较对照组有明显的增高 ($P < 0.05$ 或 $P < 0.01$)。

讨 论

实验中观察到服药组血清中睾丸酮值较正常对照组有显著地提高, 而 LH 值与对照组相比未见明显变化。血中睾丸酮的提高, 似乎说明了长期服用棉酚后并不引起睾丸间质细胞合成睾丸酮功能的损害。从临床观察, 服药者也并没有出现性功能障碍现象, 但近年来已有人报道棉酚对间质细胞有影响^(1,4,6); 动物服棉酚后血中睾丸酮和 LH 下降^(3,7,8); 体外培养也证明棉酚可抑制睾丸间质细胞的功能^(9,10), 本文中测得 T 含量较正常组有明显提高, 是否意味着由于精子发生障碍后所导致 LH 的应激反应, 此结果尚待进一步研究。

一般认为 FSH 水平与生精上皮损害程度成正比, 而 FSH 受睾丸生精上皮分泌的抑制素的调节。服棉酚过量, 使生精上皮受损害, 所以出现无精症同时有 FSH 升高。本实验结果与张桂元所得的结果相一致⁽¹¹⁾。

关键词 棉酚; 促性腺激素; 甾体激素

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参 考 文 献

1. 戴荣禧等. 棉酚抗生育作用的研究 IV. 大白鼠长期服棉酚睾丸退化的观察. 实验生物学报 1980, 13:193.
2. Zhi-ping GU, et al. Morphological changes in testes and epididymides of rats after gossypol. 中国药理学报 1983, 1:40.
3. 顾芝萍. 国外棉酚研究一瞥. 生殖与避孕 1983, 3:8.
4. 吕德滨等. 服节育量棉酚损伤精原细胞十例报告. 黑龙江省计划生育科技论文摘要选编 1982
5. WHO. Programme for the Provision of Assay Reagents for the Radioimmunoassay of Matched Hormone in Reproductive Physiology: Method Manual. 4th ed. Geneva. 1980
6. 王一飞等. 正常男性与服生棉子油后不育症患者睾丸组织的比较定量组织学观察. 生殖与避孕 1982, 2:31.
7. Chang CC, et al. Studies on Gossypol. 1. Toxicity antifertility and endocrine analysis in male rats. Intl J Fertil 1982, 27:213.
8. 梁素香等. 服棉酚大白鼠血清睾丸酮和 LH 含量的放射免疫测定. 实验生物学报 1981, 14:191.
9. Hadley MA, et al. Effect of gossypol on the reproductive system of male rats. J Androl 1981, 2:190.
10. Hoshi K, et al. Action mechanism of gossypol as a male contraceptive agent: in vitro study on Leydig cell of rat. Japn J Fertil Steril 1982, 27:156.
11. 张桂元等. 服棉酚者和其它原因所致的无精症患者血中促性腺激素与甾体激素的变化. 生殖与避孕 1983, 3:31.

CHANGES OF SERUM CONCENTRATIONS OF TESTOSTERONE, LH AND FSH IN MEN TAKING GOSSYPOL

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ABSTRACT The serum concentrations of testosterone, LH and FSH in healthy men and in men taking gossypol were determined by radioimmunoassay. Gossypol acetic acid was given orally at a daily dose of 15 mg until infertility appeared, followed by 15 mg on alternate days for 1~79 months. 141 cases were divided into a control group of 66 cases and a medication group of 75 cases. The medication group was subdivided into 6 sub-groups, according to the various durations of medication. Results indicated that the serum concentration of testosterone, LH and FSH in the group were 18.6 ± 7.6 nmol/l, 9.1 ± 5.2 IU/l and 7.2 ± 4.1 IU/l respectively. The serum testosterone and FSH levels in the medication groups, with the exception of the first group (12 months), were significantly higher than that of the control group ($p < 0.01$). There were no significant difference between values of serum LH in all of the medicated groups and control group ($p > 0.05$). The higher FSH and testosterone levels indicated severe damage of the germinal epithelium without obvious damage of the Leydig cells in men taken gossypol acetate.

Key words Gossypol acetate; Gonadotropin; Steroid hormone

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