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Communications

Systemic blood pressure in open-angle glaucoma, low tension glaucoma, and the normal eye

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The object of the present study was to investigate the hypothesis that a low systemic blood pressure might be associated with so-called low tension glaucoma: the rather unexpected result was an association between open-angle glaucoma and vascular hypertension. Theoretically, the pressure in the ophthalmic artery as shown by ophthalmodynamometry is likely to be a better index of blood pressure in arteries in the eyeball than the systemic blood pressure measured at the upper arm; however, in practice, we have the impression that the latter estimate has less observer error and so it has been chosen for this study. A good correlation seems to exist between ophthalmic artery and brachial artery pressure (Smith and Cogan, 1959; Johnson and Drance, 1968a).

The relationship between ischaemia of the optic nerve and retina, blood pressure, and glaucoma has been studied by several authors in various ways:

(*a*) *Optic nerve ischaemia and glaucoma*

Schnabel (1885) introduced the term "cavernous optic atrophy" and Wolff (1947) agreed that the condition was the result of ischaemia. Duke-Elder (1962) also considers arteriosclerosis, etc., to be important in open-angle glaucoma.

(*b*) *Low tension glaucoma and low blood pressure*

Weekers (1942) and Sjögren (1946) noted that patients with low tension glaucoma often have low blood pressure.

(*c*) *Lowering of blood pressure and increased field loss*

These have been observed in glaucoma by several authors, for example Harrington (1959) and Lobstein, Bronner, and Nordmann (1960).

(*d*) *Glaucoma, blood pressure (including perfusion pressure), and atherosclerosis*

(i) LOW BLOOD PRESSURE

Sachsenweger (1963) and Ebner (1967) found a more rapid deterioration in the visual fields in glaucoma patients with low blood pressure than in those with either high or normal blood pressure. Lobstein and Herr (1966) showed that, in glaucoma, field loss was greater the lower the blood pressure.

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(ii) HIGH BLOOD PRESSURE

Kümmell (1911) and Vele (1933) found higher blood pressures in glaucoma patients of all types than in controls of similar age. Elschnig (1917) could find no such difference. Weinstein (1935) also found higher blood pressure in glaucoma patients than in normal subjects but observed that the scatter of the values was very wide and concluded that hypertension did not predispose to glaucoma. Calhoun (1929) and Dienstbier, Balík, and Kafka (1950) reported an association between hypertension or vascular disease and glaucoma, but controls were lacking, as with Sugar (1950) who noted no direct relation between elevated blood pressure and elevated ocular tension but an association between glaucoma and hypertensive vascular sclerosis.

Mirzatas (1965), using ophthalmodynamometry, found higher diastolic pressures in patients with chronic simple glaucoma than in normal subjects. There was no difference in systolic pressures. In chronic simple glaucoma high diastolic pressure was associated with high intraocular pressure. Bettelheim (1967) found no relationship between intraocular pressure and orbital blood pressure determined by ophthalmodynamography.

(iii) BLOOD FLOW AND PERFUSION PRESSURE

Reese and McGavic (1942) showed that a small ratio between systolic or diastolic blood pressure and ocular tension was associated with a greater amount of field loss than a large ratio between blood pressure and ocular tension. Hager (1966) used ophthalmodynamography to demonstrate a poor orbital blood flow in patients with low tension glacoma. François and Neetens (1970) found a correlation between the degree of field loss in glaucoma and a "gradient" which takes into account the ophthalmic artery pressure, estimated by ophthalmodynamometry, and the intraocular pressure.

Drance (1968) studied patients with open-angle glaucoma by ophthalmodynamography. Their diastolic perfusion pressures were either lower than in normal subjects, or there was a history of severe bleeding myocardial infarction, or arteriosclerotic heart disease; see also Drance, Wheeler, and Pattullo (1968) and Johnson and Drance (1968b). Begg, Drance, and Sweeney (1971) found evidence of extraocular small vessel disease in patients showing disc haemorrhages along with a sudden advance in field loss.

(*e*) *Artificial elevation of ocular tension and visual field changes*

Gafner and Goldmann (1955) and Goldmann (1956), using skiascotometry and quantitative perimetry, demonstrated a focal diminution in the sensitivity of the Bjerrum area in early cases of simple glaucoma who had no detectable disturbances of the visual field examined by other means. Artificial increase in the ocular tension of normal persons caused the same disturbances. The minimal pressure necessary to produce these effects correlated closely with the pressure in the ophthalmic artery. Inhalation of air with a low oxygen content, or compression of the blood vessels in the neck with a sphygmomanometer cuff, also caused diminished sensitivity in the visual field, but the pattern of this was different from that caused by increased ocular tension. Drance (1962) showed that field loss increased with artificial increase in intraocular pressure (by means of a suction cup) more in severely affected glaucomatous eyes than in less affected ones; similarly, in individual patients, increasing field loss resulting from artificially raised pressure was more marked in the more affected of a pair of glaucomatous eyes. Hayreh (1969) showed that acute elevation of the intraocular pressure in monkeys selectively obliterated the vessels of choroidal origin in the optic disc and circumpapillary choroid. Blumenthal, Gitter,

Best, and Galin (1970) found that, as the intraocular pressure was artificially raised by suction ophthalmodynamometry, the vessels to the optic disc and circumpapillary choroid collapsed before the remaining choroidal vessels and the central retinal artery.

Methods

It is likely that a number of variables would obscure any relationship between systemic blood pressure and ocular tension in open-angle glaucoma: for example, myopic eyes probably tend to suffer from low tension glaucoma (Perkins, 1959; Winstanley, 1959)—their large size, especially disc size, may make them unduly susceptible to ocular tension even within the "normal range" (see Discussion).

Accordingly, each of eleven patients with low tension glaucoma was carefully matched with one open-angle glaucoma patient and one normal control for refractive error within the range $\pm 1{\cdot}50$ D sph. Only one eye of each patient was included, the eyes giving the better match for refractive error being selected. Similarly, the patients were matched for sex and age because these are important factors in both blood pressure and ocular tension; age-matching was difficult because priority was given to refractive error—the range +9 to −13 years was accepted. A matched pairs 't' test applied to the differences in refractive errors and ages between the three groups showed that they were not significant; an F test showed no significant difference between the range of ages in the three groups.

Many other possibly important characteristics had to be ignored, *e.g.* state of atherosclerosis, nutrition, obesity, etc.

The blood pressure in the brachial artery in the upper arm was estimated by the standard mercury sphygmomanometer after the patient had been resting *recumbent for at least 15 minutes.* The systolic pressure was taken to corrrespond with the appearance of any sound as the column of mercury fell, and diastolic pressure as the sudden diminution in volume of the sound (or its disappearance when no diminution was obvious) as the mercury continued to fall. The readings were all taken by one or other of the present authors.

A total of 33 subjects was studied in the following groups, only one eye from each patient being included:

low tension glaucoma (11 patients); open-angle glaucoma (11 patients); normal (11 subjects).

The following criteria for inclusion in the first two categories were adopted:

(1) Pathological cupping of the disc.

(2) A field defect of the type found in open-angle glaucoma.

(3) Angle of anterior chamber open at a time of "elevated" pressure and judged unlikely to close.

(4) (*i*) *For low tension glaucoma:* maximum ocular tension never more than 23 mm. Hg (ten of the eleven subjects had had repeated tensions taken during at least one morning as well as on many separate occasions at clinic attendances). Mean age 71·7 years (range 58–85); mean refractive error −0·93 D sph. (range +3·25 to −7).

(*ii*) *For open-angle glaucoma:* maximum recorded ocular tension on at least one occasion of 24 mm. Hg or more. Mean age 68 years (range 60–82); mean refractive error −0·66 D sph. (range +4 to −6).

The "normal" controls were obtained from two sources: (*a*) Five from the outpatient clinic; they had attended because of vitreous floaters (2), macular degeneration (1), meibomian cyst (1), and corneal ulcer (1—the normal eye was used); (*b*) Six came from the refraction clinic.

Mean ocular tension was 15·4 mm. Hg (S.D. 2·86) at the one examination on which it was done; appearances of discs were within normal limits. The mean age was 68 years (range 56–75) and mean refractive error −0·56 D sph. (range +3 to −5·5).

Results

Fig. 1 shows the mean systolic and diastolic blood pressures in the three groups. Fig. 2 shows the correlation between applanation tension and diastolic blood pressure when the open-angle glaucoma and low tension glaucoma groups were combined.

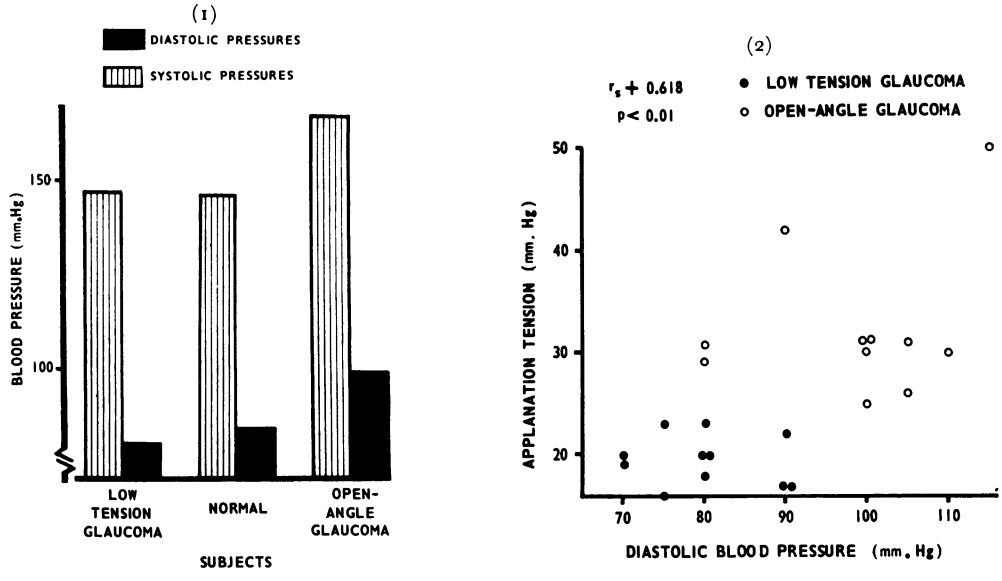

FIG. 1 *Bar charts of systemic blood pressure measured from the brachial artery after at least 15 minutes recumbency.*

Eleven subjects were in each group. Systolic and diastolic readings were significantly greater in open-angle glaucoma than in either normal controls (systolic $0{\cdot}02 < P < 0{\cdot}05$; *diastolic* $P < 0{\cdot}01$*) or in low tension glaucoma (systolic* $0{\cdot}02 < P < 0{\cdot}05$; *diastolic* $P < 0{\cdot}001$*). Between the low tension glaucoma and normal control groups there were no significant differences in blood pressure*

FIG. 2 *Scattergram of maximum recorded applanation tension and diastolic blood pressure, the latter after 15 minutes' recumbency, in eleven patients with open-angle glaucoma and eleven patients with low tension glaucoma. A significant correlation between systolic blood pressure and maximum recorded applanation tension was also found;* $r_s = +0{\cdot}373$ $(0{\cdot}01 < P < 0{\cdot}05)$

The Table shows the statistical analyses; the significant results are:

(1) For open-angle *versus* low tension glaucoma, both systolic and diastolic pressures were significantly greater in open-angle glaucoma. The difference was more significant for diastolic pressure ($P < 0{\cdot}001$) than systolic pressure ($0{\cdot}02 < P < 0{\cdot}05$).

Table *Systemic blood pressure in three groups: low tension glaucoma, open-angle glaucoma, and normal controls, eleven in each group*

Mean blood pressure (mm. Hg)	*Low tension glaucoma*	versus		*Open-angle glaucoma*	versus		*Normal controls*	versus		*Low tension glaucoma*
Systolic	147	t 2·439	P 0·02 < P < 0·05*	169	t 2·316	P 0·02 < P < 0·05*	146	t 0·047	P > 0·90†	147
Diastolic	80	t 5·646	P < 0·001*	99	t 3·187	P < 0·01*	84	t 0·714	P 0·40 < P < 0·50†	80

A matched pairs Student's 't' test was used to compare differences
* = significant results † = not significant

(2) For open-angle glaucoma *versus* normal controls, both systolic and diastolic pressures were greater in open-angle glaucoma. Again the difference was more significant for diastolic pressure ($P<0{\cdot}01$) than systolic pressure ($0{\cdot}02<P<0{\cdot}05$).

(3) For low tension glaucoma considered along with open-angle glaucoma, the higher the applanation tension, the higher was the diastolic blood pressure to a high level of significance; $P<0{\cdot}01$ by a Spearman rank correlation test; $r_s = +0{\cdot}618$. A correlation between a high applanation tension and high systolic blood pressure was also present; $0{\cdot}01<P<0{\cdot}05$; $r_s = +0{\cdot}373$.

(There was no significant difference in blood pressure between normal controls and low tension glaucoma).

Discussion

CRITERIA OF GROUPS

An objection to our criteria for subdivision into the three categories could reasonably be that repeated measurement of ocular tension throughout a full period of 24 hours was not done in any group of cases. Because of this, it is possible that some cases have been wrongly classified; however, if so, the differences we have found would tend to be *less* than the differences which in fact exist. Accordingly, we submit that a real difference exists between our three groups on the basis of the admittedly arbitrary criteria for open-angle glaucoma of maximum recorded ocular tension greater than 23 mm. Hg and for low tension glaucoma of maximum recorded tension not greater than 23 mm. Hg. Another important defence against objections to our criteria for groups is the correlation between applanation tension and blood pressure in the 22 patients with low tension and open-angle glaucoma: any grouping must involve an arbitrary cut-off point in what appears to be a continuous series.

Tonography and provocative tests were not included as criteria.

The careful control for refractive error, age, and sex has probably been important in revealing the difference found. However, control for axial length was less stringent: in low tension glaucoma it was almost significantly greater than in open-angle glaucoma ($t = 1{\cdot}826$ $0{\cdot}05<P<0{\cdot}10$). Also the 15 minutes (at least) of recumbency has probably reduced the variance of blood pressure to "accentuate" the differences between means.

Conclusion

The conclusion seems justified that chance is a very unlikely explanation for the finding of a tendency for relatively high blood pressure to be associated with open-angle glaucoma.

HYPOTHESES

There are three possible explanations for the association:

(*a*) Open-angle glaucoma is a factor in producing relatively high blood pressure.

(*b*) Relatively high blood pressure is a factor in producing open-angle glaucoma.

(*c*) Both open-angle glaucoma and relatively high blood pressure share a common cause or causes.

We consider that (*a*) is unlikely, although it *is* possible that anxiety about a disease which the patients know they have affects the blood pressure; however, if that were so, there should also be a similar effect in low tension glaucoma. A more likely explanation is (*b*); the capillary circulation at the disc may be the more precarious the higher the blood pressure. It may well be that explanation (*c*) is valid possibly in addition to (*b*), *e.g.* the trabecular meshwork and/or the ciliary epithelium may be affected by the same process(es)

which produce(s) vascular hypertension. The problem might be best studied experimentally in primates, but a study of ocular tension in vascular hypertensives from different causes would probably be valuable. A study of a large group of "normals" is planned; this would be useful even if no correlation were found in them between ocular tension and blood pressure. We are also collecting and analysing data from a large series of patients with open-angle glaucoma and their first-degree relatives.

It should be noted that the differences between these groups would probably be reduced or eliminated by a consideration of perfusion pressure. No significant difference was found between the normal and open-angle glaucoma when:

$$\frac{\text{systolic} - \text{diastolic B.P.}}{2} + \text{diastolic B.P.} - \text{ocular tension}$$

was considered.

MECHANICAL AND OTHER FACTORS

We have no really satisfactory explanation for the relatively normal blood pressure in low tension glaucoma. (It should be noted that the ocular tension was significantly higher than in the normal ($P<0.01$), though significantly lower than in open-angle glaucoma ($P<0.001$); accordingly treatment to reduce ocular tension would seem just as important as in open-angle glaucoma). A multifactorial aetiology in low tension glaucoma seems especially likely. For example, mechanical factors may play a part, related to greater axial length with or without myopia which probably tends to be associated with low tension glaucoma (Perkins and Winstanley, 1959; Tomlinson and Leighton, 1972). The retinal nerve fibres in the eye with a great axial length (and a high cup/disc area ratio: Tomlinson and Phillips, 1969, and probably a large disc) may have less "slack", especially at the disc, than in a more normal eye, so that a quite small degree of cupping may stretch them or kink them over the edge of the disc or the cribiform plate. However, a similar argument might suggest that the supplying blood vessels are more attenuated before pathological cupping starts. That there seems to be more "slack" at the upper half of the disc may explain why the lower field is normally spared until late in the disease; the papillo-macular bundle may suffer less damage also because it passes through the cribiform plate quite peripherally. Another or a related factor may be a tendency for the blood supply of the inferior half of the disc to be less well developed than in the upper half because the foetal fissure is inferior.

The large disc which probably exists in the eye with a great axial length may be a factor in making it more susceptible to pathological cupping than the normal or small disc (Phillips, 1971). The "force" tending to bow the disc backwards depends primarily on *pressure* $\times$ *area*. (A 10 per cent. increase in diameter will, of course, produce a 21 per cent. increase in area.) The bowing is a result of (*a*) bending and (*b*) stretching, the effect of area being greater on the former especially at small deflections than the latter.

Summary

In eleven patients who had low tension glaucoma, with ocular tension never more than 23 mm. Hg, the brachial diastolic and systolic blood pressures were significantly less than in eleven patients with open-angle glaucoma (ocular tension 24 mm. Hg, or more) who had been matched for age, sex, and refractive error. A closely matched group of eleven normal controls (with ocular tensions, however, significantly less than the patients with low tension glaucoma) had blood pressures which were significantly less than in open-angle glaucoma but very similar to those with low tension glaucoma.

In the combined groups of eleven with low tension plus eleven with open-angle glaucoma, significant associations were found between a high ocular tension and a high diastolic blood pressure ($P<0.01$) and also a high systolic blood pressure ($0.01<P<0.05$).

We consider that the likeliest explanation for these factors is that the capillary circulation at the optic disc is more precarious in a patient with a relatively raised blood pressure than in a patient with a normal blood pressure; however, it may well be that the process(es) producing relative vascular hypertension may also affect the trabecular meshwork, ciliary epithelium, etc., to produce raised intraocular pressure.

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