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苍砂白芥汤结合 GnRH-a 治疗子宫肌瘤疗效及其卵巢功能、血清 bFGF、NF- κ B 水平影响 *

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摘要 目的:探讨苍砂白芥汤结合 GnRH-a 治疗子宫肌瘤疗效及其卵巢功能、血清 bFGF、NF- κ B 水平影响。方法:选取 2019 年 5 月至 2021 年 5 月于我院接受治疗的 110 例子宫肌瘤患者为本次研究对象,将患者分为观察组和对照组,每组 55 例。对照组患者接受 GnRH-a 治疗,观察组接受苍砂白芥汤结合 GnRH-a 治疗,对比两组临床治疗总有效率、孕酮(P)水平、卵泡刺激素(FSH)水平、雌二醇(E₂)水平、血管内皮生长因子(VEGF)水平、碱性成纤维细胞生长因子(bFGF)水平、基质金属蛋白酶 3(MMP-3)水平、核转录因子- κ B 亚型 P65(NF- κ B P65)水平、肿瘤特异性生长因子(TSGF)水平。结果:观察组总有效率较对照组高($P<0.05$);两组治疗前 P、FSH、E₂ 水平比较无差异($P>0.05$),两组治疗后 P、FSH、E₂ 水平均有所下降,且观察组均低于对照组($P<0.05$);两组患者治疗前 VEGF、bFGF、MMP-3 水平比较无差异($P>0.05$),两组患者治疗后 VEGF、bFGF、MMP-3 水平均有所降低,且观察组均低于对照组($P<0.05$);两组治疗前 NF- κ B P65、TSGF 水平比较无差异($P>0.05$),两组治疗后 NF- κ B P65、TSGF 水平均有所下降,且观察组低于对照组($P<0.05$)。结论:使用苍砂白芥汤结合 GnRH-a 治疗子宫肌瘤,可提高临床治疗效果,调节性激素水平,改善 VEGF、bFGF、MMP-3、NF- κ B P65、TSGF 水平,值得临床推广使用。

关键词: 苍砂白芥汤; GnRH-a; 子宫肌瘤

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The Efficacy of Cangsha Baijie Decoction Combined with GnRH-a in the Treatment of Uterine Fibroids and Its Effects on Ovarian Function, Serum bFGF and NF- κ B Levels*

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ABSTRACT Objective: To investigate the efficacy of Cangsha Baijie Decoction combined with GnRH-a in the treatment of uterine fibroids and its effects on ovarian function, serum bFGF and NF- κ B levels. **Methods:** A total of 110 patients with uterine fibroids who were treated in our hospital from May 2019 to May 2021 were selected as the research objects. The patients were divided into an observation group and a matched group, with 55 cases in each group. The matched group received GnRH-a treatment, and the observation group received Cangsha Baijie decoction combined with GnRH-a treatment. The total effective rate, progesterone (P) level, follicle-stimulating hormone (FSH) level, estradiol (E₂) level, vascular endothelial growth factor (VEGF) level, basic fibroblast growth factor (bFGF) level, matrix metalloproteinase 3 (MMP-3) level, nuclear transcription factor- Levels of κ B isoform P65 (NF- κ B P65), tumor-specific growth factor (TSGF) levels. **Results:** The total effective rate of clinical treatment in the observation group was higher than the matched group ($P<0.05$). The levels of P, FSH, and E₂ in the two groups decreased post-treatment, and the observation group was lower than the matched group ($P<0.05$). The levels of VEGF, bFGF and MMP-3 in the two groups were decreased post-treatment, and the observation group was lower than the matched group ($P<0.05$). The levels of NF- κ B P65 and TSGF in the two groups decreased post-treatment, and the observation group was lower than the matched group ($P<0.05$). **Conclusion:** The use of Cangsha Baijie decoction combined with GnRH-a in the treatment of uterine fibroids can improve the clinical therapeutic effect, regulate the levels of sex hormones, and improve the levels of VEGF, bFGF, MMP-3, NF- κ B P65, and TSGF, which is worthy of clinical promotion.

Key words: Cangsha Baijie decoction; GnRH-a; Uterine fibroids

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前言

子宫肌瘤是较常见良性肿瘤,因子宫平滑肌细胞增生所致,好发于30~50岁女性^[1]。患者主要临床表现为月经量多、不规则的阴道出血等,严重影响身心健康和生活质量^[2]。子宫肌瘤治疗方式包括药物治疗、期待疗法、手术切除等,药物治疗适用于治疗症状较轻、子宫体积小于2个月妊娠子宫大小、不宜通过手术治疗的患者;期待疗法适用于治疗体积小且无症状患者;手术治疗可促使临床症状快速缓解,但会对机体产生创伤,而且存在不同程度的手术适应症,所以,针对早期子宫肌瘤常建议选用药物治疗^[3,4]。促性腺激素释放激素激动剂(GnRH-a)治疗子宫肌瘤并发异常子宫出血具有确切的疗效,但停药后易复发,导致子宫肌瘤出现增大^[5]。如果长期GnRH-a可导致闭经、情绪改变、性欲下降等不良事件,部分患者甚至出现心血管疾病和骨质疏松^[6]。中医治疗妇科疾病经验独到,尤其对于崩漏等症状的治疗。苍砂白芥汤具有软坚散结、化瘀活血之功效,用于治疗子宫肌瘤具有很好的效果^[7]。目前,关于苍砂白芥汤结合

GnRH-a治疗子宫肌瘤的疗效尚不确切,本文从疗效和对卵巢功能、血清bFGF、NF- κ B水平影响进行分析,旨在为临床治疗子宫肌瘤提供参考依据。

1 资料与方法

1.1 一般资料

选取2019年5月至2021年5月于我院接受治疗的110例子宫肌瘤患者为研究对象,根据数字随机表法将患者分为观察组和对照组,每组55例。本研究经本院医学伦理委员会审核批准。

纳入标准:符合《妇产科学》^[8]中关于子宫肌瘤的诊断标准,且经临床检查确诊为子宫肌瘤;近3个月未服用影响性激素水平的药物;临床资料齐全;患者知情同意。

排除标准:合并肝脏、肾脏、心脏、脑等重要器官基础性疾病;合并泌尿系统、免疫系统和造血系统疾病者;精神疾病以及智力低下者;对本研究使用药物过敏者。

两组患者基本资料对比无差异($P>0.05$),如表1所示。

表1 一般资料对比
Table 1 Comparison of general data

Groups	n	Age (year, $\bar{x} \pm s$)	Fibroids straight path (cm, $\bar{x} \pm s$)	body mass index (kg/m ² , $\bar{x} \pm s$)	Number of fibroids(n)	
					Solitary fibroids	multiple fibroids
Observation group	55	32.35 $\pm$ 2.43	4.36 $\pm$ 1.05	23.86 $\pm$ 1.12	16	39
Matched group	55	31.78 $\pm$ 2.52	4.29 $\pm$ 1.12	24.13 $\pm$ 1.25	18	37
χ^2/t	-	1.208	0.338	1.193	0.170	
P	-	0.230	0.736	0.235	0.680	

1.2 方法

对照组患者接受GnRH-a治疗,具体治疗方法如下:于月经来潮第1天皮下注射长效GnRH-a3.75 mg,间隔4周再次注射,连续治疗6个月。

观察组接受苍砂白芥汤结合GnRH-a治疗,GnRH-a治疗方法同对照组。苍砂白芥汤组方成分如下:胆南星6g、砂仁6g、炙甘草6g、肉桂6g、没药9g、地龙9g、白芥子9g、僵蚕9g、香附9g、苍术12g、山楂15g、昆布15g、丹参20g,清水煎服,每天1剂,分为3次温服。连续治疗6个月,经期停药。

1.3 观察指标

(1)比较临床治疗效果。判定标准:痊愈:子宫肌瘤以及临床症状全部消失;显效:子宫肌瘤体积减小50%以上,临床症状显著改善;有效:子宫肌瘤体积减小30~50%,临床症状有所改善;无效:子宫肌瘤体积不变或者减小10%,临床症状无明显改善,部分患者甚至出现子宫肌瘤体积增大情况。总有效率=(痊愈例数+显效例数+有效例数)/总例数 $\times$ 100%。

(2)比较卵巢功能。抽取患者治疗前后空腹静脉血,以3000 r/min离心后取血清,通过化学发光法测定孕酮(Progesterone, P)、卵泡刺激素(Follicle-stimulating Hormone, FSH)、雌二醇(Estradiol, E2)等血清性激素水平。

(3)抽取患者治疗前后空腹静脉血3 mL,以3000 r/min离心后取血清,通过全自动生化仪测定患者血管内皮生长因子

(Vascular endothelial growth factor, VEGF)、碱性成纤维细胞生长因子(Basic fibroblast growth factor, bFGF)、基质金属蛋白酶3(Matrix metalloproteinase-3, MMP-3)水平。

(4)抽取患者治疗前后空腹静脉血,通过酶联免疫法测定患者血清核转录因子- κ B亚型P65(Nuclear factor- κ B P65, NF- κ B P65)水平,通过化学发光法测定血清肿瘤特异性生长因子(Tumor SP ECIFIC Grow Factor, TSGF)水平。

1.4 统计学方法

采取SPSS 20.0分析,(n/%)表示计数指标,用 χ^2 检验;($\bar{x} \pm s$)表示计量指标,用t检验; $P<0.05$ 示差异有统计学意义。

2 结果

2.1 比较临床治疗效果

观察组治疗总有效率较对照组高($P<0.05$),如表2所示。

2.2 比较卵巢功能

两组治疗前P、FSH、E₂水平比较无差异($P>0.05$),两组治疗后均有所下降,且观察组均低于对照组($P<0.05$),如表3所示。

2.3 比较VEGF、bFGF、MMP-3水平

两组患者治疗前VEGF、bFGF、MMP-3水平比较无差异($P>0.05$),两组患者治疗后VEGF、bFGF、MMP-3水平均有所降低,且观察组均低于对照组($P<0.05$),如表4所示。

表 2 比较临床治疗效果(n,%)

Table 2 Comparison of clinical treatment effects (n, %)

Groups	n	Recure	Effective	Efficient	Invalid	Total efficiency
Observation group	55	27(49.09%)	15(27.27%)	11(20.00%)	2(3.64%)	53(96.36%)
Matched group	55	18(32.73%)	13(23.64%)	16(29.09%)	8(14.55%)	47(85.45%)
χ^2	-	-	-	-	-	3.960
<i>P</i>	-	-	-	-	-	0.047

表 3 比较卵巢功能($\bar{x} \pm s$)Table 3 Comparison of ovarian function ($\bar{x} \pm s$)

Groups	n	P (pmol·L ⁻¹)		FSH (μg·L ⁻¹)		E ₂ (μg·L ⁻¹)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Observation group	55	30.54± 2.86	9.67± 1.21 [#]	22.79± 3.91	15.97± 1.46 [#]	386.56± 22.83	158.57± 11.56 [#]
Matched group	55	30.75± 2.97	10.43± 1.87 [#]	22.67± 3.84	16.64± 1.47 [#]	385.58± 21.91	166.12± 12.32 [#]
<i>t</i>	-	0.378	2.531	0.162	2.398	0.230	3.314
<i>P</i>	-	0.706	0.013	0.872	0.018	0.819	0.001

Note: Compared with the Pretherapy, [#]*P*<0.05, the same below.

表 4 比较 VEGF、bFGF、MMP-3 水平($\bar{x} \pm s$)Table 4 Comparison of the levels of VEGF, bFGF and MMP-3 ($\bar{x} \pm s$)

Groups	n	VEGF (ng/mL)		bFGF (μg/L)		MMP-3 (ng/L)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment	Pretherapy	Post-treatment
Observation group	55	1.73± 0.16	0.79± 0.08 [#]	211.39± 12.91	93.47± 7.66 [#]	79.58± 2.63	37.58± 1.76 [#]
Matched group	55	1.72± 0.19	0.85± 0.10 [#]	212.17± 11.84	98.34± 7.47 [#]	79.88± 2.71	40.13± 1.42 [#]
<i>t</i>	-	0.299	3.475	0.330	3.376	0.589	8.363
<i>P</i>	-	0.766	0.001	0.742	0.001	0.557	<0.001

2.4 比较 NF-κB P65、TSGF 水平

两组治疗后 NF-κB P65、TSGF 水平均有所下降,且观察组低于

两组治疗前 NF-κB P65、TSGF 水平比较无差异(*P*>0.05), 对照组(*P*<0.05),如表 5 所示。

表 5 比较 NF-κB P65、TSGF 水平($\bar{x} \pm s$)Table 5 Comparison of the levels of NF-κB P65 and TSGF ($\bar{x} \pm s$)

Groups	n	NF-κB P65 (ng/L)		TSGF (U/L)	
		Pretherapy	Post-treatment	Pretherapy	Post-treatment
Observation group	55	80.53± 3.56	43.29± 2.78 [#]	64.35± 4.93	45.67± 3.36 [#]
Matched group	55	80.62± 3.37	48.65± 2.14 [#]	64.67± 4.86	49.74± 3.17 [#]
<i>t</i>	-	0.136	11.331	0.343	6.534
<i>P</i>	-	0.892	<0.001	0.732	<0.001

3 讨论

子宫肌瘤又称子宫纤维瘤或者纤维肌瘤,是育龄期女性常见疾病^[9]。该病主要因子宫平滑细胞增生所致,致使患者出现子宫大小改变、子宫形态变化、白带异常等问题,严重影响生活质量^[10]。现代医学认为子宫肌瘤的发生和发展与患者自身的雌孕激素水平、免疫功能水平息息相关^[11]。西医保守治疗主要采用

激素类药物治疗,利用促性腺激素释放激素对人体的激素水平进行调节,其效果可靠,但会引发一系列不良反应,严重者用药期间出现闭经,进而限制应用范围^[12]。中医学理论认为,子宫肌瘤归属于“石瘕”“癥瘕”范畴,起初为气病,久而久之伤及血,多种致病因素致使气伤,造成机体营卫不行,进而外邪入体,并留滞,日久形成癥瘕,抑制气血运行,不通则导致气滞血瘀,出现血瘀和痰湿互结之像,最终造成子宫肌瘤^[13-15]。中医认为子宫

肌瘤治疗应以活血化瘀、消痰散结为主,故本文选用苍砂白芥汤结合 GnRH-a 治疗子宫肌瘤,并观察其疗效。

本研究结果显示,观察组临床治疗总有效率较对照组高 ($P<0.05$);两组治疗后 P、FSH、 E_2 水平均有所下降,且观察组均低于对照组 ($P<0.05$)。与肖秀娟^[16]及马静毅^[17]等研究结果相似。分析可知:P 可加快阴道上皮细胞脱落、减少粘液分泌,使增殖期子宫内膜转化为分泌期内膜^[18]。FSH 可加快卵泡发育和成熟,其产生过程受卵巢雌性激素 E_2 的反馈调控和下丘脑促性腺释放激素的控制,对女性生殖功能具有关键作用^[19]。 E_2 可调节女性器官及副性征的生产发育^[20]。因苍砂白芥汤中所含的僵蚕可发挥化痰散结、祛风定惊之效;胆南星可发挥熄风定惊、清热化痰之效;地龙与僵蚕、胆南星同效,可发挥行经之效;没药可发挥消肿生肌、活血止痛之效;香附能够散肝气之郁,若肝气调则会血行畅;肉桂可发挥散寒止痛、补火助阳、活血通经之效;白芥子可发挥散结通络止痛、温肺豁痰利气之效;砂仁可发挥温脾止泄、化湿开胃之效;昆布可发挥消痰利水、软坚散结之效;苍术、丹参均为君药,其中丹参可发挥活血化瘀消癥之效;苍术可发挥健脾祛湿之效;山楂可发挥行气散瘀、消食化积之效;炙甘草作为方中使药,可调和上述诸药。诸药合用,可活血化瘀,调节激素水平。因此,该药物可将子宫肌瘤变性、增生得到吸收和消散^[21-23];两组患者治疗后 VEGF、bFGF、MMP-3 水平均有所降低,且观察组均低于对照组 ($P<0.05$);与徐蓉^[24]等人研究结果相似,子宫肌瘤患者通过中药桂枝茯苓丸联合平消胶囊治疗,可降低血清 VEGF、MMP-3、bFGF 水平。说明中药治疗子宫肌瘤可改善血液指标。VEGF 可促使血管通透性提高,诱导细胞外基质,促使细胞外基质变性,进而加快血管内皮细胞增殖速度,促使新血管形成,对子宫肌瘤的血液供应产生促进作用^[25]。bFGF 可促进大部分细胞进行增殖、分化和侵袭,其能够参与新血管形成肌瘤组,最终提升子宫组织的血液灌注^[26]。而 MMP-3 可对细胞外基质产生降解作用,促使内皮细胞的通透性改变,进而加快肿瘤细胞的增殖以及侵袭、转移^[27]。因苍砂白芥汤中地龙可抑制多种肿瘤细胞;昆布中含有昆布多糖,可抑制肿瘤细胞增殖;丹参可改善微循环和血液粘滞性,具有抗肿瘤作用;胆南星可抑制癌细胞增生;苍术中含有苍术挥发油和茅术醇,可发挥抗肿瘤作用;山楂可对肿瘤细胞生长产生抑制作用,因此诸药合用可显著降低 VEGF、bFGF、MMP-3 水平,有利于患者恢复^[28];两组治疗前 NF- κ B P65、TSGF 水平比较 ($P>0.05$),两组治疗后 NF- κ B P65、TSGF 水平均有所下降,且观察组低于对照组 ($P<0.05$)。与马二梅^[29]等研究结果相似。NF- κ B 具有多向调节性能,其亚型 NF- κ B P65 可对子宫平滑肌的增殖、分化产生诱导作用,促使肌瘤形成。TSGF 可结合于内皮细胞的生长因子受体,促使子宫平滑肌细胞进行有丝分裂,同时作用于肿瘤血管增生,进而促进子宫肌瘤发生。中药汤剂可抗肿瘤,同时可改善机体微循环。苍砂白芥汤中所含的僵蚕、砂仁、地龙等具有促使血管扩张,改善微循环的效果^[30]。

综上所述,使用苍砂白芥汤结合 GnRH-a 治疗子宫肌瘤,可提高临床治疗效果,调节性激素水平,改善 VEGF、bFGF、MMP-3、NF- κ B P65、TSGF 水平,值得临床推广使用。

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