Acta Medica Okayama

Volume 11, *Issue* 1 1957 *Article* 4

APRIL 1957

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Abstract

The existence of autonomic adjustment functions of eye pressure was demonstrated in various ways, both clinically and experimentally. It is possible to consider that in normal condition, I.O.P. is controlled autonomically like cardiac or respiratory rate irrespective of the internal or external influences of the body. The auther calls such a phenomenon "autonomic eye pressure adjustment function". The mechanism of this physiological function will be reported on in articles to follow.

Acta Med. Okayama 11, 1, 23—30 (1957)

STUDIES ON THE ETIOLOGY OF GLAUCOMA PART I. EXISTENCE OF THE AUTONOMIC EYE PRESSURE ADJUSTMENT FUNCTION

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Received for Publication Feb. 20, 1957

Introduction

Glaucoma has been of the most important and interesting problems in recent ophthalmology. The author has been studying this subject, especially the etiology of glaucoma, for the past 10 years.

First of all, the mechanism controlling intra-ocular pressure has been investigated from several points. Some important physiological functions, such as blood pressure, pulse and respiratory rate, are controlled automatically by an autonomic nervous system, however little is known about what controls intraocular pressure. Many attempts have been made to demonstrate the autonomic eye pressure adjustment functions as the basic and fundamental problems in our serial studies on glaucoma.

Experiments and Results

1. The relations between general blood pressure and intra-ocular pressure

Although there are a considerable number of works on the relationship between general blood pressure and intra-ocular pressure, many aspects of this connection remain unclear. (v. HIPPEL. u. GRUNHAGEN[1], WESSELY[2], WEGNER[3], BARANY[4], YADA[5], TAMURA[6], OHASHI) The author has investigated this problem clinically and experimentally.

a. Age and intra-ocular pressure

It is generally accepted that blood pressure increases in proportion to a person's age. If intraocular pressure has a parallel relation with blood pressure, it must also increase with age. Clinical investigations were made on 1282 normal people from the ages of 8 to 92, however no increase of intraocular pressure seemed to accompany an increase in age (Table 1). On the contrary, a decrease in intraocular pressure was found in older people. The same tendency has heen reported by WEGNER[3] and OHASHI. For example, a comparison of the intraocular pressures of a group

Table 1. Relation Between I. O. P. and Age

Age	Number of eyes	I. O. P. in Average
8—19	218	19.986±0.158 mmHg
—29	220	20.862±0.245
—39	224	19.268±0.129
—49	162	19.586±0.203
—59	180	19.980±0.176
—69	120	19.118±0.276
—79	132	18.712±0.258
—92	26	18.120±0.279
Total	1286	19.725±0.0924

$r = -0.14425 \pm 0.02736$

of persons under 59 years old with that of a group above 60 years old, showed that the I. O. P. in the former group was 19.936±0.182 mmHg and that of the latter group, 18.65±0.271 mmHg.

Statistic analysis in these two numbers showed a significant difference.

$$\therefore \quad \frac{M_1 - M_2}{\sqrt{m_1^2 + m_2^2}} = 4.01 > 3$$

b. Maximum and Minimum-blood pressures and I. O. P.

In 472 cases of healthy persons, aged 8 to 80 and in 177 cases of patients who had abnormally high or low blood pressure, the relation between blood pressure at maximum and minimum points and I. O. P. was examined clinically and statistically. In both groups the 472 healthy persons, (Tables 2, 3) and the ones with abnormal blood pressure (121 cases of essential hypertension, 22 cases of renal hypertension, 24 cases of heart disease and 10 cases of hypotension), no significant relationship between blood pressure and I. O. P. could be found.

Table 2. Relation between Maximum Brachial Artery Pressure (B. A. P.) and I. O. P. in Normal Condition

B. A. P. (mm. Hg)	I. O. P. (mm. Hg)											
	30.6 – 32.5	28.6 – 30.5	26.6 – 28.5	24.6 – 26.5	22.6 – 24.5	20.6 – 22.5	18.6 – 20.5	16.6 – 18.5	14.6 – 16.5	12.6 – 14.5	10.6 – 12.5	Total
101—110		1			5	2	11	5	1	1		26
111—120				2	13	28	71	53	29	3	4	203
121—130		3	6	13	25	19	92	68	28	3	3	260
131—140			11	12	28	39	73	42	28		2	235
141—150	2	3	6	7	4	18	45	27	13	4	5	134
151—160			5	6	6	6	13	24	8	1	1	70
161—170		1					5	3	5	2		16
Total	2	8	28	40	81	112	310	222	112	14	15	944

$r = 0.07072 \pm 0.0324$

Table 3. Relation between Minimum Brachial Artery Pressure (B. A. P.) and I. O. P. in Normal Condition

B. A. P. (mmHg)	I. O. P. (mm. Hg)										
	30.6 – 32.5	28.6 – 30.5	26.6 – 28.5	24.6 – 26.5	22.6 – 24.5	20.6 – 22.5	18.6 – 20.5	16.6 – 18.5	14.6 – 16.5	12.6 – 14.5	10.6 – 12.5	Total
31—40			1	2	2		4					9
41—50				2	3	8	14	12	8			47
51—60			6	4	6	25	58	29	19	3		150
61—70		3	8	18	33	41	102	75	39	7	6	332
71—80	2	3	9	6	31	20	79	80	28	2	3	263
81—90		2	4	8	6	18	53	26	18	2	6	143
Total	2	8	28	40	81	112	310	222	112	14	15	944

$r = 0.01802 \pm 0.03256$

Average of I. O. P. ……………………………21.21 ± 0.198 mmHg
Average of maximum blood pressure…………64.83 ± 1.827 mmHg
Correlation coefficient ……………………$r = 0.08123 \pm 0.0528$
Average of minimum blood pressure…………89.379 ± 1.136 mmHg
Correlation coefficient ……………………$r = 0.0927 \pm 0.0527$

From the above clinical and statistical observations, I. O. P. seems to have little relation to general blood pressure, but seems to be independently controlled in maintaining the physiological value.

c. Relation between the pressure of a circulating fluid in the head and I. O. P.[7]

For the purpose of clarifying experimentally the relation between general blood pressure and I. O. P. under simple conditions, an artificial circulation experiment using rabbits was made. Irrigation, with a normal salin solution through the bilateral carotid arteries, was undertaken with the different pressure, and I. O. P. variations were recorded by manometry.

In the rabbits which died half-way through the circulation experiment, the I. O. P. rose gradually, together with the increase of fluid pressure, and then maintained a maximum value at a certain level (Table 4).

In living rabbits, however, the I. O. P. temporarily increased following a rise in fluid pressure, and then after a while decreased however it seemed to have a tendency to return to its initial value. A variation of I. O. P. following a variation of circulating fluid pressure is less intensive in a living rabbit than in a dead one (Table 5).

This phenomenon suggests that in living rabbits there is a certain

Table 4. Relation between Fluid Pressure (F. P.) and I. O. P. in the Circulation Experiment. (in dead rabbit)

Rabbit No.	Duration after death	Variation of F. P. (mm. Hg)	Variation of I. O. P. (mm. Hg)	Time required to get the constant I. O. P.
1	5 min.	90→150	25→27	1′
1	10 min.	150→ 50	27→25	5′ 20″
2	22 min.	10→150	9→34	12′ 36″
2	50 min.	90→150	Typically elevated	1′ 6″
2	70 min.	150→ 50	Dropped	3′ 45″
3	15 min.	90→ 50	30→25	30″
3	23 min.	90→150	Elevated	/
3	35 min.	90→ 10	Dropped	/
7	10 min.	90→150	22→34	5′
7	20 min.	90→ 30	22→13	2′
8	20 min.	90→ 30	22→12	1′ 10″
8	25 min.	30→ 90	12→22	1′ 20″

Table 5. Relation between Fluid Pressure (F. P.) and I. O. P. in the Circulation Experiment. (in living rabbit)

Rabbit No.	Variation of F. P. (mmHg)	Variation of I. O. P. (mmHg)	Time until the maximum I. O. P.	Time until the constant I.O.P.
9	90→150	22→25→22	40″	1′ 24″
10	150→ 90	25→19→25	42″	1′ 12″
10	90→150	22→25→22	24″	48″
12	90→150	18→21→18	30″	1′ 30″
16	90→150	19→23→20.5	54″	1′ 30″
18	90→150	13→16.5→14	2′ 15″	4′
19	90→150	19→21→19.5	24″	2′ 6″

physiological autonomic eye pressure adjustment function which adjusts I. O. P. to any variation in th general blood pressure.

2. The influence of eyeball-compression on I. O. P.[8]

Variation in I. O. P. which was artificially caused by compression of the eyeball was examined. Using rabbits anesthetized with Urethan, the eyeballs were compressed by an ophthalmodinamometor, with twenty-two gm pressure being exerted upon the cornea. The variations of I. O. P. were then recorded by manometry. A sudden increase of I. O. P. occurred just after the compression of the eyeball, this was followed by a gradual decrease in pressure which continued for 5 to 10 minutes (an average of 6.6 minutes) until finally the I. O. P. returned to its initial level. At the moment of the removal of compression, a sudden decrease of I. O. P.

occurred. However the pressure gradually returned to normal in from 4 to 10 minutes (an average of 7.35 minutes). This phenomenon suggests that the autonomic eye pressure adjustment function is in the eye itself. (Table 6).

Table 6. Result of the Compression Experiment

Rabbit No.	Initial I.O.P. (mmHg)	Power of compres-sion (gm)	Duration of the compres-sion (min)	I.O.P. immediate-ly after the compression (mmHg)	Time required to recover (min)	I.O.P. immediate-ly after the removal of compression (mmHg)	Time required to recover (min)
1	16.0	22.0	10	32.0	5	14.5	4.8
2	20.5	22.0	10	25.0	6	16.5	10
3	25.0	22.0	10	28.0	7	23.5	7
4	26.0	22.0	10	29.0	10	25.0	5
5	28.0	22.0	15	30.5	5	26.5	10
Average	23.1	22.0		26.9	6.6	21.2	7.35

3. Consensual ophthalmotonic reaction

WEEKERS[9, 10] and others have reported that if a variation of I. O. P. occurred in one eye, a related alteration was provoked in the other eye. *Weekers* called this reaction "a Reaction ophthalmotonique consensuelle." To examine autonomic adjustment functions of eye pressure further, the following experiment was made, using rabbits[11]. The I. O. P. of one eye was artificially raised (60—80 mmHg) or lowered (10 mmHg) by compression or suction with a normal salin solution through the canula inserted in a vitreous and then the I. O. P. of the other eye and the blood pressure of the carotid artery were recorded simultaneously by manometry. If the I. O. P. was raised artificially in one eye, (Table 7) a lowering of I. O. P. was found in the other eye. If the I. O. P. in one eye was lowered artificially, a raising of the I. O. P. in the other eye was demonstrated. Hence, it is presumable that there is a certain function preventing the change of I. O. P. when an abnormal variation of I. O. P. is created.

IMACHI[12] has reported a similar phenomenon in the development of sympathetic glaucoma and explained that if the I. O. P. of one eye is raised abnormally by an increased tonus of the sympathetic nervous system, the tonus of the parasympathetic nervous system is increased through an oculo-vago-reflex, and consequently a lowering of the I. O. P. in the other eye takes place. This phenomenon is understood as a protective reaction against a destruction of the visual function.

Table 7. Variation of I. O. P. and Blood Pressure Following the Sudden Increase of I. O. P. of the Opposite Eye

Rabbit No.	Original side		Influencing eye		Systemic blood pressure	
	Value of increased I. O. P. (mmHg)	Duration of increased I. O. P. (min)	Initial I. O. P. (mmHg)	Type of variation	Initial pres-sure (mmHg)	Type of variation
28	60	2.2	26.5	Slight elevation just after the compression→drop→1 mmHg down	88	2—3 mmHg down→recover
29	80	1.0	21.5	Gradual drop 0.2 mmHg	78	10 mmHg down→recover
30	〃	1.7	27.0	Gradual drop (0.1 mmHg)	80	no variation
31	〃	1.2	27.5	First rapidly, then gradually dropped. (1.0 mmHg)	94	First 28 mmHg down→gradually increase but still lower
33	〃	2.0	28.0	no variation	95	no variation
34	〃	1.5	25.5	no variation	95	First 4—5 mmHg down→recover
35	〃	〃	23.0	no variation	115	no change
36	〃	〃	21.5	Gradual drop (0.5 mmHg)	87	no change
44	〃	2.5	32.0	Gradual drop (0.7 mmHg)	82	First 5 mmHg down→recover
45	〃	2.2	25.5	Gradual drop (0.2 mmHg)	92	Increase from the beginning (6 mmHg)

4. Phasic variations of I. O. P.

It is a well known fact that I. O. P. does not always have a constant value and that there is some physiological variation in it. The diurnal variation of a healthy eye, however, is very small in value and never exceeds 3 or 4 mmHg (ADLER)[13] or 5 mmHg (DUKE-ELDER)[14]. However in a glaucomatous eye, the diurnal variation is considerable and sometimes exceeds 50 mmHg.

The I. O. P. of 62 healthy eyes, of 44 eyes with simple glaucoma, and of 22 eyes with congestive glaucome were measured 6 times daily with a 4 hour interval between each measurement. Abnormal diurnal I. O. P. variations, exceeding 5 mmHg, occurred in only 4.5% of the normal eyes, but in 86.4% of the eyes with simple glaucoma and in 91.7% with congestive glaucoma (Table 8).

The above seem to indicate that under normal healthy conditions there seems to exist a physiological function which constantly maintains the I. O. P. at a certain level irrespective of the external or internal

Table 8. Phasic Variation of I. O. P.

	Value of diurnal variation (mmHg)				
	Under 5	6—10	11—20	21—30	Above 31
Healthy eye	4.5%	95.5%			
Simple glaucoma	13.6%	45.5%	25.0%	13.6%	2.3%
Congestive glaucoma	8.3%	0 %	66.7%	16.7%	8.3%

influence of the body.

5. Provocative tests.

There are many provocative tests of glaucoma as a supplemental diagnostic procedure. The diagnostic principle of these tests seems to be an evaluation of the responces of I. O. P. to a certain load on normal and glaucomatous eyes.

Several provocative tests were employed at our clinic[15]. For instance, in the liability test, the difference between I. O. P. before and after this test was 1.5 to 9.5 mmHg (an Average of 4.6 mmHg) in 20 healthy eyes, and from 2 to 58 mmHg (an Average of 11.9 mmHg) in 45 eyes with primary glaucoma. This fact indicates that the capacity for resistance to an extra load in a healthy eye is greater than that in a glaucomatous eye.

Conclusion

The existence of autonomic adjustment functions of eye pressure was demonstrated in various ways, both clinically and experimentally. It is possible to consider that in normal condition, I. O. P. is controlled autonomically like cardiac or respiratory rate irrespective of the internal or external influences of the body.

The auther calls such a phenomenon "autonomic eye pressure adjustment function".

The mechanism of this physiological function will be reported on in articles to follow.

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