·临床研究·

固定联合制剂拉坦前列素/噻吗洛尔早晨与晚间应用的比较

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Comparison of once daily morning *vs* evening dosing of fixed combinations latanoprost/timolol

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Abstract

• AIM: To evaluate the effect and safety of morning *vs* evening once daily of fixed combinations latanoprost/timolol maleate therapy in primary open angle glaucoma or in ocular hypertensive patients.

• METHODS: This study was prospective, observational clinial research. All ophthalmology examinations and 24 hours IOP testing were performed at the beginning of the study of latanoprost /timolol maleate. At 1 month follow-up, 24 hours IOP was tested and recorded the results and side effects. One week after stopping treatment, this was then changed to evening dosing once daily with fixed combinations of latanoprost/timolol maleate. After 1 month follow-up, 24 hours IOP was tested, the results and side effects were recorded. The IOP and side effects in two groups were then compared.

• RESULTS: Thirty-two patients completed this study. There was a significant reduction at each time point in the 24-hour diurnal curve of both morning (17.3 ± 3.1mmHg) and evening (17. 1 ± 2. 7mmHg) dosed patients, compared to the baseline IOP (21. 1 ± 3. 3mmHg) (P < 0. 01). When the morning and evening dosing groups were compared directly, the 6:00 time point was statistically lower with evening dosing (16.4 ± 2.3mmHg) *vs* morning dosing (17. 9 ± 2. 8mmHg) (P < 0. 05). A trend was observed, which indicated greater daytime reduction with night-time dosing, whereas morning dosing tended to give lower night-time pressure. There was a significantly lower mean range of diurnal pressure with evening (3. 6 ± 1. 6mmHg) *vs* morning (4. 4 ± 1. 6mmHg) dosing (P < 0. 05). There was no significant difference between two groups of side effects (P > 0. 05).

• CONCLUSION: This study suggests that fixed combinations latanoprost/timolol maleate both given once daily in the morning and evening can effectively reduce the IOP for the 24-hour diurnal curve and are well tolerated with few side effects. There is a significantly stable 24 hour IOP lowering in evening dosed fixed combinations of latanoprost /timolol maleate. .

• KEYWORDS: fixed combinations; glaucoma; intraocular pressure

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摘要

目的:对早晨与晚间应用固定联合制剂拉坦前列素/噻吗洛尔(适利加),1 次/d 治疗开角型青光眼和高眼压症疗效及其安全性的比较。

方法:本研究为前瞻性、观察性的临床研究,患者入组前先进行全面的眼科检查,并进行 24h 眼压测定,早晨开始应用固定联合制剂拉坦前列素/噻吗洛尔,1 次/d,1mo 后随访,测量其 24h 眼压曲线,记录就诊的观察结果及副作用。停用 1wk 后嘱患者改为晚间应用固定联合制剂拉坦前列素/噻吗洛尔,1 次/d,应用 1mo 后再测量 24h 眼压曲线,记录就诊的观察结果及副作用,比较两次随访中 24h 眼压及副作用的差别。

结果:本研究共入组 32 例患者,早晨组平均眼压(17. 3 ± 3. 1mmHg)和晚间组平均眼压(17. 1 ± 2. 7mmHg)均较基线眼压(21. 1 ± 3. 3mmHg)降低(P < 0. 01)。在 6:00 相比较,晚间组的平均眼压(16. 4 ± 2. 3mmHg)较早晨组的平均眼压(17. 9 ± 2. 8mmHg)明显降低(P < 0. 05)。晚间组应用固定联合制剂拉坦前列素/噻吗洛尔可以维持较低的白天眼压,早晨组应用固定联合制剂拉坦前列素/噻吗洛尔可以维持较低的夜间眼压。晚间应用固定联合制剂拉坦前列素/噻吗洛尔平均 24h 眼压波动(3. 6 ± 1. 6mmHg),较早晨组(4. 4 ± 1. 6mmHg)低(P < 0. 05)。两组副作用均无统计学差异(P > 0. 05)。

结论:本研究显示早晨应用固定联合制剂拉坦前列素/噻吗洛尔与晚间应用固定联合制剂拉坦前列素/噻吗洛尔 1 次/d 均能有效的降低 24h 眼压,患者的耐受性好,副作用少,但晚间应用固定联合制剂拉坦前列素/噻吗洛尔更能有效的维持 24h 眼压的稳定。

关键词:固定联合制剂;青光眼;眼压
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0 引言

固定联合制剂拉坦前列素/噻吗洛尔(Xalcom, Pharmacia, Peapack, New Jersey, USA)是拉坦前列素和噻吗洛尔的联合制剂,文献显示其与单用两种药物相比,能够更有效地降低眼压,并有良好的耐受性[1]。以往的研究显示单独每晚1次应用拉坦前列素可以降低眼压26%~35%[2-5],但是我们知道噻吗洛尔夜间无降低眼压的作用,所以本研究对早晨与晚间应用固定联合制剂拉坦前列素/噻吗洛尔,1次/d治疗开角型青光眼和高眼压症的疗效进行比较,以期对今后的临床工作有所帮助。

1 对象和方法

1.1 对象 我们选取2010-06/08在山西省眼科医院就诊的开角型青光眼和高眼压患者32例,记录患者的年龄、性别、诊断、杯盘比、视野及用药情况,并进行24h眼压测定作为基线。排除有外伤史、手术史、干眼,角膜不正常影响压平眼压测量的准确性的患者,排除有严重的呼吸系统疾患、心血管疾病、肝肾功能不全的患者。

1.2 方法 患者每天早晨8:00应用固定联合制剂拉坦前列素/噻吗洛尔,1次/d,1mo后随访时记录就诊的观察结果及副作用,测量其24h眼压;停用1wk后再嘱患者改为每日晚上20:00应用固定联合制剂拉坦前列素/噻吗洛尔,1次/d,1mo后随访时再记录就诊的观察结果及副作用,再测量24h眼压,比较两者的差别。24h眼压每4h测量1次,患者再医院留观1d。压平眼压计每次测量3次,取其平均值。

统计学分析:采用SPSS 13.0软件进行统计学分析,三组眼压比较采用重复测量的方差分析,两两比较采用LSD-t法,各时间点两组眼压比较采用t检验,两组副作用比较采用卡方检验进行分析,$P<0.05$为差异有统计学意义。

2 结果

2.1 早晚用药疗效的比较 患者32例中,男18例,女14例。平均年龄65.9±11.8岁,5例患者为高眼压症,其余为27例患者为开角型青光眼,随访2mo。入组前用一种抗青光眼的药物为7例患者,两种以上抗青光眼的药物的患者为25例。所有患者均为既往治疗未能充分降低眼压或希望简化治疗而换用固定联合制剂拉坦前列素/噻吗洛尔每日给药1次。换用固定联合制剂拉坦前列素/噻吗洛尔后,分组主效应有统计学差异,早晨组和晚间组眼压均低于基线眼压($P<0.05$),时间主效应无统计学差异($P>0.05$),分组与时间的交互效应无统计学意义($P>0.05$)。早晨组和晚间组各时间点眼压比较,在6:00晚间组的平均眼压(16.4±2.3mmHg)较早晨组的平均眼压(17.9±2.8mmHg)明显降低($P<0.05$,表1)。其他时间段的眼压相差不明显($P>0.05$)。早晨组平均眼压(17.3±3.1mmHg)和晚间组平均眼压(17.1±2.7mmHg)均较基线眼压(21.1±3.3mmHg)降低($P<0.01$),早晨组和晚间组平均眼压无统计学差异($P>0.05$)。24h眼压波动早晨组较夜间组大($P>0.05$)。

2.2 副作用 表2显示,换用固定联合制剂拉坦前列素/噻吗洛尔的副作用,两组副作用均无统计学差异($P>0.05$)。

表1 基线与换用适利加后早晨与晚间用药的24h眼压

($\bar{x}\pm s$, mmHg)

	基线眼压	早晨用药	夜间用药
6:00	27.2±2.6	17.9±2.8	16.6±2.3
10:00	24.5±2.7	18.1±3.0	18.2±3.1
14:00	21.6±3.1	17.8±3.8	17.6±2.1
18:00	22.5±2.9	16.8±3.2	16.8±2.4
22:00	19.7±3.4	16.3±2.5	16.9±2.6
2:00	19.6±3.2	15.6±2.6	17.1±2.1
24h眼压波动	5.7±1.6	4.4±1.6	3.6±1.6

表2 换用固定联合制剂拉坦前列素/噻吗洛尔的副作用 例

副作用	早晨用药	晚间用药
结膜充血	6	6
眼部刺激症状	3	3
眼部炎症反应	3	2
干眼症	1	1
眼睑皮肤反应	1	1

3 讨论

固定联合制剂拉坦前列素/噻吗洛尔(适利加)是近年上市的新的抗青光眼药物。许多研究显示,拉坦前列素和噻吗洛尔联合用药可比单独的应用拉坦前列素或噻吗洛尔明显的降低眼压[6],分别降低1.1mmHg和2.9mmHg。但是拉坦前列素夜间降眼压的效果要好于白天用药[2,7],而噻吗洛尔眼药水夜间用药不如白天用药,那么固定联合制剂拉坦前列素/噻吗心胺是早晨用药还是夜间用药,两种方式用药对24h眼压的控制情况文献中未有报道,我们通过对早晨与晚间应用固定联合制剂拉坦前列素/噻吗洛尔(适利加),1次/d治疗开角型青光眼和高眼压症疗效的比较,确定降眼压的效果及安全性。

本研究选取开角型青光眼和高眼压的患者,分别早上用固定联合制剂拉坦前列素/噻吗洛尔(适利加),1次/d,1mo测量24h眼压后停药1wk后改为晚上用药,1次/d,1mo后再测量24h眼压,比较两次降眼压效果及其副作用。

以往的文献显示,固定联合制剂拉坦前列素/噻吗洛尔(适利加)1次/d的疗效优于各自单用的疗效[3,4,8],并且至少与其它两种给药次数多的药物联合制剂的疗效相似[9-11],本研究结果与这些试验一致。32例患者参加这次研究,早晨组(17.3±3.1mmHg)和晚间组(17.1±2.7mmHg)的24h眼压曲线明显较基线眼压(21.1±3.3mmHg)降低($P<0.01$)。早晨组与晚间组在6:00相比较,晚组间(16.4±2.3mmHg)较早晨组(17.9±2.8mmHg)眼压明显降低($P<0.05$)。晚间应用适利加可以维持较低的白天眼压,早晨应用适利加可以维持较低的晚间眼压。晚间应用适利加平均24h眼压波动(3.6mmHg)较早晨应用适利加平均24h眼压波动(4.3mmHg)明显低($P<0.05$),更能维持24h眼压的稳定性。这提示我们在今后的临床应用中要根据患者的24h眼压来嘱患者早晨或晚间用药,如果24h眼压波动较大者,选用晚间用药。两组副作用无区别,结膜充血及眼部刺激是最常见的副作用,在整个随访期间,无患者中途停药,患者对每日给药1次治疗方案的依从性好,很少出现忘记使用滴眼液的情况,更能够容易遵医嘱使用滴眼液。

本研究显示早上应用适得加与晚间应用适利加1次/d均能有效的降低24h眼压,且副作用少,但晚上应用适利加更能有效的维持24h眼压的波动。

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