

doi: 10.13241/j.cnki.pmb.2018.04.036

马来酸噻吗洛尔眼液联合拉坦前列素眼液对原发性开角型青光眼患者眼压的影响

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摘要 目的:探讨马来酸噻吗洛尔眼液联合拉坦前列素眼液对原发性开角型青光眼患者眼压的影响。**方法:**选取2015年1月-2016年5月在我院接受治疗的原发性开角型青光眼患者84例,其中给予马来酸噻吗洛尔眼液治疗的42例记为对照组,给予拉坦前列素眼液联合马来酸噻吗洛尔眼液治疗的42例记为观察组,两组均治疗6个月。对比两组患者治疗过程中的眼压变化情况,并对比两组患者的临床总有效率、药物依从性和并发症情况。**结果:**观察组治疗2、4、6个月后的眼压均显著低于对照组($P<0.05$),观察组患者治疗6个月后的眼压差值大于对照组($P<0.05$)。两组患者治疗2、4、6个月后的眼压呈下降趋势,两两比较差异均有统计学意义($P<0.05$)。观察组的临床总有效率95.24%显著高于对照组的80.95%($P<0.05$)。两组患者在治疗过程中结膜充血、眼内异物感、眼睛疼痛、视力模糊、味觉异常以及总并发症发生率对比差异不显著($P>0.05$)。观察组患者的药物依从性比例显著低于对照组($P<0.05$)。**结论:**马来酸噻吗洛尔眼液联合拉坦前列素眼液治疗原发性开角型青光眼患者具有较好的临床疗效,可显著降低患者眼压,同时具有较好的安全性,但药物依从性较差。

关键词:拉坦前列素眼液;马来酸噻吗洛尔眼液;开角型青光眼;高眼压

中图分类号:R775 **文献标识码:**A **文章编号:**1673-6273(2018)04-763-04

Effect of Latanoprost Eye Drops Combine with Timolol Maleate Eye Drops on Intraocular Pressure in Patients with Primary Open Angle Glaucoma

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ABSTRACT Objective: To investigate the effect of Latanoprost eye drops combine with timolol maleate eye drops on intraocular pressure in patients with primary open angle glaucoma. **Methods:** 84 cases patients with primary open angle glaucoma in our hospital from January 2015 to May 2016 were selected, 42 cases were given timolol maleate eye drops treatment as the control group, 42 cases were given latanoprost eye drops combined with timolol maleate eye drops treatment as the observation group, the two groups were treated for 6 months. The intraocular pressure of two groups were compared in the course of treatment, the clinical efficacy, drug compliance and complications of the two groups were compared. **Results:** In the 2,4 and 6 months after the treatment, the intraocular pressure of observation group were significantly lower than the control group ($P<0.05$). The difference between before treatment and 6 months after treatment of observation group were higher than the control group($P<0.05$). Two groups of patients after treatment for 2, 4, 6 months after the intraocular pressure showed a downward trend, the differences were statistically significant ($P<0.05$). The total effective rate of the observation group was 95.24% higher than that of the control group (80.95%) ($P<0.05$). The conjunctival congestion, intraocular foreign body sensation, eye pain, blurred vision, allotropicgeusia, total complication rate of two groups were no statistical significance ($P>0.05$), the drug compliance rate of the observation group was significantly lower than that of the control group($P<0.05$). **Conclusion:** Latanoprost eye drops combine with timolol maleate eye drops has good clinical efficacy in patients with primary open angle glaucoma, can significantly reduce intraocular pressure, and has better security, but the drug compliance is poor.

Key words: Latanoprost eye drops; Timolol maleate eye drops; Open angle glaucoma; High intraocular pressure

Chinese Library Classification(CLC): R775 **Document code:** A

Article ID: 1673-6273(2018)04-763-04

前言

原发性开角型青光眼是一种眼内压间断性或持续性升高的眼病,临床症状常表现为视力下降,眼球疼痛,眼压相对增高,视神经逐渐萎缩及视野缩小^[1,2]。原发性开角型青光眼多是一种双眼性疾病,双眼多先后发病,且是终身进展性疾病,由于

病发后会对视觉神经造成不可逆转的损坏,即使在手术治疗后也很难恢复正常视力,若任由病情发展可导致患者失明^[3,4]。据相关研究报道^[5,6],原发性开角型青光眼是导致我国失明人数上升的主要疾病之一,因此对原发性开角型青光眼患者进行及时有效的治疗具有重要的意义。马来酸噻吗洛尔眼液是目前临床治疗青光眼的常用药,可通过减少房水的生成来起到降低眼压

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(收稿日期:2017-04-28 接受日期:2017-05-22)

的效果,对于原发性开角型青光眼具有良好疗效^[7,8]。拉坦前列素眼液是一种前列腺素类似物,可通过增加房水的流出来间接性的降低角膜和虹膜间房水的含量,进而降低眼内压,起到治疗原发性开角型青光眼的作用^[9,10]。本文旨在探讨马来酸噻吗洛尔眼液联合拉坦前列素眼液对原发性开角型青光眼患者眼压的影响,以期临床选择更合适的治疗方案提供参考,现做如下报道。

1 资料与方法

1.1 一般资料

选取2015年1月-2016年5月在我院接受治疗的青光眼患者84例作为研究对象,纳入标准:①所有患者均符合中华医学会眼科学分会青光眼学组制定的《我国原发性青光眼诊断和治疗专家共识》中有关青光眼的诊断标准^[11];②患者眼内压 ≥ 21 mmHg,房角开放;③患者及其家属对本次研究知情同意。排除标准:①对本次研究药物过敏者;②过往做过眼科手术者;③急性闭角型青光眼病史或房角关闭者;④妊娠期或哺乳期妇女;⑤合并有严重的眼部感染者。采用乱数表法将患者分为观察组和对照组各42例。观察组男24例,女18例,年龄21-71岁,平均年龄 (52.32 ± 10.31) 岁,病程5个月-8年,平均病程 (1.72 ± 0.64) 年,病侧:左眼5例,右眼6例,双眼31例。对照组男23例,女19例,年龄22-70岁,平均年龄 (51.93 ± 11.15) 岁,病程5个月-8年,平均病程 (1.67 ± 0.70) 年,病侧:左眼5例,右眼6例,双眼31例。两组患者的一般资料比较差异无统计学意义($P>0.05$),可行组间比较。本次研究经医院伦理委员会批准通过。

1.2 治疗方法

对照组患者给予马来酸噻吗洛尔滴眼液治疗(武汉五景药

业有限公司,国药准字:H42021078,规格:5 mL:25 mg),1滴/次,2次/d,用药时间为清晨8:30和夜晚20:30,连续用药6个月。观察组患者在对照组的基础上给予拉坦前列素眼液(华润紫竹药业股份有限公司,国药准字H20020198,规格:2.5 mL/瓶),1滴/次,1次/d,用药时间为20:30,连续用药6个月。

1.3 观察指标

分别于治疗前、治疗2个月后、治疗4个月后、治疗6个月后测量两组患者眼内压,同时计算治疗6个月后和治疗前的眼压值之差。疗效评价标准如下^[12],显效:与用药前的基线眼压相比,眼压降低20%及以上,患者临床症状明显好转或完全恢复;有效:眼压较基线眼压降低5%~20%,患者临床症状有所改善;无效:眼压较基线眼压降低5%或以下,患者临床症状无改变。总有效率=(显效例数+有效例数)/总例数 $\times 100\%$ 。分别于治疗前和治疗6个月后测量两组患者的舒张压、收缩压和心率。记录患者的药物依从性和治疗过程中的并发症情况。

1.4 统计学方法

选用SPSS19.0对所有数据进行统计分析,有效率、药物依从性等计数资料以率(%)表示,采用 χ^2 检验,平均年龄、眼压等计量资料以均值 $\pm$ 标准差($\bar{x} \pm s$)表示,采用t检验,以 $\alpha=0.05$ 为检验标准。

2 结果

2.1 两组患者治疗过程中的眼压变化情况对比

治疗前两组患者的眼压比较差异不显著($P>0.05$),观察组治疗2、4、6个月后的眼压均显著低于对照组($P<0.05$),观察组患者治疗6个月后与治疗前的眼压差值大于对照组($P<0.05$)。两组患者治疗2、4、6个月后的眼压呈下降趋势,两两比较差异均有统计学意义($P<0.05$)。详见表1。

表1 两组患者治疗过程中的眼压变化情况对比(mmHg)

Table 1 Comparison of intraocular pressure of the two groups in the course of treatment(mmHg)

Groups	n	Before treatment	2 months after treatment	4 months after treatment	6 months after treatment	The difference between before treatment and 6 months after treatment
Control group	42	25.41 $\pm$ 2.63	19.56 $\pm$ 2.31 ^a	18.35 $\pm$ 1.98 ^{ab}	16.33 $\pm$ 1.57 ^{abc}	9.21 $\pm$ 2.24
Observation group	42	25.39 $\pm$ 2.58	18.33 $\pm$ 2.21 ^a	17.12 $\pm$ 1.79 ^{ab}	15.28 $\pm$ 1.36 ^{abc}	10.47 $\pm$ 2.31
t	-	0.035	2.493	2.986	3.276	2.538
P	-	0.972	0.015	0.004	0.002	0.013

Note: Compared with before treatment, ^a $P<0.05$; Compared with after 2 months after treatment, ^b $P<0.05$; Compared with 4 months after treatment, ^c $P<0.05$.

2.2 两组患者治疗后临床总有效率对比

观察组的临床总有效率95.24%显著高于对照组的80.95%($P<0.05$)。详见表2。

2.3 两组患者治疗过程中并发症情况对比

两组患者在治疗过程中结膜充血、眼内异物感、眼睛疼痛、视力模糊、味觉异常以及总并发症发生率对比差异无统计学意义($P>0.05$)。详见表3。

表2 两组患者治疗后临床总有效率对比

Table 2 Comparison of the total clinical effective rate of the patients in the two groups

Groups	n	Markedly effective	Effective	Invalid	Total effective rate
Control group	42	24(57.14)	10(23.81)	8(19.05)	34(80.95)
Observation group	42	27(64.29)	13(30.95)	2(4.76)	40(95.24)
X ²	-				4.086
P	-				0.043

2.4 两组患者药物依从性对比

观察组患者的药物依从性比例为 54.76%(23/42), 对照组

患者的药物依从性比例为 80.95%(34/42), 两组比较差异有统计学意义($\chi^2=6.604, P=0.010$)。

表 3 两组患者治疗过程中并发症情况对比[n(%)]

Table 3 Comparison of complications between the two groups in the course of treatment[n (%)]

Groups	n	Conjunctival congestion	Intraocular foreign body sensation	Eye pain	Blurred vision	Allotriogeusia	Total complication rate
Control group	42	2(4.76)	2(4.76)	5(11.90)	3(7.14)	4(9.52)	16(38.10)
Observation group	42	4(9.52)	4(9.52)	3(7.14)	5(11.90)	6(14.29)	22(52.38)
X ²	-	0.179	0.179	0.138	0.138	0.454	1.730
P	-	0.672	0.672	0.710	0.710	0.500	0.188

3 讨论

青光眼是仅次于白内障的全球第二大致盲性疾病,因病失明的人群中约有 8.0%是因青光眼所致,虽青光眼的集中人群为中老年人,但是近年来儿童青少年的青光眼患病率不断上升,这一现象已逐渐引起人们的重视,因此寻找快速有效的治疗方案成为近年来眼科工作者的重点^[13,14]。临床上将青光眼分为:原发性青光眼、先天性青光眼、继发性青光眼、混合型青光眼,虽然每种类型的青光眼临床症状及特点有所差别,但均表现为患者眼压升高,因此治疗青光眼的基本思路就是降低患者眼压^[15,16]。将青光眼患者的眼压降低并控制在一定数值内,这个数值内的眼压能够阻止或缓解青光眼患者的视觉神经损害,稳定视觉神经、视网膜神经纤维层,眼压数值范围的上限在临床上称为目标眼压^[17,18]。目标眼压并不是一个确切的数字,而应该根据患者的病情来确定。《中国青光眼临床工作指南》中提到:患者治疗前眼压值越低、病情越严重则设定的目标眼压应相应降低。在为青光眼患者设定治疗方案时,应先设定好目标眼压,再选择最为合适的用药方案^[19,20]。

在本次研究中,观察组治疗 2、4、6 个月后的眼压均显著低于对照组($P<0.05$),两组患者治疗 6 个月后的差值比较差异有统计学意义($P<0.05$)。两组患者治疗 2、4、6 个月后的眼压呈下降趋势,两两比较差异均有统计学意义($P<0.05$)。观察组治疗后的临床总有效率 95.24%显著高于对照组的 80.95%($P<0.05$)。这说明单用马来酸噻吗洛尔滴眼液治疗和马来酸噻吗洛尔眼液联合拉坦前列素眼液治疗原发性开角型青光眼高眼压患者均有较好临床疗效,能有效的降低患者眼压,改善临床症状,但观察组治疗效果优于对照组。究其原因,拉坦前列素眼液中的主要活性成分是前列腺素的类似物,为选择性受体激动药,该物质无活性,但在渗透到角膜后可水解为游离酸,该活性物质对房水的产生并无影响,但可以促进房水通过眼角素层流出,因而能减少眼球中房水的含量,起到降低眼压的作用^[21-23]。拉坦前列素眼液还可疏通青光眼患者眼球小梁筛网结构,进而改善患者的临床症状^[24]。马来酸噻吗洛尔眼液是一种非选择性-肾上腺能受体阻滞剂,能够减少房水的生成,从而从根本上减少眼球中房水的含量,降低患者眼内压,达到治疗原发性开角型青光眼的目的^[25,26]。由于拉坦前列素眼液和马来酸噻吗洛尔眼液降压机制不同且不冲突,因此两种药物联合治疗具有一定的协同作用,可以更好的治疗原发性开角型青光眼患者

^[27,28]。本次研究显示观察组药物依从性低于对照组($P<0.05$),这主要是因为对照组是单药治疗,从而简化了用药过程,因此依从性更高^[29,30]。同时本次研究结果还显示两组患者治疗过程中结膜充血、眼内异物感、眼睛疼痛等并发症比较差异无统计学意义($P>0.05$),这说明两种治疗方案都有近似的安全性,虽然有部分患者在治疗过程中出现一些不良反应,但症状均较为轻微,且在治疗结束停药后均恢复正常,提示两种治疗方案具有较好的安全性。

综上所述,马来酸噻吗洛尔眼液联合拉坦前列素眼液治疗原发性开角型青光眼高眼压患者具有较好的临床疗效,可显著降低患者眼压,同时具有较好的安全性,但药物依从性较差。

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