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坦洛新联合托特罗定对老年膀胱过度活动综合症患者 P2X3 受体表达的影响 *

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摘要 目的：探讨坦洛新联合托特罗定对老年膀胱过度活动综合症患者 P2X3 受体表达的影响。**方法：**收集我院收治的膀胱过度活动综合症患者 60 例，随机分为对照组和实验组，每组各 30 例，对照组患者给予盐酸坦洛新缓释胶囊，实验组患者在对照组的基础上给予酒石酸托特罗定。观察并比较所有患者的最大尿流速率、膀胱残余尿量、排尿次数、单次最大尿量水平以及患者的治疗效果。**结果：**治疗后，两组患者治疗后单次最大尿量、最大尿流速率均升高(P<0.05)，膀胱残余尿量、排尿次数以及 P2X3 水平均降低(P<0.05)；与对照组相比，实验组患者治疗后单次最大尿量、最大尿流速率较高(P<0.05)，膀胱残余尿量、排尿次数以及 P2X3 水平较低(P<0.05)；实验组患者临床总有效率与对照组相比较高(P<0.05)。**结论：**坦洛新联合托特罗定能够显著提高老年膀胱活动度综合征患者临床疗效，可能与其降低患者血清 P2X3 受体水平有关。

关键词：坦洛新；托特罗定；膀胱过度活动综合症；P2X3 受体

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Effect of Tamsulosin Combined with Tolterodine on the Expression of P2X3 Receptor in Elderly Patients with Bladder Hyperactivity Syndrome*

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ABSTRACT Objective: To investigate the effect of tamsulosin combined with tolterodine on the expression of P2X3 receptor in elderly patients with bladder hyperactivity syndrome. **Methods:** 60 cases of elderly patients with bladder hyperactivity syndrome from our hospital were selected and randomly divided into the control group and the experiment group, 30 cases in each group. The control group was treated by tamsulosin hydrochloride sustained release capsules and the experiment group was treated on the basis of control group with Tolterodine. The maximum urinary flow rate, residual urine volume, urinary frequency, maximum urine volume and treatment effect were tested and compared after treatment. **Results:** Compared with before treatment, the one time maximum urine volume, maximum urine flow rate were higher in both groups after treatment (P<0.05), the residual urine volume, urinary frequency and P2X3 level were lower (P<0.05). Compared with the control group after treatment, the one time maximum urine volume, maximum urine flow rate were higher in the experiment group (P<0.05), the residual urine volume, urinary frequency and P2X3 level were lower (P<0.05), the clinical total effective rate were higher(P<0.05). **Conclusion:** Tamsulosin combined with Luoding could significantly improve the clinical efficacy of elderly patients with bladder hyperactivity syndrome, which might be related to the decrease of serum P2X3 receptor level.

Key words: Tamsulosin; Tolterodine; Overactive bladder syndrome; P2X3 receptor

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前言

膀胱过度活动症(Overactive bladder，OAB)是以尿急为核心症状的症候群，是临床泌尿外科的常见疾病[1]。临床上常以日间尿频和夜尿增多、急迫性尿失禁等为主要症状，也可伴有急性尿路感染或膀胱尿道的局部病变[2,3]。膀胱过度活动症严重影响了患者的生活质量，给患者的日常生活及社会活动带来严重影响[4]。近年来，老年膀胱过度活动症的发病率显著上升，已经引起临床的高度重视。膀胱过度活动症的病因及发病机制比较复杂，涉及到膀胱的感觉功能，中枢及外周神经系统等多个方

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面,因此至今尚不能完全明确[5,6]。目前对于膀胱过度活动症的药物治疗上普遍以抗胆碱能药物作为首选用药[7]。托特罗定片是目前临床常用的治疗膀胱过度活动症的抗胆碱能药物,是竞争性 M 受体拮抗剂,研究表明[8]其对膀胱的选择性较强,高于其对唾液腺的选择性, 与其他药物相比不良反应明显减少,但近年来的报道显示[9]仍有部分患者的疗效不令人满意。坦洛新为肾上腺素受体拮抗剂,研究表明其能够提高最大尿流率及平均尿流率,缓解尿道痉挛,改善膀胱过度活动症的临床症状[10]。本研究通过观察老年膀胱过度活动综合症患者 P2X3 受体表达水平的变化,探讨坦洛新联合托特罗定对老年膀胱过度活动综合症的治疗作用及其机制,现报道如下。

1 资料与方法

1.1 临床资料

收集 2014 年 1 月 ~2015 年 6 月于我院治疗的 60 例膀胱过度活动症患者,随机分为实验组和对照组,每组 30 例。实验组组内男性 12 例,女性 18 例,患者平均年龄(66.56± 1.28)岁;对照组内患者平均年龄(69.41± 1.71)岁,男性 14 例,女性 16 例。所有患者均符合《中国泌尿外科疾病诊断治疗指南》[11]中关于膀胱过度活动症的诊断标准。所有患者均无心脑血管疾病以及肝肾功能不全;患者无膀胱实质性病变;患者无感染性疾病以及恶性肿瘤。所有患者在实验前均未服过实验相关药物且对实验药物无过敏。所有对象均签署知情同意书同意。两组患者一般资料具有可比性(P>0.05)。

1.2 方法

所有患者入院后均给予常规治疗,对照组患者给予盐酸坦洛新缓释胶囊 (江苏恒瑞医药股份有限公司产品, 国药准字 H20050392)0.2 mg/ 次,1 次 /d,睡前口服;实验组患者在对照组的基础上给予酒石酸托特罗定(南京美瑞制药有限公司,国药准字 H20000602)2 mg/ 次,2 次 /d,口服。治疗期间注意患者状况,治疗连续 4 周。

1.3 观察指标

1.3.1 最大尿流速率(MFR)以及膀胱残余尿量(RUV)水平检测 对所有患者治疗前后的最大尿流速率(MFR)以及膀胱残余尿量(RUV)水平等尿流动力学水平进行检测。

1.3.2 排尿次数以及单次最大尿量水平检测 对所有患者治疗前后患者日平均排尿次数以及单次最大尿量水平进行检测

1.3.3 P2X3 受体水平检测 治疗前后取所有患者清晨空腹取静脉血 2 mL,离心取上清,采用酶联免疫分析法,严格按照试剂盒的步骤,检测患者血清 P2X3 受体水平。

1.3.4 临床疗效评价标准 患者临床症状明显改善,尿急、尿频等症状消失,尿流率 >20 mL/s 为治愈。患者治疗后临床症状基本消失,尿流率 >15 mL/s,尿急、尿频等症状基本消失为显效;患者治疗后临床症状减轻,尿流率 >10 mL/s,尿急、尿频等临床症状缓解为有效;患者治疗后症状无明显改善为无效。

1.4 统计学分析

采用 SPSS 19.0 统计软件进行分析, 计量数据以均数± 标准差($\bar{x}$± s)表示,采用 t 检验;计数资料以%表示,采用卡方检验,以 P<0.05 认为差异有统计学意义。

2 结果

2.1 两组患者最大尿流速率(MFR)以及膀胱残余尿量(RUV)水平比较

治疗后, 两组患者最大尿流速率与治疗前相比均升高,膀胱残余尿量均降低(P<0.05);与对照组相比,实验组患者最大尿流速率较高,膀胱残余尿量较低(P<0.05),见表 1。

表 1 两组患者治疗前后最大尿流速率(MFR)以及膀胱残余尿量(RUV)水平比较($\bar{x}$± s)

Table 1 Comparison of the MFR and RUV levels of patients between two groups before and after treatment($\bar{x}$± s)

		MFR	RUV
Experimental group	Before treatment	9.36± 2.73	81.37± 22.19
	After treatment	16.92± 3.18*#	25.16± 8.22*#
Control group	Before treatment	9.26± 3.11	83.53± 26.72
	After treatment	12.63± 3.03*	33.26± 11.79*

注:与治疗前相比,*P<0.05;与对照组相比,#P<0.05。

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

2.2 两组患者排尿次数以及单次最大尿量水平比较

治疗后,两组患者排尿次数与治疗前相比降低,单次最大尿量升高(P<0.05);与对照组相比,实验组患者排尿次数较低,单次最大尿量较高(P<0.05),见表 2。

表 2 两组患者治疗前后排尿次数以及单次最大尿量水平比较($\bar{x}$± s)

Table 2 Comparison of the urinary frequency and maximum urine volume of patients between two groups before and after treatment($\bar{x}$± s)

		Micturition frequency (Times)	Single maximal urine volume(mL)
Experimental group	Before treatment	15.22± 3.17	112.62± 33.14
	After treatment	6.16± 2.11*#	301.27± 89.62*#
Control group	Before treatment	16.29± 4.81	109.26± 41.72
	After treatment	9.92± 3.16*	276.15± 73.15*

注:与治疗前相比,*P<0.05;与对照组相比,#P<0.05。

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

表 3 两组患者临床疗效的比较【例(%)】

Table 3 Comparison of the clinical curative effect of patients between two groups[n(%)]

	Cure	Excellent	Effective	Invalid	Total effective rate
Experimental group	12(40.0)	9(30.0)	8(26.67)	1(3.33)	29(96.67)*
Control group	5(16.67)	7(23.33)	10(33.33)	8(26.67)	22(73.33)

注:与对照组相比,*P<0.05。

Note: Compared with the control group, *P<0.05.

2.3 两组患者临床治疗效果比较

治疗后,实验组(96.67%)的治疗总有效率显著高于对照组(73.33%)(P<0.05),具体见表 3。

2.4 两组患者血清 P2X3 水平比较

治疗后,两组患者的血清 P2X3 水平与治疗前相比均显著降低(P<0.05);与对照组相比,实验组患者的 P2X3 水平较低(P<0.05),见表 3。

表 4 两组患者治疗前后血清 P2X3 水平比较(ng/mL, $\bar{x}\pm$ s)

Table 4 Comparison of the serum P2X3 level of patients between two groups before and after treatment(ng/mL, $\bar{x}\pm$ s)

	Before treatment	After treatment	t	P
Experimental group	15.73± 4.27	6.14± 1.22	3.387	0.001
Control group	14.28± 3.16	10.33± 2.79	2.431	0.016
t	1.489	3.143	-	-
P	0.089	0.004	-	-

3 讨论

膀胱过度活动症以尿急为主要症状,常伴有尿频、夜尿以及急迫性尿失禁等症状,可表现为逼尿肌的过度活动(detrusor overactivity or detrusor instability)[12]。近年来的研究表明[13]膀胱过度活动症的发病率随着年龄的升高而升高,其女性患者多于男性。因此,膀胱过度活动症已经成为了临床的常见疾病,受到广泛关注。托特罗定是新一代毒蕈碱受体拮抗剂,对 M 受体存在专一性和高度亲和性,可阻断乙酰胆碱与 M 受体结合,抑制逼尿肌收缩,从而改善膀胱的感觉功能,由于其器官选择性强,从而既能保证疗效又最大限度的减少副作用[14]。坦洛新主要作用于存在于膀胱颈和后尿道的肾上腺素受体,通过阻断其受体发挥抑制逼尿肌的收缩、降低尿道压的作用[15]。

近年来,随着 P2X 受体信号途径对于调节膀胱充盈感觉以及膀胱逼尿肌收缩的临床研究的深入,P2X 受体的作用受到重视[16]。研究表明[17]P2X 的各亚型均可在人的膀胱平滑肌上表达,主要分布于膀胱上皮下层所支配的逼尿肌的神经束,与感觉传导相关,是近年来研究发现的一种能够参与体内感觉功能的嘌呤受体。目前认为 P2X3 与膀胱的伤害性疼痛传导有关,其水平的升高能够导致排尿次数的增多[18]。临床研究证实[19,20] P2X3 受体与膀胱的感觉和以及顺应性密切相关,临床的常见疾病如神经源性逼尿肌不稳定、急迫性尿失禁以及间质性膀胱炎等都有膀胱内 P2X3 受体的异常表达,提示其与膀胱过度活动症的发病也具有密切关系。本研究结果显示治疗后,两组患者的 P2X3 水平与治疗前相比均降低,提示其与膀胱过度活动症有关;与对照组相比,实验组患者的 P2X3 水平较低(P<0.05),表明坦洛新联合托特罗定在提高老年膀胱活动度综合征患者临床疗效的同时可显著降低 P2X3 受体水平。

综上所述,坦洛新联合托特罗定能够显著提高老年膀胱活动度综合征患者临床疗效,可能与其降低患者血清 P2X3 受体水平有关。

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