

Isosorbide and intraocular pressure

O. P. KULSHRESTHA AND R. N. MITTAL

Department of Ophthalmology, Ravindra Nath Tagore Medical College, Udaipur, India

There is growing interest in the use of osmotic agents in lowering intraocular pressure in cases of glaucoma.

A drug recently put on clinical trial is isosorbide, an oral hyperosmotic agent introduced by Treon, Gongwer, and Rueggeberg (1965). It is a dihydric alcohol formed by the removal of two molecules of water from sorbitol, a sugar alcohol. Becker, Kolker, and Krupin (1967) first used it to reduce intraocular pressure with significant results. Barry, Khoury, and Brooks (1969) found a reduction in intraocular pressure within 30 to 60 minutes, after the administration of 75 g. isosorbide. Krupin, Kolker, and Becker (1970) hold the view that oral isosorbide in similar doses is as effective as oral glycerol with fewer side-effects. Wisznia, Lazar, and Leopold (1970) used it on 28 patients with various types of glaucoma.

Materials and methods

Thirty patients with various types of glaucoma (including open-angle glaucoma, acute congestive glaucoma, secondary glaucoma due to various causes, and absolute glaucoma) were treated with a 50 per cent. solution of isosorbide. In all, 58 eyes were studied, of which eighteen with normal intraocular pressure offered an opportunity to study the effect in normal eyes. The patients were examined clinically to reach the diagnosis.

Each patient was given isosorbide $1/5$ g./kg, bodyweight. Intraocular pressure was recorded with the Schiötz tonometer before the administration of the drug and every 15 minutes thereafter for 2 hours, and then every 30 minutes for a further 4 hours. The patients were asked to report any headache, nausea, diuresis, vomiting, diarrhoea, back pain, abdominal cramp, or other side-effects. The urine was examined before and after administration of the drug.

Results

The oral administration of 1.5 g./kg. bodyweight of isosorbide resulted in a fall in intraocular pressure in hypertensive eyes from 9 to 32 mm. Hg (mean 16.3). The average reduction in intraocular pressure was 30.016 per cent. of the initial level.

The fall in pressure in eyes with normal intraocular pressure ranged from 2 to 9.5 mm. Hg (mean 4.61).

The action of the drug starts within 30 to 45 minutes, the lowest pressure levels are reached after 60 to 90 minutes, and the effect lasts for 3 to 5 hours.

Side-effects were minimal. Four patients complained of slight headache and nausea; other symptoms were diarrhoea and vomiting (Table I, overleaf).

Table I Effects of oral isosorbide 1.5 g./kg. bodyweight on thirty patients of glaucoma

Case no.	Type of glaucoma	tension	Initial Eye	IOP after administration of isosorbide (hrs)						Side-effects
				½	1	2	3	4	5	
1	Secondary	R	20.5	14.5	11	12	14.5	14.5	16	None
	Lens-induced	L	82	69	59	59	64	69	82	
2	Secondary	R	20.5	20.5	17	17	17	20.5	20.5	None
	Lens-induced	L	47	43	37	37	43	47	47	
3	Chronic simple	R	59	51	37	37	51	59	59	None
	L	L	17	14.5	12	12	14.5	14.5	14.5	
4	Chronic simple	R	17	11	10	10	14.5	17	17	None
	L	L	55	43	40	43	51	55	55	
5	Chronic simple	R	64	64	47	47	47	55	55	None
	L	L	82	82	69	55	59	64	64	
6	Chronic simple	R	59	59	51	51	51	59	59	None
	L	L	Recently operated for glaucoma							
7	Chronic simple	R	26.5	22	16	16	19	26.5	26.5	None
	L	L	17	14.5	12	12	14.5	17	17	
8	Absolute	R	20.5	20.5	17	17	20.5	10.5	10.5	None
	L	L	59	59	51	51	51	59	59	
9	Angle-closure	R	17	11	10	12	14.5	17	17	None
	L	L	82	59	51	51	64	82	82	
10	Absolute	R	47	40	37	37	43	47	47	None
	L	L	14.5	12	12	12	12	14.5	14.5	
11	Secondary	R	47	40	34	34	40	47	47	Headache
	Lens-induced	L	17	14.5	13	14.5	14.5	17	17	
12	Secondary	R	46	39	36	33	42	46	46	None
	Lens-induced	L	10	8.5	8.5	8.5	8.5	10	10	
13	Chronic simple	R	59	47	43	51	55	55	55	None
	L	L	69	55	47	51	59	59	69	
14	Chronic simple	R	51	43	34	37	43	43	51	None
	L	L	51	43	37	40	47	47	47	
15	Angle-closure	R	47	40	34	37	43	47	47	None
	L	L	59	47	40	47	51	59	59	
16	Chronic simple	R	32	26.5	20.5	20.5	26.5	32	32	Headache Loose motion
	L	L	75	64	47	47	55	69	75	
17	Chronic simple	R	51	43	37	37	40	51	51	None
	L	L	47	40	32	32	37	47	47	
18	Chronic simple	R	Phthisis bulbi							None
	L	L	59	51	47	51	51	59	59	
19	Chronic simple	R	69	59	55	55	55	64	69	None
	L	L	29	22	19	19	20.5	24	24	
20	Angle-closure	R	69	51	37	37	37	51	69	None
	L	L	43	32	25	25	25	40	43	
21	Chronic simple	R	69	59	51	51	55	69	69	Nausea Vomiting
	L	L	64	59	51	51	51	64	64	
22	Chronic simple	R	69	69	59	64	64	69	69	None
	L	L	22	22	18	17	17	22	22	
23	Angle-closure	R	34	24	19	19	19	22	34	None
	L	L	14.5	11	9	9	9	12	14.5	
24	Aphakic	R	59	51	40	40	43	51	59	None
	L	L	17	13	11	11	13	17	17	
25	Chronic simple	R	51	43	34	34	37	43	43	Headache
	L	L	36	24	17	17	17	20.5	36	
26	Angle-closure	R	69	55	43	43	43	59	69	None
	L	L	22	17	14.5	14.5	14.5	19	22	
27	Secondary	R	55	43	40	40	40	51	55	None
	lens-induced	L	17	14.5	14.5	14.5	14.5	14.5	17	
28	Angle-closure	R	50	42	36	36	42	50	50	None
	L	L	12	10	10	10	12	12	12	
29	Secondary	R	50	46	36	36	39	46	50	None
	lens-induced	L	12	11	10	10	10	12	12	
30	Aphakic	R	42	42	36	33	39	39	42	None
	L	L	17	14.5	13	13	13	17	17	

Discussion

In the present study isosorbide effectively lowered the intraocular pressure; the higher the initial pressure, the greater was the fall observed (Table II).

Table II Average fall in tension

Group	Initial tension (mm. Hg)	No. of cases	Initial average tension (mm. Hg)	Fall in tension (mm. Hg)	Time of maximum action (min.)
I	Up to 22	18	16.91	4.61	49.2
II	From 22 to 50	15	41.56	13.0	60.0
III	Above 50	25	63.60	18.28	56.0

Becker and others (1967) reported a mean fall in intraocular pressure of 16 mm. Hg in hypertensive eyes after the administration of isosorbide 2 g./kg. bodyweight. The lowest pressure levels were reached between 1 and 2 hours and the pressure often remained depressed for more than 5 hours. Wisnia and others (1970) observed a mean fall of 12.2 mm. Hg, and we observed a fall of 16.3 mm. Hg from a higher initial level (52.58 mm. Hg) in 58 minutes.

When the drug is not combined with miotics like pilocarpine or eserine, the intraocular pressure rises again within 3 to 6 hours.

We have observed a mean fall of 4.61 mm. Hg from an initial level of 16.91 mm. Hg in eyes with normal intraocular pressure.

An orally-administered drug tends to be somewhat slower in its action but it is safer. Glycerol has the disadvantage that it produces nausea and vomiting; this creates problems in the management of acute glaucoma, especially if used preoperatively and its value in diabetic patients is limited because it undergoes metabolism and increases the need for insulin.

Summary

The use is reported of oral isosorbide to reduce intraocular pressure in eighteen normal eyes and forty eyes with glaucoma. The drug reduced the intraocular pressure in both normal and glaucomatous eyes, with minimal side-effects. It is a useful addition to the oral drug therapy of glaucoma.

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References

- BARRY, K. G., KHOURY, A. H., and BROOKS, M. H. (1969) *Arch. Ophthalm. (Chicago)*, **81**, 695
 BECKER, B., KOLKER, A. E., and KRUPIN, T. (1967) *Ibid.*, **78**, 147
 KRUPIN, T., KOLKER, A. E., and BECKER, B. (1970) *Amer. J. Ophthalm.*, **69**, 737
 MEHRA, K. S., SINGH, R., CHAR, J. N., RAJYASHREE, K. (1971) *Arch. Ophthalm. (Chicago)*, **85**, 167
 TREON, J. F., GONGWER, L. E., and RUEGGERBERG, W. H. C. (1965) *Proc. Soc. exp. Biol. (N.Y.)*, **119**, 39
 WISZNIA, K. I., LAZAR, M., and LEOPOLD, I. H. (1970) *Amer. J. Ophthalm.*, **70**, 630