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茵栀黄颗粒联合蓝光治疗新生儿病理性黄疸的疗效及对患儿心肌酶谱的影响*

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摘要 目的:探讨茵栀黄颗粒联合蓝光治疗新生儿病理性黄疸的疗效及对患儿心肌酶谱的影响。**方法:**选取 2015 年 2 月至 2016 年 12 月于我院就诊的 80 例新生儿病理性黄疸患儿,随机分为观察组和对照组,每组各 40 例。根据两组患儿的临床症状有针对性地给予常规治疗,对照组在此基础上加用蓝光照射治疗,观察组加用蓝光照射联合茵栀黄颗粒进行治疗,两组均持续治疗一个星期。比较两组的临床疗效、治疗前后血清心肌酶、胆红素水平的变化以及不良反应的发生情况。**结果:**治疗前,两组患儿的血清总胆红素(TBIL)、直接胆红素(DBIL)水平比较差异不明显($P>0.05$);治疗后,两组 TBIL、DBIL 水平均较同组治疗前显著降低($P<0.05$),且观察组显著低于对照组,差异有统计学意义($P<0.05$)。治疗前,两组患儿血清乳酸脱氢酶(LDH)、肌酸激酶(CK)、肌酸激酶同工酶(CK-MB)水平比较差异不显著($P>0.05$);治疗后,两组血清 LDH、CK、CK-MB 水平均较同组治疗前显著降低($P<0.05$),且观察组显著低于对照组,差异有统计学意义($P<0.05$)。治疗后,两组不良反应的发生情况比较差异无统计学意义($P>0.05$)。**结论:**茵栀黄颗粒联合蓝光照射治疗新生儿黄疸较单用蓝光照射治疗可显著提高临床疗效,显著改善患儿血清胆红素及心肌酶谱水平,且安全性较高。

关键词:茵栀黄颗粒;新生儿病理性黄疸;疗效;心肌酶谱

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Clinical Effect of Yinzhihuang Granules Combined with Blue Light Treatment on Neonatal Pathological Jaundice and Influence on the Serum Muscle Enzyme Spectrum*

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ABSTRACT Objective: To explore the clinical efficacy of Yinzhihuang granules combined with blue light in the treatment of neonatal pathological jaundice and the effect on myocardial enzymes. **Methods:** 80 cases of patients with neonatal pathological jaundice treated in our hospital from February 2015 to December 2016 were randomly divided into two groups (control group and observation group), with 40 cases in each group. All patients were given routine treatment according to the clinical symptoms, and patients in control group were treated with blue light irradiation. Patients in the observation group were treated with Yinzhihuang granules combined with blue light irradiation. Both groups were treated continuously for one week. The clinical efficacy, serum myocardial enzymes, bilirubin levels and incidence of adverse reactions of two groups were compared. **Results:** Before treatment, there was no significant difference in the serum total bilirubin (TBIL) and direct bilirubin (DBIL) levels between the two groups ($P>0.05$). After treatment, the levels of serum bilirubin in both groups were both significantly decreased ($P<0.05$), and the TBIL and DBIL levels in the observation group were significantly lower than those in the control group. Before treatment, there was no significant difference in the serum lactate dehydrogenase (LDH), creatine kinase (CK) and creatine kinase isoenzyme (CK-MB) between the two groups ($P>0.05$). After treatment, the levels of myocardial enzymes of both groups were significantly decreased ($P<0.05$), and the LDH, CK and CK-MB levels in observation group were significantly lower than those of the control group ($P<0.05$). After treatment, there was no significant difference in the incidence of adverse reactions between the two groups ($P>0.05$). **Conclusion:** Yinzhihuang granules combined with blue light can significantly improve the clinical efficacy, the serum bilirubin, the myocardial enzyme spectrum, and is more secure in the treatment of neonatal jaundice compared with the treatment of blue light irradiation alone.

Key words: Yinzhihuang Granules; Neonatal jaundice; Curative effect; Myocardial enzymes

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前言

新生儿黄疸是儿科的临床常见疾病之一,又称新生儿高胆红素血症,指胆红素代谢异常的新生婴儿血清胆红素水平过高且大量积聚于体内而导致皮肤、巩膜等出现黄疸症状^[1]。临床上将其分为生理性黄疸和病理性黄疸,其中生理性黄疸仅有轻微食欲不振而无其他严重症状,一般在早期进行开奶干预,保证奶量供给充足并尽早建立肠道正常菌群,促使黄疸自行消退^[2]。病理性黄疸可引发肝、脑、心、肾等重要脏器损害,如不采取及时有效的治疗措施,可致病情加重、黄疸加深或消退后重复出现。病理性黄疸还会累及中枢神经系统,并引发胆红素脑病,早期重度黄疸尤其严重,可导致不可逆的脑损伤及后遗症,对新生儿的身体健康及生长发育产生极大威胁^[3]。目前,临床上治疗新生儿黄疸的方法主要采用光疗,而近年应用中医药的治疗方法亦有报道^[4]。本研究主要探讨了茵栀黄颗粒联合蓝光照射治疗新生儿病理性黄疸的疗效以及对患儿心肌酶谱的影响,现将结果报道如下。

1 资料与方法

1.1 一般资料

选取 2015 年 2 月至 2016 年 12 月于我院就诊的病理性黄疸患儿 80 例,将其随机分为观察组和对照组各 40 例。其中,观察组:男 19 例,女 21 例,年龄 3-18 天,平均年龄 (5.73 ± 1.49) 天,体重 2.7-7.1 kg,平均体重 (3.19 ± 1.62) kg,早产儿 9 例,足月儿 29 例,过期儿 2 例;对照组:男 22 例,女 18 例,年龄 2-17 天,平均年龄 (5.46 ± 1.79) 天,体重 2.7-6.8 kg,平均体重 (3.32 ± 1.54) kg,早产儿 9 例,足月儿 27 例,过期儿 4 例。两组患儿临床基线资料比较差异无统计学意义($P>0.05$),具有可比性。

病例纳入标准:根据《实用儿科学》^[5],纳入研究对象的所有患儿均符合新生儿病理性黄疸的诊断标准。病例排除标准:伴有心、肝、肾等脏器严重器质性病变的患儿;伴发颅内出血、新生儿感染性疾病、新生儿肝炎、胆管阻塞等疾病的患儿;由新生儿溶血病、其他先天性遗传代谢病所致的新生儿黄疸、阻塞性黄疸的患儿;年龄超过 28 天,临床确诊为新生儿胆道闭锁的患儿;对药物出现严重过敏的患儿。

1.2 治疗方法

两组均根据患儿具体情况给予常规治疗以及喂养、护理,

保证奶量供给充足,保暖、补液、纠酸,纠正便秘、防止低血糖。在此基础上,对照组患儿采用蓝光照射治疗,观察组采用蓝光照射联合茵栀黄颗粒进行治疗。蓝光照射治疗采用间歇光疗方式,选取波长 420-480 nm 的蓝色荧光灯双面光疗,将患儿置于暖箱内,用黑色眼罩保护眼睛,外阴部用纸尿裤遮挡,根据黄疸程度每日 1 次或隔日 1 次进行蓝光照射,每次 10 h,具体方法参照《新生儿黄疸行光照疗法的护理问题及干预措施》^[6]。仪器采用上海四菱医用恒温设备有限公司 8502D 型婴儿光疗暖箱。观察组加用茵栀黄颗粒(鲁南厚普制药有限公司,国药准字 Z20030028)治疗,1 g/次,每日 3 次,加温开水 5-10 mL,溶解后汤勺喂服。两组患儿均连续治疗一周。

1.3 观察指标

对两组患儿的临床治疗效果及治疗前后的血清胆红素水平、心肌酶谱水平进行观测。

入院时检测两组患儿血清总胆红素及间接胆红素值,入院后每次光疗前监测经皮总胆红素值(采用日本 Konica minolta sensing 公司, JM-103 型经皮黄疸检测仪)。治疗前后采集两组患儿清晨空腹外周静脉血 5 mL,进行肝素钠抗凝处理,采用全自动生化分析仪(BECKMAN COULTER AU5800)检测血清心肌酶和胆红素指标,包括总胆红素(TBIL)、直接胆红素(DBIL)及乳酸脱氢酶(LDH)、肌酸激酶(CK)、肌酸激酶同工酶(CK-MB)水平。

1.4 统计学处理

数据采用 SPSS17.0 统计学软件进行处理分析。本研究中,血清胆红素、心肌酶谱等各项指标均服从正态分布,以 $(\bar{x} \pm s)$ 表示,治疗前后组内比较、治疗后组间比较均行 t 检验。以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 两组患儿治疗前后血清胆红素水平的比较

两组患儿治疗前血清 TBIL、DBIL 水平比较无显著性差异($P>0.05$)。治疗后,两组患儿血清 DBIL、TBIL 水平均显著低于治疗前($P<0.05$);且观察组血清 TBIL 水平 $(52.13 \pm 4.71) \mu\text{mol/L}$ 显著低于对照组 $[(95.42 \pm 6.11) \mu\text{mol/L}]$ ($P<0.05$),观察组血清 DBIL 水平 $(38.52 \pm 3.87) \mu\text{mol/L}$ 显著低于对照组 $[(56.48 \pm 4.41) \mu\text{mol/L}]$ ($P<0.05$)。见表 1。

表 1 两组治疗前后血清胆红素水平的比较($n=40, \bar{x} \pm s$)

Table 1 Comparisons of the serum bilirubin levels between two groups before and after treatment($n=40, \bar{x} \pm s$)

Groups	Time	TBIL($\mu\text{mol/L}$)	DBIL($\mu\text{mol/L}$)
Control group	Before treatment	296.26 $\pm$ 32.44	221.53 $\pm$ 21.62
	After treatment	95.42 $\pm$ 6.11*	56.48 $\pm$ 4.41*
Observation group	Before treatment	310.32 $\pm$ 31.07	217.67 $\pm$ 18.94
	After treatment	52.13 $\pm$ 4.71**	38.52 $\pm$ 3.87**

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

2.2 两组患儿治疗前后心肌酶谱水平的比较

治疗前,两组心肌酶谱各项指标水平比较差异不显著($P>0.05$)。治疗后,两组心肌酶谱各项指标水平均显著降低($P<0.05$);

治疗后,观察组血清 LDH 水平 $[(171.21 \pm 11.07) \text{U/L}]$ 显著低于对照组 $[(181.84 \pm 10.48) \text{U/L}]$,血清 CK 水平 $[(234.27 \pm 31.22) \text{U/L}]$ 显著低于对照组 $[(261.66 \pm 32.54) \text{U/L}]$,观察组 CK-MB 水

平 $[(38.28 \pm 4.11) \text{U/L}]$ 显著低于对照组 $[(41.73 \pm 3.92) \text{U/L}]$,差异 均有统计学意义($P < 0.05$)。见表 2。

表 2 两组治疗前后心肌酶谱水平的比较($n=40, \bar{x} \pm s$)

Table 2 Comparison of the myocardial enzyme spectrum between two groups before and after treatment($n=40, \bar{x} \pm s$)

Groups	Time	LDH(U/L)	CK(U/L)	CK-MB(U/L)
Control group	Before treatment	248.32 $\pm$ 28.34	364.82 $\pm$ 37.97	52.31 $\pm$ 4.88
	After treatment	181.84 $\pm$ 10.48*	261.66 $\pm$ 32.54*	41.73 $\pm$ 3.92*
Observation group	Before treatment	251.49 $\pm$ 30.17	369.43 $\pm$ 35.54	51.85 $\pm$ 5.19
	After treatment	171.21 $\pm$ 11.07*#	234.27 $\pm$ 31.22*#	38.28 $\pm$ 4.11*#

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

3 讨论

新生儿黄疸指因胆红素代谢异常导致的新生儿胆红素水平过高而出现的皮肤、黏膜和巩膜黄染等现象,是儿科常见病之一,其病理因素主要有胆红素生成过多、胆汁排泄障碍、肝脏胆红素代谢障碍等^[7]。新生儿黄疸分为生理性及病理性,其中病理性黄疸对患儿中枢神经系统影响严重,且具有不可逆性,若治疗不当,可引发胆红素脑病及各种后遗症,严重者甚至导致死亡^[8]。导致病理性黄疸的原因为新生儿体内的血清胆红素生成量过大,而小儿体内缺乏与之结合的血浆白蛋白,因而体内的游离胆红素水平升高,患儿肝脏内缺乏代谢胆红素的相关酶类,肝细胞功能尚不成熟,摄取胆红素能力低下,因此处理胆红素的能力较低,同时少数患儿患有先天性胆道闭锁、肝炎或者先天性代谢缺陷症等疾病,因此容易引发病理性黄疸^[9,10]。临床治疗主要有促进胆红素排泄并减少其重吸收等措施,同时保障对患儿的心肌酶谱保护和免疫保护,治疗方式主要有蓝光照射、苯巴比妥(酶诱导剂)及人血白蛋白等治疗^[11]。

蓝光照射安全有效,可明显降低未结合胆红素的水平^[12],其作用机制为蓝光照射器发射的波长主峰在 425-480 nm,人体内血清胆红素的最高吸收波长 460-465 nm,二者十分接近,故经蓝光照射后,血清游离胆红素可以水溶性胆红素异构体的形式,以胆汁及尿液形式代谢排出,降低血清中胆红素水平^[12,13]。蓝光治疗过程中应注意照射时间及照射间隔的设定,且照射时需做好患儿眼睛及会阴部的保护措施^[12]。研究表明蓝光会引起皮疹、腹泻、核黄素缺失及青铜症等不良反应,因此仅依赖光疗干预,发热、呕吐、腹泻、皮疹等不良反应的发生率较高;且蓝光的穿透力较弱,仅可转化皮肤和浅层皮下组织的未结合胆红素,而对深层组织的胆红素无法起效^[14]。因此,目前临床上治疗新生儿病理性黄疸通常选择蓝光照射与药物联合的治疗方法,其中茵栀黄作为一种安全有效的治疗黄疸的中成药备受关注^[15]。

新生儿病理性黄疸属中医“胎黄”范畴,孕妇的饮食习惯不当以及情志不舒或导致胎禀湿蕴,湿热郁结于肝、胆并移至胞胎,或因胎产之时、出生之后婴儿感受湿热邪毒,最终引发黄疸;其治疗常以泻下退黄及清热利湿为法^[16-21]。茵栀黄颗粒中成药提取物将茵陈、栀子、黄芩和金银花以现代制剂工艺制备成口服中成药,具有清热解毒、利湿退黄之功效,用于肝胆湿热引发的黄疸^[22-27]。方中^[28]茵陈苦泄下降,善清热利湿退黄,为治黄疸之要药,能促进胆汁中胆酸、胆红素等的排泄;栀子清利三焦湿热,其主要活性成分栀子苷可促进胆汁分泌;黄芩苦寒燥湿,

清热解毒,通泻胃肠郁热,可改善毛细血管通透性并增加胆囊收缩,促进胆汁排泄,从而降低胆红素水平;金银花清热解毒,具有抑菌和杀菌作用。诸药合用可加强清利湿热、利胆退黄的效果。现代药理研究表明^[29]茵栀黄能诱导肝脏酶系统,促进肝脏对胆红素的代谢,抑制胆红素生成,增强肝脏对胆红素的摄取、结合以及排泄水平;同时还可通过干预肠循环从而促进肠壁蠕动,泻热通便,减少未结合胆红素的重吸收,有效降低血清中未结合胆红素,从而达到治疗黄疸的目的。此外,茵栀黄颗粒还能抑制 D-氨基半乳糖对肝脏产生的急性损伤,并降低异硫氰酸引发的血清胆红素,从而保护肝脏。黄疸患儿血清胆红素相关指标如 TBIL、DBIL 水平明显较高,血清胆红素有潜在神经毒性,胆红素水平过高时会损伤线粒体、细胞膜等,产生脂质过氧化反应,损害心肌,导致患儿心肌酶谱异常。心肌酶谱中,CK 由细胞胞质和线粒体产生,存在于心肌、骨骼肌及平滑肌等细胞,LDH 由肝、脑等器官产生,CK-MB 为心肌特异性酶。上述指标水平的升高程度可提示心肌细胞的受损程度^[30]。本研究应用茵栀黄颗粒联合蓝光照射治疗新生儿病理性黄疸,结果显示两组治疗后血清胆红素指标 TBIL 水平、DBIL 水平显著降低,且观察组显著低于对照组,提示茵栀黄起到了显著的降低胆红素的作用,原因可能是茵栀黄具有清热解毒,利湿退黄等功效,可有效减轻肝细胞损伤并促进肝细胞修复和再生,因而增强肝脏解毒及疏泄的功能,即促进对胆红素摄取、结合和排泄的能力,有效降低患儿血清胆红素水平。两组治疗后心肌酶谱各项指标 LDH、CK、CK-MB 水平均显著降低,且观察组显著低于对照组,表明蓝光联合茵栀黄颗粒治疗可显著降低患儿心肌酶谱水平,提示茵栀黄颗粒治疗在蓝光降酶抗菌基础上可进一步增加胆红素的排泄,保护心肌细胞。原因可能是茵栀黄通过降低患儿高水平胆红素,减少胆红素在患儿心肌组织内的沉积,因而减少血清胆红素通过损伤线粒体、细胞膜等方式产生的脂质过氧化反应,起到保护心肌细胞的效果。治疗后,两组患儿的不良反应结果比较差异无统计学意义,提示茵栀黄颗粒治疗安全性较好。

综上所述,茵栀黄颗粒联合蓝光照射治疗新生儿黄疸较单用蓝光照射治疗可显著提高临床疗效,显著改善患儿血清胆红素及心肌酶谱水平,且安全性较高。

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