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雌激素替代疗法对内分泌失调女性内分泌轴功能的影响*

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摘要 目的：探讨雌激素替代疗法对内分泌失调女性内分泌轴功能的影响。**方法：**选取 2014 年 9 月至 2018 年 2 月到本院就诊的 186 例内分泌失调女性患者当作研究对象，根据治疗方法的不同将其分为观察组(给予雌激素替代疗法)100 例与对照组(给予常规药物)86 例，两组均治疗 3 个月，比较两组治疗前 TC、TG、LDL-C、HDL-C 水平、黄体生成素(LH)和雌二醇(E2)水平的变化、疗效与不良反应的发生情况。**结果：**观察组与对照组治疗后的总有效率分别为 98.0%和 88.4%，观察组明显高于对照组(P<0.05)。观察组治疗后的血清 HDL-C、E2 值较对照组显著增加，血清 TC、TG 与 LDL-C、FSH 水平均较对照组明显降低(P<0.05)。观察组与对照组治疗期间的主要不良反应为乳房胀痛、乳房包块、肝功能异常、下肢水肿等，组间对比差异无统计学意义(P>0.05)，所有不良反应经过对症处理后好转。**结论：**雌激素替代疗法治疗内分泌失调女性能调节内分泌轴功能，提高治疗效果，改善临床症状，促使血脂分泌平衡，且安全性好。

关键词：雌激素替代疗法；内分泌失调；内分泌轴功能；女性；血脂

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Effects of Estrogen Replacement Therapy on the Endocrine Axis Function of Endocrine Disorder Women*

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ABSTRACT Objective: To investigate the effect of estrogen replacement therapy on the endocrine axis function of women with endocrine disorders. **Methods:** 186 cases of female patients with endocrine disorders from September 2014 to February 2018 were selected as research subjects. According to the different treatment methods, they were divided into the observation group (100 cases, estrogen replacement therapy) and the control group (86 cases, conventional drugs). Both groups were treated for 3 months. The changes of TC, TG, LDL-C and HDL-C levels, luteinizing hormone (LH) and estradiol (E2) levels, curative effect and incidence of adverse reactions were compared between the two groups before and after treatment. **Results:** The total effective rates of observation group and control group after treatment were 98.0% and 88.4% respectively, which was significantly higher in the observation group than that of the control group (P<0.05). The serum HDL-C and E2 values of observation group were significantly higher than those of the control group after treatment. The levels of serum TC, TG and LDL-C and FSH were significantly lower than those in the control group (P<0.05). Breast pain, breast mass, abnormal liver function and edema of lower extremities were found in both groups during the treatment. No significant difference between the groups (P>0.05). All the adverse reactions were improved after treatment. **Conclusion:** Estrogen replacement therapy can regulate the function of the endocrine axis, improve the treatment effect and promote the balance of blood lipid secretion in the treatment of endocrine disorder women with high safety.

Key words: Estrogen replacement therapy; Endocrine disorders; Endocrine axis function; Female; Blood lipid

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前言

内分泌失调(endocrine dyscrasia)为机体内激素反馈调节机制失衡而出现的疾病，该病多发病于女性，也多发病于女性围绝经期[1]。该病可影响 20%左右的女性，在临床上主要表现为烦躁易怒、烘热汗出、血压升高、心悸失眠等症状，可诱发出现雄

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激素血症、高胰岛素血症、卵巢囊性增大等疾病的发生，影响患者妇女的身心健康[2,3]。内分泌失调可导致脂代谢紊乱，研究显示围绝经期妇女 TC、TG、LDL-C 的上升显著，其中高甘油三酯症的发生率最高[4,5]，且随着年龄的增长，HDL-C 异常的发生率也在逐渐增加[6]。

内分泌失调的具体发病机制还不完全明确，研究表明其与神经内分泌系统异常密切相关 [7]。下丘脑 - 垂体 - 性腺轴(Hypothalamic-pituitary-adrenal，HPA) 在哺乳动物各种生命活动中发挥至关重要的调节作用，内分泌失调患者多呈现 HPG 异常，使肾上腺源与卵巢源的雄激素过分泌、黄体生成素 / 卵泡刺激素比率升高和促性腺激素释放激素脉冲频率异常[8]。研究表明围绝经期妇女能通过神经 - 内分泌的自我调节达到新的平衡而无自觉症状，但很多妇女则可因性激素减少，精神、心理、神经、内分泌和代谢失衡发生内分泌失调[9,10]。

激素替代疗法(hormone replacement therapy，HRT)为内分泌失调的主要治疗方法，并且也有很好的降血脂作用[11,12]。但激素替代疗法的长期应用可造成体重增加、乳房胀痛、阴道出血等并发症[13,14]。本研究主要探讨了雌激素替代疗法对内分泌失调女性内分泌轴功能的影响，以阐明该方法的作用机制，促进改善内分泌失调女性患者的预后。现总结报道如下。

1 资料与方法

1.1 一般资料

采用多回顾性、平行、总结性研究方法，选取 2014 年 9 月至 2018 年 2 月到本院就诊的 186 例内分泌失调女性患者当作研究对象。所有患者均签订知情同意书，研究得到了医院伦理委员会的批准。纳入标准：符合内分泌失调的诊断标准；女性；年龄 45-55 岁；可以全程参与本次研究；临床资料完整。排除标准：长期吸烟、酗酒；存在严重或不稳定状态的躯体疾病；近 1 个月内曾服用雌激素制剂或针对更年期症状的保健药品；临床资料缺项；妊娠与哺乳期妇女；研究中无法根据要求用药与生活者。根据治疗方法的不同将所有患者分为观察组(给予雌激素替代疗法)100 例与对照组(给予常规药物)86 例，两组患者的一般资料比较差异无统计学意义，具有可比性，见表 1。

表 1 两组一般临床资料对比

Table 1 Comparison of the general data between two groups

Groups	n	Age(year)	BMI(kg/m2)	Course of disease (year)	Educational level (primary school and below/middle school/University)	Disease condition (mild/moderate/severe)
Observation group	100	48.32± 3.11	23.49± 2.19	1.53± 0.78	22/50/28	80/16/4
Control group	86	48.19± 4.88	23.10± 3.48	1.59± 0.24	18/50/18	73/10/3
P		0.198	0.573	0.744	0.466	0.671

1.2 治疗方法

对照组：给予患者口服坤泰胶囊(贵阳新天药业股份有限公司，国药准字 Z20000083，0.5 g/g)4 粒，3 次 /d。观察组：在对照组治疗的基础上给予雌激素替代疗法治疗，口服戊酸雌二醇(国药准字 J20130009，拜耳医药保健有限公司)1mg，1 次 /d。在患者无经潮时服药，若有经潮，则在来潮 5 d 以后服药。两组都治疗观察 3 个月。

1.3 观察指标

(1) 疗效标准：(显效 + 有效)/ 组内例数× 100.0%= 总有效率。显效：临床主要症状不适症状减轻，临床症状改良 Kupperman 评分减少≥ 80%；有效：临床主要症状不适症状部分减轻，Kupperman 评分减少≥ 50%；无效：无达到上述标准甚或恶化。(2)血脂测定：在治疗前与治疗后由我院检验科测定血脂，有月经者须在月经期第 2-4 等抽血检测 TC、TG、LDL-C、HDL-C，无停经着可等到下个月经周期进行检测。(3)不良反应发生情况。(4) 在治疗前后抽取患者的空腹静脉血 3-5 mL，4℃ 3000 rpm 分离上层血清，采用化学免疫发光法检测黄体生成素(LH)和雌二醇(E2)含量，检测试剂由罗氏公司提供，严格按照操作说明书进行操作。

1.4 统计学分析

选择 SPSS 22.00 软件对本研究数据进行统计学分析，计量资料以均数± 标准误表示，计数资料以率表示，组间比较分别采用 t 检验、卡方检验，以 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组治疗前后血脂变化的对比

治疗后，观察组的 HDL-C 值较治疗前显著增加($P<0.05$)，TC、TG 与 LDL-C 值较治疗前明显降低($P<0.05$)，对照组治疗前后血脂水平对比差异无统计学意义($P>0.05$)，观察组 HDL-C 值显著高于对照组，而 TC、TG 与 LDL-C 值明显低于对照组($P<0.05$)，见表 2。

2.2 两组的临床疗效对比

治疗后，观察组与对照组的总有效率分别为 98.0% 和 88.4%，观察组明显高于对照组($P<0.05$)，见表 3。

2.3 两组治疗前后血清 FSH、E2 水平的变化对比

两组治疗后血清 FSH 水平较治疗前明显降低，而血清 E2 水平明显高于治疗前($P<0.05$)，观察组治疗后血清 FSH 水平显著低于对照组，而血清 E2 水平明显高于对照组($P<0.05$)，见表4。

2.4 两组不良反应情况的对比

观察组与对照组治疗期间的主要不良反应为乳房胀痛、乳房包块、肝功能异常、下肢水肿等，其发生率组间对比差异无统计学意义($P>0.05$)，所有不良反应经过对症处理后好转，见表5。

3 讨论

内分泌系统属于内分泌腺与内分泌细胞所组成的重要性调节系统，在维持机体的生长发育与代谢等方面发挥重要作

表 2 两组治疗前后血脂水平的变化对比(mmol/L)

Table 2 Comparison of the changes of blood lipid before and after treatment between two groups (mmol/L)

Groups	n	TC		TG		LDL-C		HDL-C	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	100	5.79± 0.78	5.56± 0.55*#	1.65± 0.22	1.54± 0.52*#	3.82± 0.24	3.70± 0.55*#	1.50± 0.42	1.60± 0.32*#
Control group	86	5.80± 0.42	5.77± 0.94	1.66± 0.42	1.64± 0.78	3.82± 0.62	3.78± 0.81	1.50± 0.67	1.53± 0.42

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

表 3 两组治疗后的临床疗效对比

Table 3 Comparison of the curative effect after treatment between two groups

Groups	n	Obviously effective	Effective	Invalid	Effective rate
Observation group	100	90	8	2	98.0%*
Control group	86	66	10	10	88.4%

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

表 4 两组治疗前后血清 FSH、E2 水平的变化对比(μmol/L)

Table 4 Comparison of the changes of serum FSH and E2 levels before and after treatment betwen two groups (μmol/L)

Groups	n	E2		FSH	
		Before treatment	After treatment	Before treatment	After treatment
Observation group	100	16.30± 4.32	33.29± 4.02*#	89.21± 22.30	73.09± 15.30*#
Control group	86	16.49± 5.11	25.39± 3.92#	89.82± 21.73	80.39± 21.77#

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

表 5 两组治疗期间不良反应发生情况对比

Table 5 Comparison of the incidence of adverse reactions during the treatment between two groups

Groups	n	Breast tenderness	Breast mass	Abnormal liver function	Edema of lower extremity
Observation group	100	2(2.0%)	1(1.0%)	1(1.0%)	1(1.0%)
Control group	86	1(1.2%)	2(2.3%)	1(1.2%)	0(0.0%)

用。正常的生理条件下,多种激素共同实现机体功能的动态化平衡。当机体内分泌系统出现紊乱时,激素分泌失衡,可出现内分泌失调[15],患者在临床上可出现一系列精神和躯体的症状,影响患者妇女的身心健康[16,17]。虽然部分患者能通过神经 - 内分泌的自我调节达到新的平衡而无自觉症状,但是多数患者由于体内雌激素水平急剧下降,可导致冠心病、骨质疏松与痴呆症的发病率增加[18]。现代研究显示导致内分泌失调的原因比较多,特别是随着年龄的增加,使得围绝经期女性的内分泌失调发生率非常高;而在产、胎、经等特殊时期,女性很容易遭受寒、暑、热、风等外邪的影响,导致气机失调,从而导致内分泌失调;焦虑情绪严重时会导致气血紊乱,从而引发内分泌失调;营养不充足很容易导致内分泌失调 [19]。当前治疗该病尚无特效药物,单独进行药物治疗,只能达到治标的目的,而无法治本。

激素替代治疗是目前临床上用于内分泌失调女性的主要治疗方法,其中雌、孕激素合用适合有完整子宫的女性。与其他药物联合的序贯用药能够模拟正常的月经周期,对患者的身心状态影响比较小[20]。本研究显示观察组治疗后的 HDL-C 值增加,TC、TG 与 LDL-C 值降低,临床总有效率高于对照组。从机制上分析,雌激素具有调控血脂代谢的作用,随着性激素水平的下降,从而导致血脂代谢的紊乱。有研究表明雌激素能够介入血浆 TC 代谢,对 TC 下降及排泄有着促进作用,能够降低血浆 TC 含量,能促进患者血脂平衡。雌激素替代疗法对血脂也呈现不同的改变规律, 低剂量雌激素并不一定对血脂更有利,特别是雌激素替代疗法改善血脂的作用机制,是以后关注的焦点[21]。相关研究表明雌激素替代疗法不但可显著改善内分泌失调各种症状,还可缓解血脂紊乱与血脂谱,从而对心血管起到有效保护[22]。

正常机体的各类型激素会保持一个动态性的平衡状态,体内激素分泌过多或过少便会导致内分泌失调。长期雌激素不足可加重骨质疏松、老年痴呆症与冠心病发病率增高等[23]。在治疗中,当前多选择进行雌激素替代疗法干预,可以帮助妇女顺利渡过围绝经期,并可有效地预防骨质疏松。有研究显示内分泌失调患者的卵巢功能下降,体内雌激素的含量下降,体内能量的过剩,使得体型变得肥胖,患者就需要补充一定激素,以保持生理平衡[24,25]。本研究显示观察组与对照组治疗期间的主要不良反应为乳房胀痛、乳房包块、肝功能异常、下肢水肿等,所有不良反应经过对症处理后好转,表明雌激素替代疗法的应用具有很好的安全性。

内分泌失调女性异常的卵巢类固醇生成、高胰岛素血症和下丘脑-垂体-性腺轴内分泌紊乱之间存在着复杂的相互作用[26]。在 HPA 轴中，下丘脑合成的促肾上腺皮质激素释放激素能够促进垂体前叶合成和分泌促肾上腺皮质激素(ACTH)，而促肾上腺皮质激素主要作用于肾上腺皮质的束状带和网状带，同时分别促进分泌糖皮质激素和合成雄激素[27]。研究显示妇女机体雌激素减少时会导致出现一系列的神经内分泌失调的症状[28]。内分泌异常、肾上腺雄激素过多、卵巢类固醇生成异常可影响卵泡生成和排卵，若此时进行合理干预可有效改善和促进内分泌失调女性患者卵巢中卵泡发育和生育能力的适当恢复[29]。也有研究显示围绝经期卵巢功能的衰退表现为雌激素分泌下降，去甲肾上腺素转化率增加，使下丘脑体温调节中枢下调，促使患者产生精神神经症状及血促性腺激素变化[30]。本研究显示两组治疗后观察组治疗后血清 FSH 水平显著低于对照组，而血清 E2 水平明显高于对照组，表明雌激素替代疗法可协同反馈性抑制垂体的性功能调节轴，避免了过度的 FSH 或 LH 异常导致的患者血管舒张功能障碍的发生。

内分泌失调疾病很难根治，雌激素替代疗法虽然有一定的效果，但是也需要借助多种治疗方案实现内外结合、标本同治的目的。使用雌激素替代疗法有明确的指征，必需低剂量，尽量从绝经早期开始用药，并定时进行体检。对有子宫的患者使用时必须加用孕激素以对抗子宫内膜增生，保护子宫内膜，以免诱发子宫内膜癌[31]。

总之，雌激素替代疗法治疗内分泌失调女性能调节内分泌轴功能，提高治疗效果，改善临床症状，促使血脂分泌平衡，且安全性好。

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