CLINICAL RESEARCH

Prevalence of diabetes in glaucoma

ROY MAPSTONE, CHARLES V CLARK

Abstract

Oral glucose 75 g was given to 352 patients with chronic glaucoma, acute glaucoma, or ocular hypertension and 73 patients without glaucoma. The proportion of patients with shallow anterior chambers who showed an abnormal response was significantly greater than that in patients with deep anterior chambers and in the control group ($p < 0.005$). The probability of developing an abnormal response to oral glucose tests increased as the depth of the anterior chamber decreased; these two variables showed a significant negative linear correlation ($r = -0.79$, $p < 0.001$). The high prevalence of autonomic dysfunction in patients with shallow anterior chambers and glaucoma may explain this association. Because of this, acute glaucoma should be regarded as a symptom of diabetes.

Introduction

An association between diabetes, chronic (open angle) glaucoma, and ocular hypertension has been recognised for some years,[1-3] but acute (closed angle) glaucoma has a low prevalence in patients with diabetes.[4] This does not necessarily suggest that a low prevalence of diabetes exists in patients with acute glaucoma.

During a longitudinal study of a group of patients with acute glaucoma or ocular hypertension it became clear that there was probably an increased incidence of type 2 diabetes in that sample. This study was therefore done to determine the relation between diabetes, the primary glaucomas, and ocular hypertension.

St Paul's Eye Hospital, Liverpool L3 9PF
ROY MAPSTONE, MD, FRCS, consultant ophthalmic surgeon
CHARLES V CLARK, MB, CHB, research registrar
Correspondence to: Mr R Mapstone.

Patients and methods

As new and old patients attended the glaucoma clinic they were included in this study with the following criteria: all patients with acute glaucoma and one eye that had not developed the disease spontaneously and was not being treated with a miotic; all patients with chronic glaucoma who were not being, and had not been, treated with a miotic; and patients with ocular hypertension—that is, an intraocular pressure ≥ 21 mm Hg and no known predisposing cause and no evidence of glaucomatous damage—if they were not being, and had not been, treated with a miotic. Patients with secondary glaucoma were excluded.

A control group of 73 patients was selected with the following criteria: minimum age 40, no upper limit; new patients attending a general ophthalmic clinic for the first time; and no evidence of primary or secondary glaucoma. Patients with visually disabling cataracts were excluded.

DIABETIC STATE

No patient was pregnant, and anyone taking a diabetogenic drug was excluded. If a patient was a known diabetic that diagnosis was accepted and a glucose tolerance test not done. Other patients had an oral glucose tolerance test done according to the recommendations of the expert committee of the World Health Organisation[5]—that is, after at least three days of unrestricted diet, followed by an 11-14 hour overnight fast, the patient was given oral glucose 75 g in 300 ml water to be drunk within five minutes. Intravenous blood glucose was measured at zero time and at one and two hours after ingestion of glucose. Two abnormal patterns of response were recognised: if the fasting blood glucose concentration was ≥ 8 mmol/l (144 mg/100 ml) or the two hour sample was ≥ 11 mmol/l (198 mg/100 ml), or both, then that response was classed as diabetic. No patient, however, was classed as diabetic unless that response was obtained on two separate occasions. If the fasting blood glucose concentration was < 8 mmol/l and the two hour sample ≥ 8 mmol/l but < 11 mmol/l then that response was classed as impaired glucose tolerance.

ANTERIOR CHAMBER ANGLE

The appearance of the angle was assessed with a slit beam and the Van Herrick method,[6] each patient being classed as having wide or narrow angle eyes. This assessment was always made before the result of a glucose tolerance test was known, so three groups of patients were recognised: those with open angle glaucoma or ocular hypertension

and wide angle eyes; those with open angle glaucoma or ocular hypertension and narrow angle eyes; and those with closed angle glaucoma.

AXIAL ANTERIOR CHAMBER DEPTH

Axial anterior chamber depth—that is, the distance between the posterior corneal surface and the anterior lens surface—was measured with a Haag Streit meter. The depth of the fellow eye was measured in patients with closed angle glaucoma; in the other groups the depth of the right eye was measured. All measurements were made before the results of a glucose tolerance test were known.

Statistical methods used were χ^2 with Yates's correction, linear regression analysis, and Pearson's correlation coefficient.

Results

The table shows the statistical results in the four groups of patients; each group shows similar patterns of age and a preponderance of women. Fifty five patients had diabetes, of whom one was dependent on insulin. The proportion of abnormal responses to a glucose tolerance test in the patients with wide angle eyes (20 of 109) was not significantly different from that in the control group ($\chi^2=0{\cdot}02$, $p>0{\cdot}5$). In the patients with narrow angle eyes and those with closed angle glaucoma, however, the proportions were significantly different ($\chi^2=8{\cdot}28$ and 9·01, respectively, $p<0{\cdot}005$). Even after multiple comparisons these differences remained significant at less than the 1% level.

Statistical details of patients

	Wide angle eyes	Narrow angle eyes	Closed angle glaucoma	Control group
No of cases	109	101	142	73
Mean (SD) age (years)	65·1 (8·3)	67·7 (8·6)	66·1 (10·4)	66·2 (9·8)
Mean (SD) anterior chamber depth (mm)	2·61 (0·34)	2·01 (0·27)	1·87 (0·28)	2·44 (0·42)
Cases of diabetes (known diabetics)	9 (4)	17 (8)	24 (7)	5 (0)
Cases of impaired glucose tolerance	11	21	29	7
Men/women	45/64	35/66	40/102	18/55

If the clinical diagnosis is ignored and patients with ocular hypertension or primary glaucoma are classed according to their axial anterior chamber depth the probability, at any one depth, of showing an abnormal response to an oral glucose test decreases in a linear fashion as the depth increases (figure 1). There is a significant negative linear correlation between these two variables ($r=-0{\cdot}79$, $p<0{\cdot}001$); the regression equation is: probability = 0·9 − depth × 0·3. Figure 2 also shows the relation of the two hour blood glucose concentration against anterior chamber depth, excluding 19 known diabetics, 16 of whom had an anterior chamber depth $\leqslant 2{\cdot}2$ mm.

Discussion

These results do not support the view that impaired glucose tolerance and diabetes can be associated with a particular clinical type of glaucoma. They do suggest that, given glaucoma, an association exists between diabetes and the anatomical dimensions of the anterior segment of the eye, the clinical diagnosis being of secondary importance. In fact, if the clinical diagnosis is ignored and account is taken of anterior chamber depth only the shallower the anterior chamber the greater is the probability of a patient with that attribute showing an abnormal response to an oral glucose test (fig 1).

The lens of the eye of a diabetic is larger than that of a non-diabetic,[7] and the association described above might simply reflect this, which suggests that one effect of diabetes is to reduce the depth of the anterior chamber, and so the eye is more likely to get closed angle glaucoma. This is probably not an adequate explanation because an eye with a shallow anterior chamber will not necessarily get glaucoma—most will not.[8] Also, closed angle glaucoma is an acute event that demands an equally acute change in the anterior segment. A change in the thickness of the lens is usually gradual, so some other event or combination of events is necessary.

Acute glaucoma is often precipitated in fellow eyes, at high risk because the presenting eye has already developed the disease, by using drugs to increase the autonomic activity within the anterior segment of the eye.[9,10] Specifically, if pilocarpine and phenylephrine drops are instilled the pupil dilates in a mid-position, parasympathetic and sympathetic activity are at a maximum, and so the block force of the pupil apposing iris to lens is also at a maximum.[11] Consequently the diaphragm of the iris and the lens moves forwards, the iris touches the cornea, and the angle of the anterior chamber closes, producing acute glaucoma in 60% of such eyes.[12] This means that about one third of fellow eyes at high risk never develop acute closed angle glaucoma, mainly because the diaphragms of the iris and lens do not translate sufficiently.[13] The crucial factor that determines whether or not an eye develops acute glaucoma is not, therefore, the absolute value of the depth of the anterior chamber but how much it can decrease in response to autonomic stress. This in

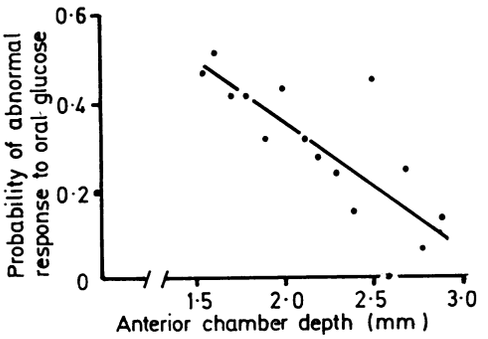

FIG 1—Probability of developing abnormal response to oral glucose test against anterior chamber depth.

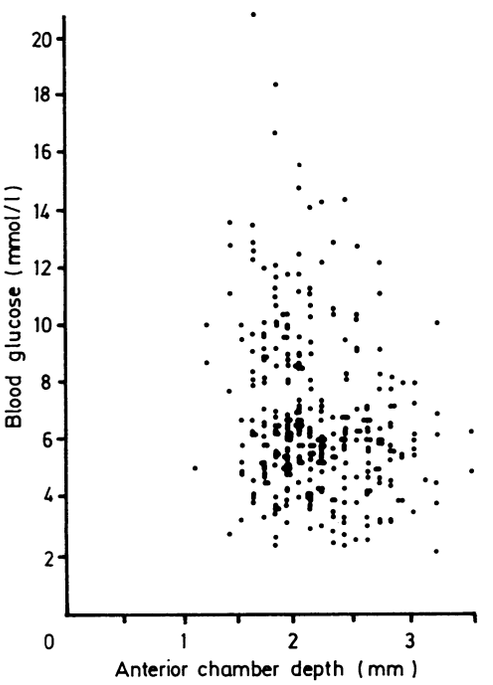

FIG 2—Plot of two hour blood glucose concentration against anterior chamber depth.

Conversion: SI to traditional units—Glucose: 1 mmol/l ≈ 18 mg/100 ml.

turn is largely determined by the response of the sphincter and dilator muscles to autonomic agonist drugs.

In a group of 112 patients with spontaneous acute glaucoma 65 (58%) showed evidence of systemic autonomic dysfunction with standard autonomic function tests (Valsalva's ratio, variation of heart rate during deep breathing, immediate response of heart rate to standing and lying, and decrease in systolic blood pressure in response to standing),[14] compared with a prevalence of 7% in a control group matched for age and sex without glaucoma. Also, the pupils of diabetics are partially denervated and show a supersensitivity to topically applied autonomic mediators—both sympathetic and parasympathetic.[15 16]

Perhaps the observed association between diabetes and acute glaucoma described above is a consequence of autonomic dysfunction within the anterior segment of the eye. Because of this dysfunction some anterior segments develop a heightened response to autonomic mediators, endogenously released or exogenously applied, and the diaphragm of the iris and lens moves forwards and closes the angle. The shallower the anterior chamber at the outset the greater the probability of this occurring.

We thank Dr R Vogel, Merck Sharp & Dohme Ltd, for computer facilities. CVC is in receipt of the R D Lawrence research fellowship from the British Diabetic Association.

References

1 Armstrong JR, Daily RK, Dobson HL, Girard L. The incidence of glaucoma in diabetes mellitus. *Am J Ophthalmol* 1960;**50**:55-68.
2 Becker B. Diabetes mellitus and primary open angle glaucoma. *Am J Ophthalmol* 1971;**71**:1-16.
3 Wilensky JY, Podos SM, Becker B. Prognostic indicators in ocular hypertension. *Arch Ophthalmol* 1974;**91**:200-2.
4 Nielsen NV. The prevalence of glaucoma and ocular hypertension in Type 1 and 2 diabetes mellitus. *Acta Ophthalmol (Copenh)* 1983;**61**:662-72.
5 World Health Organisation expert committee on diabetes mellitus. *WHO Tech Rep Ser* 1980; No 646.
6 Van Herrick W, Shaffer RN, Schwartz A. Estimation of width of angle of anterior chamber. *Am J Ophthalmol* 1969;**68**:626-9.
7 Brown N, Hungerford J. The influence of the size of the lens in ocular disease. *Trans Ophthalmol Soc UK* 1982;**102**:359-63.
8 Mapstone R. Clinical significance of a narrow angle. *Trans Ophthalmol Soc UK* 1978;**98**:216-8.
9 Mapstone R. Acute shallowing of the anterior chamber. *Br J Ophthalmol* 1981; **65**:446-51.
10 Mapstone R. Glaucoma. In: Davidson SI, ed. *Recent advances in ophthalmology*. Edinburgh: Churchill Livingstone, 1983.
11 Mapstone R. Provocative tests in closed angle glaucoma. *Br J Ophthalmol* 1976;**60**:115-9.
12 Mapstone R. The fellow eye. *Br J Ophthalmol* 1981;**65**:410-3.
13 Mapstone R. The pathological physiology of primary closed angle glaucoma. In: Cairns JE, ed. *Glaucoma*. London: Grune & Stratton (in press).
14 Mapstone R, Clark CV. The prevalence of autonomic neuropathy in glaucoma. *Trans Ophthalmol Soc UK* (in press).
15 Sigsbee B, Torkelson R, Kadis G, Wright JW, Reeves AG. Parasympathetic denervation of the iris in diabetes mellitus. *J Neurol Neurosurg Psychiatry* 1974;**37**:1031-5.
16 Smith SE, Smith SA, Brown PM, Fox C, Sonksen PH. Pupillary signs in diabetic autonomic neuropathy. *Br Med J* 1978;ii:924-7.

(Accepted 11 April 1985)

Selective consumption of large platelets during massive bleeding

CRAIG B THOMPSON

Abstract

To see whether selective consumption of either small or large platelets occurs during haemostasis in vivo the mean platelet volume was studied in six patients who developed thrombocytopenia after trauma. The mean platelet volume at the onset of thrombocytopenia was significantly lower than that on admission ($p < 0.01$): selective loss of large platelets had occurred.

Introduction

Recent reports have shown that mean platelet volume is increased in patients after acute myocardial infarction.[1 2] It has been suggested that this increase may contribute to the myocardial infarction as large platelets are more active than small ones in assays of in vitro aggregation. Sewell *et al* suggested, however, that the increase is the result of selective consumption of small platelets in vivo.[3] Despite in vitro evidence that large platelets are selectively consumed during platelet aggregation there is no direct evidence that similar selection occurs in vivo.[4 5] To test whether selective consumption of either large or small platelets occurs during in vivo haemostasis I studied the mean platelet volume in patients who developed thrombocytopenia after trauma.

Department of Medicine, University of Washington School of Medicine, Seattle, Washington, United States of America
CRAIG B THOMPSON, MD, department of medicine

Correspondence to: Dr C B Thompson, Fred Hutchinson Cancer Research Center, 1124 Columbia Street, Seattle, Washington 98104, USA.

Patients and methods

I studied six patients who were admitted as emergencies after major trauma or rupture of an aortic aneurysm and who initially had a normal platelet count and mean platelet volume, but developed thrombocytopenia within 24 hours after admission. Patients with a history of recent major illness or laboratory evidence of acute ethanol intoxication were excluded.

Complete blood counts, including platelet and mean platelet volume, were obtained (Coulter S+ counter) using blood samples anticoagulated with edetic acid.[2] Each sample was measured twice, the first analysis being done immediately on receipt in the laboratory to determine the platelet count and the second at least two hours after collection to confirm that the mean platelet volume had stabilised. No appreciable variation in the platelet count was observed between the two determinations. The patients' charts were reviewed to ensure that they had been receiving antiplatelet drugs. Initial blood samples were obtained before the patients received any blood products. Blood volume was maintained by giving either packed red blood cells or modified whole blood free of cryoprecipitate and platelets (on average 10 (SD 2) units, range 8-13 units). None of the patients received a transfusion of platelets before developing thrombocytopenia, but all patients received platelets for generalised vascular oozing within 24 hours after admission.

On admission the mean platelet count was 283 (SD 78) $\times 10^9$/l (range 218-398 $\times 10^9$/l) and mean platelet volume 9·0 (0·5) fl (range 8·5-9·8 fl), well within the normal ranges for the laboratory. All the patients developed thrombocytopenia (mean platelet count 95 (30) $\times 10^9$/l, range 61-146 $\times 10^9$/l) during the 24 hours after admission, necessitating transfusion of platelets. The mean platelet volume at the