

Prevention of the immediate intraocular pressure rise following argon laser trabeculoplasty

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SUMMARY A prospective, randomised double-masked study was undertaken to compare the effect of pretreatment with acetazolamide or placebo on the immediate intraocular pressure (IOP) rise following argon laser trabeculoplasty. One hundred eyes (100 patients) underwent 180° of laser treatment with a mean of 59 spots of 50 µm size and 800 to 1000 mW power. The IOP was measured during the first three hours after laser treatment, at 24 hours, and at two months. Forty-six patients (92%) in the placebo group had an immediate rise of IOP. The mean rise (SD) for these patients was 8.6 (7.1) mmHg. Fifteen patients (30%) in this group had an IOP rise of greater than 10 mmHg. Nine patients (18%) receiving acetazolamide had an immediate rise of IOP. The mean rise for these patients was 4.3 (3.1) mmHg, and no patient had an increase in IOP of greater than 8 mmHg. Acetazolamide appears to be effective in preventing a critical IOP rise after argon laser trabeculoplasty ($p < 0.0001$).

Argon laser trabeculoplasty has gained widespread acceptance as a valuable tool for the control of glaucoma. Its efficacy in the short term has been established,^{1,2} and recent reports are encouraging with regard to long term control.³⁻⁷ Its mode of action has not been clearly elucidated, though an increase in outflow facility has been demonstrated.^{1,8-11} A variety of complications of laser trabeculoplasty have been reported,¹²⁻¹⁶ the most serious being an immediate rise in intraocular pressure. Eyes already severely compromised by chronically raised intraocular pressure are susceptible to further damage from acute pressure elevations which may lead to field loss or loss of central vision.^{1,12,14,15,17}

It has been suggested that the extent of trabecular meshwork treated, as well as the number of burns, their energy, and placement, have a bearing on the degree of the pressure rise; though attention to these details may reduce the incidence of raised pressure, they do not eradicate it.¹⁶⁻²⁰ Several forms of pretreatment, including topical 4% pilocarpine,²¹ ALO 2145 (para-aminoclonidine),^{22,23} oral glycerin,²⁴ and oral acetazolamide,²⁵ have been reported to reduce

the frequency and severity of the pressure rise, while pretreatment with topical corticosteroid,²⁶ indomethacin,²⁷⁻³⁰ and flurbiprofen^{30,31} had no statistically significant effect.

We performed a prospective, randomised, double-masked study to evaluate the effectiveness of oral acetazolamide in preventing this pressure rise. A significant rise of IOP after argon laser trabeculoplasty is usually apparent by two hours, peaking between two and three hours and then declining; rarely a rise is first detected beyond this time.^{17,32-34} Oral acetazolamide reaches a peak plasma concentration one hour after administration of the drug (Fig. 1), the greatest fall in IOP occurs after two hours (Fig. 2) and declines only slightly up to six hours.^{35,36} Administration of acetazolamide one hour before argon laser trabeculoplasty should produce maximum IOP reduction to coincide with the period of potential maximum IOP elevation.

Patients and methods

In this controlled study all patients were white, aged 65 or over, and had uncontrolled open-angle glaucoma as defined by an IOP greater than 21 mmHg and progressive visual field loss. All were on the maximum tolerated topical therapy and none were

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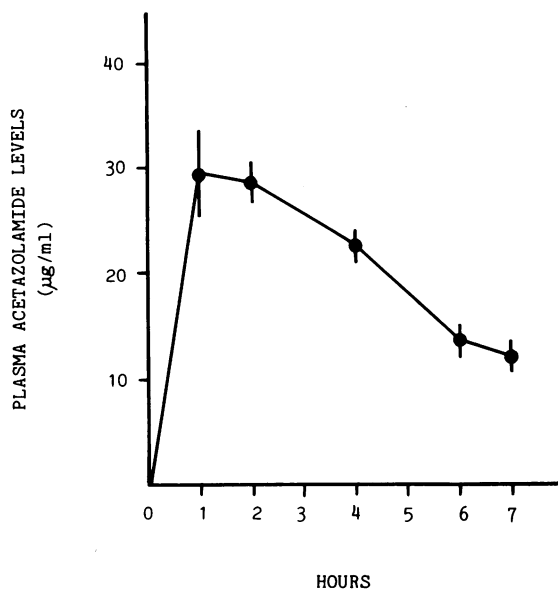


Fig. 1 Average plasma concentration (with SE) following oral administration of acetazolamide 500 mg in ocular hypertensive patients. Modified with permission from Friedland BR et al.³⁵

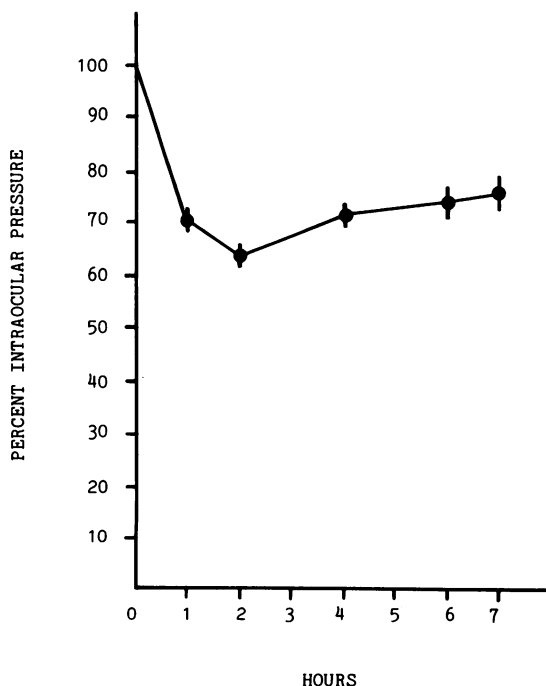


Fig. 2 Percentage (SE) of initial IOP following oral administration of acetazolamide 500 mg. Modified with permission from Friedland BR et al.³⁵

receiving acetazolamide, which in our experience is poorly tolerated in this age group. One eye of each patient was included in the study. None had previously undergone laser trabeculoplasty. If bilateral treatment was required, the eye treated first was included. Informed consent was obtained from all patients.

Before each treatment the patients underwent ophthalmic assessment of both eyes, which included best corrected Snellen visual acuity, slit-lamp examination of the anterior segment, and applanation tonometry. The patient was then randomly selected to receive either two 250 mg tablets of acetazolamide (group 1) or two placebo tablets (group 2). The medication selected was masked to both the patient and the physician. Acetazolamide or placebo were given orally, and one hour later the IOP was measured again immediately before argon laser trabeculoplasty. Topical anaesthesia was given with 0.4% oxybuprocaine. An antireflective Goldmann three-mirror contact lens was used to view the trabecular meshwork. A mean of 59 (SD 4.4) laser burns of 800 to 1000 mW power, 50 µm spot size, and 0.1 second duration were applied to the anterior trabecular meshwork. The burns were applied evenly over 180°, and the power was titrated to achieve blanching of the meshwork with occasional bubble formation. Blue-green argon laser light was used for all treatments and was delivered by a Coherent model 900 laser. The power output of the laser was measured at the start of the study and found to be 95% of the laser meter reading. All the laser treatments were applied by one of the authors (TM) and all examinations were conducted by the other (DE).

After laser treatment the IOP in both eyes and the degree of anterior segment inflammation in the treated eye were determined at 30 minutes, one hour, two hours, three hours, and 24 hours by the classification of Kimura *et al.*³⁷ Excessive intraocular pressure elevation was treated with 500 mg of intravenous acetazolamide and the patient monitored until the IOP had returned to baseline levels. An excessive IOP rise was defined as an increase of more than 30% or 10 mmHg above pretreatment levels provided the peak IOP was greater than 30 mmHg, after Krupin *et al.*³² Following laser trabeculoplasty the patients continued all their initial antiglaucomatous treatment with additional prednisolone 0.5% eye drops four times a day for three days. A further IOP check was made at two months.

Statistical data are reported as mean and SD, and were analysed by Student's *t* test, Fisher's exact test, Spearman's rank correlation coefficient, and multivariate regression analysis where appropriate. Values of *p* less than 0.05 were considered significant.

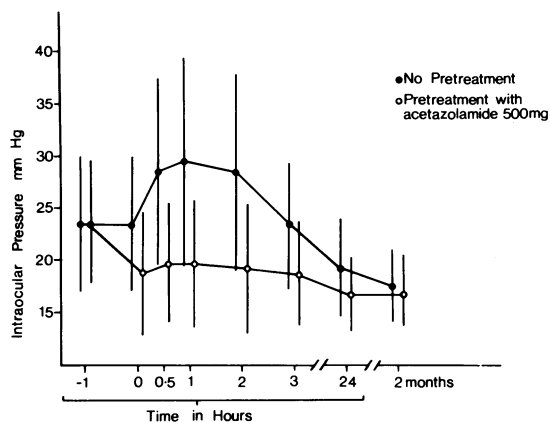


Fig. 3 Mean intraocular pressure (SD) before and after argon laser trabeculoplasty in patients receiving either acetazolamide (group 1) or placebo (group 2) pretreatment.

Results

One hundred eyes of 100 patients were treated. The mean age of group 1 was 74.0 years (SD 6.0) and of group 2 was 74.6 years (SD 5.9). The sex ratios were 27 female and 23 male in group 1, and 26 female and 24 male in group 2. None of the patients had secondary glaucoma or chronic narrow-angle glaucoma. Six patients in group 1 and seven in group 2 had pseudoexfoliative glaucoma; the remaining patients had chronic open-angle glaucoma. The mean pretreatment IOP in group 1 was 23.6 (6.1) mmHg and in group 2 23.7 (6.5) mmHg. There was

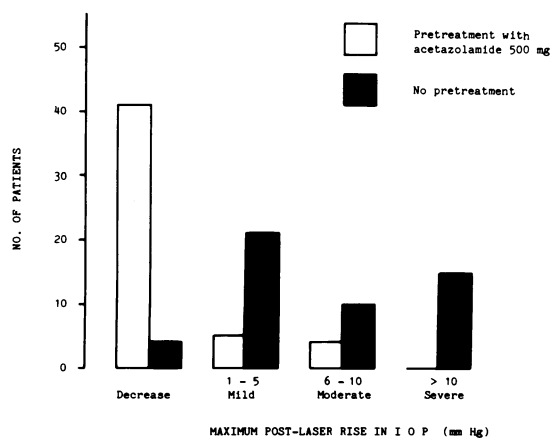


Fig. 4 Maximum intraocular pressure change following argon laser trabeculoplasty in patients receiving either acetazolamide (group 1) or placebo (group 2) pretreatment. Distribution is significantly different ($p < 0.0001$).

Table 1 Time elapsed from laser trabeculoplasty at which maximum IOP rise occurred

Time (hours)	0.5	1	2	3	24	Total
Number of patients						
Group 1 (acetazolamide)	2	3	3	1	0	9
Group 2 (placebo)	13	19	13	0	1	46

no significant difference between the mean pretreatment IOPs of the two groups ($p > 0.3$). Two patients in each group had a pretreatment IOP greater than 35 mmHg. The mean (with SD) IOPs before and after laser treatment at each examination time are presented in Fig. 3. The mean pressures were significantly lower in the acetazolamide pretreated patients (group 1) from time zero to 24 hours ($p < 0.001$ at time zero, 30 minutes, one, two, and three hours, and $p < 0.01$ at 24 hours). There was no significant difference at two months ($p > 0.3$).

The numbers of patients in each group showing either a decrease or a mild, moderate, or severe increase in postlaser IOP are represented in Fig. 4, and the time at which the maximum IOP increase occurred is shown in Table 1. One patient with pseudoexfoliative glaucoma in group 2 experienced a rise of 5 mmHg (21%) over the pretreatment IOP at 24 hours; in all other cases the maximum increase had occurred by three hours. Nine patients (18%) in group 1 had a postlaser rise in IOP ranging from 1 to 8 mmHg, mean 4.3 (SD 3.1) mmHg. The mean rise for the group as a whole was 0.8 (2.1) mmHg. None of the rises in pressure were significant as defined by Krupin *et al.*³² In group 2 46 patients (92%) had a postlaser rise in pressure, the range being 1 to 25 mmHg, mean 8.6 (7.1) mmHg. The mean rise for the group as a whole was 7.8 (7.2) mmHg. Fifteen patients (30%) had a significant increase in IOP as defined by Krupin *et al.*³² In these patients intravenous acetazolamide was administered and produced satisfactory reduction in IOP in all cases.

There was a highly significant increased risk of an immediate postlaser IOP rise in group 2 compared with group 1 ($p < 0.0001$, Fisher's exact test). The amplitude of the rise was also significantly higher in group 2 ($p < 0.01$). We found no significant difference in the risk of a critical postlaser pressure rise between patients with pseudoexfoliation and those without ($p > 0.3$, Fisher's exact test). There was no significant difference in the pressure drop at two months between the two groups; the mean pressure drop for group 1 was 6.8 (4.9) mmHg and for group 2 6.2 (5.5) mmHg. An excessive postlaser rise in intraocular pressure did not significantly compromise the result-

ing IOP at two months (Spearman's rank correlation coefficient).

Stepwise multivariate regression analysis showed there was no correlation between the postlaser pressure rise and age, sex, pretreatment IOP, previous antiglaucoma medication, number of burns administered, or postlaser inflammatory score. It also established that the only variable significantly to affect the pressure drop at two months was the initial IOP: the greater the initial IOP the greater the fall in IOP. This concurs with the findings of other authors.^{1 15 16}

Discussion

The risk of an intraocular pressure rise immediately after laser trabeculoplasty has been widely reported and is confirmed by our study. The cause of the rise has not been elucidated. It has been suggested that prostaglandins released as part of the inflammatory response following laser trabeculoplasty may be the cause, as certain prostaglandins applied topically have been shown to increase the IOP.³⁸ However, prostaglandin inhibitors have shown no beneficial effect.²⁶⁻³¹ Inflammatory debris silting up the trabecular meshwork has been implicated, but our study and others have found no correlation between inflammatory scores and postlaser IOP rises.^{27 30 31} It seems more probable that localised structural changes and oedema in the trabecular meshwork resulting from the laser burn temporarily reduce aqueous outflow, leading to a rise in IOP. This may be aggravated by an exudative response of the damaged trabecular cells producing a transient pseudomembrane,³⁹ further blocking egression of aqueous.

All investigators agree that an acute increase in intraocular pressure is deleterious and can lead to further loss of visual field or loss of central vision in a glaucomatous eye. Although Hoskins *et al.*¹³ did not find pretreatment with acetazolamide effective, we agree with Brooks *et al.*²⁵ that acetazolamide confers a high degree of safety. Our results of a large prospective, randomised series showed that pretreatment with 500 mg of oral acetazolamide is effective in decreasing both the frequency and the magnitude of the immediate IOP rise after argon laser trabeculoplasty. Pretreatment with acetazolamide had no effect on the results of argon laser trabeculoplasty at two months. None of our patients reported side effects from acetazolamide beyond slight paraesthesiae and mild gastrointestinal disturbance.

This study shows that the safe and widely available drug acetazolamide is of major value in preventing an acute pressure rise in patients undergoing argon laser trabeculoplasty.

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Neither of the authors has any financial, commercial, or proprietary interest in acetazolamide.

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