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The Effect of α_2-Agonist on IOP Rise Following Nd-YAG Laser Iridotomy

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We have tested the effect of topical administration of 0.5 % para-amino-clonidine (PAC), an adrenergic alpha 2 agonist, on intraocular pressure (IOP), protein and prostaglandin E_2 (PGE_2) concentration in aqueous humor following the laser application to the iris of albino rabbits. The irides received Q-switched Nd: YAG laser irradiation with the energy level ranging from 2 to 80 mJ with and without topical administration of PAC one-hour prior to and immediately following laser irradiation. The IOP was measured with an Alcon pneumotonometer prior to and hourly for 6-hours following laser application. Aqueous humor was withdrawn prior to and at 0.5, 1, 2, 4 hours following laser irradiation for determining protein (Lowry method) and PGE_2 (radioimmunoassay). Four to 6 rabbits were used for each experiment. The increase in IOP, protein and PGE_2 concentration following laser irradiation was demonstrated to be dependent on the amount of laser energy. PAC significantly suppressed the IOP rise and the elevation of protein content, while it failed to affect the increase in PGE_2.

Key words : Nd: laser iridotomy, para-amino-clonidine, protein, prostaglandin E_2, intraocular pressure

INTRODUCTION

Q-switched Nd: YAG laser iridotomy is a simple and timesaving method of eliminating pupillary block in angle-closure glaucoma.

However, Nd: YAG laser iridotomy (Nd: YAG LI) often brings about an immediate IOP rise and inflammatory responses of the anterior segment [1, 2]. The mechanism of IOP rise after Nd: YAG LI is still obscure [1, 3, 4] and there is no reliable means but preoperative, topical administration of para-aminoclonidine (PAC: adrenergic alpha 2 agonist) for circumventing this particular complication [5-8]. In attempts to elucidate the effects of PAC on the response of ocular tissues to laser irradiation, we conducted animal experiments where the IOP response to Q-switched Nd: YAG laser irradiation to the iris was measured along with that of aqueous protein and prostaglandin E_2 and the effects of PAC on these factors were determined [9, 10].

MATERIALS AND METHODS

Albino rabbits weighing 2-3 kg were used. Nd: YAG laser irradiation was carried out with a Q-switched Nd: YAG laser apparatus (Topaz, Lasag) with total energy level ranging from 2 to 80 mJ.

IOP study

The rabbits underwent Nd: YAG laser irradiation of the iris in one eye only, and the fellow eye served as an untreated control. IOP was measured by a pneumotonometer at 0, 0.5, 1, 2, 4 and 24 hours after laser irradiation.

The effect of para-amino-clonidine pretreatment on the IOP response to Nd: YAGLI was studied in the following manner. PAC ophthalmic solution 0.5 % was instilled in one eye and the contra lateral, fellow eye

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Table 1

The amount of laser energy and IOP change
ΔIOP (mmHg)

	Lasered eye		Untreated fellow eye			
2mJ	−0.5	±2.1	+0.5	± 2.4	n=4	N.S.
16mJ	+2.0	±1.6	+1.5	± 1.0	n=4	N.S.
24mJ	+8.9	±3.1	+0.75	± 1.7	n=4	P<0.025
48mJ	+16.25	±2.9	+2.75	± 3.3	n=4	P<0.01
80mJ	+14.0	±1.4	+0.25	± 0.5	n=4	P<0.005

ΔIOP = Maximum postlaser IOP-Base line IOP

Table 2

The amount of laser energy and IOP change
ΔIOP (mmHg)

	PAC-treated		Untreated with PAC			
2mJ	+0.75	± 2.5	+0.75	± 2.6	n=4	N.S.
16mJ	−4.25	± 1.3	−1.0	± 1.3	n=4	P<0.05
24mJ	−2.5	± 0.6	+4.3	± 2.2	n=4	P<0.005
48mJ	−4.25	± 5.2	+5.25	± 3.6	n=4	P<0.025
80mJ	−6.0	± 0.8	+8.1	± 8.0	n=4	P<0.025

ΔIOP = Maximum postlaser IOP-Base line IOP

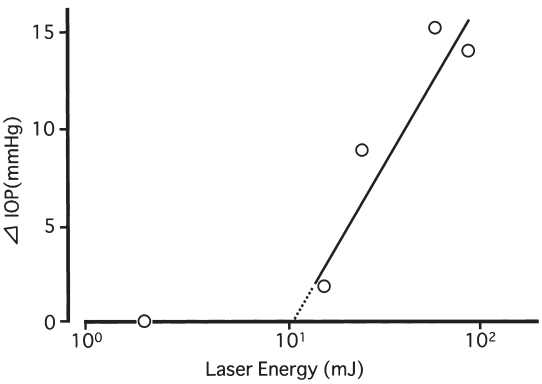

Fig. 1 The amount of laser energy and the change in intraocular pressure. The change in intraocular pressure (mm Hg) is calculated by subtracting the maximum postlaser IOP from baseline IOP.

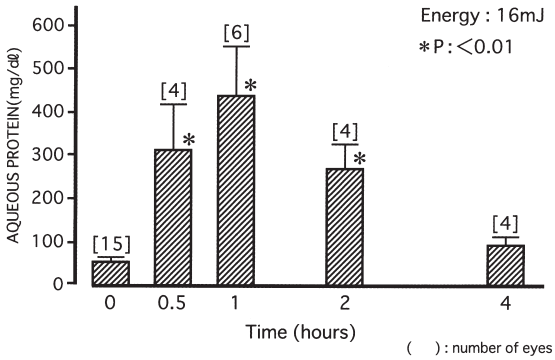

Fig. 2 The concentration of aqueous protein after Nd: YAGLI with total energy output of 16 mJ. Asterick indicate statisfically significant difference from time 0 (Wilcoxon rank sum test)

received placebo 1 hour prior to and immediately after Nd: YAG laser irradiation of the iris in both eyes. IOP was measured by a pneumotonometer at time 0, 0.5, 1, 2, 4 and 24 hours. For the determination of protein and PGE_2 content in aqueous humor, aqueous humor was aspirated from the anterior chamber of each eye with a 26 gauge needle one hour after the laser irradiation. Aqueous protein concentration was analyzed using the method of Lowry [11]. The content of PGE_2 in aqueous humor was determined by radioimmunoassay [12]. For each energy level a total of 8 to 12 rabbits were used for either protein or PGE_2 determination.

RESULTS

IOP rise:

The amount of laser energy and the resultant IOP change are shown in Table 1 and Fig. 1. Energy level of 2 and 16 mJ failed to induce a significant difference in IOP between the lasered and the untreated, fellow eyes. However, the energy level of 24, 48 and 80 mJ brought about a statistically significant IOP rise as compared with the untreated fellow eye.

The effect of PAC treatment on the IOP change following Nd: YAG laser irradiation is summarized in Table 2.

An increase in IOP of variable degree was observed in the control eyes that had not received PAC at 0.5-6 hours after YAG laser irradiation. While, IOP failed to rise in the contra lateral eyes treated with PAC. The difference in IOP change between the PAC-treated and the untreated eyes was of statistical significance for all energy levels but 2 mJ.

At the higher energy levels (16, 24, 48 and

Table 3 One hour after the laser irradiation, aqueous humor was aspirated from the anterior chamber of each eye with 26G needle.

The amount of laser energy and aqueous protein content (mg/dℓ)

	PAC-treated	Placebo-treated		
0mJ	46.4 ± 6.4	51.1 ± 7.0	n=4	N.S.
2mJ	68.15± 4.4	177.3 ± 63.3	n=4	P<0.025
16mJ	64.4 ± 14.2	431.25±232.3	n=4	P<0.05
24mJ	191.8 ±197.5	777.7 ±749.2	n=3	N.S.
48mJ	159.1 ±178.0	860.8 ±654.0	n=4	P<0.05
80mJ	248.8 ±293.8	1037.8 ±546.7	n=4	P<0.05

Table 4 One hour after the laser irradiation, aqueous humor was aspirated from the anterior chamber of each eye with 26G needle.

The amount of laser energy and aqueous PG E_2 (pg/mℓ)

	PAC-treated	Placebo-treated		
0mJ	37.8± 3.4	32.75± 3.40	(4)	N.S.
2mJ	400.0± 22.6	332.5 ±164.2	(4)	N.S.
16mJ	2125.0±1024.3	1865.0 ±756.0	(4)	N.S.
24mJ	1075.0± 263.0	950.0 ± 56.0	(4)	N.S.
80mJ	1100.0± 81.6	910.0 ±108.6	(4)	N.S.

( ) : number of eyes

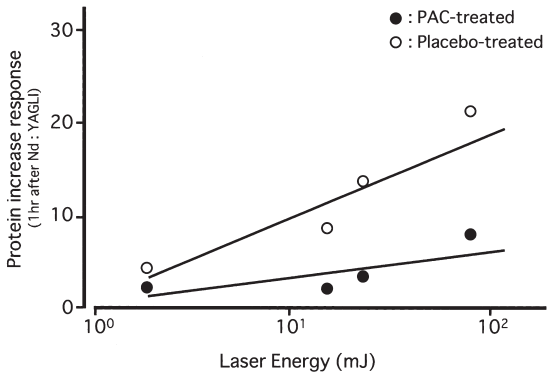

Fig. 3 The amount of laser energy and aqueous protein content. At the energy level between 16 and 80 mJ, the concentrations of aqueous protein of the placebo-treated eye (○) were 4-6 times higher than in PAC treated eye (●).

80 mJ) the IOP rise was statistically, significantly less in the PAC-treated as compared with the untreated with PAC.

Aqueous protein:

The change of aqueous protein with time after Nd: YAG laser irradiation (total energy: 16 mJ) is shown in Fig. 2. One hour after Nd: YAG laser irradiation, the highest concentration of aqueous protein was noted. Based on these results, we decided to determine the aqueous protein concentration at 1 hour period.

Aqueous protein content was found to be dependent on the amount of laser energy. When PAC ophthalmic solution 0.5 % was instilled in one eye 1 hour prior to and immediately after laser application to both eyes (at time 0 in each animal), the aqueous protein concentration was significantly less in PAC treated eyes than in the placebo-treated (Table 3). At the energy level between 16 and 80 mJ, the concentrations of aqueous protein of the placebo-treated eye were 4-6 times higher than in PAC treated eye (Fig. 3).

PGE_2 in aqueous humor:

The amount of laser energy and aqueous PGE_2 is shown in Table 4. There was no statistically significant difference in PGE_2 concentration between the PAC-treated and the placebo-treated eyes. Thus, pretreatment of PAC failed to affect the increase of PGE_2 after Nd: YAG LI.

DISCUSSION

Recently, Goluboric reported intracameral injection of PGE_2 produced a long-lasting increase in IOP and protein concentration of the aqueous humor [13]. The increase in

PGE_2 and protein content was demonstrated in rabbits aqueous humor following the laser application to iris and the postlaser IOP rise was found to be directly proportional to the increase in aqueous protein and PGE_2 content [4, 9, 14]. Subsequent studies revealed the inhibitors of PG synthesis significantly reduced but failed to completely prevent the IOP rise following laser application to iris or trabecular meshwork in glaucoma patients.

Para-Amino-clonidine (PAC) is also known to prevent IOP rise in the laser iridotomy [5-8]. However, the biochemical and pharmacological mechanism of the prevention of IOP rise after lase iridotomy by PAC has not been studied until now. Present study shows that the treatment with PAC ophthalmic solution before and at the completion of YAG laser irradiation significantly suppresses the IOP rise and the increase of protein concentration, but failed to affect the increase in PGE_2 following Nd: YAG laser irradiation. The results seem to indicate that PGs do not constitute the sole group of causative factors involved with the development of IOP rise and that the other factors such as the increase of protein content also play an important role in the postlaser IOP elevation. Thus, the further studies are still needed to clarify the mechanism of postlaser IOP elevation.

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