Changes in Aqueous Outflow After In Vitro Neodymium:Yttrium Aluminum Garnet Laser Cyclophotocoagulation

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To examine the possible role of transscleral outflow routes, enucleated human and porcine eyes underwent noncontact neodymium:yttrium aluminum garnet (Nd:YAG) laser cyclophotocoagulation 3 mm posterior to the limbus. Pars plana lesions were verified histologically. The eyes were perfused with saline solution at 50 mm Hg perfusion pressure, placing the tip of the needle into the hyaloid orbicular space. The outflow facility was 0.072 μl/min/mm Hg in paired controls and 0.105 μl/min/mm Hg in human lasered eyes, a difference of 31%. In porcine eyes the difference was 43%. Since concepts of aqueous production, impaired circulation, and inflammation do not apply to enucleated eyes, the increase may be related to pars plana transscleral flow facilitated by disruption of the neuroepithelial barrier. Invest Ophthalmol Vis Sci 31:1834-1838, 1990

Although descriptions of cycloablation have concentrated on the destruction of aqueous producing tissues, more recent interest has focused on aspects of inflammation and increased outflow facility. The latter was thought to be related to changes in the trabecular meshwork after freezing and increased transscleral flow due to scleral changes after sonication or laser application. To investigate further the possibility of transscleral flow after laser application, paired enucleated human eyebank eyes which are incapable of aqueous production and vascular and/or inflammatory response were perfused with normal saline solution. The increased facility of outflow found after neodymium:yttrium aluminum garnet (Nd:YAG) laser cyclodestruction suggests improved transneuroepithelial and transscleral flow as one contributing factor in the long-term lowering of pressure.

Materials and Methods

Fourteen unmatched enucleated porcine eyes, 6–8 hr old, packed in ice, were obtained from a slaughterhouse. Eyes were discarded if they showed any gross abnormalities when viewed with a hand-held magnifier. Seven eyes were selected at random and assigned to the laser group. The remaining seven unaltered eyes served as controls. Laser treatments were applied using the LASAG Microruptor II Nd:YAG laser (Thun, Switzerland) at 10 J, 20 msec, and a retrofocus of 9 (approximately 3 mm). Due to the increased pigmentation and thickness of porcine sclera, 10 J were required to obtain visible lesions comparable to those produced at 5–6 J in human eyes at the pars plana. Through preliminary experiments on porcine eyes, the distance between the limbus and the mid pars plana was measured to be an average of 4 mm. Forty laser applications were given for 360°, 4-mm posterior to the surgical limbus.

Ten pairs of matched enucleated human eyes, 1–4 days old, without gross pathologic or surgical alterations, were obtained from the Lions Eye Bank of Delaware Valley. One eye from each pair was randomly assigned to the laser group, and the other eye served as a control. Laser treatments were applied using the LASAG Microruptor II Nd:YAG laser at 5–6 J, 20 msec, and a retrofocus of 9. Forty applications were given for 360°, 3-mm posterior to the limbus, as used in some clinical studies.

Immediately after laser treatment all eyes were stabilized in a surgical tray with saline moist towelettes to prevent drying and to maintain a constant perfusion temperature of 22°C. A 30-G, 1/2-inch infusion needle (Becton-Dickinson, Rutherford, NJ) was inserted 2 mm from the limbus, and slowly advanced intraocularly until seen with the indirect ophthalmo-
scope. The needle was then withdrawn a distance of 7 mm, so that the tip was positioned internally close to the pigment epithelium in the porcine equivalent of the canal of Hannover. Similarly, in human eyes undergoing perfusion, the tip of the needle was inserted 3-mm posterior to the limbus and withdrawn 6 mm to enter the canal of Hannover, or the superficial anterior cortical gel. Glue was used to seal the ocular penetration site of the needle completely.

A simple quantitative perfusion apparatus consisted of a reservoir of 500 ml of normal saline solution (0.9% sodium chloride; Abbott Laboratories, North Chicago, IL) connected by polyethylene intravenous tubing (Venoset 78 with cair clamp; Abbott) to the 30-G ½-inch needle placed in the eyes. The height of the saline reservoir was varied to establish the desired intraocular pressure. A U-shaped mercury manometer tube with a custom port to accommodate the infusion needle was used to verify the pressures before each perfusion. The infusion lines were fully opened for 30 min to allow for pressure equilibration of the eyes with the infusion system. After equilibration, an air bubble was introduced (time, 0) into the intravenous infusion lines of both the lasered and the control eye, close to the saline reservoirs. The initial position of the lower air-bubble meniscus was marked (distance, 0 mm). The progression of the meniscus was measured with a 1-mm division tape measure every 15 min for 2 hr. These distances were converted to inflow volumes by determining the amount of fluid held by a given length of tubing.

Seven pairs of unmatched porcine eyes were perfused at 100 mm Hg (Fig. 1), six pairs of human eyes at 100 mm Hg (Fig. 2), and four pairs of human eyes at 50 mm Hg (Fig. 3). The perfusion lines to be connected to the lasered eye and its control were randomly selected in both porcine and human eye perfusions to reduce systematic error. During perfusion, shallowing of the anterior chamber was not noted. As in previous studies, it was assumed that global inflow equaled the sum of conventional and nonconventional outflow at steady state.9 Outflow values were averaged for the 15-min intervals up to 2 hr, and standard deviations were calculated. The paired t-test was used to test for statistical significance at the usual level of 0.05. After perfusion the eyes were fixed in 7% formaldehyde. They were dissected in the equatorial meridian, and pars plana burns were verified in all lasered eyes. Gross photographs were taken and representative sections were submitted for routine histology as described elsewhere.2

Results

Compared with controls, the rate of outflow was increased by 43% in porcine eyes (Fig. 1) and by 28–31% in human eyes (Figs. 2, 3). In human eyes,
the facility of outflow at 50 mm Hg was 0.072 in controls versus 0.105 µl/min/mm Hg in lasered eyes, and at 100 mm Hg, it was 0.061 versus 0.085 µl/min/mm Hg, respectively. The facility of outflow was decreased for higher pressures. All differences were statistically significant at the usual confidence levels of 0.05, two sided. Postperfusion gross examination of lasered human eyes showed pars plana lesions at the 3-mm laser focus used (Fig. 4C). Histologic sections showed disruptions of the pigmented pars plana epithelium (Fig. 4D) in experimental eyes which were not found in fellow control eyes (Figs. 4A–B). The scleral changes after noncontact Nd:YAG laser were minimal on microscopic examination.

Discussion

Our results showed that passive outflow of intraocular fluid was increased after in vitro conventional laser cycloablation. Perfusion of enucleated eyes has been used extensively in the past and, as in our experiment, derived its internal consistency from randomization and permutation of the experimental eyes versus paired controls. Outflow was increased by 28–43% in all lasered porcine and human eyes, making laser treatment the only independent variable which could account for the difference within each pair. It is possible that the greater effectiveness in porcine eyes was related to pigmentation and higher total energy levels as suggested by more explosive absorption during laser treatment.

The rate of outflow was low; however, it was comparable to rates reported for enucleated eyes perfused from the vitreous compartment, possibly implicating a component of vitreous in the increased resistance to outflow.

In cycloablation, four pathomechanisms of pressure lowering have been proposed. First, the destruction of aqueous-producing epithelium may reduce aqueous production. This concept demands exact focus of the laser on the corona ciliaris and requires more laser energy than would be needed at the pars...
processes resulting in less absorption of light, the pig-
mentation of the ciliary muscle blocking transmis-
sion of transscleral light to the epithelium, and the
increased vascularization of the ciliary processes resulting in
more heat dissipation. The combination of these
anatomic details may interfere with the creation of a
lesion of therapeutic degree at the corona ciliaris
level. In addition, as discussed previously, there may
be no apparent damage to the aqueous-producing ep-
ithelium when applying the usual clinical focus at
2–3-mm posterior to the limbus.

The second pathogenic theory of pressure lowering
in ablation is mediation by the inflammatory process
which may be more important in the acute phase. Two
phases have been distinguished for cyclocryo-
pxey based on increased facility of outflow. Mediation
by prostaglandins and other eicosanoids is likely
to occur to some extent in cycloablation, and it is
independent of anatomic ciliary atrophy or the loca-
tion of the ablation. One possible group of media-
tors are prostaglandins that enhance uveoscleral out-
flow.

A third mechanism is vascular compromise of the
ciliary circulation. This may play some role even
though the uvea is rich in collaterals and most of the
ciliary blood supply comes from the long posterior
ciliary arteries and anterior ciliary arteries, ie, from
the major arteriolar circle of the ciliary body. This
mechanism would apply only when the arteriolar cir-
cle is photoablated extensively, requiring a focus
much more anterior than that commonly used. Ante-
rior focus with short exposures may account for hy-
phema and other hemorrhagic complications.

The fourth mechanism is pressure-dependent pas-
sive outflow through the sclera: this has been postu-
lated for ultrasound and laser application. In
creased outflow was actually measured after cryo-
pxey, however, this was ascribed to alterations in the
trabecular meshwork. It has not been determined
whether histologic scleral alterations are needed to
increase the transscleral rate of flow to a range where
it would make a therapeutic difference. The volumet-
ric rate of flow would depend on both pressure head
and scleral changes. The fact that cycloablation is
effective without apparent scleral damage suggests
that scleral changes may be an adjunct in the lower-
ing of pressure. In our in vitro study histologic scleral
damage was minimal, yet increased outflow was pre-
sent suggesting that the neuroepithelium and not the
sclera may be the main barrier to passive outflow.

Key words: aqueous outflow, cyclodestruction, noncontact
Nd:YAG laser, pars plana photofiltration

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