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阿立哌唑与利培酮对男性精神分裂症患者性功能、甲状腺素水平及糖脂代谢的影响*

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摘要 目的:探讨阿立哌唑与利培酮对男性精神分裂症患者性功能、甲状腺素水平及糖脂代谢的影响。**方法:**选取我院于2016年1月至2017年10月期间收治的92例精神分裂症患者。根据数表法将患者随机分为对照组(n=46)与研究组(n=46),对照组给予利培酮治疗,研究组给予阿立哌唑治疗,两组均治疗8周。观察两组患者临床疗效、性功能、糖脂代谢、甲状腺素水平。**结果:**研究组患者临床总有效率为84.78%(39/46),高于对照组的78.26%(36/46),但差异无统计学意义(P>0.05)。研究组治疗前后性欲、性唤起以及性高潮比较差异无统计学意义(P>0.05);对照组治疗后上述指标低于治疗前和研究组(P<0.05)。研究组治疗前后三碘甲状腺原氨酸(T3)、甲状腺素(T4)、游离三碘甲状腺原氨酸(FT3)比较差异无统计学意义(P>0.05),游离甲状腺素(FT4)低于治疗前(P<0.05);对照组治疗后T4、FT3以及FT4低于治疗前和研究组(P<0.05)。研究组治疗前后总胆固醇(TC)、甘油三酯(TG)、高密度脂蛋白胆固醇(HDL-C)、低密度脂蛋白胆固醇(LDL-C)、空腹血糖(FPG)以及餐后2 h血糖(2hPG)比较差异无统计学意义(P>0.05);对照组治疗后TG、HDL-C、FPG以及2hPG高于治疗前和研究组(P<0.05)。**结论:**阿立哌唑对男性精神分裂症患者的性功能、甲状腺素水平及糖脂代谢影响较小,与利培酮均具有较好的治疗效果,可做进一步推广应用。

关键词:阿立哌唑;利培酮;男性;精神分裂症;性功能;甲状腺素;糖脂代谢

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Effects of Aripiprazole and Risperidone on Sexual Function, Thyroxine Level and Glycolipid Metabolism in Male Schizophrenic Patients*

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ABSTRACT Objective: To investigate the effects of aripiprazole and risperidone on sexual function, thyroxine level and glycolipid metabolism in male schizophrenic patients. **Methods:** 92 cases of schizophrenia who were treated in our hospital from January 2016 to October 2017 were selected,the patients were divided into control group (n=46) and study group (n=46) according to the number table method. The control group was treated with risperidone, and the study group was treated with aripiprazole, the two groups were treated for 8 weeks. The clinical efficacy, sexual function, glycolipid metabolism and thyroxine level were observed between the two groups. **Results:** The total clinical effective rate of the patients in the study group was 84.78% (39/46), which was higher than 78.26% (36/46) of the control group, but the difference was not statistically significant (P>0.05). There were no significant differences in sexual desire, sexual arousal and orgasm between the study group before and after treatment (P>0.05), the above indexes in the control group were lower than those before treatment and the study group (P<0.05). There was no significant difference in the triiodothyronine (T3), thyroxine (T4) and free triiodothyronine (FT3) in the study group before and after treatment (P>0.05), free thyroxine (FT4) was lower than before treatment (P<0.05), after treatment, T4, FT3 and FT4 in the control group were lower than before treatment and in the study group (P<0.05). There were no significant differences in total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), fasting blood glucose (FPG) and postprandial 2H blood glucose (2hPG) in the study group before and after treatment (P>0.05). The TG, HDL-C, FPG and 2hPG in the control group after treatment were higher than those before treatment and study group (P<0.05). **Conclusion:** Aripiprazole has less effect on sexual function, thyroxine level and glycolipid metabolism in male schizophrenic patients, and risperidone has good therapeutic effect and can be used for further promotion and application.

Key words: Aripiprazole; Risperidone; Male; Schizophrenic; Sexual function; Thyroxine level; Glycolipid metabolism

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前言

精神分裂症是临床上常见的一组病因不明的重性精神病，多发于青壮年人群。该病病程较长,且易反复发作,部分患者会

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出现认知衰退以及精神残疾等临床症状,给患者、家庭以及社会带来较大的负担[1-3]。药物治疗是精神分裂症的主要治疗方式,常规的药物治疗可以缓解绝大多数的临床症状[4,5]。近年来,新型抗精神病药物如阿立哌唑、利培酮等已被临床逐渐接受,阿立哌唑是一种新型的非典型抗精神病药物,该药具有上调多巴胺功能的不足、下调多巴胺功能的亢进等作用[6,7],另外,利培酮为苯丙异噁唑衍生物,是新一代的抗精神病药,常用于治疗急性和慢性精神分裂症[8,9]。然而临床有关上述两种药物对男性精神分裂症患者甲状腺素水平影响的报道较为少见。因此,本研究通过分析阿立哌唑与利培酮治疗男性精神分裂症患者的疗效,旨在为临床选择治疗药物提供数据支持。

1 资料与方法

1.1 一般资料

选取我院于 2016 年 1 月至 2017 年 10 月期间收治的精神分裂症患者 92 例。纳入标准:(1)所有患者均符合精神分裂症的诊断标准[10];(2)患者均为男性;(3)年龄处于 18-60 之间;(4)入院前一个月内未接受过抗精神病药物治疗者;(5) 性功能正常者;(6) 患者家人知情本次研究并签署知情同意书。排除标准:(1)伴有严重的心肝肾等脏器功能障碍者;(2)伴有糖尿病及内分泌疾病者;(3)伴有高血压、高血脂、心脑血管疾病者;(4)对本研究使用药物存在禁忌症者;(5)伴有明显冲动、自杀、自残以及暴力倾向者。根据随机数字表法将患者分为对照组(n=46) 与研究组 (n=46), 其中对照组年龄 21-59 岁, 平均(34.95± 4.01)岁;病程 3 个月 -5 年,平均(2.78± 0.78)年。研究组年龄 19-57 岁,平均(35.25± 3.28)岁;病程 5 个月 -6 年,平均(2.65± 0.91)年。两组患者一般资料比较无差异(P>0.05),均衡可比。本研究符合我院伦理委员会制定的相关规定,并已通过伦理委员会的审核。

1.2 治疗方法

对照组患者给予利培酮(西安杨森制药有限公司,国药准字:H20010309,规格:1 mg)口服治疗,初始剂量为 2 mg/d,治疗剂量为 4-6 mg/d,平均(4.27± 0.19)mg/d。研究组给予阿立哌唑口腔崩解片 (成都康弘药业集团股份有限公司, 国药准字:H20060521,5 mg)口服治疗,初始剂量为 10 mg/d,治疗剂量为 20-30 mg/d,平均(24.46± 1.31)mg/d。两组患者均从小剂量用药逐情加量,2 周内达到治疗剂量标准, 研究期间均未服用其他药物,两组均治疗 8 周。

1.3 观察指标

采用阳性与阴性症状量表(PANSS)评价患者临床疗效,疗效判定标准[11]:PANSS 减分率 >75%则表明痊愈,50%<PANSS 减分率≤ 75%则表明显效,30%<PANSS 减分率≤ 50%则表明有效,PANSS 减分率≤ 30%则表明无效, 总有效率 = 痊愈率 + 显效率 + 有效率。分别于治疗前、治疗后采用自制男性性功能量表对所有患者性功能进行评价,该量表分为性欲、性唤起、性高潮三个项目,总分 100 分,分数越高表明性功能状况越好。分别于治疗前后采集患者清晨空腹静脉血 10 mL,送往我院检验科,3000 r/min 离心 10 min,取上清液,冷藏待测。取 5 mL 采用增强化学发光法检测三碘甲状腺原氨酸(T3)、甲状腺素(T4)、游离三碘甲状腺原氨酸(FT3)以及游离甲状腺素(FT4)水平,取 5 mL 采用罗氏 Modular 全自动生化分析仪检测总胆固醇(TC)、高密度脂蛋白胆固醇(HDL-C)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C),试剂盒均购自上海雅培生物科技有限公司,操作步骤严格遵循试剂盒中的操作指南进行。同时检测患者空腹血糖(FPG)、餐后 2 h 血糖(2hPG)。

1.4 统计学方法

采用 SPSS20.0 处理数据,性功能相关评分、甲状腺素指标等计量资料用均数± 标准差($\bar{x}$± s)表示,采用 t 检验,总有效率等计数资料以率(%)表示,采用 x^2 检验,将 α=0.05 作为检验标准。

2 结果

2.1 两组患者临床疗效比较

研究组患者临床总有效率为 84.78%(39/46), 高于对照组的 78.26%(36/46),但差异无统计学意义(P>0.05);详见表 1。

表 1 两组患者临床疗效比较[n(%)]

Table 1 Comparison of the clinical efficacy of the two groups[n(%)]

Groups	n	Recovery	Effective	Good	Invalid	Total effective rate
Control group	46	18(39.13)	7(15.22)	11(23.91)	10(21.74)	36(78.26)
Study group	46	21(45.65)	8(17.39)	10(21.74)	7(15.22)	39(84.78)
x^2	-					0.649
P	-					0.420

2.2 两组患者治疗前后性功能比较

两组患者治疗前性欲、性唤起以及性高潮比较无差异(P>0.05); 研究组治疗前后上述指标比较差异无统计学意义(P>0.05); 对照组治疗后上述指标低于治疗前和研究组(P<0.05);详见表 2。

2.3 两组患者治疗前后甲状腺素比较

两组患者治疗前 T3、T4、FT3 以及 FT4 比较无差异(P>0.05); 研究组治疗前后 T3、T4、FT3 比较差异无统计学意义(P>0.05),FT4 低于治疗前(P<0.05);对照组治疗后 T4、FT3 以及 FT4 低于治疗前和研究组(P<0.05);详见表 3。

2.4 两组患者治疗前后糖脂代谢比较

两组患者治疗前 TC、TG、HDL-C、LDL-C、FPG 以及 2hPG 比较无差异(P>0.05);研究组治疗前后上述指标比较差异无统计学意义(P>0.05);对照组治疗后 TG、HDL-C、FPG 以及 2hPG 高于治疗前和研究组(P<0.05);详见表 4。

3 讨论

精神分裂症的复发率较高,长期服药维持治疗仍是目前缓解病情以及降低复发率的有效途径,但是抗精神病药物治疗后所引起的血糖、血脂以及甲状腺素代谢紊乱已经逐渐引起临床

表 2 两组患者治疗前后性功能比较($\bar{x}\pm s$,分)

Table 2 Comparison of sexual function before and after treatment between the two groups ($\bar{x}\pm s$, scores)

Groups	n	Sexual desire		Sexual arousal		Orgasm	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	46	7.43± 0.82	6.88± 1.27*	24.32± 1.12	21.52± 1.24*	23.24± 1.38	22.72± 0.64*
Study group	46	7.26± 0.73	7.39± 0.82	23.89± 1.55	23.91± 1.12	23.78± 1.82	24.63± 0.71
t		1.050	2.288	1.525	9.318	1.604	13.552
P		0.296	0.024	0.131	0.000	0.112	0.000

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

表 3 两组患者治疗前后甲状腺素比较($\bar{x}\pm s$,ng/mL)

Table 3 Comparison of thyroxine before and after treatment between the two groups($\bar{x}\pm s$, ng/mL)

Groups	n	T3		T4		FT3		FT4	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control group	46	1.13± 0.35	1.01± 0.22	9.51± 2.05	8.23± 1.62*	3.16± 0.53	2.78± 0.45*	0.96± 0.23	0.68± 0.25*
Study group	46	1.16± 0.22	1.09± 0.19	9.57± 1.64	8.92± 1.53	3.09± 0.64	2.98± 0.47	0.99± 0.22	0.79± 0.27*
t		0.492	1.867	0.155	2.100	0.571	2.085	0.639	2.028
P		0.624	0.065	0.877	0.039	0.569	0.040	0.524	0.046

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

表 4 两组患者治疗前后糖脂代谢比较($\bar{x}\pm s$,mmol/L)

Table 4 Comparison of glycolipid metabolism before and after treatment between the two groups($\bar{x}\pm s$, mmol/L)

Groups	n	Time	TC	TG	HDL-C	LDL-C	FPG	2hPG
Control group	46	Before treatment	4.09± 0.55	1.27± 0.34	1.21± 0.36	2.23± 0.50	4.75± 0.49	5.10± 0.55
		After treatment	4.27± 0.81	2.08± 0.65*	1.43± 0.32*	2.22± 0.63	5.41± 0.53*	5.81± 0.49*
Study group	46	Before treatment	4.05± 0.85	1.22± 0.55	1.33± 0.41	2.26± 0.59	4.78± 0.62	5.16± 0.61
		After treatment	3.99± 0.96	1.35± 0.63&	1.24± 0.45&	2.23± 0.59	4.71± 0.68&	5.21± 0.58&

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

工作者们的广泛关注,尤其针对男性精神分裂症患者,服用抗精神病药物后易引发其性功能障碍[12-14]。因此,寻找安全有效的药物治疗男性精神分裂症患者具有积极的临床意义。目前,氯氮平、阿立哌唑、利培酮等均是临床常用的抗精神病药物,其中阿立哌唑属于新药,安全性高且不良反应较少[15,16],而利培酮在治疗阳性以及阴性症状及其所伴发的情感症状中效果较好[17,18]。

本研究针对男性精神分裂症患者分别给予阿立哌唑与利培酮治疗,结果表明研究组患者临床总有效率为 84.78%,高于对照组的 78.26%,但差异无统计学意义(P>0.05)。提示阿立哌唑与利培酮疗效相当,均可显著提升患者治疗效果,改善预后。另外,研究组治疗前后性欲、性唤起以及性高潮比较差异无统计学意义(P>0.05);对照组治疗后上述指标低于治疗前和研究组(P<0.05)。表明阿立哌唑治疗男性精神分裂症患者,对其性功能影响较小,而利培酮则可影响其性功能不良状况。抗精神病药主要是通过下丘脑多巴胺、垂体催乳素以及外周性腺睾酮三个方面来影响患者的性功能状况。因阿立哌唑属于多巴胺、5-HT 稳定剂,在中脑边缘通路会产生功能性拮抗作用,并且可在中脑皮层通路产生功能性激动作用,对 D2、D3 受体具有较强的亲和力,因此,对患者性功能影响不大[19-21]。而利培酮具有较强的多巴胺受体拮抗作用,易引发患者锥外体系反应,如失眠、视物模糊以及体重增加等,从而影响患者的性功能[22-24]。本次研究还显示,研究组治疗前后 T3、T4、FT3 比较差异无统计学意义(P>0.05),FT4 低于治疗前(P<0.05);对照组治疗后 T4、FT3 以及 FT4 低于治疗前和研究组(P<0.05)。表明阿立哌唑治疗对精神分裂症患者甲状腺素水平影响不大,而利培酮则会引起患者 T4、FT3 以及 FT4 降低,由于 T4、FT3 以及 FT4 均是临床检验甲状腺功能是否正常的常用指标,若上述指标水平降低,易引发甲减,继而导致低白蛋白血症。分析其原因,可能是由于利培酮类抗精神病药物在阻断丘脑下部结节受体时对患者内分泌功能产生影响,从而影响甲状腺素水平[25-27]。此外,研究组治疗前后 TC、TG、HDL-C、LDL-C、FPG 以及 2hPG 比较差异无统计学意义(P>0.05);对照组治疗后 TG、HDL-C、FPG 以及 2hPG 高于治疗前和研究组(P<0.05)。提示精神分裂症患者经阿立哌唑治疗后,其血糖、血脂各项指标基本不受影响,而经利培酮治疗后,血糖、血脂部分指标发生变化。目前,抗精神病类药物引起患者血糖、血脂影响的主要机制可能与多巴胺受体以及 H1 受体的阻断作用有关,可能引起胰岛素释放不足、胰岛素抵抗以及葡萄糖利用受损,这些结果均和血糖、血脂的变化密切相关[28-30]。

综上所述,利培酮对男性精神分裂症患者性功能、甲状腺素水平及糖脂代谢均有影响,而阿立哌唑则可有效减少此类影响,并且阿立哌唑与利培酮疗效相当,临床医师工作者们可根据患者实际情况合理用药,确保患者治疗效果以及预后。

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