

doi: 10.13241/j.cnki.pmb.2017.01.030

戊酸雌二醇与坤宁安丸对更年期综合征女性激素水平及免疫功能的影响*

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摘要 目的:探讨戊酸雌二醇联合坤宁安丸对女性更年期综合征患者血清激素水平及免疫功能影响。**方法:**收集我院就诊或住院治疗的 120 例更年期综合征患者,随机分为实验组和对照组,每组 60 例。对照组患者给予戊酸雌二醇治疗,实验组患者在对照组基础上给予坤宁安丸治疗。分别于治疗前后对患者血清卵泡刺激素(FSH)、雌二醇(E2)、CD3⁺、CD4⁺、CD8⁺ 水平及 Kupperman 评分、临床疗效进行检测并比较。**结果:**与治疗前相比,治疗后两组患者的 FSH、CD8⁺、KI 评分水平均下降($P<0.05$),E2、CD3⁺CD4⁺ 水平均升高($P<0.05$);与对照组相比,实验组患者的 FSH、CD8⁺、KI 评分水平较低($P<0.05$),E2、CD3⁺、CD4⁺ 水平较高,临床治疗总有效率较高($P<0.05$)。**结论:**戊酸雌二醇联合坤宁安丸能够升高更年期综合征患者血清 E2 水平,降低 FSH 水平,并提高患者的免疫功能,临床疗效较好。

关键词: 戊酸雌二醇;坤宁安丸;更年期综合征;免疫功能

中图分类号:R711.75 文献标识码:A 文章编号:1673-6273(2017)01-119-04

Effects of Estradiol Valerate Combined with Kunningan Pill on the Serum Hormones Levels and Immune Function of Patients with Climacteric Syndrome*

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ABSTRACT Objective: To investigate the estradiol valerate combined Kunningan Pill on serum hormone level and immune functions in patients with climacteric syndrome. **Methods:** 120 cases of menopausal syndrome in our hospital were selected and randomly divided into the experiment group and the control group with 60 cases in each group. The control group were treated with estradiol valerate tablets 1 mg/time, 1 times/d; the patients in the experiment group were given Kunningan Pill based on the control group, 3 g/time, 3 times/d, oral. Treatment for 8 consecutive weeks. After the treatment, the serum follicle stimulating hormone (FSH), estradiol (E2), CD3⁺, CD4⁺, CD8⁺, Kupperman score and the clinical efficacy of patients were detected and compared. **Results:** Compared with before treatment, the FSH, CD8⁺, Ki score levels decreased ($P<0.05$), E2, CD3⁺, CD4⁺ levels were significantly increased ($P<0.05$) after treatment of two groups of patients; compared with the control group, FSH, CD8⁺, Ki score levels were lower ($P<0.05$), E2, CD3⁺, CD4⁺ levels were higher, clinical treatment of total efficiency was higher ($P<0.05$). **Conclusion:** Estradiol valerate combined Kunningan Pill can increased menopausal syndrome patients, the level of serum E2, reduce FSH levels, enhance the immune function and the clinical.

Key words: Estradiol valerate; Kunningan Pill; Climacteric syndrome; Immune function

Chinese Library Classification(CLC): R711.75 **Document code:** A

Article ID: 1673-6273(2017)01-119-04

前言

更年期综合征是由于卵巢功能衰退引起内分泌和生物学改变引起的一系列临床症状^[1],发病率为 80%,其中 10%~15%的妇女因症状严重而被迫就医,临床以潮热、多汗、抑郁

等为其主要症状,是妇科常见病、多发病^[2]。戊酸雌二醇是第一个国产的天然雌激素^[3]。研究证实^[4]长期服用激素有致癌的潜在因素且有一些不良反应,加之部分药品价格较贵,因此在临床应用方面受到了局限。祖国医学中大量的临床实践总结本病病位在肝肾,为肝郁肾虚,瘀浊内生之证^[5]。坤宁安方是在中医

* 基金项目:湖北省自然科学基金项目(SJ970572)

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(收稿日期:2016-08-01 接受日期:2016-08-23)

理论的指导下,由经方桂枝加龙骨牡蛎汤化裁而来,为补阴摄阳之主方^[6]。本方以疏肝调肝为要,兼顾健脾益肾具有疏肝益肾健脾、调和营卫的功效^[7]。本实验通过观察更年期综合征患者血清激素水平及免疫功能的变化,探讨其对女性更年期综合征的治疗效果,现将结果报道如下。

1 资料与方法

1.1 临床资料

收集 2013 年 5 月~2014 年 11 月于我院就诊的 120 例更年期综合征患者,患者符合更年期综合征的诊断标准,有更年期综合征的相关症状,所有患者年龄在 43~58 岁;患者无卵巢以及其他生殖系统疾病;所有患者无肝肾功能不全,无心脑血管疾病;所有患者对实验药物无过敏反应,实验前未服用过类似药物;所有患者签署知情同意书同意进行实验。根据就诊先后顺序分为实验组和对照组,每组 60 例。实验组患者平均年龄(51.34±1.02)岁;对照组患者平均年龄(50.41±1.26)岁。所有患者均符合《中医病证诊断疗效标准》中关于更年期综合征的诊断标准。两组患者一般资料具有可比性(P<0.05)。

1.2 方法

两组患者入院后均给予相应的治疗措施。对照组患者给予戊酸雌二醇片(拜耳医药保健有限公司广州分公司生产 批准文号:H20120369)1 mg/次,1 次/d;实验组患者在对照组基础上给予坤宁安丸(院内自制 药物组成:桂枝、白芍、柴胡、龙骨、牡蛎、当归等,提取制成浓缩水蜜丸)3 g/次,3 次/d,口服。治疗连续 8 周。

1.3 观察指标

1.3.1 患者血清激素水平检测 所有患者治疗前后取外周静脉血 3 mL,采用放射免疫法,检测患者血清血清卵泡刺激素(FSH)、雌二醇(E2)水平。

1.3.2 患者 T 淋巴细胞 CD 亚群水平检测 所有患者治疗前后取外周静脉血 3 mL,采用免疫荧光法,对患者 CD3⁺、CD4⁺、CD8⁺ 水平进行检测。

1.3.3 患者 KI 评分水平检测 治疗前后根据 Kupperman 评分,对患者的各症状进行检测,共统计潮热、汗出、眩晕、头痛、失眠等 13 种症状,各症状的程度分无、轻、中、重 4 种程度,程度因子与指数乘积和即为 KI 指数。

1.4 临床疗效

治疗结束后,采用 KI 评分对患者的临床疗效进行评价。与治疗前相比,治疗后患者 KI 评分下降超过 80%为完全缓解;患者评分下降在 50%~80%之间为显效;有效:患者评分下降在 20%~49%之间为有效;患者评分下降低于 20%为无效。

1.5 统计学分析

采用 SPSS 19.0 统计软件进行分析。计量数据以均数±标准差($\bar{x} \pm s$)表示,采用 t 检验;计数资料以%表示,采用 χ^2 检验。所有数据比较,以 P<0.05 认为差异有统计学意义。

2 结果

2.1 两组患者治疗前后血清 FSH 和 E2 水平比较

治疗后,两组患者的 E2 水平与治疗前相比均升高(P<0.05),FSH 水平均下降(P<0.05);与对照组相比,实验组患者的 E2 水平较高(P<0.05),FSH 水平较低(P<0.05),见表 1。

表 1 两组患者治疗前后 FSH, E2 水平比较($\bar{x} \pm s$)

Table 1 Comparison of the serum FSH, E2 levels between two groups before and after treatment($\bar{x} \pm s$)

		FSH(IU/L)	E2(ng/L)
Experimental group	Before treatment	90.17±4.28	6.93±1.82
	After treatment	43.17±6.14**	61.71±7.82**
Control group	Before treatment	89.92±7.13	6.27±1.29
	After treatment	55.82±5.38*	49.19±5.18*

Note: Compared with before treatment, *P<0.05; Compared with the control group, **P<0.05.

2.2 两组患者治疗前后 CD3⁺、CD4⁺、CD8⁺ 水平比较

治疗后,与治疗前相比,两组患者的 CD3⁺、CD4⁺ 水平均升

高,CD8⁺ 水平降低 (P<0.05); 与对照组相比,实验组患者的 CD3⁺、CD4⁺ 水平较高,CD8⁺ 水平较低(P<0.05),见表 2。

表 2 两组患者治疗前后 CD3⁺、CD4⁺、CD8⁺ 水平比较(ng/mL, $\bar{x} \pm s$)

Table 2 Comparison of the serum levels of CD3⁺, CD4⁺ and CD8⁺ between two groups before and after treatment (ng/mL, $\bar{x} \pm s$)

		CD3 ⁺	CD4 ⁺	CD8 ⁺
Experimental group	Before treatment	44.13±6.43	24.47±5.38	35.72±5.29
	After treatment	60.12±8.22**	41.84±5.13**	22.63±3.84**
Control group	Before treatment	45.03±6.11	25.53±7.09	36.27±3.99
	After treatment	53.28±5.99	35.38±4.11*	28.82±4.11*

Note: compared with before treatment, *P<0.05; Compared with the control group, **P<0.05.

2.3 两组患者治疗前后 KI 评分比较

治疗后,与治疗前相比两组患者的 KI 评分均下降(P<0.05);与对照组相比,实验组患者的 KI 评分水平较低(P<0.05),见表 3。

2.4 两组患者的临床疗效比较

治疗后,实验组的治疗总有效率与对照组相比比较高(P<0.05),具体见表 4。

表 3 两组患者治疗前后 KI 评分比较($\bar{x} \pm s$)Table 3 Comparison of the KI score between two groups before and after treatment($\bar{x} \pm s$)

	Before treatment	After treatment
Experimental group	26.84 $\pm$ 3.18	12.38 $\pm$ 2.11* [#]
Control group	26.34 $\pm$ 2.89	17.93 $\pm$ 2.07*

Note: compared with before treatment, *P<0.05; compared with the control group, [#]P<0.05.

表 4 两组患者的临床疗效比较(% , $\bar{x} \pm s$)Table 4 Comparison of the Clinical curative effect between two groups(% , $\bar{x} \pm s$)

	Complete remission	Excellent	Effective	Invalid	Total effective rate
Experimental group	31(51.67)	18(30.0)	10(16.67)	1(1.67)	59(98.33)*
Control group	24(40.0)	14(23.33)	11(18.33)	11(18.33)	49(81.67)

Note: Compared with the control group, *P<0.05.

3 讨论

更年期综合征是一种人类生命自然发展过程中出现的疾病。对于更年期综合征的诊治是医学界关注的热点^[8]。中医对更年期综合征的理论认识源远流长,历代医家关于其病因病机论述进行了大量的临床实践研究^[9]。在绝经前后,随着肾气的衰微,精血不足,冲任二脉也随之衰少,最终导致女性绝经^[10]。部分女性在此时期阴阳失调而导致一系列症状,所以本病以肾虚为基础,肝郁是关键因素加之阴阳失调、气血失和,导致是病发生^[11]。

全方由桂枝、白芍、龙骨、牡蛎、柴胡、当归等药物组成。本病的主要病因为肝郁所致^[12],故方中以疏肝为主,兼顾补肾健脾、调和营卫。方中柴胡,味苦,性微寒,为疏肝解郁之要药^[13]。历代医家认为:肝脏喜调达,恶抑郁,能够升发诸阳。更年期患者多有肝火炽盛,肝阳上亢等证,采用柴胡能够升发,枢转少阳之机;白芍苦、酸、微甘,能够滋阴养血柔肝^[14]。肝脏具有肝阴易亏,肝阳易亢的病理特点,因此选用白芍养血滋补肝体。当归,健脾养血,又可滋养肝血,与白芍合用,一开一合,互相为用,行气缓急,对患者气郁之症具有较好的疗效^[15]。山药性甘、平,为平补之剂,功能健脾补肾。党参有滋补脾胃,安神解郁之功。茯苓具有宁心安神,交通心肾的功效,且与龙牡合用,能安神定志^[16]。龙骨有镇惊安神之功,能镇安精神,固涩滑脱的功效,并在收敛中具有开通之力。牡蛎始载于《神农本草经》,具有镇静安神的功效。与龙骨常相须为用,同用治心神不安、惊悸怔忡等症。桂枝功能助阳化气,温通经脉。能振奋脾阳,与白芍二者配合,从阴阳两个方面能调整脾胃功能。

妇女进入更年期,雌激素水平明显下降,雌激素的长期缺乏会增加心血管疾病发生的风险,补充雌激素可改善潮热等症状^[17]。本实验结果显示:治疗后,两组患者的血清 E2 水平升高,FSH 水平下降,其中实验组患者的 E2 水平较高,FSH 水平较低。有研究证实坤宁安可以改善更年期综合征患者激素内环境,坤宁安提高患者的 E2、FSH 水平不是通过增加外周组织中雄激素转化,而是通过提高患者卵巢功能,延缓卵巢衰老而实现的。

现代研究表明^[18]坤宁安的组方对中枢神经系统功能会产生一定的影响,调节植物神经功能。方中的桂枝中桂皮醛以及柴胡中的柴胡粗皂苷还具有镇静作用,龙骨对骨骼肌的兴奋产

生抑制作用,发挥较好的镇静作用。近年来的研究显示^[19]皮肤、激素、免疫分子三者之间的相互作用,构成了 " 神经—内分泌—免疫网络 ",其中任何一环的紊乱都会影响其它系统的功能。更年期综合征患者神经内分泌失调会对免疫系统产生影响,免疫系统功能下降,患者内分泌系统发生改变^[20]。本实验结果显示:治疗后,与治疗前相比,两组患者的调高免疫应答能力的 CD3⁺、CD4⁺ 水平均升高,调低免疫应答能力的 CD8⁺ 水平降低,而实验组患者的 CD3⁺、CD4⁺ 水平较高,CD8⁺ 水平较低。本实验组方中柴胡中的柴胡多糖能够改善细胞免疫功能;白芍也能够增强体液免疫反应的特异性;当归可以促进脾淋巴细胞的增高,同时能促进淋巴细胞形成抗体;党参中的党参醇提物能够增加其淋巴细胞转化,提高抗体效价。因此,诸药合用,对更年期综合征患者的免疫功能的调节具有较为明显的作用。

综上所述,戊酸雌二醇联合坤宁安丸能够升高更年期综合征患者血清 E2 水平,降低 FSH 水平,并提高患者的免疫功能,临床疗效更好。

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