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硝苯地平片联合酒石酸托特罗定片对 TURP 术后膀胱过度活动症的应用效果分析 *

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摘要 目的：探讨硝苯地平片联合酒石酸托特罗定片用于经尿道前列腺电切术(TURP)术后膀胱过度活动症的临床效果及安全性。**方法：**选择 2015 年 8 月至 2017 年 8 月我院接诊的 103 例 TURP 术后出现膀胱过度活动症的患者作为本研究对象，通过随机数表法将其分为试验组 52 例和对照组 51 例。两组均给予常规处理，对照组在此基础上口服酒石酸托特罗定片，2 mg/ 次，2 次 /d；试验组在对照组基础上联合硝苯地平片口服，5 mg/ 次，3 次 /d；两组均连续用药 7d。比较两组临床疗效，治疗前后膀胱过度活动症(OABSS)评分、国际前列腺症(IPSS)评分、膀胱痉挛次数、排尿情况的变化以及不良反应的发生情况。**结果：**治疗后，试验组和对照组临床疗效总有效率分别为 92.31%(48/52)和 76.47%(39/51)，OABSS 评分分别为(2.69± 0.58)分和(4.76± 0.62)分，IPSS 评分分别为(5.02± 0.80)分和(7.86± 1.15)分，24h 膀胱痉挛次数分别为(0.65± 0.48)次和(1.10± 0.61)次，24h 尿急次数分别为(0.88± 0.32)次和(1.59± 0.54)次，24h 排尿次数分别为(5.52± 1.02)次和(7.24± 0.97)次，夜间排尿次数分别为(0.73± 0.45)次和(1.39± 0.70)次，24 h 平均尿量分别为(227.07± 16.68)mL 和(196.65± 15.07)mL，试验组临床总有效率和 24 h 平均尿量均显著高于对照组($P<0.05$)，OABSS 评分、IPSS 评分、24 h 膀胱痉挛次数、24 h 尿急次数及 24h 排尿次数均显著低于对照组($P<0.05$)。两组不良反应发生率比较差异无统计学意义($P>0.05$)。**结论：**硝苯地平片联合酒石酸托特罗定片治疗 TURP 术后膀胱过度活动症患者的临床疗效明显优于单用酒石酸托特罗定片，其可更有效促进膀胱功能恢复，且不增加不良反应。

关键词：经尿道前列腺电切术；膀胱过度活动症；硝苯地平片；酒石酸托特罗定片；临床疗效；安全性

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Analysis of the Effect of Nifedipine Tablets Combined with Tolterodine Tartrate Tablets on the Overactive Bladder Syndrome after TURP*

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ABSTRACT Objective: To study the clinical effect and safety of nifedipine tablets combined with tolterodine tartrate tablets on the overactive bladder syndrome after transurethral resection of the prostate(TURP). **Methods:** 103 patients with overactive bladder syndrome after TURP who received therapy from August 2015 to August 2017 in our hospital were selected as research objects, according to random number table, those patients were divided into the 52 cases of treatment group and the 51 cases of control group. The were given routine treatment, on the basis of this, the control group was taken Tolterodine Tartrate Tablets orally, 2 mg/times, 2 times/d; on the basis of the control group, the treatment group was given nifedipine tablets orally, 5 mg/times, 3 times/d, the 2 groups was used continuously 7d. The clinical effects, the changes of Overactivity of bladder symptom score (OABSS) score, the International Prostatic Disease(IPSS) score, bladder spasm times and urination condition before and after the treatment, and the adverse reactions in the 2 groups were compared. **Results:** After treatment, the total effective rates of the treatment group and the control group were 92.31% (48/52) and 76.47% (39/51) respectively, the OABSS scores were(2.69± 0.58) scores and (4.76± 0.62) scores respectively, the IPSS scores were(5.02± 0.80) scores and(7.86± 1.15) scores respectively, the 24 h bladder spasm times were (0.65± 0.48) times and (1.10± 0.61) times respectively, the 24 h urgent urination times were(0.88± 0.32) times and(1.59± 0.54) times respectively, the 24 h urination times were(5.52± 1.02) times and (7.24± 0.97) times respectively, the nocturnal urination times were(0.73± 0.45)times and(1.39± 0.70) times respectively, 24 h mean urine volume were (227.07± 16.68)mL and (196.65± 15.07)mL respectively, the total clinical effective rate and 24h mean urine

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volume in the treatment group were significantly higher than that of the control group ($P<0.05$), the OABSS scores, IPSS scores, 24 h bladder spasm times, 24 h urgent urination times and 24 h urination times were significantly lower than that of 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:** The clinical effect of Nifedipine tablets combined with tolterodine tartrate tablets on the overactive bladder syndrome after TURP is better than that of tolterodine tartrate tablets alone, which can effectively promote the recovery of bladder function, without increasing adverse reactions.

Key words: Transurethral resection of the prostate; Overactive bladder syndrome; Nifedipine tablets; Tolterodine Tartrate Tablets; Clinical effect; Safety

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前言

前列腺增生是男性较为常见的泌尿系统疾病,发病率可随着年龄的增长而逐渐增加,而随着病情逐渐进展,患者可出现尿频、尿急、尿失禁等症状,严重者甚至出现泌尿系统感染、肾功能损害等,严重影响患者的生活质量[1,2]。手术治疗仍是良性前列腺增生患者的重要治疗方案, 其中经尿道前列腺电切术(TURP)是治疗的金标准,可快速完整的切除增生腺体[3,4]。但临床实践表明 TURP 术后有部分患者会出现膀胱过度活动症,发生率约为 18%~31%,不利于术后膀胱功能的恢复[5,6]。

酒石酸托特罗定片作为一种型强效竞争性的 M 胆碱能受体拮抗剂,可改善尿频、尿急等下尿路症状,是目前治疗膀胱过度活动症的常用药物,但也有部分患者疗效不佳[7,8]。研究表明钙离子通道拮抗剂在治疗逼尿肌不稳定中具有一定辅助效果,可能有助于改善膀胱功能[9]。因此,本研究主要探讨了钙离子通道拮抗剂硝苯地平片联合酒石酸托特罗定片对 TURP 术后膀胱过度活动症患者的临床疗效和安全性,现将结果报道如下。

1 资料与方法

1.1 一般资料

选择我院 2015 年 8 月至 2017 年 8 月接诊的 103 例 TURP 术后膀胱过度活动症患者,纳入标准[10]:① 术前诊断为良性前列腺增生,并于我院顺利完成 TURP 治疗;② TURP 术后出现膀胱过度活动症症状,包括尿频(24 h 排尿次数>8 次)、尿急(突然强烈无法避免的尿意)、夜尿频(起夜>2 次)等症状,每次尿量<200 mL,有尿不尽感,并经尿动力学、B 超、肛门指检等确诊;③ 膀胱过度活动症(OABSS)评分≥ 5 分或国际前列腺症(IPSS)评分≥ 8 分;④ 术后无前列腺增生症状,前列腺特异抗原(PSA)<5 μg/L;⑤ 签署研究知情同意书。排除标准[11]:① 术前膀胱容量<200 mL,和(或)逼尿肌收缩无力等症状;② 术前合并严重尿路感染;③ 术前即有膀胱过度活动症症状;④ 合并严重胃肠道疾病、重症肌无力者;⑤ 合并肝、肾、心等功能严重障碍者;⑥ 对胆碱能受体拮抗剂、钙离子通道拮抗剂等过敏。

通过随机数表法将患者分为试验组 52 例和对照组 51 例,两组年龄、BMI、前列腺增生病程、术前前列腺体积、膀胱过度活动症症状比较差异无统计学意义($P>0.05$),具有可比性,见表 1。

表 1 两组一般资料比较($\bar{x}\pm s$)

Table 1 Comparison of the general information between two groups($\bar{x}\pm s$)

Groups	n	Age(years)	BMI(kg·m^{-2})	Course of prostatic hyperplasia (yers)	Preoperative prostate volume(ml)	Symptoms of overactive bladder		
						Frequent micturition	Urgent urination	Incontinence
Treatment group	52	61.63± 10.41	21.80± 1.58	3.83± 0.81	67.55± 14.04	50(96.15)	52(100.00)	16(30.77)
Control group	51	62.25± 8.80	21.89± 1.51	3.92± 0.56	66.95± 15.29	49(96.08)	51(100.00)	17(33.33)

1.2 治疗方法

两组均给予常规处理内容,包括膀胱训练、盆底肌训练、定时排尿等。对照组在此基础上给予酒石酸托特罗定片(规格:每片 2 mg,厂家:鲁南贝特制药有限公司,国药准字 H20000614)治疗,2 mg/ 次,2 次 /d; 试验组在对照组基础上联合硝苯地平片(规格:每片 10 mg,厂家:山东方明药业集团股份有限公司,国药准字 H37022634)治疗,5 mg/ 次,3 次 /d;均持续治疗 7d。

1.3 观察指标

观察治疗前、治疗 7 d 后以下指标的变化:① OABSS 评分,评价内容包括白天排尿次数、夜间排尿次数、尿急和急迫性尿失禁, 其中分数 3~5 分表示轻度,6~11 分表示中度,≥ 12 分为重度;② IPSS 评分,总共 7 个问题,其中 0~7 分表示轻度,8~19 分表示中度,20~35 分表示重度; ③ 记录两组 24 h 膀胱痉挛次数、24 h 尿急次数、24 h 排尿次数、夜间排尿次数以及 24 h 平均尿量。并记录两组治疗期间不良反应的发生情况。

1.4 疗效评价标准

连续治疗 7 d 后,参考文献[12]评价疗效。治愈:尿频、尿急、夜尿频等症状完全消失, 尿流动力学检查显示正常; 有效:尿频、尿急、夜尿频等症状部分改善,尿流动力学检查显示基本恢复正常;无效:未满足上述标准。总有效率 = 显效率 + 有效率。

1.5 统计学分析

数据采用 SPSS 18.0 软件进行分析。计量资料以 ($\bar{x}\pm s$)表示,组间、组内比较分别使用独立、配对样本 t 检验,计数资料以率表示,组间比较采用 χ^2 检验,以 $P<0.05$ 表示差异具有统

计学意义。

2 结果

2.1 两组临床疗效的比较

治疗后，试验组临床疗效总有效率显著高于对照组（$P<0.05$），见表 2。

表 2 两组临床疗效的比较(例，%)

Table 2 Comparison of clinical efficacy between two groups (n, %)

Groups	n	Cure	Valid	Invalid	Total effective rate
Treatment group	52	30(57.69)	18(34.62)	4(7.69)	48(92.31)*
Control group	51	19(37.25)	20(39.22)	12(25.53)	39(76.47)

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

2.2 两组治疗前后 OABSS 评分、IPSS 评分的比较

两组治疗后 OABSS 评分、IPSS 评分较治疗前均明显降低（$P<0.05$），且试验组 OABSS 评分、IPSS 评分均明显低于对照组($P<0.05$)，见表 3。

表 3 两组治疗前后 OABSS 评分、IPSS 评分的比较($\bar{x}\pm s$，分)

Table 3 Comparison of the OABSS scores, IPSS scores between two group before and after treatment($\bar{x}\pm s$, scores)

Groups	n	Time	OABSS scores	IPSS scores
Treatment group	52	Before treatment	10.17± 1.46	18.54± 2.81
		After treatment	2.69± 0.58*#	5.02± 0.80*#
Control group	51	Before treatment	10.16± 1.57	18.43± 2.99
		After treatment	4.76± 0.62*	7.86± 1.15*

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

2.3 两组膀胱痉挛次数、排尿情况比较

两组治疗后 24 h 膀胱痉挛次数、24 h 尿急次数、24 h 排尿次数、夜间排尿次数较治疗前均明显减少，24 h 平均尿量明显增加($P<0.05$)，试验组 24 h 膀胱痉挛次数、24 h 尿急次数、24 h 排尿次数、夜间排尿次数均明显少于对照组，24 h 平均尿量比对照组显著增多($P<0.05$)，见表 4。

表 4 两组治疗前后膀胱痉挛次数、排尿情况的比较($\bar{x}\pm s$)

Table 4 Comparison of the bladder spasm times, urination condition in two groupsbefore and after treatment($\bar{x}\pm s$)

Groups	n	Time	24 h bladder spasm times (times)	24 h urgent urination times (times)	24 h urination times(times)	Nocturnal urination times (times)	24 h mean urine volume(mL)
Treatment group	52	Before treatment	3.46± 0.50	3.37± 0.69	11.62± 1.66	3.23± 0.47	172.03± 11.53
		After treatment	0.65± 0.48*#	0.88± 0.32*#	5.52± 1.02*#	0.73± 0.45*#	227.07± 16.68*#
Control group	51	Before treatment	3.47± 0.50	3.35± 0.69	11.65± 1.60	3.20± 0.49	171.27± 11.84
		After treatment	1.10± 0.61*	1.59± 0.54*	7.24± 0.97*	1.39± 0.70*	196.65± 15.07*

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

2.4 两组不良反应的发生情况

试验组出现 2 例口干、1 例恶心，未见便秘、感染、消化不良等不良反应，对照组出现 2 例口干，总发生率分别为 5.77%(3/52)、3.92%(2/51)，两组比较差异无统计学意义($P>0.05$)。

3 讨论

膀胱过度活动症是 TURP 治疗后常见的并发症，其发生原因可能是术中对肌肉、神经的损伤以及术后导管气囊对膀胱三角区的压迫等所产生的不良刺激，对逼尿肌功能产生损伤，致使逼尿肌过度活度、膀胱感觉敏感等，形成膀胱过度活动症，加上手术过程中操作不良等因素，可导致膀胱出口持续性梗阻，直接损伤了逼尿肌功能，且容易加重术后疼痛感[13,14]。患者发病后可出现尿急、尿频等症状，不利于术后恢复[15,16]。

目前，针对膀胱过度活动症的治疗方案主要包括膀胱训练、盆底肌训练、生活方式干预和药物治疗等，旨在降低膀胱副交感神经的兴奋性，缓解临床症状，其中药物治疗是临床医学者的研究重点[17,18]。既往临床上通常选择解痉镇痛药物，但由于膀胱痉挛的出血时间迅速且持续时间较短，镇痛药物需要一定时间方可发挥作用，效果往往不理想[19,20]。而抗胆碱能药物的使用逐渐在膀胱过度活动症的治疗中体现出优势，已成为治疗该病的一线药物。酒石酸托特罗定片是一种新型的强效的毒蕈碱受体拮抗剂，可通过对乙酰胆碱、胆碱能受体之间的结合产生竞争性抑制作用，发挥抑制逼尿肌不自主收缩的效果[21,22]。但也仍有部分患者单一用药疗效不明显，较多研究认为联合用药的

方式可有助于提高疗效[23,24]。

近年来，有研究显示逼尿肌不稳的发生可能和平滑肌细胞中的钙稳态失衡密切相关，并认为钙离子通道拮抗剂可能对逼尿肌不稳有一定疗效[25]。Fry CH 等[26]动物实验显示钙离子通道拮抗剂可通过对细胞外钙离子内流产生阻滞作用，从而抑制膀胱逼尿肌的收缩，促进平滑肌松弛，有利于排尿功能的恢复。硝苯地平片属第一代钙离子通道拮抗剂，可舒张平滑肌[27]。张广明等[28]等在常规治疗基础上联合硝苯地平用于女性膀胱过度活动症患者的研究显示其可进一步促进排尿情况，效果明显。

本研究将硝苯地平联合酒石酸托特罗定片用于治疗 TURP 术后膀胱过度活动症患者，结果显示经过 7 d 的治疗后，联合用药的患者在 OABSS 评分、IPSS 评分、膀胱痉挛次数、排尿情况的改善明显优于单独使用酒石酸托特罗定片的患者，且临床疗效总有效率高达 92.31%，高于单独用药患者，分析原因可能是由于逼尿肌本身也是属于一种平滑肌，逼尿肌的不稳和钙稳态失衡之间又存在着密切联系，通过给予硝苯地平的使用可直接作用于逼尿肌平滑肌细胞，减少并延缓 Ca^{2+} 向细胞中的移动，降低细胞内 Ca^{2+} 浓度，修复钙稳态失衡的情况，并对膀胱逼尿肌的收缩产生抑制作用，使逼尿肌松弛，最终改善排尿功能、帮助疾病恢复[29,30]。硝苯地平联合酒石酸托特罗定片可发挥协同作用，阻断 M3 受体作用，进一步促进膀胱功能的恢复。此外，联合用药并未增加药物不良反应，提示用药安全性高。

综上所述，硝苯地平片联合酒石酸托特罗定片治疗 TURP 术后膀胱过度活动症患者的临床疗效明显优于单用酒石酸托特罗定片，其可更有效促进膀胱功能恢复，且不增加不良反应。但本研究也存在着样本量不足、随访时间过短等不足，此后仍需进一步研究。

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