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Ocular effects of acute hyperglycaemia

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SUMMARY Intraocular pressure and levels of glucose in plasma were recorded during a standard glucose tolerance test for 54 patients with chronic simple or low-tension glaucoma, and osmolality in plasma was also recorded for 12 patients. Significant correlations between the rates of change of these variables were not obtained, but the overall response of intraocular pressure correlated with the overall increase of plasma glucose, which also correlated with the increase of osmolality. These results show that the changes in refraction associated with acute hyperglycaemia arise from adjustments in fluid balance between intraocular compartments.

Transient changes in refraction may accompany the onset of diabetes mellitus or arise during periods of impaired control of established cases, myopia associated with hyperglycaemia being the most common finding in man.[1] Duke-Elder[1 2] reviewed these effects and concluded that change in the refractive power of the lens was probably involved, though the exact mechanism was uncertain. It is probable that various influences apply, arising from systemically induced changes in intraocular fluid balance, and we have examined some changes arising during a standard glucose tolerance test.

Patients and methods

Patients. Standard two-hour oral glucose tolerance tests using a 75 g load were performed on patients with chronic simple or low-tension glaucoma, who additionally showed disc haemorrhages or levels of glucose in randomly timed samples of plasma above a low arbitrary limit of 5 mmol/l. Simultaneous values for intraocular pressure, plasma glucose, and plasma osmolality were recorded for 7 male and 5 female patients aged 54–73, mean age 63·3 years. Values for intraocular pressure and glucose in plasma only were recorded for a further 16 males and 26 female patients aged 35–88, mean age 66·2 years, in an overall group of 23 male patients of mean age 66·6 years and 31 female patients of mean age 66·3 years. All patients were fasting without restriction of water, glucose was taken in ⅓ pint (200 ml) of water over a short interval between 0930 and 1000, and no further fluid was allowed during the test. Blood pressures were also recorded before and during the test, but no significant changes were observed.

Methods. Intraocular pressures were determined with a Goldmann applanation tonometer after routine examination of the eye. Values were recorded before and at 30 minute intervals during the glucose tolerance

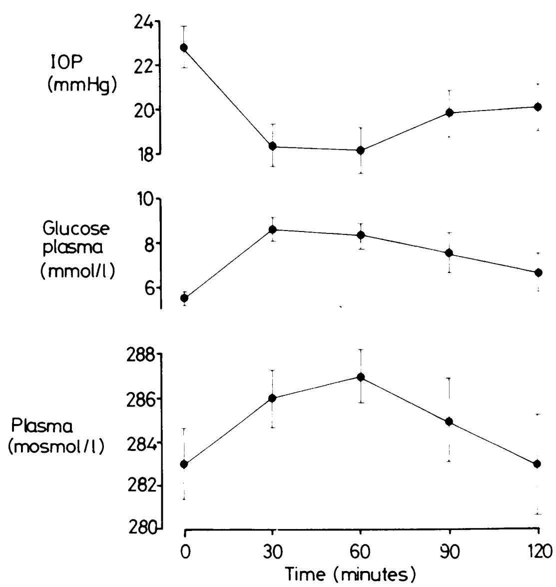

Fig. 1 *Changes in intraocular pressure, glucose, and osmolality in plasma recorded for 12 subjects undertaking a standard glucose tolerance test. Results shown are mean ± 1 SD.*

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Table 1 *Changes in intraocular pressure, plasma glucose, and plasma osmolality arising at 0, 30, 60, 90, and 120 minutes during a standard oral glucose tolerance test in 12 patients*

No.	*age*	*sex*		*Intraocular pressure mmHg* 0	30	60	90	120	I	*Plasma glucose mmol/l* 0	30	60	90	120	I	*Plasma osmolality mosmol/l* 0	30	60	90	120	I
1	61	F	R	14	10	10	12	10	10·75	4·6	6·5	7·9	8·6	10·0	11·9	293	291	296	295	295	5·4
			L	14	11	11	12	11													
2	68	F	R	26	20	22	21	21	15·5	5·0	9·0	7·9	9·0	9·0	12·9	299	281	279	285	276	–
			L	26	21	22	23	23													
3	64	F	R	26	24	22	22	20	13·0	6·6	12·7	13·7	15·2	13·1	25·05	272	281	285	281	282	36·0
4	65	M	R	24	20	17	17	19	21·0	5·6	7·1	8·1	8·0	7·4	7·3	283	293	299	287	284	30·5
			L	24	20	16	17	19													
5	61	M	R	24	18	18	18	19	20·25	4·8	8·8	12·5	13·3	10·1	22·85	281	291	302	298	296	55·5
			L	24	18	18	18	20													
6	58	M	R	19	16	17	18	19	6·5	5·0	7·0	6·4	6·2	5·0	4·6	291	284	287	283	281	–
			L	19	16	17	17	19													
7	71	F	R	22	19	18	20	22	8·5	4·6	8·1	5·8	4·8	4·3	4·92	283	281	276	283	270	–
			L	22	20	18	20	22													
8	58	M	R	24	22	20	18	23	12·5	7·4	10·9	10·8	4·4	2·3	6·14	287	291	291	285	285	7·33
			L	24	20	20	20	23													
9	62	M	R	23	20	19	25	24	8·5	5·0	7·3	7·5	8·8	7·8	10·0	284·5	284·5	287	287·5	287	6·75
			L	22	18	17	20	20													
10	68	M	R	27	19	20	24	23	14·25	5·6	9·2	8·1	6·8	6·3	7·65	281	287	288	286	285	20·0
			L	22	18	18	22	21													
11	54	F	R	22	16	18	20	20	12·5	5·5	8·9	7·3	6·6	5·1	6·14	281	288	286	285	280	15·6
			L	28	22	24	26	28													
12	73	M	R	24	16	18	22	21	17·25	5·5	8·4	6·3	5·0	4·4	3·54	284	287	285	286	280	5·3
			L	24	16	18	21	22													

I: Overall integrated response.

test. Venepuncture was also then performed, with a cuff but without delay, for determination of glucose in plasma by an automated hexokinase method, and of plasma osmolality by a Wescor model 5100B vapour pressure osmometer with at least duplicate estimations. Refraction was not performed.

Assessment of data. Relationships between the rate of change of intraocular pressure, plasma glucose, and osmolality were assessed by comparison of the changes arising between 0 and 30 minutes after the glucose load. The extent of the overall changes during the test was assessed by integration of the area over or under the curve (Fig. 1) by the trapezoidal rule and with the start value taken as baseline. The data provided, representing rate and extent of change for each variable, were then subject to regression analysis determining intervariable correlation coefficients and their levels of significance on direct and transformed variables (see below) by the method of least squares.

Results

Changes in intraocular pressure, plasma glucose, and osmolality recorded for the first group of 12 patients are shown in Fig. 1 and in Table 1. Regression analysis did not establish any significant correlation between the rates of change of these variables as defined above. With the integrated overall responses a significant linear correlation was found between plasma glucose and osmolality ($r=0·753$, $p<0·02$), but neither variable showed a linear or other correlation with intraocular pressure, the closest relationship arising between osmolality and reciprocal intraocular pressure ($r=0·571$, $0·1<p<0·2$).

Data on intraocular pressure and plasma glucose for the remaining 42 patients is shown in Table 2, the time course of the changes being similar to that shown for the smaller group in Fig. 1. Regression analysis of the combined data for 54 patients did not show a significant correlation between rates of change of intraocular pressure and plasma glucose. A non-linear correlation for the integrated overall responses of these variables was shown, for a power regression ($r=0·287$, $p<0·05$) and a double reciprocal plot ($r=0·512$, $p<0·001$). This non-linear relationship between the overall responses for intraocular pressure and plasma glucose was not established for the first group of 12 patients, apparently through sampling variation, as values for intraocular pressure were less widely distributed for the first group than with the overall group, the difference in variance being significant at the $p<0·05$ level.

Glucose tolerance status of the patients in this survey was not previously known. One patient in the second group was found to be diabetic, and four patients in the first group and seven in the second

Table 2 *Changes in intraocular pressure, plasma glucose arising at 0, 30, 60, 90, and 120 minutes during a standard glucose tolerance test in a further 42 patients*

No. age, sex				*Intraocular pressure mmHg*						*Plasma glucose*					
				0	*30*	*60*	*90*	*120*	*I*	*0*	*30*	*60*	*90*	*120*	*I*
13	77	F	R	16	14	13	15	15	6·0	4·4	7·1	6·0	5·6	5·4	6·0
			L	16	14	14	15	15							
14	76	M	R	24	14	12	20	28	23·25	3·8	7·2	9·4	8·2	7·8	15·4
			L	24	16	16	20	19							
15	72	M	R	36	20	24	24	28	28·75	8·0	13·0	8·0	5·4	4·8	5·0
			L	22	16	16	16	19							
16	54	F	R	26	20	19	24	25	14·5	4·0	5·4	5·0	4·4	4·4	3·0
			L	25	19	19	24	24							
17	66	F	R	25	14	14	22	22	28·0	4·0	6·6	7·2	6·0	5·0	8·3
			L	26	14	14	22	23							
18	44	F	R	17	14	16	18	20	2·7	4·4	6·6	3·8	3·2	2·9	0·2
			L	17	14	19	20	20							
19	76	M	R	19	14	19	20	20	10·0	4·0	5·0	5·2	4·4	2·9	2·45
			L	19	14	14	14	16							
20	50	M	R	18	13	14	14	13	16·5	5·2	7·2	5·9	5·0	4·2	2·62
			L	20	16	14	14	17							
21	62	F	R	18	12	10	14	14	18·0	5·2	5·6	7·2	4·8	5·0	1·48
			L	16	12	10	14	14							
22	77	F	R	42	36	34	39	42	18·5	6·0	13·6	10·4	10·4	10·0	18·4
			L	42	34	34	38	42							
23	50	F	R	23	16	16	21	22	14·75	4·8	6·4	5·6	5·6	5·2	3·4
			L	22	16	16	21	22							
24	65	F	R	31	23	20	26	26	30·6	4·3	6·4	7·0	5·4	5·2	5·35
			L	29	20	18	18	24							
25	69	M	R	35	28	28	32	33	18·5	4·8	6·2	7·0	5·4	2·6	3·96
			L	35	28	26	33	33							
26	69	F	R	25	28	28	22	23	16·0	5·0	9·2	9·8	8·4	7·0	13·0
			L	25	20	20	22	25							
27	72	M	R	20	12	16	16	17	19·0	4·8	11·8	13·8	11·7	11·3	26·15
			L	20	11	15	15	17							
28	88	F	R	30	20	22	24	25	26·75	5·5	8·6	13·0	11·0	11·5	19·1
			L	28	18	20	22	22							
29	75	M	R	26	20	21	22	22	20·5	4·8	11·8	11·2	10·8	10·5	22·25
			L	36	30	31	24	34							
30	55	F	R	18	12	16	16	18	10·0	4·4	8·5	6·6	6·0	4·8	7·9
			L	18	12	16	16	18							
31	78	F	R	36	28	30	30	32	20·25	4·4	8·0	7·8	7·8	4·6	10·5
			L	28	22	22	23	25							
32	75	F	R	16	11	12	14	15	11·5	4·0	7·2	7·0	5·4	5·2	8·2
			L	16	11	12	14	15							
33	75	F	R	24	18	21	23	23	12·25	3·8	8·5	7·6	7·4	7·4	13·9
			L	24	18	20	21	22							
34	80	M	R	26	18	20	20	20	23·0	5·6	8·8	9·4	9·8	9·0	12·9
			L	26	18	20	20	20							
35	45	F	R	14	8	8	12	14	14·0	3·6	6·8	5·0	5·0	3·4	5·9
			L	14	8	8	12	14							
36	54	F	R	16	10	10	12	12	17·5	4·4	6·6	6·8	3·2	2·9	4·2
			L	16	10	10	12	14							
37	54	F	R	20	14	14	16	17	16·75	6·0	8·6	10·0	8·8	7·6	10·2
			L	19	13	13	17	17							
38	35	F	R	15	8	8	10	10	22·25	5·0	8·0	7·6	7·3	7·2	9·0
			L	16	10	8	10	10							
39	77	M	R	34	25	24	28	30	25·5	4·8	7·6	7·6	6·7	5·2	7·7
			L	26	18	17	21	22							
40	76	F	R	36	25	26	28	32	31·0	5·2	9·2	9·6	6·2	5·4	9·5
			L	34	24	25	26	30							
41	73	M	R	24	14	17	21	25	15·63	4·6	7·6	7·6	6·4	5·0	8·0
			L	24	16	20	24	26							
42	52	M	R	34	24	24	25	24	32·5	4·0	6·0	6·2	5·0	4·0	5·0
			L	32	22	21	26	24							
43	74	F	R	30	24	24	27	32	15·1	6·0	10·2	8·0	7·6	5·4	7·5
			L	32	26	26	28	32							

Table 2 continued *Changes in intraocular pressure, plasma glucose arising at 0, 30, 60, 90, and 120 minutes during a standard glucose tolerance test in a further 42 patients*

No. age, sex				*Intraocular pressure mmHg*						*Plasma glucose mmol/l*					
				0	*30*	*60*	*90*	*120*	*I*	*0*	*30*	*60*	*90*	*120*	*I*
44	51	M	R	22	16	16	18	19	18·5	4·8	8·2	8·0	7·0	4·8	8·8
			L	24	17	17	20	21							
45	73	F	R	24	16	16	21	20	19·0	5·6	10·0	13·4	12·8	10·8	22·0
			L	22	15	15	20	20							
46	74	F	R	19	16	16	17	18	7·75	6·2	10·8	10·6	9·2	8·3	13·0
			L	17	15	15	15	17							
47	66	M	R	28	22	21	22	26	19·75	5·4	6·0	4·2	3·6	2·8	0·4
			L	29	24	23	22	26							
48	51	M	R	30	25	24	25	25	22·25	13·7	20·3	21·5	22·7	20·6	26·8
			L	39	32	30	32	32							
49	75	M	R	28	22	21	22	26	19·75	5·4	6·0	4·2	3·6	2·9	0·2
			L	29	24	23	22	26							
50	75	F	R	20	16	17	20	20	8·0	5·0	7·6	7·3	6·4	5·2	6·4
			L	20	16	17	18	20							
51	75	M	R	26	20	20	17	21	22·75	4·4	9·0	11·4	12·5	10·0	22·5
			L	20	14	14	12	16							
52	76	F	R	20	20	14	12	16	15·0	4·8	8·0	6·4	5·8	6·0	6·4
			L	18	18	12	12	14							
53	66	F	R	20	17	15	16	20	11·5	4·6	6·0	5·0	5·2	4·8	2·5
			L	21	18	16	18	21							
54	54	F	R	26	22	24	25	25	5·25	5·2	8·2	10·4	6·2	4·2	8·9
			L	22	18	24	21	22							

I: Integrated response.

group showed impaired glucose tolerance as defined by standard criteria.[3]

Discussion

This study has shown that the overall fall of intraocular pressure arising acutely after a glucose load can be related to the overall increase of plasma glucose and that the change in glucose is related to plasma osmolality. Previous studies[2] have shown that myopia in human diabetes is related to the degree of acute hyperglycaemia. Our data suggest that hyperglycaemia can also be related to changes of intraocular pressure and plasma osmolality. The eye is a multicompartment system, and changes in fluid balance probably affect these compartments at different rates, the overall effect of acute hyperglycaemia in man being myopia. Chronic hyperglycaemia in diabetes mellitus is associated with a small rise in intraocular pressure,[4,5] probably through different mechanisms. The lack of a clear relationship in our study between the initial rates of change of intraocular pressure and glucose and osmolality in plasma probably reflects the complexity of balanced shifts of fluid and solute involving the various intraocular components, and may be clarified by detailed studies of the progress of myopia and intraocular dimensions during hyperglycaemia.

Our observations do not identify the mechanism of the changes in refraction arising with hyperglycaemia but strongly suggest that changes in fluid balance between intraocular compartments are involved. The lens is probably the seat of these changes; aphakic subjects are not affected. Possible effects include changes in lens shape and refractive index, perhaps promoted by sorbitol accumulation and fluid entry, and changes in lens position relative to the retina. Vere and Verel[6] also noted that hyperglycaemia and myopia were associated with different effects on the red reflex, and proposed that hyperglycaemia produced independent effects on the lens, including anterior opacification. Alloxan-diabetic rabbits become hypermetropic, an affect controlled by inhibition of aldose reductase.[7] However, such inhibitions have other biochemical effects, and as yet there is no direct evidence of osmotically significant polyol accumulation within the lens of human diabetes, unlike the clear effects arising with galactose-based disorders.[8] Changes in lens capsule basement membrane as induced by prolonged hyperglycaemia in rats may also modify lens deformability.[9]

The fall of intraocular pressure observed in association with hyperglycaemia may represent increased loss from or reduced entry of fluid into the anterior chamber. Effects on the posterior chamber may also arise. The retinal circulation in the rabbit is poorly developed in comparison with man, and the different effects of hyperglycaemia on refraction in these species[7] could result from unbalanced effects on anterior and posterior chambers, and consequent changes in lens position, which remain to be assessed.

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