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· 临床研究 ·

强脉冲光联合氨甲环酸片对黄褐斑患者皮肤生理参数、面部症状及血清激素水平的影响*

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摘要 目的:观察黄褐斑患者经氨甲环酸片和强脉冲光联合治疗后,患者皮肤生理参数、面部症状及血清激素水平的变化情况。**方法:**按随机数字表法将我院2020年2月至2022年10月收治的128例黄褐斑患者分为对照组(强脉冲光治疗,n=64)和观察组(强脉冲光联合氨甲环酸片治疗,n=64),对比两组患者的面部症状评分、皮肤生理参数、血清激素水平和不良反应发生率。**结果:**两组治疗3个月后黄褐斑面积及严重程度评分(MASI)、皮损颜色评分、皮损面积评分下降,且观察组低于对照组($P<0.05$)。两组治疗3个月后经皮水分丢失(TEWL)下降,且观察组低于对照组;表皮油脂含量、角质层含水量升高,且观察组高于对照组($P<0.05$)。观察组治疗3个月后卵泡生成激素(FSH)、睾酮(T)、雌二醇(E₂)、黄体生成激素(LH)下降,且观察组低于对照组($P<0.05$)。两组不良反应发生率组间对比未见差异($P>0.05$)。**结论:**黄褐斑患者在强脉冲光治疗基础上联合氨甲环酸片,面部症状改善效果更佳,同时可更好的调节皮肤生理参数及血清激素水平,未见明显的不良反应发生风险升高,具有较好的安全性。

关键词:强脉冲光;氨甲环酸片;黄褐斑;面部症状;皮肤生理参数;激素

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Effects of Intense Pulsed Light Combined with Tranexamic Acid Tablets on Skin Physiological Parameters, Facial Symptoms and Serum Hormone Levels in Chloasma Patients*

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ABSTRACT Objective: To observe the changes of skin physiological parameters, facial symptoms and serum hormone levels in chloasma patients after combine treatment with tranexamic acid tablets and intense pulsed light. **Methods:** According to the random number table method, 128 chloasma patients admitted to our hospital from February 2020 to October 2022 were divided into control group (intense pulsed light treatment, n=64) and observation group (intense pulsed light combined with tranexamic acid tablets, n=64), the facial symptom scores, skin physiological parameters, serum hormone levels and incidence of adverse reactions were compared in two groups. **Results:** After 3 months of treatment, the area and severity score (MASI), lesion color score, and lesion area score of the two groups decreased, and the observation group was lower than the control group ($P<0.05$). After 3 months of treatment, transcutaneous water loss (TEWL) decreased in both groups, and the observation group was lower than the control group; The content of epidermal oil and water in the stratum corneum increased, and the observation group was higher than the control group ($P<0.05$). After 3 months of treatment, the levels of follicle stimulating hormone (FSH), testosterone (T), estradiol (E₂), and luteinizing hormone (LH) decreased in the observation group was lower than the control group ($P<0.05$). There was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Chloasma patients combined with tranexamic acid tablets on the basis of intense pulsed light treatment have better improvement of facial symptoms, and can better regulate skin physiological parameters and serum hormone levels, there is no obvious increase in the risk of adverse reactions, with good safety.

Key words: Intense pulsed light; Tranexamic acid tablets; Chloasma; Facial symptoms; Skin physiological parameters; Hormone

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前言

黄褐斑是一种常见色素增加性皮肤病,可造成患者面部皮肤受损^[1]。黄褐斑的病因复杂,受到日晒、炎症反应、遗传易感性、皮肤屏障受损、性激素水平异常、黑色素合成增加、血管等多种因素的影响^[2]。目前关于黄褐斑的治疗方式尚未统一,强脉冲光是临床常用的治疗方案之一,通过将极强的能量瞬间形成能量密度极高的巨脉冲,发射到病变组织中,致使黑素细胞内的黑素颗粒爆破,但单纯治疗效果有限^[3-4]。氨甲环酸片是一种合成的氨基酸类抗纤溶药,能够减少酪氨酸代谢的最后产物黑素的合成,有褪色作用,近年来已逐渐被应用于黄褐斑的治

疗^[5]。本研究观察黄褐斑患者经氨甲环酸片和强脉冲光联合治疗后,患者皮肤生理参数、面部症状及血清激素水平的变化情况,报道如下。

1 资料与方法

1.1 一般资料

按随机数字表法将我院 2020 年 2 月至 2022 年 10 月收治的 128 例黄褐斑患者分为对照组(强脉冲光治疗,n=64)和观察组(强脉冲光联合氨甲环酸片治疗,n=64)。本研究方案通过我院伦理学委员会批准进行。两组患者一般资料对比未见统计学差异($P>0.05$),具体见表 1。

表 1 两组一般资料对比

Table 1 Comparison of general data in two groups

Groups	Age (years old)	Course of disease (years)	Fitzpatrick skin type	
			III type	IV type
Control group(n=64)	39.86±3.15	2.96±0.45	36	28
Observation group(n=64)	40.15±3.67	2.92±0.38	37	27
t/x^2	-0.480	0.543	0.032	
P	0.632	0.588	0.858	

1.2 纳入排除标准

纳入标准:(1)符合《中国黄褐斑诊疗专家共识(2021 版)》^[6],面部斑片界限清晰,呈对称分布,处于疾病稳定期,根据患者的病史、典型的临床表现联合玻片压诊、Wood 灯等无创检测技术确诊;(2)患者知情同意,签署知情同意书;(3)年龄≥18 岁者;(4)对本次研究用药无过敏者。排除标准:(1)合并其他慢性疾病者;(2)近半年有相关药物使用史者;(3)肾功能不全者;(4)光敏感者;(5)合并免疫功能异常者;(6)凝血功能异常、有血栓形成倾向及家族病史的患者;(7)妊娠期、哺乳期妇女;(8)瘢痕体质者;(9)继发性黄褐斑患者。

1.3 方法

对照组接受强脉冲光治疗,患者取仰卧位,彻底清洁面部皮肤,将耦合剂涂于治疗区,眼部使用遮光镜遮盖。采用科医人 M22 强光与激光系统进行治疗,患者接受能量为 15 J/cm² 的强脉冲光,采用 640 nm 滤光片,脉宽 6 ms,3 脉冲,4 周治疗一次,共三次。观察组患者在强脉冲光治疗基础上接受国药集团同济堂(贵州)制药有限公司采购的氨甲环酸片治疗[国药准字 H52020898,规格:0.25 g]口服,每次 0.25 g,一天 2 次,所有患者月经行经期间停止服药,约 1 周,治疗 3 个月。两组治疗期间及治疗后均做好防晒措施。

1.4 观察指标

(1) 治疗前、治疗 3 个月后采用黄褐斑面积和严重指数(MASI)、皮损颜色评分、皮损面积评分对患者的面部症状进行评分,多位医师共同评分取均值^[7]。(2)治疗前、治疗 3 个月后使用德国 Courage+Khazaka 公司 MPA9 多功能皮肤检测仪测定两组患者皮肤生理参数:经皮水分丢失(TEWL)、表皮油脂含量、角质层含水量。(3)抽取两组患者于治疗前、治疗后 3 个月的月经出血 2-5 天时间内,清晨空腹抽取静脉血 4 mL,采用广

州吉迪仪器有限公司采购的 JIDI-20D 台式高速离心机离心(2900 r/min 离心 13 min,离心半径 8 cm)获取上清液。采用酶联免疫吸附法检测血清激素水平: 血清卵泡生成激素(FSH),试剂盒购自上海富雨生物科技有限公司;睾酮(T),试剂盒购自上海酶联科技有限公司;雌二醇(E₂),试剂盒购自上海酶联科技有限公司;黄体生成激素(LH),试剂盒购自上海烜雅生物科技有限公司。(4)记录两组烧灼感、皮肤过敏、胃肠道不适、恶心呕吐等不良反应发生情况。

1.5 统计学方法

以 SPSS 25.0 进行数据分析。计量数据均符合正态分布以($\bar{x}\pm s$)表示,实施 t 检验。计数数据以例数或比表示,采用 x^2 检验。检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组面部症状评分对比

两组治疗前 MASI、皮损颜色评分、皮损面积评分组间比较无差异($P>0.05$)。两组治疗 3 个月后 MASI、皮损颜色评分、皮损面积评分下降($P<0.05$)。观察组治疗 3 个月后 MASI、皮损颜色评分、皮损面积评分较对照组更低($P<0.05$)。见表 2,图 1 和图 2。

2.2 两组皮肤生理参数对比

两组治疗前 TEWL、表皮油脂含量、角质层含水量组间比较无差异($P>0.05$)。两组治疗 3 个月后 TEWL 下降;表皮油脂含量、角质层含水量升高($P<0.05$)。观察组治疗 3 个月后表皮油脂含量、角质层含水量较对照组更高;TEWL 较对照组更低($P<0.05$)见表 3。

2.3 血清激素水平对比

两组治疗前 FSH、T、E₂、LH 组间比较未见统计学差异

($P>0.05$)。观察组治疗3个月后FSH、T、E₂、LH下降,且观察组低于对照组($P<0.05$),对照组治疗前、治疗3个月后FSH、T、

E₂、LH组间比较未见统计学差异($P>0.05$)。见表4。

表2 两组面部症状评分对比(± s,分)

Table 2 Comparison of facial symptom scores in two groups(± s, score)

Groups	MASI		Skin lesion color		Skin lesion area	
	Before treatment	3 months after treatment	Before treatment	3 months after treatment	Before treatment	3 months after treatment
Control group(n=64)	12.96± 2.17	8.17± 1.83*	1.91± 0.29	1.54± 0.24*	1.95± 0.26	1.58± 0.27*
Observation group(n=64)	13.25± 3.28	5.59± 2.11*	1.88± 0.26	1.17± 0.19*	1.91± 0.31	1.29± 0.33*
t	-0.590	7.390	0.616	9.670	0.791	5.441
P	0.556	0.000	0.539	0.000	0.430	0.000

Note: Compared with before treatment, * $P<0.05$.



图1 对照组治疗前后对比

Fig.1 Comparison of the control group before and after treatment

Note: Fig.1A: Vision photo of the right face before treatment, Fig.1B: Vision photo of the right face after treatment.

2.4 两组不良反应发生情况

对照组不良反应发生率为4.69%,观察组为6.25%,组间对比无差异($P>0.05$),见表5。

3 讨论

黄褐斑主要表现为黄褐色斑片,虽无全身症状或严重不适,但有损患者容貌美观性,极易引起焦虑抑郁^[8-10]。强脉冲光治疗又称光子嫩肤,利用光子产生化学作用加速角质层细胞自然脱落,进而使斑块随着皮屑脱落或者经过淋巴循环排出体外,既往用于治疗黄褐斑,具有较好的疗效,但强脉冲光治疗无法从源头控制黑色素形成,且能量控制不当可能会导致色素沉着风险升高^[11-13]。氨甲环酸是一种临床常用的抗纤溶止血药物,可竞争性干扰黑素细胞及角化细胞之间的联系,具有一定的改善黄褐斑的疗效,但长期外用会增加皮肤烧灼感、过敏等不良

反应的发生风险^[14-16]。近年来,不少研究发现^[17,18],多种模式联合治疗黄褐斑的疗效优于单一治疗。故本研究观察联合治疗的应用效果,就此展开分析。

本文的研究发现,强脉冲光联合氨甲环酸片治疗黄褐斑患者,可改善患者的面部症状。分析原因:强脉冲光可以提高表皮细胞活力与代谢水平;同时还可以降低皮肤内酪氨酸活性,减少黑色素传递^[19]。既往有研究发现^[20]:强脉冲光将激光能量射入病变组织,病变组织的黑素颗粒吸收激光能量可变大直至破碎,被免疫细胞清除。而氨甲环酸可以抑制酪氨酸酶的活性,减少黑素形成^[21]。因此,两种方式可相互协同,提高疗效。研究结果显示,强脉冲光联合氨甲环酸片治疗黄褐斑患者,可改善皮肤生理参数。究其原因:强脉冲光治疗可以加速皮表下血液循环,有效刺激真皮层中纤维组织弹性恢复^[22]。氨甲环酸可帮助提升角质层细胞中相关脱落蛋白的表达,提高皮肤屏障与皮表

**A****B**

图 2 观察组治疗前后对比

Fig.2 Comparison of the observation group before and after treatment

Note: Fig.2A: Vision photo of the right face before treatment, Fig.2B: Vision photo of the right face after treatment.

表 3 两组皮肤生理参数对比($\bar{x} \pm s$)Table 3 Comparison of skin physiological parameters in two groups($\bar{x} \pm s$)

Groups	TEWL [$\text{g}/(\text{h} \cdot \text{m}^2)$]		Oil content of epidermis($\mu\text{g}/\text{cm}^2$)		Water content of stratum corneum(%)	
	Before treatment	3 months after treatment	Before treatment	3 months after treatment	Before treatment	3 months after treatment
Control group(n=64)	28.05± 1.87	25.88± 2.46*	76.81± 5.34	86.09± 7.31*	24.13± 3.24	29.90± 4.25*
Observation group(n=64)	28.17± 1.24	21.14± 2.72*	75.13± 6.22	97.23± 8.26*	23.83± 5.05	34.15± 4.62*
t	-0.428	10.340	1.639	-8.080	0.400	-5.416
P	0.669	0.000	0.104	0.000	0.690	0.000

Note: Compared with before treatment, *P<0.05.

表 4 血清激素水平对比($\bar{x} \pm s$)Table 4 Comparison of serum hormone levels($\bar{x} \pm s$)

Groups	FSH(IU/L)		T(nmol/L)		E ₂ (nmol/L)		LH(IU/L)	
	Before treatment	3 months after treatment	Before treatment	3 months after treatment	Before treatment	3 months after treatment	Before treatment	3 months after treatment
Control group (n=64)	9.22± 1.36	9.18± 0.92	2.79± 0.33	2.71± 0.59	272.85± 27.29	271.13± 31.26	23.27± 3.25	22.92± 3.67
Observation group(n=64)	9.04± 1.27	4.13± 0.86*	2.83± 0.38	1.67± 0.65*	271.79± 30.25	211.92± 28.28*	23.30± 3.34	12.25± 2.48*
t	0.774	32.080	-0.636	9.478	0.208	15.847	-0.051	19.271
P	0.440	0.000	0.526	0.000	0.835	0.000	0.949	0.000

Note: Compared with before treatment, *P<0.05.

通透度^[23]。

性激素分泌失代偿是当前黄褐斑病因的主流观点之一,机体性激素受下丘脑-垂体-卵巢轴影响,E₂能解除谷胱甘肽的抑制从而提高酪氨酸酶活性,增加黑色素形成,且血清E₂水平与FSH、T、LH水平相互影响,表现为机体性激素分泌失代偿,

黄褐斑患者血清中FSH^[24]、T^[25]、E₂^[26]、LH^[27]等指标升高,加速黄褐斑病情进展。研究还发现,强脉冲光联合氨甲环酸片治疗黄褐斑患者,可改善血清激素水平,考虑主要是因为氨甲环酸是通过阻断黑素细胞与角质形成细胞之间的联系,抑制黑素颗粒进入角质形成细胞,这可能在一定程度上影响E₂的分泌^[28-30]。

表 5 两组不良反应发生情况 [例(%)]
Table 5 Incidence of adverse reactions in two groups [n(%)]

Groups	Burning sensation	Skin sensibility	Gastrointestinal discomfort	Nausea and vomiting	Total incidence
Control group(n=64)	2(3.13)	1(1.56)	0(0.00)	0(0.00)	3(4.69)
Observation group(n=64)	1(1.56)	1(1.56)	1(1.56)	1(1.56)	4(6.25)
	χ^2				0.151
	P				0.197

本文结果也显示,对照组的不良反应总发生率为 4.69%,观察组的为 6.25%,组间对比无差异,可见联合治疗效果较好。

综上所述,黄褐斑患者在强脉冲光治疗基础上联合氨甲环酸片,面部症状改善效果更佳,同时可更好的调节皮肤生理参数及血清激素水平,未见明显的不良反应发生风险升高,具有较好的安全性。本研究尚存在一些不足,该实验观察样本量较小、研究时间仅为 3 个月,有关黄褐斑患者在强脉冲光治疗基础上联合氨甲环酸片的远期疗效尚不清晰。其次,基于患者临床考虑,仅口服氨甲环酸片的患者病例数较少,因而缺乏单纯应用氨甲环酸片的数据对比,今后研究可延长研究时间,增加用药方案多样化,深入机制研究,以提供更为准确的结论。

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表 3 三组患者术后情况比较

Table 3 Comparison of postoperative conditions among three groups

Variables	Combined group (n=40)	U-SAPB group (n=40)	Control group (n=40)	F/H/ χ^2	P
Number of effective postoperative compressions of PCA pump (times)	5(4,7.75) ^a	6(4,10) ^a	10(8,13)	31.429	0.000
Time of first postoperative compression of PCA pump(h)	13(10,17) ^{ab}	10.5(9,13) ^a	8(6,10)	37.765	0.000
Additional analgesic need(n, %)	2(5%)	3(7.5%)	8(20%)	4.711	0.139
Nausea(n, %)	6(15%)	9(22.5%)	8(20%)	0.753	0.686
Vomiting(n, %)	5(12.5%)	7(17.5%)	7(17.5%)	0.500	0.779

Note: Compared with the Control group, ^aP<0.05; Compared with U-SAPB group, ^bP<0.05.

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