Initial Laser Trabeculoplasty Versus Initial Medications

Research supports the use of selective laser trabeculoplasty as primary therapy for open-angle glaucoma.

BY JOSEPH A. DONNELLY, BS; ELAINE M. MIGLINO; AND LAWRENCE F. JINDRA, MD

Glaucoma is a secondary optic neuropathy characterized by an acquired progressive loss of retinal ganglion cells, decreased function of the optic nerve, and a slow, insidious loss of vision.[1] The clinician's goal is to provide the best treatment options based on evidence-based medicine. This article presents current data supporting the use of laser trabeculoplasty as primary therapy for glaucoma.

ARGON LASER TRABECULOPLASTY

Laser trabeculoplasty has been a treatment for glaucoma since its introduction in 1979 by Wise and Witter in the form of argon laser trabeculoplasty (ALT).[2] The Glaucoma Laser Trial (GLT) established the efficacy of ALT at lowering IOP in previously untreated glaucoma patients.[3] In the study, ALT also had at least the same efficacy, when used as initial treatment, as timolol maleate 0.5%. The Ocular Hypertensive Treatment Study (OHTS) and the Early Manifest Glaucoma Trial (EMGT) built on the GLT by establishing the efficacy of early and effective treatment to preserve long-term visual function in glaucoma patients.[4,5]

After its introduction, ALT became an accepted adjuvant therapy for glaucoma, but the procedure had decreased efficacy when used as repeat therapy. A life table analysis from Feldman et al showed that repeat ALT was successful in 35% of eyes at 6 months, but that figure decreased to 5% at 48 months. The investigators therefore concluded that repeat ALT generally was not effective for the long-term control of open-angle glaucoma.[6] The problem is that ALT causes a fibrocellular layer to form over the trabecular meshwork, resulting in decreased aqueous outflow.[7] Cvenkel et al found increased fragmentation of the trabecular meshwork extending to Schlemm's canal and the scleral stroma.[8] Van der Zypen noted ultrastructural changes to the trabecular meshwork.[9] Prior treatment with ALT was also found to increase complications in eyes undergoing glaucoma filtering surgery. In a study by Schwartz et al, 19% of eyes that underwent trabeculectomy after ALT had a tendency to develop encapsulated blebs compared with 14% of eyes without previous ALT.[10]

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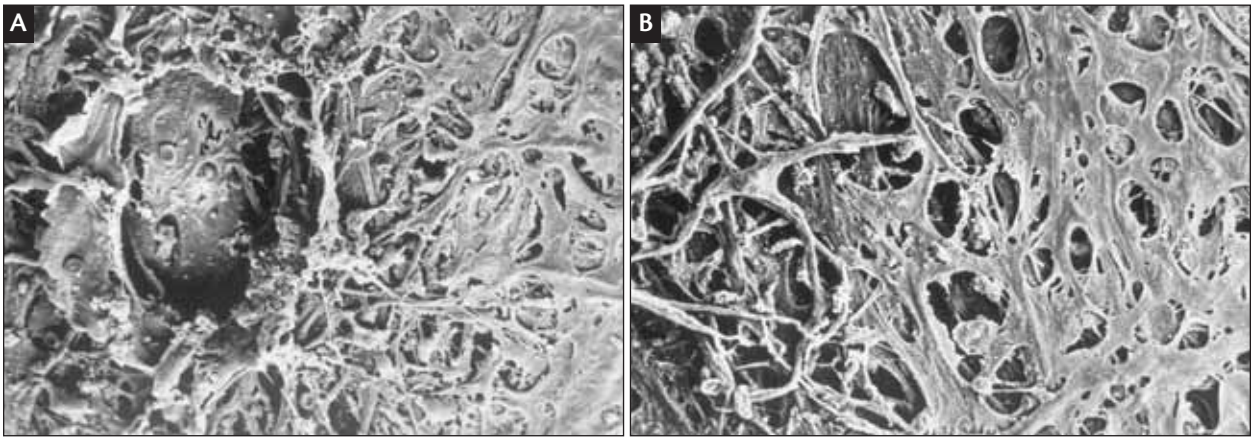
SELECTIVE LASER TRABECULOPLASTY

The brainchild of Mark A. Latina, MD,[11] selective laser trabeculoplasty (SLT) may someday be recognized as an addition to the glaucoma treatment armamentarium that is as valuable as phacoemulsification and IOLs were to cataract surgery. SLT is performed using a 532-nm, frequency-doubled, Q-switched Nd:YAG laser with a 3-ns pulse and 400-µm spot size. The system delivers a 0.4- to 1.8-mJ beam (less than 1/6,000 the fluence used in ALT) over 240º to 360º by means of approximately 120 spots, titrated to generate champagne-like bubbles without producing a significant liberation of pigment.[12] The SLT pulse selectively photolyses melanocytes in the trabecular meshwork without producing collateral cytotoxic, thermal, or coagulative damage to neighboring tissue. Alvarado et al demonstrated that SLT increases the per-



(Courtesy of Theresa R. Kramer, MD, and Robert J. Noecker, MD, MBA.)

Figure 1. Scanning electron micrographs were taken of the trabecular meshwork after ALT (A) and after SLT (B).

meability of the trabecular meshwork.[13]

SLT is believed to decrease the IOP via two mechanisms: the mechanical photodisruption of melanocytes and the cytokine-mediated recruitment of macrophages. In the mechanical model, photothermolysis of pigmented cells causes a photodisruption of melanocytes in the trabecular meshwork. Using electron microscopy, Kramer and Noecker noted well-defined craters after ALT but no coagulative necrosis or disruption of the trabecular beams in eyes treated with SLT (Figure 1); the only ultrastructural evidence of laser-tissue interaction after SLT was cracking of intracytoplasmic pigmentary granules.[14] In the cytokine-mediated model, cytokines trigger a systemic recruitment of macrophages to the trabecular meshwork. The macrophages are then upregulated to express matrix metalloproteases,[15] leading to an actual remodeling of the trabecular meshwork. There is a growing body of evidence to suggest that a cytokine-mediated inflammatory response is the primary mechanism of action for SLT, but further study is ongoing to elucidate the exact mechanism by which SLT reduces the IOP.

CLINICAL STUDIES

When used as primary (initial) therapy, SLT decreases IOP with significant efficacy. Recent data from a clinical case series of more than 8 years' duration and a mean follow-up period of 750 days are a continuation of unpublished studies from 2005 and 2007.[16-18] In a retrospective chart review, investigators collected data on 1,363 eyes that underwent SLT as primary therapy from a total of more than 3,000 eyes treated with SLT. They found a 31% long-term reduction in mean IOP, from a mean of 18.8 to 13.0 mm Hg, which was consistent with measured reductions in IOP in previous studies.[19-21] Success rates were also consistent with those reported in previous studies[19-21]: 93% of eyes treated with primary SLT required no further intervention, 6% of eyes required one repeat SLT, and 1% of eyes required medications to control the IOP. These data have been consistent over 8 years' time, as the size and length of the study have increased.

Using life table analysis over 8 years in continuation of a 2008 study,[22] the cumulative probability of success for SLT as primary therapy was 92%. In a study of 1,612 eyes treated with primary SLT, there was a 9% repeat rate among those with 4 to 6 years of follow-up; for these eyes, an average of 5 years elapsed between initial and repeat SLT.[23] In a study of eyes with a mean follow-up of 1,152 days, the mean IOP decreased by 34% after SLT as primary therapy.[24] Lai et al reported a 33% decrease in IOP in 24 eyes after SLT with 5 years of follow-up.[25] These results are in contrast to the relatively poorer efficacy of ALT demonstrated by Baez and Spaeth, who showed that, over 5 years, only 60% of treated patients maintained adequate IOP without the need for further filtering surgery.[26]

Primary treatment with SLT has certain advantages over primary treatment with medications. First, diurnal fluctuations in IOP were observed less often after primary treatment with SLT versus eyes treated with medications primarily and then treated with secondary SLT therapy.[27] It is theorized that the enhanced pharmacokinetics and improved IOP can decrease patients' need for glaucoma medications as well as reduce clinical concerns about patients' adherence to and compliance with medical therapy.

SLT's ability to lower IOP has been observed in cases of exfoliative as well as pigmentary glaucoma, albeit with use of lower energy levels.[28] The treatment of pigmentary glaucoma requires lower energy settings with fewer spots needed, whereas the treatment of exfoliative glaucoma usually requires higher energy, also with fewer spots. In both cases, all things being equal, the total energy used

for the treatment of these forms of glaucoma is less than that used for the treatment of primary open-angle glaucoma. Although SLT works due to an interaction with pigmented particles, it has been shown that the procedure is suitable for use in both blue and brown eyes; care must be taken with brown eyes, however, to use enough energy to achieve a therapeutic effect.[29]

Clinical practice has confirmed the notion that the low-energy, selective photothermolysis of SLT makes it an option for treatment in eyes with narrow angles. The photodestructive nature of ALT makes it inappropriate for use in these cases because of the peripheral anterior synechiae that can form due to the procedure's photocoagulative mechanism of action and the subsequent burning and scarring that result from the treatment. In contrast, the low-energy, cold-laser nature of SLT (at 1/6000 the fluence of ALT) does not appear to have the energy to cause, make, or form peripheral anterior synechiae.

Although SLT has been shown to work in many forms of glaucoma, it is our experience that the procedure is not indicated for the treatment of total angle closure, neovascular glaucoma, or active uveitic glaucoma.

ECONOMICS

The clinical benefits aside, primary treatment with SLT can result in significant cost savings for patients and for the health care system. The 5-year cumulative costs were approximately $6,571 and $6,363, respectively, for medications and filtering surgery compared with $4,838 for laser trabeculoplasty.[30] These reductions in cost combined with the benefits of IOP reduction and a lesser need for patients' compliance represent the strengths of SLT compared with other treatment modalities.

CONCLUSION

The GLT established the clinical rationale for laser trabeculoplasty as a primary treatment for glaucoma. In our clinical experience, SLT has been a safe and effective primary therapy for several types of glaucoma, a means of decreasing IOP by enhancing aqueous outflow. One of this modality's strengths is its ability to produce a significant treatment effect without accompanying photocoagulative damage to the trabecular meshwork (unlike ALT), which theoretically makes it clinically amenable for use as repeat therapy. A large and growing body of clinical research supports the use of SLT as a safer, more effective, and more cost-efficient primary treatment for open-angle glaucoma than initial pharmacological therapy. ■

Joseph A. Donnelly, BS, is a medical student at Albert Einstein College of Medicine, Yeshiva University, Bronx, New York.

Lawrence F. Jindra, MD, is an assistant clinical professor of ophthalmology, Columbia University in New York, and chief, Division of Ophthalmology, Winthrop University Hospital in Mineola, New York. Dr. Jindra may be reached at drlfjind@optonline.net.

Elaine M. Miglino is research manager at Floral Park Ophthalmology in Floral Park, New York.

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