

Refractive Correction and Glaucoma

The first in a two-part series focuses on refractive procedures for patients with glaucoma.

BY RICHARD A. LEWIS, MD

Our goal in treating patients with glaucoma is to preserve their visual acuity to the greatest extent possible. Historically, however, we have avoided discussing refractive correction with them and thus ignored a salient fact: our patients want to see well. They are excited about successful cataract surgery, not about achieving a decrease in their IOP. Despite little hard data on how to approach refractive correction in these individuals, the topic is worthy of discussion.

WHAT DO WE MEAN BY REFRACTIVE CORRECTION?

Refractive correction includes a wide range of treatment options. It is as commonplace as a prescription for glasses or contact lenses. It may also take the form of cataract surgery or refractive lens exchange with the implantation of a monofocal lens, a phakic IOL, an aspheric lens, or one of the new accommodating or multifocal IOLs. Additional surgical options include conductive keratoplasty, LASIK, Epi-LASIK, and PRK.

BENEFITS

The advantage of refractive correction is obvious: sharper vision. Although many glaucoma patients will be satisfied with spectacles or contact lenses, a lot of them wish for the clearer visual acuity that only surgical intervention can achieve. Moreover, certain occupations (eg, airline pilot) require better visual acuity than is possible with glasses or contact lenses in some cases.

Highly myopic patients with glaucoma who undergo cataract surgery or refractive lens exchange often have residual sphere or astigmatism postoperatively. LASIK may be an appropriate means of fine-tuning their visual outcome. Additionally, removing the crystalline lens from moderately-to-highly hyperopic eyes during cataract surgery or refractive lens exchange could actually

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help avoid angle-closure glaucoma as well as control IOP.

Perhaps most important to consider is that, by discussing refractive correction with our patients, we are ensuring that they receive well-informed counsel about its compatibility with the management strategies for their glaucoma. Physicians who do not perform certain refractive procedures themselves can consider partnering with a refractive surgeon who will refer the patient back to them for continued management.

CONCERNS

Certainly, due to the risk of infection, contact lenses are not the best choice in patients who will soon undergo filtration surgery or who have a functioning bleb. The risk of an infected bleb, dysesthesia, and other ocular problems in patients wearing contact lenses after trabeculectomy warrants a discussion of alternative forms of refractive correction, including spectacles, excimer laser treatment, and cataract surgery. Of course, any surgical intervention also carries risks.

A possible objection to refractive surgery involving excimer laser ablation is that such procedures make interpreting the correct IOP challenging. Alternative devices such as the Pascal Dynamic Contour Tonometer (SMT Swiss Microtechnology AG, Port, Switzerland) do not solve the problem. The management of glaucoma

involves more than simply monitoring IOP, however. We also track the appearance of the optic nerve and perform visual field testing, neither of which is affected by laser ablation. Before and after refractive surgery, it is essential that patients with glaucoma undergo baseline visual field testing and imaging of their optic nerves. The new baseline is important for clinical follow-up. In certain circumstances, it can address the question of whether the refractive procedure contributed to visual loss.

CONCLUSION

To avoid the subject of refractive correction in patients with glaucoma is to ignore reality. Instead, we should recognize that they want to see well and take a proactive approach regarding their visual acuity. In doing so, we are ensuring the oversight of their total vision care by physicians well versed in glaucoma management, including establishing a new baseline IOP, visual field testing, and the assessment of the optic disc. Most important, however, is that these patients maintain a continuity of follow-up, something that may be lost in a busy refractive surgery practice. □

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ISTALOL® (timolol maleate ophthalmic solution) 0.5%

Brief Summary of Prescribing Information

Sterile

INDICATIONS AND USAGE

ISTALOL ophthalmic solution is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

CONTRAINDICATIONS

ISTALOL is contraindicated in patients with (1) bronchial asthma; (2) a history of bronchial asthma; (3) severe chronic obstructive pulmonary disease (see WARNINGS); (4) sinus bradycardia; (5) second or third degree atrioventricular block; (6) overt cardiac failure (see WARNINGS); (7) cardiogenic shock; or (8) hypersensitivity to any component of this product.

WARNINGS

As with many topically applied ophthalmic drugs, this drug is absorbed systemically. The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate (see CONTRAINDICATIONS).

Cardiac Failure

Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition of beta-adrenergic receptor blockade may precipitate more severe failure.

In Patients Without a History of Cardiac Failure continued depression of the myocardium with beta-blockade agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of cardiac failure, ISTALOL should be discontinued.

Obstructive Pulmonary Disease

Patients with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease other than bronchial asthma or a history of bronchial asthma, in which ISTALOL is contraindicated (see CONTRAINDICATIONS), should, in general, not receive beta-blockers, including ISTALOL.

Major Surgery

The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to major surgery is controversial. Beta-adrenergic receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli. This may augment the risk of general anesthesia in surgical procedures. Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents. If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of adrenergic agonists.

Diabetes Mellitus

Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or in diabetic patients (especially those with latent diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia. (Thyroidectomy)

Beta-adrenergic blocking agents may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm.

PRECAUTIONS

General

Because of potential effects of beta-adrenergic blocking agents on blood pressure and pulse, these agents should be used with caution in patients with cardiovascular insufficiency. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of therapy with ISTALOL, alternative therapy should be considered. There have been reports of bacterial keratitis associated with the use of multiple dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface (see PRECAUTIONS, Information for Patients).

Information for Patients

Choroidal detachment after filtration procedures has been reported with the administration of aqueous suppressant therapy (e.g., timolol). Angle-closure glaucoma in patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil. Timolol maleate has little or no effect on the pupil. ISTALOL should not be used alone in the treatment of angle-closure glaucoma.

Anaphylaxis: While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

Muscle Weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness). Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

Information for Patients

Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures. Patients should also be instructed that ocular solutions, if handled improperly or if the tip of the dispensing container contacts the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions (see PRECAUTIONS, General).

Patients should also be advised that if they have ocular surgery or develop an intermittent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidosage container.

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, or cardiac failure should be advised not to take this product (see CONTRAINDICATIONS).

Patients should be advised that ISTALOL contains benzalkonium chloride which may be absorbed by soft contact lenses. Contact lenses should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following ISTALOL administration.

Drug Interactions

Although ISTALOL used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with ISTALOL and epinephrine has been reported occasionally.

Beta-adrenergic blocking agents: Patients who are receiving a beta-adrenergic blocking agent orally and ISTALOL should be observed for potential additive effects of beta-blockade, both systemic and on intraocular pressure. The concomitant use of two topical beta-adrenergic blocking agents is not recommended.

Calcium antagonists: Caution should be used in the coadministration of beta-adrenergic blocking agents, such as ISTALOL, and oral or intravenous calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, coadministration should be avoided.

Calcium channel-blocking drugs: Close observation of the patient is recommended when a beta blocker is administered to patients receiving calcium channel-blocking drugs such as verapamil, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may result in vertigo, syncope, or postural hypotension.

Digitalis and calcium antagonists: The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

Quinidine: Potentiated systemic beta-blockade (e.g., decreased heart rate) has been reported during combined treatment with quinidine and timolol, possibly because quinidine inhibits the metabolism of timolol via the P-450 enzyme, CYP2D6. Quinidine: Oral beta-adrenergic blocking agents may potentiate the rebound hypertension which can follow the withdrawal of clonidine. There have been reports of exacerbation of rebound hypertension with ophthalmic timolol maleate.

Injectable epinephrine (see PRECAUTIONS, General, Anaphylaxis)

Pregnancy

Teratogenic Effects—Pregnancy Category C. Teratogenicity studies with timolol in mice, rats, and rabbits at oral doses up to 50 mg/kg/day (7,000 times the systemic exposure following the maximum recommended human ophthalmic dose) demonstrated no evidence of fetal malformations. Although delayed fetal ossification was observed at this dose in rats, there were no adverse effects on postnatal development of offspring. Doses of 1000 mg/kg/day (142,000 times the systemic exposure following the maximum recommended human ophthalmic dose) were maternotoxic in mice and resulted in an increased number of fetal resorptions. Increased fetal resorptions were also seen in rabbits at doses of 14,000 times the systemic exposure following the maximum recommended human ophthalmic dose. In this case without apparent maternotoxicity.

There are no adequate and well-controlled studies in pregnant women. ISTALOL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

Timolol maleate has been detected in human milk following oral and ophthalmic drug administration. Because of the potential for serious adverse reactions from ISTALOL in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

No overall differences in safety or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS

The most frequently reported adverse experiences have been burning and stinging upon instillation in 38% of patients treated with ISTALOL. Additional events reported with ISTALOL at a frequency of 4 to 10% include: blurred vision, catarrh, conjunctival injection, headache, hypotension, infection, itching and decreased visual acuity. The following additional adverse experiences have been reported less frequently with oral administration of this or other timolol maleate formulations:

BODY AS A WHOLE

Asthenia/fatigue and chest pain.

CARDIOVASCULAR

Bradycardia, arrhythmia, hypotension, syncope, heart block, cerebral vascular accident, cerebral ischemia, cardiac failure, worsening of angina pectoris, palpitation, cardiac arrest, pulmonary edema, edema, claudication, Raynaud's phenomenon, and cold hands and feet.

DIGESTIVE

Nausea, diarrhea, dyspepsia, anorexia, and dry mouth.

IMMUNOLOGIC

Systemic lupus erythematosus.

NERVOUS SYSTEM/PSYCHIATRIC

Dizziness, increase in signs and symptoms of myasthenia gravis, paresthesia, somnolence, insomnia, nightmares, behavioral changes and psychic disturbances including depression, confusion, hallucinations, anxiety, disorientation, nervousness, and memory loss.

SKIN

Alopecia and psoriasisiform rash or exacerbation of psoriasis.

HYPERSENSITIVITY

Signs and symptoms of systemic allergic reactions, including angioedema, urticaria, and localized and generalized rash.

RESPIRATORY

Bronchospasm predominantly in patients with pre-existing bronchospastic disease, respiratory failure, dyspnea, nasal congestion, cough and upper respiratory infections.

ENDOCRINE

Masked symptoms of hypoglycemia in diabetic patients (see WARNINGS).

SPECIAL SENSES

Signs and symptoms of ocular irritation including conjunctivitis, blepharitis, keratitis, ocular pain, discharge in e., crusts, foreign body sensation, itching and tearing, and dry eye; ptosis; decreased corneal sensitivity; corneal edema; visual disturbances including refractive changes and diplopia; pseudophthalmos; choroidal detachment following filtration surgery (see PRECAUTIONS, General); and irrititis.

UROGENITAL

Retroprostatic fibrosis, decreased libido, impotence, and Peyronie's disease.

The following additional adverse effects have been reported in clinical experience with ISTALOL maleate or other OPA beta-blocking agents and may be considered potential effects of ophthalmic timolol maleate: ALLERGIC: Erythematous rash, hives combined with itching and sore throat, laryngospasm with respiratory distress; BODY AS A WHOLE: Excessive pain, decreased exercise tolerance, weight loss; CARDIOVASCULAR: Worsening of arterial insufficiency, vasodilation; DIGESTIVE: Gastrointestinal pain, hyperemesis, vomiting, mesenteric arterial thrombosis, ischemic colitis; HEMATOLOGIC: Thrombocytopenic purpura, thrombocytopenic purpura, agranulocytosis; ENDOCRINE: Hypoglycemia, hypoglycemia; SKIN: Pruritus, skin irritation, increased pigmentation, sweating; MUSCULOSKELETAL: Arthralgia; NERVOUS SYSTEM/PSYCHIATRIC: Vertigo, local weakness, diminished concentration, reversible mental depression progressing to cataplexy, an acute reversible syndrome characterized by disorientation for time and place, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometric tests; RESPIRATORY: Rhinitis, bronchial obstruction; UROGENITAL: Urination difficulties.

OVERDOSAGE

There have been reports of inadvertent overdose with ISTALOL ophthalmic solution resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest (see also ADVERSE REACTIONS).

As in vitro hemodialysis study using ¹⁴C timolol added to human plasma or whole blood, showed that timolol was mainly dialyzed from these fluids; however, a study of patients with renal failure showed that timolol did not dialyze readily.

DOSE AND ADMINISTRATION

ISTALOL ophthalmic solution is available at a concentration of 0.5 percent. The starting dose is one drop of 0.5 percent ISTALOL in the affected eye(s) once a day in the AM. If the patient's intraocular pressure is not at a satisfactory level on this regimen, concomitant therapy with other agents for lowering intraocular pressure can be instituted. The concomitant use of two topical beta-adrenergic blocking agents is not recommended (see PRECAUTIONS, Drug Interactions, Beta-adrenergic blocking agents).

Storage

Store at 15-25°C (59-77°F).

Rx Only

Manufactured for: SENJU Pharmaceutical Co., Ltd., Osaka, Japan 541-0046.

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