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布林佐胺联合噻吗洛尔治疗开角型青光眼的临床效果观察及安全性评价*

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摘要 目的：探讨布林佐胺联合噻吗洛尔治疗开角型青光眼的临床效果及安全性。**方法：**选择 2016 年 9 月至 2018 年 9 月在我院接受治疗的 150 例开角型青光眼患者，采用抽签法分为观察组(n=76)和对照组(n=74)。对照组给予噻吗洛尔治疗，观察组在对照组的基础上给予布林佐胺治疗。比较两组患者的临床疗效、治疗前后眼压、视野平均光敏度、视野平均缺损、视网膜神经纤维层厚度(RNFLT)、视盘盘沿面积(NRA)、泪膜破裂时间(BUT)、收缩期峰值血流速度(PSV)、舒张末期血流速度(EDV)及阻力系数(RI)水平的变化及并发症的发生情况。**结果：**治疗后，观察组和对照组总有效率分别为 96.72%，79.66%，观察组显著高于对照组(P<0.05)；观察组眼压、视野平均光敏度、视野平均缺损水平及 RI 均显著低于对照组(P<0.05)，PSV、EDV、BUT 显著高于对照组(P<0.05)。两组并发症总发生率分别为 3.95%、9.46%，差异无统计学意义(P<0.05)。**结论：**布林佐胺联合噻吗洛尔用于开角型青光眼患者的效果显著，可有效改善患者眼压、视敏度，且安全性较高。

关键词：布林佐胺；噻吗洛尔；慢性鼻窦炎；开角型青光眼；安全性

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Curative Efficacy of Brinzolamine Combined with Timolol in the Treatment of Open Angle Glaucomaand Its Safety*

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ABSTRACT Objective: To study the curative efficacy of brinzolamine combined with timolol in the treatment of open angle glaucoma and its safety. **Methods:** 150 patients with open-angle glaucoma who were treated in our hospital from September 2016 to September 2018 were selected and divided into the observation group (n=76) and the control group (n=74) by lottery. The control group was treated with timolol, and the observation group was treated with brinzolamine on the basis of control group. The clinical curative effect, the average intraocular pressure, vision light sensitivity, average visual defect, retinal nerve fiber layer thickness (RNFLT) along the area (NRA), it appears, DVD disk rupture time (BUT), systolic peak velocity (PSV), end-diastolic velocity (EDV), the change of drag coefficient (RI) levels and the occurrence of complications were compared between the two groups before and after treatment. **Results:** After treatment, the total effective rate of observation group and control group was 96.72% and 79.66%, respectively, which was significantly higher in the observation group than that in the control group (P<0.05). The iop, average photosensitivity of visual field, average defect level of visual field and RI in the observation group were significantly lower than those in the control group (P<0.05), while the PSV, EDV and BUT were significantly higher than those in the control group(P<0.05). The total incidence of complications in the two groups was 3.95% and 9.46%, respectively, with no statistically significant difference (P<0.05). **Conclusion:** Brinzolamide combined with timolol has a remarkable effect on patients with open-angle glaucoma, which can effectively improve the intraocular pressure and visual acuity of the patients with high safety.

Key words: Brinzoamine; Timolol; Chronic sinusitis; Open Angle glaucoma; Security

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前言

青光眼是一种不可逆转但可以预防的致盲眼病，机体眼内压间断或持续升高的一种眼病，开角型青光眼包括原发性和继

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发性两组，临床原发性病例居多，临床表现为视盘凹陷增大、视网膜神经纤维层缺损等症状，晚期还会出现视盘萎缩，颜色苍白，伴有全周的视盘旁脉络膜视网膜萎缩，最终导致失明。因此，控制眼压是治疗青光眼最有效的方法[1-3]。

噻吗洛尔是治疗青光眼的常用药物，起效快，耐受性好，但单一用药效果欠佳，不能将眼压降至正常水平[4,5]。布林佐胺是一种新型的碳酸酐酶抑制剂，可减少房水分泌，同时减少碳酸氢盐离子的生成减少了钠和水的转移，从而降低了水的渗透压，从而降低了眼压[6-8]。目前，联合治疗开角型青光眼已成为一种新趋势，但也存在一定的局限性。因此，本研究主要探讨了布林佐胺联合噻吗洛尔治疗开角型青光眼的临床效果及安全性。

1 资料与方法

1.1 一般资料

选择 2016 年 9 月至 2018 年 9 月在我院接受治疗的 150 例开角型青光眼患者。采用抽签法分为 2 组，观察组 76 例，男 45 例，女 31 例，年龄 38~49 岁，平均(43.57± 1.15)岁，病程 2~10 月，平均(6.34± 2.15)月；对照组 74 例，男 40 例，女 34 例，年龄 39~50 岁，平均 (43.41± 1.16) 岁，病程 2~11 月，平均 (6.36± 2.17)月。两组基线资料比较无明显差异，具有可比性。

1.2 诊断标准

西医诊断标准，参照《青光眼专题》[9]，(1)矫正视力≥ 0.3；(2)中央角膜厚度 500~600 μm；(3)影像检查证实。

1.3 纳入标准和排除标准

纳入标准：(1)符合上述诊断标准；(2)年龄＞18 岁；(3)无明显药物过敏史；(4)角膜、泪膜稳定良好；(5)签署知情同意书。排除标准：(1)严重肝肾疾病者；(2)患有意识障碍、精神障碍者；(3)伴有恶性肿瘤患者；(4)妊娠、围产、哺乳期妇女的患者；(5)严重脑血管疾病；(6)未按规定用药；(7)角膜炎、结膜炎者；(8)依从性较差者。

1.4 方法

两组患者均根据需要卧床休息、镇静等基础治疗。对照组给予噻吗洛尔(规格：5 mL：12.5 mg，生产厂家：湖北远大天天明制药有限公司，国药准字：H20045947)1~2 滴，1 d 1~2 次。观察组在对照组的基础上加用布林佐胺(规格：5 mL：50 mg，生产厂家：Alcon Laboratories(UK) Ltd.，国药准字：H20140976)1~2 滴，1 d 1~2 次。

1.5 观察指标

采用眼压测量仪测定眼压；采用光学相干断层扫描技术测定 RNFLT、NRA；BUT 在裂隙灯滴入荧光素测定；采用彩色超声多普勒显像仪测定 PSV、EDV，自动计算 RI；记录两组并发症发生情况。

疗效评定标准：显效：临床症状消失，眼压 10~21 mmHg；有效：临床症状明显改善，眼压 21~30 mmHg；无效：临床症状无改善。

1.6 统计学分析

以 SPSS18.0 软件包处理，符合正态分布的计量资料用均数± 标准差($\bar{x}\pm s$)表示，组间比较采用独立样本 t 检验，计数资料以率表示，组间比较采用 x^2 检验，以 $P<0.05$ 表示差异具有统计学意义。

2 结果

2.1 两组疗效比较

治疗后，观察组和对照组总有效率分别为 96.72%，79.66%，观察组显著高于对照组，差异有统计学意义($P<0.05$)，见表 1。

表 1 两组疗效的比较[例(%)]

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

Groups	n	Excellent	Valid	Invalid	Total effective rate
Observation group	76	48(63.16)	21(27.63)	7(9.21)	69(90.79)
Control group	74	29(19.19)	23(31.08)	22(29.73)	52(70.27)
x^2 value					10.122
P value					0.001

2.2 两组治疗前后眼相关指标的比较

治疗前，2 组眼压、视野平均光敏度及视野平均缺损水平无明显差异；治疗后，2 组眼压、视野平均光敏度及视野平均缺损水平均显著改善，且观察组上述指标均低于对照组($P<0.05$)，见表 2。

表 2 2 组治疗前后眼相关指标比较($\bar{x}\pm s$)

Table 2 Comparison of the eye-related indexes between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	Intraocular pressure(mmHg)		Field average light sensitivity(dB)		Mean field defect(dB)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	76	34.51± 3.92	22.49± 3.56	14.96± 3.74	22.06± 3.94	17.05± 3.94	12.39± 2.74
Control group	74	34.49± 3.89	30.57± 3.02	15.02± 3.79	16.12± 3.25	16.98± 3.85	15.98± 3.29
t value		0.031	14.971	0.098	10.058	0.110	7.269
P value		0.975	0.000	0.922	0.000	0.913	0.000

2.3 2 组治疗前后 RNFLT、NRA 及 BUT 的比较

治疗后，2 组 RNFLT、NRA 水平无显著变化，且观察组 BUT 显著高于对照组(P<0.05)，见表 3。

表 3 2 组 RNFLT、NRA 及 BUT 比较($\bar{x}\pm s$)

Table 3 Comparison of RNFLT, NRA and BUT in two groups before and after treatment($\bar{x}\pm s$)

Groups	n	RNFLT(μm)		NRA(mm)		BUT(s)	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	76	106.51± 5.74	107.24± 6.24	1.65± 0.18	1.62± 0.21	13.74± 2.65	14.56± 2.51
Control group	74	106.85± 6.89	106.67± 6.31	1.64± 0.21	1.63± 0.18	13.81± 2.71	12.25± 2.14
t value		0.329	0.556	0.313	0.313	0.159	6.058
P value		0.743	0.579	0.754	0.755	0.873	0.000

2.4 2 组治疗前后网膜中央动脉血流参数的比较

治疗前，2 组 PSV、EDV 及 RI 水平无明显差异；治疗后，2 组 PSV、EDV 及 RI 水平均较治疗前显著改善，且观察组 PSV、EDV 均高于对照组，RI 低于对照组(P<0.05)，见表 4。

表 4 2 组治疗前后网膜中央动脉血流参数比较($\bar{x}\pm s$)

Table 4 Comparison of blood flow parameters in central omental artery between the two groups before and after treatment($\bar{x}\pm s$)

Groups	n	PSV(cm/s)		EDV(cm/s)		RI	
		Before the treatment	After treatment	Before the treatment	After treatment	Before the treatment	After treatment
Observation group	76	7.79± 2.12	12.54± 2.74	2.79± 0.61	3.96± 0.81	0.65± 0.07	0.58± 0.05
Control group	74	7.81± 2.13	8.09± 2.35	2.81± 0.62	2.94± 0.54	0.66± 0.08	0.64± 0.08
t value		0.058	10.664	0.199	9.049	0.815	5.524
P value		0.954	0.000	0.842	0.000	0.416	0.000

2.5 2 组并发症比较

2 组并发症总发生率为 3.95%、9.46%，组间差异无统计学意义(P<0.05)，见表 5。

表 5 2 组并发症发生情况的比较[例(%)]

Table 5 Comparison of the incidence of complications between the two groups[n(%)]

Groups	n	Conjunctival congestion	Dry eye	Blurred vision	The total incidence of
Observation group	76	1	2	0	3(3.95)
Control group	74	3	2	2	7(9.46)
x^2 value					1.831
P value					0.176

3 讨论

青光眼是我国常见的眼科疾病，可分为原发和继发两组，由视神经病变、视野缺损等原因所致，严重时还会导致患者失明[10-12]。据世界卫生组织调查估计，该病发病率较高，已达到 8000 万人[13-15]。药物治疗是开角型青光眼的首选方法。因此，寻找一种使用安全有效的药物使病情得到控制，在临床具有重要意义。

噻吗洛尔是一种强有力的β 受体阻滞剂，通过抑制睫状体上皮细胞受体介导的生成来降低眼压，是治疗开角型青光眼的常用药物[16-19]，但其单一治疗效果欠佳，故较多学者提出联合治疗，提高临床疗效[20]。布林佐胺与人类睫状体碳酸酐酶同工酶Ⅱ有很强的亲和力，主要通过抑制房水生成的碳酸酐酶同工酶-Ⅱ减少房水的生成，从而而降低眼压，同时该药滴眼剂可避免口服制剂的全身副作用[21-23]。国外研究显示布林佐胺可通过强效抑制碳酸酐酶同工酶的活性而减少房水生成[24]。本研究结果显示联合布林佐胺治疗的患者总有效率为 96.72%，明显高于单独使用噻吗洛尔的患者，且并发症发生率为 3.95%，低于对照组，提示联合布林佐胺治疗开角型青光眼安全有效，能明显提高患者的治疗效果，降低不良反应发生率。Nilanjana Deb-Joardar[25]等研究显示布林佐胺不用口服，不会与集体内碳酸酐酶同工酶结合产生反应，因此减少了并发症。本研究还显

示联合布林佐胺治疗的患者眼压、视野平均光敏度及视野平均缺损水平明显低于对照组，说明联合治疗的患者眼压降低后，机体视神经的损伤得到减少和加重。分析其原因是因为噻吗洛尔能可以有效的降低眼压和血管输出，从而减轻收缩力，减轻视盘和视神经水肿现象，从而治疗青光眼；而布林佐胺与可以有效的降低眼压、视神经水肿，联合用药可提高治疗效果。

青光眼发生时眼压升高，压迫视神经，RNFLT 变薄，NRA 缩小，视野缩小。因此，检测 RNFLT、NRA 可判断患者视力损伤程度[26-28]。BUT 是干眼症常用的指标，是判断泪液分泌是否健康的重要指标。本研究结果显示患者治疗后 RNFLT、NRA 无明显差异，可能是因为视神经损伤恢复需要较长时间，而本研究观察时间较短。联合治疗的患者 BUT 显著高于对照组。Makashova N V[29]等研究也显示布林佐胺治疗原发性开角型青光眼效果显著，可改善患者 BUT 水平。分析其原因是因为噻吗洛尔可引起视神经和眼内血管收缩，使眼内血流量减少；布林佐胺则可引起视网膜内 CO_2 增高，产生扩血管作用，增加眼灌注压。青光眼患者视神经损伤的主要原因是血流减少和阻力指数升高[30]。本结果也显示联合布林佐胺治疗的患者 PSV、EDV 均高于对照组，RI 低于对照组，提示联合治疗能改善患者网膜中央动脉血流参数。

综上所述，布林佐胺联合噻吗洛尔用于开角型青光眼患者的效果显著，可有效改善患者眼压、视敏度，且安全性较高。

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