Effectiveness and Safety of Dorzolamide–Timolol Alone or Combined with Latanoprost in Open-Angle Glaucoma or Ocular Hypertension

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BACKGROUND: Treatment of glaucoma is aimed at reducing intraocular pressure (IOP) to prevent further damage to the optic nerve. For patients who do not respond to monotherapy, combination treatment may be effective in achieving therapeutic reduction or target IOP.

OBJECTIVE: To evaluate the effectiveness and safety of dorzolamide 2% with timolol 0.5% alone or combined with latanoprost in reducing IOP in a real-world setting.

METHODS: A prospective, open-label, multicenter, nonrandomized interventional study was designed. Three hundred fifty patients with primary open-angle glaucoma or ocular hypertension and uncontrolled IOP after latanoprost monotherapy for 4 or more weeks were treated with combination dorzolamide–timolol twice daily added to their existing latanoprost therapy (D/T-Add-On; n = 280) or dorzolamide–timolol twice daily monotherapy (D/T-Switch; n = 70). The primary effectiveness outcome measure was the change in IOP after 6 and 12 weeks of treatment.

RESULTS: Of the total population, 313 patients completed this trial (248 D/T-Add-On; 65 D/T-Switch). After 12 weeks, the mean ± SD IOP decrease was –6.3 ± 3.6 mm Hg (–28.1%) and –5.8 ± 4.9 mm Hg (–23.5%) in the D/T-Add-On and D/T-Switch groups, respectively (both $p < 0.001$). Therapeutic response rates (defined as IOP reduction >20%) after 12 weeks of treatment for the D/T-Add-On and the D/T-Switch groups were 66.4% (186/280) and 52.9% (37/70), respectively. There were 116 predominantly mild, nonserious adverse events attributed to the study drugs, reported by 86 (24.6%) patients. The most frequent adverse events were eye irritation (n = 42; 12.0%) and taste perversion (n = 15; 4.3%). No serious adverse events related to the study medications were reported.

CONCLUSIONS: In patients with primary open-angle glaucoma or ocular hypertension and elevated IOP while on monotherapy with latanoprost, switching to dorzolamide–timolol or combining dorzolamide–timolol with latanoprost are effective and safe treatment options for reducing IOP and achieving therapeutic response.

KEY WORDS: dorzolamide–timolol, intraocular pressure, latanoprost, ocular hypertension, open-angle glaucoma.

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First-line treatment for patients with primary open-angle glaucoma (POAG) and ocular hypertension (OHT) consists of monotherapy to reduce intraocular pressure (IOP); however, many patients remain uncontrolled and may experience deterioration of their condition despite treatment. For some patients with insufficient response to monotherapy, switching to another agent or initiating combination therapy may be beneficial. These patients may benefit from a strategy that combines drugs with different mechanisms of action to induce a greater reduction in IOP and achieve therapeutic response. The results of controlled clinical trials have shown that combination therapy consisting of β-adrenergic antagonists, carbonic anhydrase inhibitors, and prostaglandin analogs is effective in reducing IOP for patients not responding to monotherapy.[1-5] However, generalization of the results from controlled clinical trials to the target population and a real-life setting is often difficult due to the highly selected sample of patients and the application of treatment under strict protocols and controlled conditions. Properly designed Phase 4, open-label studies with treatment protocols and subject selection procedures that more closely emulate real-world practice are required to address these issues and to provide data that better represent the real-life setting.

The triple drug regimen of fixed combination dorzolamide 2.0% and timolol 0.5% (dorzolamide–timolol) added to latanoprost in patients not at target IOP with their existing latanoprost monotherapy has not been previously assessed in a real-life, routine clinical care setting. The Phase 4 study presented here used an open-label, prospective cohort design to assess the real-life safety and effectiveness of adding dorzolamide–timolol to the existing latanoprost monotherapy regimen or replacing latanoprost monotherapy with dorzolamide–timolol in patients with

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POAG or OHT who had not achieved their therapeutic target after treatment with latanoprost monotherapy.

Methods

STUDY DESIGN

This was an open-label, prospective cohort, multicenter study (investigators listed in Appendix I). The study was approved by an independent ethics review board (IRB Services, Aurora, Ontario, Canada). Eligible patients signed an informed consent form prior to the performance of study procedures. Follow-up duration was 12 weeks, with clinical assessments at baseline, 6 weeks, and 12 weeks. All visits and assessments were scheduled to be conducted in the morning, at approximately the same time for each patient.

At baseline, patients were assessed for eligibility and underwent a review of their medical history, with emphasis on glaucoma history and associated risk factors, specifically presence of hypertension, diabetes, or a family history of glaucoma. Vital sign measurements, prior and concomitant medication use, and adverse effects related to the patient's existing latanoprost therapy were recorded. Ocular assessments of IOP (Goldmann applanation tonometry), visual acuity (best-corrected Snellen), visual field (unless performed in the previous 12 mo) and slit-lamp examination including funduscopy were also performed. Visual field loss was described as the presence or absence of each of the following characteristics for each eye: generalized depression, nasal step, arcuate scotoma, hemifield loss, and central island. The patient's "worse eye," based on IOP measurement and the physician's decision, was selected and evaluated during the study.

For follow-up visits at 6 and 12 weeks, patients were instructed to administer their study medications at least 2 hours before their scheduled assessment. During the follow-up visits, vital sign and IOP measurements on the worse eye were conducted and changes to concomitant drugs were recorded. Assessment of treatment adherence was ascertained by the number of missed doses of study medication since the previous visit as reported by the patient. Details regarding all adverse events were documented. During the final study visit at 12 weeks, the slit-lamp examination was repeated.

PATIENTS

Patients were recruited from a random sample of 33 community-based ophthalmologists from across Canada. The following inclusion criteria were applied to identify potentially eligible subjects:

1. age 18 years or older;
2. diagnosis of POAG or OHT;
3. treatment with latanoprost monotherapy for 4 or more weeks, but IOP remained uncontrolled, defined as: (a) IOP greater than 21 mm Hg with latanoprost monotherapy; (b) deterioration of the visual field regardless of IOP target; (c) target IOP not achieved with latanoprost monotherapy; and (d) insufficient response to latanoprost monotherapy (IOP reduction <15%);
4. with the exception of POAG or OHT, in otherwise good health;
5. women could not be pregnant or breast-feeding, and if of child-bearing potential, must be using an effective method of contraception.

The following exclusion criteria were applied:

1. presence of fundus pathology likely to change during the study or to influence IOP (background of diabetic retinopathy permitted);
2. presence of any contraindication to the use of dorzolamide–timolol including bronchospasm, chronic obstructive pulmonary disease, or severe renal impairment (serum creatinine >1.7 mg/dL or creatinine clearance <30 mL/min);
3. use of any medication, including oral carbonic anhydrase inhibitors, that is contraindicated to the use of dorzolamide–timolol or that would produce significant risk to the patient or influence IOP (eg, clonidine, corticosteroids, oral β-blocking agents);
4. treatment with any other investigational drug within 4 weeks.

TREATMENT ASSIGNMENT

Treatment was based on the previous response to latanoprost treatment. Specifically, patients who fulfilled inclusion criterion 3(a), 3(b), or 3(c) were treated with combination therapy of dorzolamide–timolol and latanoprost (D/T-Add-On group); for patients with insufficient response to latanoprost treatment (inclusion criterion 3(d)), latanoprost therapy was discontinued and was replaced by dorzolamide–timolol (D/T-Switch group). Patients who fulfilled criterion 3(d) received priority with respect to treatment assignment over patients who met inclusion criteria 3(a), 3(b), and 3(c).

Subjects in the D/T-Add-On group administered 1 drop twice daily (morning and bedtime) of fixed combination dorzolamide 2% plus timolol 0.5% and 1 drop once daily of latanoprost 0.005% as prescribed. Subjects in the D/T-Switch group had their existing latanoprost therapy discontinued and administered 1 drop twice daily (morning and bedtime) of fixed combination dorzolamide 2% plus timolol 0.5% only. All patients were treated for 12 weeks.

OUTCOME MEASURES

The primary effectiveness outcome measure was the absolute and percent change in IOP between baseline and 12 weeks of treatment. Secondary effectiveness outcome measures were the absolute and percent change in IOP between

baseline and 6 weeks and between 6 and 12 weeks and the proportion of patients achieving a therapeutic response at 12 weeks. Therapeutic response was defined as a decrease greater than 20% in IOP from baseline. The proportion of patients achieving greater than 10%, greater than 15%, greater than 25%, and greater than 30% IOP reduction from baseline was also assessed. Safety was assessed by the incidence of treatment-emergent adverse events.

STATISTICAL ANALYSIS

Descriptive statistics were produced for all study variables including patient characteristics, treatment, and outcome variables. For continuous variables, the mean ± SD and 95% confidence interval of the mean were reported. For categorical variables, frequency distributions were reported. Statistical significance was defined as p less than 0.05. The sample size requirement of 207 patients per group with an estimated 15–20% attrition rate was calculated for 5% significance and 80% power to detect a 20% change in IOP between the baseline and 12-week assessment.

Student's *t*-test for paired samples was used to test the statistical significance of within-group changes in IOP from baseline to 6 and 12 weeks and between 6 and 12 weeks. Repeated measures analysis of variance was used to assess the overall effect of time on IOP for each group. To be compatible with the real-world setting of this study and in accordance with the intent-to-treat approach, effectiveness analyses were conducted on observed cases, including all patients, regardless of adherence to the study protocol. No imputations or replacement of missing data were used. Data on patients who withdrew during the study were reported up to the time of the last known follow-up. Patients withdrawn for any reason were considered treatment failures. Patients who received at least one dose of the study medication were included in the safety analysis. Adverse events were described using the MedDRA dictionary of terms, version 9.0. The analyses were performed using SPSS version 12.0 for Windows (SPSS Inc., Chicago, IL).

Results

PATIENT DISPOSITION

A total of 350 eligible patients from across Canada were enrolled in the study. Of these, 70 (20.0%) patients fulfilled inclusion criterion 3(d) and were therefore assigned to the D/T-Switch group. The remaining 280 (80.0%) patients were assigned to the D/T-Add-On group on the basis of inclusion criteria 3(a) (n = 124; 35.4%), 3(b) (n = 21; 6.0%), and 3(c) (n = 137; 39.1%). There were 37 (10.6%) patients who were discontinued from the study. Of these, 15 (40.5%) were withdrawn before the 6-week assessment and 22 (59.5%) after this visit. Twenty-three (6.5%) patients withdrew due to adverse events, 5 (1.4%) were lost to follow-up, 5 (1.4%) withdrew consent, 3 (0.8%) involved protocol violations, and 1 (0.3%) patient was withdrawn by the treating physician due to lack of efficacy.

PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

The patient baseline characteristics and demographics are described in Table 1. During the 12 months prior to study entry, an abnormal visual field was reported in 248 (70.9%) patients, primarily as generalized depression (28.0%), arcuate scotoma (27.1%), and nasal step (26.9%). Normal findings for the baseline slit-lamp examination were reported for the majority (88.9–98.0%) of patients, depending on the specific structure examined. Ten (2.9%) patients reported having taken timolol in the past and 1 (0.3%) patient had taken dorzolamide. No patients reported previously taking combination dorzolamide–timolol.

IOP MEASUREMENTS

The majority of the IOP measurements (62.9% of baseline, 83.3% at week 6, 85.0% at week 12) were taken between 0700 and 2359. IOP measurements for the 2 treatment groups at each visit are described in Table 2. For both groups, significant ($p < 0.001$) mean absolute and percent

Table 1. Demographics and Baseline Patient Characteristics

Characteristic	Dorzolamide–Timolol Add-on (n = 280)	Dorzolamide–Timolol Switch (n = 70)	Total (N = 350)
Age, y (mean ± SD)	68.6 ± 11.3	66.4 ± 11.4	68.2 ± 11.3
Age ≥65 y, n (%)	184 (65.7)	37 (52.9)	221 (63.1)
Sex, n (%)			
female	161 (57.5)	37 (52.9)	198 (56.6)
male	119 (42.5)	33 (47.1)	152 (43.4)
Race, n (%)			
white	238 (85.0)	68 (97.1)	306 (87.4)
Asian	18 (6.4)	2 (2.9)	20 (5.7)
black	18 (6.4)	0 (0.0)	18 (5.1)
other	6 (2.1)	0 (0.0)	6 (1.7)
Glaucoma diagnosis, eye affected, n (%)			
both eyes	245 (87.5)	59 (84.3)	304 (86.9)
right eye only	18 (6.4)	5 (7.1)	23 (6.6)
left eye only	17 (6.1)	6 (8.6)	23 (6.6)
Comorbidities and glaucoma risk factors, n (%)			
hypertension	140 (50.0)	39 (55.7)	179 (51.1)
family history of glaucoma	89 (31.8)	23 (32.9)	112 (32.0)
visual field defect	197 (70.4)	51 (72.9)	248 (70.9)
myopia	74 (26.4)	25 (35.7)	99 (28.3)
type 2 diabetes	41 (14.6)	9 (12.9)	50 (14.3)
ocular hypertension	25 (8.9)	2 (2.9)	27 (7.7)

reductions in IOP were observed at 6 and 12 weeks of follow-up compared with baseline (Table 3). The changes in IOP between weeks 6 and 12 were not statistically significant for either group.

Therapeutic response rates for the 2 study groups are described in Table 4. After 12 weeks of treatment, 223 (63.7%) of the 350 patients enrolled had achieved therapeutic response greater than 20% IOP reduction from baseline. Therapeutic response greater than 20% was achieved by 186 (66.4%) patients in the D/T-Add-On group and 37 (52.9%) patients in the D/T-Switch group.

ADVERSE EVENTS

There were 116 (D/T-Add-on = 85; D/T-Switch = 31) nonserious adverse events reported by 86 (24.6%) patients (D/T-Add-on = 61 [21.8%]; D/T-Switch = 25 [35.7%]), which were attributed by the treating physician to the study medications. The majority of these events were mild or moderate (76.7% and 19.0%, respectively). The most frequently reported adverse events were eye irritation (n = 42; 12.0%) and bad taste in the mouth (n = 15; 4.3%). There were 5 treatment-emergent nonserious adverse events of severe intensity (eye irritation, diarrhea, nausea, gout, and headache) reported by 1 (0.4%) patient in the D/T-Add-On group. No serious adverse events were reported.

ADHERENCE

Overall adherence to treatment was high. The majority of the patients (71.4% at the 6-week assessment and 67.3% at the 12-week assessment) reported not missing any dorzolamide–timolol treatment doses. For dorzolamide–timolol, the mean number of drops missed was 6.6 of 84 (7.9%) at the 6-week assessment and 4.6 of 168 (2.7%) at the 12-week assessment. For latanoprost, the mean number of drops missed was 2.1 of 42 (5.0%) and 3.5 of 84 (4.2%) at the 6- and 12-week assessments, respectively.

Table 2. Intraocular Pressure

Visit	Dorzolamide–Timolol Add-on, mm Hg	Dorzolamide–Timolol Switch, mm Hg
Baseline		
n	280	70
mean ± SD	21.89 ± 4.50	22.74 ± 4.77
95% CI	21.36 to 22.42	21.61 to 23.88
Week 6		
n	266	69
mean ± SD	15.86 ± 3.93	17.63 ± 3.58
95% CI	15.38 to 16.33	16.77 to 18.49
Week 12		
n	248	65
mean ± SD	15.64 ± 3.84	17.31 ± 3.72
95% CI	15.16 to 16.12	16.39 to 18.23

Discussion

Glaucoma and, specifically, POAG refer to a group of chronic and progressive disorders that lead to damage of the optic nerve and gradual, irreversible loss of vision.[6,7] Recent evidence and current guidelines suggest that early and aggressive reduction of IOP may not only prevent optic nerve damage and visual field loss, but also preclude the progression of glaucoma.[6,8-10]

Table 3. Change in Intraocular Pressure

Time Period	Dorzolamide–Timolol Add-on, mm Hg		Dorzolamide–Timolol Switch, mm Hg	
	Absolute Change	% Change	Absolute Change	% Change
Week 6 to baseline				
n	266		69	
mean ± SD	–6.01 ± 3.72	–26.72 ± 14.06	–5.20 ± 4.91	–20.77 ± 17.88
95% CI	–6.46 to –5.56	–28.42 to 25.02	–6.38 to –4.02	–25.06 to –16.47
p value[a]	0.001	0.001	0.001	0.001
Week 12 to baseline				
n	248		65	
mean ± SD	–6.31 ± 3.56	–28.08 ± 13.00	–5.81 ± 4.85	–23.47 ± 17.98
95% CI	–6.76 to –5.87	–29.70 to –26.45	–7.02 to –4.61	–27.92 to –19.01
p value[a]	0.001	0.001	0.001	0.001
Week 12 to week 6				
n	248		65	
mean ± SD	–0.03 ± 2.35	0.98 ± 15.32	–0.16 ± 3.04	0.10 ± 18.79
95% CI	–0.32 to 0.26	–0.94 to 2.90	–0.91 to 0.60	–4.56 to 4.75
p value[a]	0.840	0.314	0.676	0.966
Overall p value[b]	<0.001	NA	<0.001	NA

NA = not applicable.
[a]Based on paired Student's *t* test for within groups.
[b]Based on repeated-measures analysis of variance for overall time effect.

We evaluated the real-life therapeutic effectiveness of adding dorzolamide–timolol to latanoprost or switching from latanoprost to dorzolamide–timolol in patients with POAG or OHT who had not achieved their therapeutic target after treatment with latanoprost monotherapy. Given that dorzolamide and timolol both mediate the inflow of aqueous humor[1,11-16] while latanoprost increases humor outflow, combination treatment with these 3 agents is believed to be more effective in reducing IOP compared with any of these 3 drugs alone. The results demonstrate that combination therapy with dorzolamide–timolol is an effective and safe choice for add-on or replacement therapy in this patient population. Clinically important IOP reductions and therapeutic response rates were achieved for both study treatment groups.

Overall, these data are in agreement with results from clinical trials that have demonstrated that combining drugs may be more effective in reducing IOP than monotherapy.[2-4,17-19] Previous studies that examined the combinatory effects of dorzolamide, timolol, and latanoprost were conducted as open-label, randomized trials, in contrast to the real-life nature of our study in which treatment assignment was based on the patient's previous response to therapy.[20,21] In particular, the effectiveness of adding latanoprost to dorzolamide and timolol in patients with uncontrolled IOP after dorzolamide and timolol treatment was previously examined.[20] In patients who had uncontrolled IOP after treatment with dorzolamide and timolol, addition of latanoprost for one week was reported to produce a mean IOP reduction of 3.1 mm Hg (–16%), and 36.3% of patients experienced IOP reductions of more than 20%.[20] This compares with a mean IOP reduction of 6.3 mm Hg (–28.1%) and 66.4% of patients achieving a therapeutic response of more than 20% in the present study when dorzolamide–timolol was added to latanoprost. The shorter time of follow-up, as well as the addition of 1 drug to the preexisting 2-drug regimen in the former study, likely accounts for this difference in treatment effect. Additionally, a recent meta-analysis reported a pooled mean IOP change of –4.9 mm Hg (95% CI –5.3 to –4.5) at peak for patients given fixed combination dorzolamide–timolol after a timolol run-in period.[22]

Table 4. Therapeutic Response Rates at Week 12

Change in IOP from Baseline, %	Dorzolamide–Timolol Add-on, n (%) (n = 280)	Dorzolamide–Timolol Switch, n (%) (n = 70)
>10	233 (83.2)	53 (75.7)
>15	208 (74.3)	47 (67.1)
>20	186 (66.4)	37 (52.9)
>25	152 (54.3)	27 (38.6)
>30	116 (41.4)	21 (30.0)

IOP = intraocular pressure.

This decrease is slightly less than that observed in our study, where patients who were switched to dorzolamide–timolol experienced a mean IOP change of –5.8 mm Hg (95% CI –7.0 to –4.6). However, the population sample in the meta-analysis may have included timolol nonresponders, whereas patients in our study were latanoprost nonresponders.

Results of controlled clinical trials provide evidence regarding efficacy. However, due to the fact that controlled clinical trials enroll very selective patients who are treated under ideal conditions, the efficacy results may not always be comparable with effectiveness observed in the real-life setting and routine clinical practice. Other factors that may be related to this discordance include lack of homogeneity in patient characteristics, adherence to treatment, accessibility of care, and follow-up. Evaluations of interventions in real-life, open-label settings are therefore essential to demonstrate treatment benefit from a population-based epidemiologic perspective. Furthermore, the accumulation and aggregation of data from ongoing postmarketing studies are required to ensure that the treatment is safe and to detect signals of rare but potentially serious adverse effects. Regional, observational, real-life studies are also required to provide data and evidence of the safety and effectiveness of marketed drugs within the context of different healthcare systems that affect clinical practice and accessibility to care.

Potential limitations of single cohort, Phase 4 studies are related to the lack of a control group. However, in the current study, patients had not responded to previous treatment. Therefore, the baseline values provide control data for each patient. Given that comparisons are assessed within groups, any change in IOP should be attributed to the new treatment. Furthermore, the paradigm is compatible with a real-life setting and routine clinical practice where patients who do not respond to treatment are either treated with add-on therapy or switched to alternative treatments. Another potential weakness of this study is that treatment allocation was not randomized and patients were assigned to study groups based on their response to previous treatment with latanoprost. However, this allocation of treatment better simulates the real-life setting where physicians make treatment decisions based on the patient's response to previous therapy. The open-label design may also have introduced response bias. However, this design is necessary for emulating the real-life setting. Another perceived limitation was that the sample size requirement for the switch group was not met. However, for this group, the change from baseline was statistically significant; thus, power calculations were no longer relevant. Lastly, our assessment of adherence may have been limited by memory problems in the elderly.

The strengths of our study include the potential to generalize the results to the target Canadian population. This

was accomplished by recruiting patients from a random sample of community-based ophthalmologists from across Canada. The results of the study emulate a real-life setting, with direct implications on clinical practice, by imposing less restrictive inclusion criteria and by the inclusion of all patients in the analysis regardless of adherence to the protocol. The prospective design and sufficient sample size to detect clinically important effects are additional strengths of the study.

Conclusions

For patients with glaucoma who have elevated IOP while on treatment with latanoprost monotherapy, switching latanoprost to dorzolamide–timolol or combining dorzolamide–timolol with latanoprost are effective and well-tolerated treatment options for reducing IOP and achieving therapeutic response. The real-life nature of these results supports the benefit of combination therapy for the effective reduction of IOP in patients with open-angle glaucoma.

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Appendix I. List of Investigators

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Efectividad y Seguridad de Dorzolamida–Timolol sólo o en Combinación con Latanoprost para el Tratamiento de Glaucoma de Ángulo Abierto o Hipertensión Ocular

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EXTRACTO

TRASFONDO: El tratamiento de glaucoma está orientado a reducir la presión intraocular (IOP) para prevenir daño al nervio óptico. En los pacientes que no responden a monoterapia, la terapia de combinación puede ser efectiva en lograr una reducción terapéutica o llegar al IOP deseado.

OBJETIVOS: Evaluar la efectividad y seguridad de dorzolamida al 2% con timolol al 0.5% sólo o en combinación con latanoprost para reducir IOP en un escenario "de la vida real."

MÉTODOS: Este es un estudio prospectivo, abierto, multicentro, no aleatorizado. Trescientos cincuenta pacientes con glaucoma de ángulo abierto o hipertensión ocular que tenían IOP descontrolada después de haber recibido monoterapia con latanoprost por 4 semanas o más recibieron tratamiento con una combinación de dorzolamida-timolol 2 veces al día con su terapia existente de latanoprost (D/T-Add-On) o dorzolamida-timolol 2 veces al día como monoterapia (D/T-Switch). La medida de resultado principal fue el cambio en IOP después de 6 a 12 semanas de tratamiento.

RESULTADOS: Trescientos trece pacientes completaron el estudio, 248 en el D/T-Add-On y 65 en el D/T-Switch. Después de 12 semanas, el promedio de reducción (desviación estándar) en IOP fue de –6.3 (3.6) mm Hg (–28.1%) en el grupo D/T-Add-On y –5.8 (4.9) mm Hg (–23.5%) en el grupo D/T-Switch. Ambas reducciones fueron estadísticamente significativas ($p < 0.001$). Las tasas de respuesta terapéutica (definidas como reducciones en IOP mayores de 20%) después de 12 semanas de tratamiento para el grupo de D/T-Add-On y el grupo de D/T-Switch fueron 66.4% (186/280) y 52.9% (37/70), respectivamente. Hubo 116 eventos adversos no serios predominantemente leves atribuibles a los medicamentos en el estudio que fueron reportados por 86 (24.6%) de los pacientes. Los eventos adversos más frecuentes fueron irritación de la vista (n = 42; 12.0%) y cambios en el sentido de sabor (n = 15; 4.3%). No se reportaron eventos adversos serios relacionados a los medicamentos utilizados en el estudio.

CONCLUSIONES: En pacientes con glaucoma de ángulo abierto primario o hipertensión ocular que tenían la IOP elevada mientras estaban en monoterapia con latanoprost, se observó que el cambio a dorzolamida–timolol o a una combinación de dorzolamida–timolol con latanoprost resultó ser efectivo y seguro en reducir la IOP y lograr una respuesta terapéutica.

Traducido por Homero A Monsanto

Efficacité et Innocuité de l'Association Dorzolamide–Timolol en Monothérapie ou Combinée au Latanoprost pour le Traitement du Glaucome à Angle Ouvert ou de l'Hypertension Intraoculaire

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RÉSUMÉ

INTRODUCTION: Le traitement du glaucome vise à réduire la tension intraoculaire (TIO) dans le but de prévenir des dommages au nerf optique. Pour les patients ne répondant pas à une monothérapie, une thérapie combinée peut possiblement permettre d'atteindre la TIO cible.

OBJECTIF: Évaluer l'efficacité et l'innocuité de l'association dorzolamide 2%–timolol 0.5% seule ou combinée au latanoprost à réduire la TIO lors d'un essai pragmatique.

DEVIS EXPÉRIMENTAL: Trois cent cinquante patients ont participé à une étude prospective, multicentrique, à simple insu, et sans répartition aléatoire. Pour être éligibles, les patients devaient souffrir de glaucome à angle ouvert ou d'hypertension intraoculaire et avoir une TIO non contrôlée en dépit d'un traitement de 4 semaines ou plus au latanoprost. Les patients éligibles ont reçus soit l'association dorzolamide–timolol à raison de 2 fois par jour en plus de leur thérapie actuelle au latanoprost (D/T-Ajout), soit l'association dorzolamide–timolol en monothérapie à raison de 2 fois par jour (D/T-Remplacement). Le paramètre d'efficacité principal était le changement de TIO après 6 et 12 semaines de traitement.

RÉSULTATS: Trois cent treize patients ont complété l'étude (248 D/T-Ajout; 65 D/T-Remplacement). Après 12 semaines, la chute moyenne de TIO était de –6.3 (3.6) mm Hg (–28.1%) et –5.8 (4.9) mm Hg (–23.5%) dans les groupes D/T-Ajout et D/T-Remplacement, respectivement ($p < 0.001$ pour les 2). Le taux de réponse thérapeutique (défini comme une réduction de la TIO >20%) après 12 semaines de traitement était de 66.4% (186/280) pour le groupe D/T-Ajout et de 52.9% (37/70) pour le groupe D/T-Remplacement. Cent seize réactions indésirables, rapportés par 86 patients (24.6%), ont été attribués aux médicaments à l'étude. Ces réactions étaient pour la plupart de faible intensité et non sérieuses. Les plus fréquentes étaient l'irritation oculaire (n = 42; 12.0%) et la perversion du goût (n = 15; 4.3%). Aucun effet indésirable sérieux relié aux médicaments à l'étude n'a été rapporté.

CONCLUSIONS: Chez les patients avec un glaucome à angle ouvert ou d'une TIO élevée et chez qui la TIO n'est pas contrôlée par du latanoprost, l'ajout ou le remplacement par une association dorzolamide–timolol est efficace et sécuritaire pour réduire la TIO et obtenir une réponse thérapeutique satisfaisante.

Traduit par Suzanne Laplante