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不同证型多囊卵巢综合征患者的临床和生化特征研究 *

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摘要 目的:探讨"痰湿证"和"非痰湿证"多囊卵巢综合征(Polycystic ovary syndrome,PCOS)患者的临床和生化特征。**方法:**纳入 PCOS 患者 89 例(其中痰湿证 42 例、非痰湿证 47 例)及正常对照 52 例(其中痰湿证对照组 21 例、非痰湿证对照组 31 例),采集和比较其临床资料及血清糖脂代谢指标、性激素水平的差异。**结果:**PCOS 患者月经初潮年龄明显晚于正常对照组,两种证型 PCOS 患者均存在临床表现、性激素、糖代谢、脂代谢的异常,表现在多毛评分、黑棘皮、皮肤溢脂、痤疮发生率明显高于对照组;黄体生成素((Luteinizing hormone,LH)、黄体生成素/促卵泡激素(Follicle stimulating hormone,FSH)、雌二醇(Estradiol,E2)、睾酮(Testosterone,T)、游离雄激素指数(Free androgen index,FAI)、空腹葡萄糖(Fast blood glucose,FBG)、甘油三酯(Triglyceride,TG)水平明显高于对照组;高密度脂蛋白(High density lipoprotein,HDL)水平显著低于对照组(P<0.05)。而"痰湿型"PCOS 以体重指数(Body mass index,BMI)、腰臀比(Waist hip ratio,WHR)、收缩压、黑棘皮和皮肤溢脂发生率、FAI、FBG、空腹胰岛素(Fast Insuline,FINS)、稳态模型胰岛素抵抗指数(Homeostasis model insulin resistance index,HOMA-IR)水平增高为主;而"非痰湿型"PCOS 以 LH/FSH、LH 水平增高为主;与"非痰湿"对照组相比,"痰湿"对照组 BMI、WHR、收缩压、FBG、TG、低密度脂蛋白(Low density lipoprotein,LDL)、HOMA-IR 明显升高。**结论:**"痰湿证"PCOS 患者以糖脂代谢异常和胰岛素抵抗为主,而"非痰湿证"PCOS 患者以性腺轴紊乱和高雄激素血症为主,将 PCOS 患者分为"痰湿证"和"非痰湿证",能反映疾病不同证型的基本特点,对远期并发症的防治有指导意义。

关键词:多囊卵巢综合征;中医证型;临床研究

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A Study on the Clinical and Biochemical Characteristics of Patients with Different Syndromes of Polycystic Ovary Syndrome*

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ABSTRACT Objective: To study the clinical and biochemical characteristics of patients with polycystic ovary syndrome with different syndromes. **Methods:** The samples of 89 cases of PCOS patients (42 cases of phlegm dampness type and 47 cases of nonphlegm dampness type) and 52 cases of normal control groups (21 cases of phlegm dampness type and 31 cases of nonphlegm dampness type) were studied. The clinical data and the serum glycolipid metabolism index and sex hormone level were collected and compared. **Results:** The age of menarche of patients with phlegm dampness type and nonphlegm dampness type were later than those oif the normal control groups, the F-G score and the incidence of skin excessive fat, acne, acan-thosis nigricans in phlegm dampness type and nonphlegm dampness type were significantly increased than those of the control group with phlegm dampness type and nonphlegm dampness type, the LH, LH/FSH, E2, T, FAI, FGS, TG levels were significantly higher than those in the control group; the level of HDL was lower than that of the control group (P<0.05). The BMI, WHR, systolic blood pressure, the incidence of acanthosis nigricans and skin excessive fat, FAI, FGS, FINS, HOMA-IR levels in the phlegm dampness type were significantly increased; and the LH, LH/FSH, HDL levels in nonphlegm dampness type were signifycantly increased; between phlegm dampness type and nonphlegm dampness type in the control group. **Conclusions:** " Phlegm-damp-Ness " PCOS is mainly characterized with abnormal glucose and lipid metabolism and insulin resistance, and " non-phlegm dampness " PCOS is mainly characterized with disorders of gonadal axis and hyperandrogenism. As PCOS patients were divided into " phlegm-dampness " and " non-phlegm dampness " , it can reflect the basic characteristics and the severity of disease and guide for prevention and treatment of long-term complications.

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前言

多囊卵巢综合征(Polycystic ovary syndrome，PCOS)是妇科常见病，表现为生殖障碍和内分泌异常，在育龄期妇女中的发病率为 5%～10%[1,2]。PCOS 的病因及发病机制尚不明确，远期可发生不孕、心血管疾病、糖尿病、子宫内膜癌等并发症[3-5]，严重影响女性健康。中医学认为 PCOS 的证候分布以 " 痰湿 " 证为多见[6,7]，肥胖 PCOS 患者中属痰湿证所占比例最高[8]。肥胖的病理基础是痰湿，" 痰湿 " 现代生物学基础是糖代谢、脂代谢改变[9,10]。此外，研究表明中医证候与血清性激素变化具有相关性[11-13]。" 证 " 是机体在疾病发展过程中某一阶段的病理概括，反映的是疾病发展过程中病理变化的本质 [14]。明确不同证型 PCOS 患者的临床和生化特征对疾病证候的诊断和治疗具有重要意义。因此，本研究主要探讨了 PCOS 中医 " 痰湿证 " 和 " 非痰湿证 " 的临床特征，以期为证候研究提供借鉴。

1 资料与方法

1.1 研究对象及分组

收集 2012 年 1 月至 2013 年 6 月就诊于我院妇科门诊的的 PCOS 患者中医辨证为 " 痰湿证 "42 例为痰湿组；" 非痰湿证 "47 例为非痰湿组，另收集于我院体检中心体检的正常人群，与 " 痰湿证 " 体重指数匹配的 21 名为痰湿对照组；与 " 非痰湿证 " 体重指数匹配 31 名为非痰湿对照组。

1.2 诊断标准

PCOS 诊断参照 2003 年鹿特丹诊断标准[15]。中医痰湿证型诊断标准：根据《中医证候辨治规范》[16]、《中药新药临床研究指导原则》[17] 的中医证候临床研究指导原则等制定，主证：(1)肥胖；(2)月经后期或闭经；(3)不孕；兼证：(1)身体倦怠，沉困、嗜睡、乏力；(2)月经量少或经色淡黯；(3)胸腹痞满；(4)带下量多；(5)舌淡胖，苔白或白腻；(6)脉滑或沉涩、沉缓；其中主证具备 1 项，兼证具备 3 项，便诊断为痰湿证型。非痰湿证型诊断标准：排除痰湿证型，综合其他证型，定为非痰湿证型。

1.3 纳入及排除标准

纳入标准：(1)15~35 周岁；(2)月经来潮≥ 两年；(3)PCOS 患者符合 2003 年鹿特丹诊断标准及中医证候诊断标准；正常对照组月经周期规律，周期为 21~35 天且雄激素水平正常；(4)受试者均自愿参加研究并已经签署知情同意书。排除标准：所有受试者近 3 个月内应用影响实验结果的药物；妊娠期或哺乳期；患有严重的躯体或精神系统疾病者予以排除。

1.4 伦理许可

研究通过了黑龙江中医药大学附属第一医院伦理委员会的审批，伦理审查批件号：2010HZYLL-014，符合临床研究中的赫尔辛基宣言，在研究开始前均取得了受试者的知情同意，并签署了知情同意书。

1.5 观察指标

(1)体格检查：身高、体重、腰围、臀围、腰臀比、血压、计算体重指数(BMI)= 体重(kg)÷ 身高(m)^2、腰臀比、多毛评分、计算黑棘皮及痤疮的发生率；(2)生化指标：受试者于自然月经周期或孕激素撤退出血(地屈孕酮，10 mg，每日 1 次，连用 7 天)的 3~5 天，早晨空腹采静脉血 10 mL，室温下静置 30 min 后以 3000 r/min 离心 10 min 后分离血清，EP 管分装，置于 -80 ℃冰箱保存，待标本全部收集完一次性检测。

采用放免法测定 FSH、LH、E2、泌乳素(Prolactin，PRL)、T、AND、硫酸脱氢表雄酮 (Dehydroepiandrosterone sulfate，DHEAS)、性激素结合球蛋白 (Sex hormone binding globulin，SHBG)；化学发光法测定 FIN，以上由黑龙江省医院同位素科检测；FBG、总胆固醇(total Cholesterol，TC)、TG、LDL、HDL 由黑龙江中医药大学附属第一医院检验中心生化室测定。计算 HOMA-IR (HOMA-IR=FBG (mmol·L^{-1})× FIN (miu·L^{-1})/22.5，计算 FAI(FAI=T(nmol/L)× 100/SHBG(nmol/L))。

1.6 统计学方法

采用 SPSS21.0 统计软件对数据进行统计分析，所有的统计数据均存储在 Excel 表格中，计量资料以 $\bar{x}\pm s$ 表示，多组间比较采用单因素方差分析，两组间比较采用 SNK-q 检验，计数资料应用 x^2 检验，以 P<0.05 为差异有统计学意义。

2 结果

2.1 四组一般临床资料差异的比较

PCOS 不同证型组与相应的对照组比较，在年龄、体重指数上无差异，具有可比性；痰湿组和非痰湿组患者的初潮年龄均明显晚于对照组，P＜0.05，有统计学意义；痰湿组体重指数、腰臀比、收缩压、黑棘皮评分、溢脂发生率明显高于非痰湿组女性，痰湿组腰臀比、皮肤溢脂、收缩压发生率明显高于痰湿对照组，差异有统计学意义(P＜0.05)；痰湿组、非痰湿组多毛、黑棘皮、痤疮评分明显高于痰湿对照组、非痰湿对照组，差异具有统计学意义(P＜0.05)。

2.2 四组血清性激素水平比较

痰湿组、非痰湿组 LH、LH/FSH、E2、AND、T、FAI 水平明显高于相应对照组，差异具有统计学意义(P＜0.05)；痰湿组患者 LH 及 LH/FSH 明显低于非痰湿组，而 FAI 水平明显高于非痰湿组，差异具有统计学意义(P＜0.05)；四组女性 PRL 水平无明显差异；非痰湿组组 DHEAS 水平明显高于非痰湿对照组女性，差异具有统计学意义(P＜0.05)。

2.3 四组血糖、脂代谢的比较

痰湿组 FBG、FINS、HOMA-IR 水平明显高于非痰湿组；痰湿组和非痰湿组 FBG、TG 水平明显高于痰湿对照组、非痰湿对照组；痰湿组 HOMA-IR 水平明显高于痰湿对照组，差异具有统计学意义(P＜0.05)；非痰湿组血清 CHO、LDL 水平明显高于非痰湿对照组女性，差异具有统计学意义(P＜0.05)；痰湿组和非痰湿组 HDL 水平明显低于于痰湿对照组、非痰湿对照组，差异具有统计学意义(P＜0.05)。

3 讨论

表 1 四组一般资料的比较

Table 1 Comparison of the general information among four groups

	Phlegm dampness type	Nonphlegm dampness type	Control group of phlegm dampness type	Control group of nonphlegm dampness type
Case	42	47	21	31
Age	24.61± 3.43	24.22± 3.91	24.58± 3.45	24.10± 2.61
Menarche age	13.81± 1.51*	14.21± 1.96▲	13.10± 0.95	13.29± 1.61
BMI(kg/m²)	27.87± 3.63△	21.01± 1.82	26.77± 1.95○	20.32± 1.68
WHR	0.91± 0.08△ *	0.83± 0.07	0.86± 0.05○	0.80± 0.08
Systolic pressure(mmHg)	117.63± 7.51△ *	110.45± 10.73	113.51± 7.75○	111.15± 10.79
Diastolic blood pressure (mmHg)	76.34± 9.63*	72.48± 9.28	69.29± 7.06	71.89± 8.06
F-G score	3.37± 2.64*	3.70± 3.73▲	1.51± 1.46	2.15± 2.05
Incidence of acanthosis nigricans(%)	61.4△ *	10▲	0	0
Incidence of acne(%)	41*	75▲	54.7	48.6

Note: Comparison of phlegm dampness type and The control group of phlegm dampness type, *p＜0.05; Comparison of phlegm dampness type and nonphlegm dampness type,△ p＜0.05; Comparison of nonphlegm dampness type and The control group of nonphlegm dampness type, ▲p＜0.05; Comparison of The control group of phlegm dampness type and The control group of nonphlegm dampness type.

表 2 四组血清性激素水平的比较

Table 2 Comparison of the serum sex hormone levels among four groups

	Phlegm dampness type	Nonphlegm dampness type	Control group of phlegm dampness type	Control group of nonphlegm dampness type
Case	42	47	21	31
FSH (mIU/mL)	5.54± 1.61*	5.91± 1.77	4.56± 0.93○	5.65± 1.43
LH (mIU/mL)	9.145± 4.36△ *	12.64± 7.65▲	5.28± 2.85	6.62± 4.71
LH/FSH	1.71± 0.75△ *	2.19± 1.20▲	1.19± 0.55	1.17± 0.65
E2 (pg/mL)	50.65± 21.32*	51.12± 23.71▲	35.09± 10.94	38.55± 17.53
PRL (ng/mL)	17.93± 12.59	16.89± 7.86	17.20± 6.35	21.11± 11.18
T (ng/dl)	57.94± 26.25*	54.75± 24.92▲	25.65± 12.43	26.37± 12.85
DHEAS(μg/Dl)	235.01± 117.54	249.78± 90.32▲	240.56± 103.12	209.34± 84.92
AND (ng/mL)	4.34± 1.75*	4.71± 2.20▲	3.23± 1.32	3.05± 1.51
SHBG(nmol/L)	30.24± 30.01	44.03± 38.58	38.61± 21.75○	52.15± 19.88
FAI	10.11± 7.3△ *	6.32± 5.45▲	3.45± 3.35	2.15± 1.57

Note: Comparison of phlegm dampness type and The control group of phlegm dampness type, *p＜0.05; Comparison of phlegm dampness type and nonphlegm dampness type,△ p＜0.05; Comparison of nonphlegm dampness type and The control group of nonphlegm dampness type, ▲p＜0.05; Comparison of The control group of phlegm dampness type and The control group of nonphlegm dampness type.

3.1 不同证型 PCOS 患者的一般特征分析

大多数研究认为 PCOS 患者月经初潮年龄较早，研究表明初潮年龄和环境、营养状况、体重指数等相关[18]，本研究结果以往的报道不完全相符，可能与研究的例数、营养和环境因素有关。现代医学认为肥胖与 PCOS 的发生关系密切，肥胖是 PCOS 常见的特征表现。大多数临床和流行病学调查显示 PCOS 患者超重或肥胖的发生率为 50%～70%，PCOS 的肥胖是以腹型肥胖为特征，腹型肥胖导致血脂异常，对 PCOS 患者的远期健康有负面影响。PCOS 患者的腹型肥胖与其临床症状、IR 程度和内分泌代谢紊乱水平具有相关性[19]。本研究结果与之相符，且痰湿证更为明显。PCOS 存在明显的高血压倾向，痰湿型 PCOS 患者更为明显。大量研究表明[20]原发性高血压的发生发展与胰岛素抵抗或高胰岛素血症密切相关，IR 和 HI 是高血压的独立危险因素。

高雄激素血症的临床表现有多毛、痤疮和脱发。女性多毛症的轻重与血清雄激素水平的相关性研究报道不一致，可能与患者不同生理时期体内雄激素来源不同以及血浆 SHBG 水平有关。目前研究认为多毛症与遗传因素有关，并且与雄激素水

表 3 四组糖脂代谢水平比较

Table 3 Comparison of glucose lipid metabolism in the four groups

	Phlegm dampness type	Nonphlegm dampness type	Control group of phlegm dampness type	Control group of nonphlegm dampness
Case	42	47	21	31
FBG(mmol/L)	5.25± 0.73△ *	4.83± 0.39▲	4.65± 0.38◦	4.39± 0.46
FINS(IU/ml)	17.59± 17.46△	7.37± 5.22	12.52± 4.47◦	8.09± 3.41
HOMA-IR	4.60± 1.03△ *	1.60± 1.21	2.62± 1.06◦	1.68± 0.78
CHO(mmol/L)	4.67± 1.21	4.35± 0.67▲	4.24± 0.93	3.85± 0.47
TG(mmol/L)	1.43± 0.51*	1.25± 0.48▲	1.17± 0.54◦	0.75± 0.26
HDL(mmol/L)	1.04± 0.21△ *	1.25± 0.32▲	1.33± 0.42	1.51± 0.34
LDL(mmol/L)	3.17± 1.12	2.71± 1.09▲	2.75± 1.04◦	2.17± 0.52

Note: Comparison of phlegm dampness type and The control group of phlegm dampness type, *p＜0.05; Comparison of phlegm dampness type and nonphlegm dampness type, △ p＜0.05; Comparison of nonphlegm dampness type and The control group of nonphlegm dampness type, ▲p＜0.05; Comparison of The control group of phlegm dampness type and The control group of nonphlegm dampness type.

平升高有关。在本研究中,PCOS 组多毛评分明显高于对照组,而与痰湿证型无关,表明多毛的发生与严重程度是 PCOS 疾病本身的特点,对临床诊断 PCOS 提供参考。痤疮有多种发病因素,尤其与雄激素水平有密切关系。研究表明部分痤疮患者游离 T、DHEA 和 ANDS 高水平。本研究中 " 痰湿型 " 及 " 非痰湿型 "PCOS 患者的痤疮发生率均明显高于对照组，提示我们如果青春期和育龄期女性患者以痤疮就诊,应进一步排除是否罹患了多囊卵巢综合征。

黑棘皮症、皮肤溢脂是 PCOS 患者的一种皮肤表现。普遍认为胰岛素抵抗和肥胖是发生黑棘皮和皮肤溢脂的最常见原因。在我们的研究中,PCOS 组黑棘皮发生率明显高于对照组,且 " 痰湿型 "PCOS 黑棘皮和皮肤溢脂发生率明显高于 " 非痰湿型 "PCOS,提示 IR 是 PCOS 发病的重要病理机制,而肥胖可以加重 IR。

3.2 不同证型 PCOS 患者的血清性激素水平差异

PCOS 患者存在不同程度的性激素代谢紊乱,表现为 HA、LH/FSH 比例失调等。" 痰湿型 "、" 非痰湿型 "PCOS 患者与对照组相比均存在性激素代谢紊乱，表现在 LH、LH/FSH、E2、T、FAI 水平升高,具有统计学差异,且 " 痰湿型 "PCOS 组 FAI 明显高于 " 非痰湿型 "PCOS 组，而 " 痰湿型 "PCOS 组 LH、LH/FSH 水平明显低于 " 非痰湿型 "PCOS，差异具有统计学意义。" 痰湿型 "PCOS 患者以 FAI 升高为特点,而痰湿肥胖体质妇女性激素无明显变化。HA 是 PCOS 的重要内分泌特征,无论 PCOS 患者是否肥胖。本研究结果显示:非痰湿型 "PCOS 患者 LH 及 LH/FSH 水平更高，可见非痰湿型 PCOS 存在明显的性腺轴功能紊乱，且其 T、DHEAS 和 ANDS 水平高于对照组,而不伴有 IR 的生化特征；而 " 痰湿型 "PCOS 患者主要以 T 和 FAI 水平升高为主,伴有 IR,可能与 " 痰湿型 "PCOS 患者存在 HI 有关,HI 可抑制肝脏 SHBG 合成,使 PCOS 患者的雄激素生物活性增强。本研究结果提示 " 痰湿型 "PCOS 雄激素的主要来源是卵巢，而 " 非痰湿型 "PCOS 患者雄激素的主要来源是卵巢和肾上腺。

3.3 不同证型 PCOS 患者的糖脂代谢差异

本研究中," 痰湿型 "PCOS 组 FBG、HOMA-IR 明显高于 " 非痰湿型 "PCOS 组和痰湿型对照组,FINS 水平明显高于 " 非痰湿型 "PCOS 组，说明 " 痰湿型 "PCOS 体内存在较为明显糖代谢失常，表现为 HI、IR,HI、IR 是 PCOS 的重要病理特征[21],可能是由于 " 痰湿型 "PCOS 患者除了肥胖以外，还存在 HA 有关,两者互相作用,进一步加重 " 痰湿型 "PCOS 患者的内分泌紊乱。PCOS 脂类代谢异常[22-24]最常见的特征是 HDL 降低、LDL 和 TG 升高,脂代谢与高雄激素血症、IR、稀发排卵等密切相关。本研究结果显示两种证型 PCOS 患者 TG、LDL 均高于对照组，提示与 BMI 匹配的对照组相比，非痰湿型和痰湿型 PCOS 组更易出现血 TG 和 LDL 升高,可见 PCOS 患者比正常人更容易发生心血管疾病，已有研究证实,PCOS 患者发生心血管疾病的风险比非 PCOS 患者高[25]。另外,两种证型 PCOS 患者 HDL 低于对照组,且 " 痰湿型 "PCOS 的 HDL 水平更低;HDL 有明显的抗动脉粥样硬化作用,而高 TG 血症与动脉粥样硬化的发生相关，由此可知 " 痰湿型 "PCOS 患者更容易发生动脉粥样硬化和代谢综合征。与痰湿型相匹配的正常对照组 TG、LDL 明显高于与非痰湿型相匹配的正常对照组,说明肥胖是发生血脂异常的危险因素。所以,应该对 PCOS 患者脂代谢紊乱高度重视,在治疗上应积极纠正血脂异常,通过控制饮食和运动等方法控制体质量指数，积极预防远期并发症的发生。中医痰浊产生的机理与脂质代谢紊乱相似,《景岳全书·痰瘀》中提到 " 痰即人之津液,无非水谷之所化,此痰亦既化之物,而非不化之属也,但化得其正,则形体强,营卫充,而痰涎本皆血气;若化失其正,则脏腑病,津液败,而血气即成痰涎 "。认为正常情况下痰为人体的阴液物质,由脾胃运化的水谷而生,藏于五脏以养全身。若过食膏粱厚味,湿困脾胃;或者饮食劳倦伤脾,均可致脾的运化输布功能失常,血中脂肪升高,脂质逐渐增多聚而成痰,形成痰浊。痰浊瘀滞于体内,壅滞于胞宫,导致多囊卵巢疾病的发生。

综上," 痰湿型 " 及 " 非痰湿型 "PCOS 患者临床和生化特征存在差异,临床上应针对不同证型患者的特征进行有针对性的治疗。但本研究尚存在样本量较少,对中医证候划分较单一

等不足,需要进一步的研究明确。

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