EFFECT OF INTRAVENOUS CARDIAC GLYCOSIDES ON THE AQUEOUS HUMOUR DYNAMICS OF THE CAT*†

BY

DAVID M. WARNER AND STEPHEN M. DRANCE‡

From the Department of Ophthalmology, Faculty of Medicine, University of British Columbia, Canada

PREVIOUS investigation by Simon, Bonting, and Hawkins (1962) indicated that intravenous cardiac glycosides caused a significant fall in the rate of aqueous humour formation in the cat eye. Langham (1963), using rabbits and cats, and Becker (1963), using rabbits, were not able to demonstrate this effect. Becker, using an intravitreal injection of cardiac glycosides, was able to demonstrate a fall in intra-ocular pressure. The use of cardiac glycosides in the clinical treatment of glaucoma has been reported by Simon and others (1962), who were able to demonstrate a measurable fall in the intra-ocular pressure. Smith and Mickatavage (1963) showed that topical cardiac glycosides caused a measurable, though slight, fall in intra-ocular pressure.

This report concerns experimental work on cats. The method used by Simon and others (1962) has been substantially repeated.

Method

Adult female cats were anaesthetized with intraperitoneal Nembutal (30 mg./kg.). Additional intravenous Nembutal was administered during the course of the experiment if the depth of anaesthesia was not considered to be adequate. The head was not immobilized but was allowed to rest lightly on a platform so that the diaphragms of the transducers, the anterior chamber, and the heart were all on the same horizontal plane. The femoral artery and vein were cannulated using No. 190 and 90 polyethylene tubing respectively. Continuous pressure recordings were made, using Statham high and low level pressure transducers. Both anterior chambers were cannulated close to the limbus using a 25-gauge needle connected by short lengths of No. 90 polyethylene tubing to two Statham low-pressure transducers. The arterial and venous systems were filled with bubble-free heparinized normal saline. The anterior chamber systems were filled with bubble-free phosphate buffer pH 6.95. Continuous arterial, venous, and anterior chamber pressure tracings were made, using a Grass Polygraph with a SP1.K low-level DC pre-amplifier and 5E driver amplifiers.

After cannulation of the anterior chambers, a period of 15 to 20 minutes was allowed to elapse while the intra-ocular pressure reached a steady-state level. At this stage a reservoir connected to the anterior chamber was lowered, reducing the intra-ocular pressure by approximately half. The aqueous drainage was allowed to continue for one minute with the pressure maintained at this level. The reservoir was then disconnected and the intra-ocular pressure allowed to rise to its

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‡ Address for reprints: 2550 Willow Street, Vancouver 9, B.C., Canada.

pre-existing level (Fig. 1). The slope of this curve was measured in mm. Hg per minute and taken as an index of the aqueous inflow. When steady-state pressure levels were once again obtained, a slow intravenous injection of the appropriate cardiac glycoside was given. Digoxin in doses between 0.075 and 0.13 mg./kg. and ouabain in doses between 0.05 and 0.10 mg./kg. were used. The anterior chamber systems were then allowed to remain undisturbed for a period of 30 to 45 minutes during which time a further steady level of intra-ocular pressure was reached. Inflow rate was then again measured (Fig. 2).

FIG. 1.—Arterial pressure, venous pressure, and intra-ocular pressure tracings before administration of intravenous digoxin. Inflow rates derived from recovery rate of intra-ocular pressure, measured in mm. Hg/min.

FIG. 2.—Arterial pressure, venous pressure, and intra-ocular pressure tracings 21 minutes after injection of 0.10 mg./kg. intravenous digoxin. Inflow rates derived from recovery rate of intra-ocular pressure, measured in mm. Hg/min.

Estimations of outflow and scleral rigidity were made before and after administration of cardiac glycoside, using the methods described by Langham and Eakins (1964) and Eisenlohr and Langham (1962). The results of these estimates have not been included in this paper.

As a control six cats were used repeating the technique described above but without the injection of cardiac glycosides.

Results

The inhibition of aqueous inflow produced by cardiac glycosides was estimated by a change in slope of the recovery of intra-ocular pressure measured in mm. Hg per minute. Tables I and II (opposite) show that there has been an inhibition of 48 per cent. after the administration of digoxin and of 46 per cent. after that of ouabain. This inhibition was accompanied by a fall in the steady-state intra-ocular pressure of 17 per cent. in the digoxin studies and 15.5 per cent. in the ouabain studies. During the experiments it was noted that variations in systemic blood pressure were reflected in the intra-ocular pressure and a ratio was derived which showed that a rise in blood pressure of 11 mm. Hg caused a rise of 1 mm. Hg in the intra-ocular pressure. Applying the blood pressure/intra-ocular pressure ratio to the data obtained, it can be seen that the direction of change in the blood pressure would have tended to increase intra-ocular pressure, but that in spite of this a fall in the intra-ocular pressure was obtained with digoxin and ouabain.

The control series show that there was a 50 per cent. inhibition of recovery rate of intra-ocular pressure (Table III, overleaf). There was a fall in the steady-state intra-ocular pressure of 33 per cent. and a slight rise in the blood pressure during the course of the experiment.

TABLE I
EFFECT OF INTRAVENOUS ADMINISTRATION OF DIGOXIN ON AQUEOUS HUMOUR
DYNAMICS IN THE CAT

Date of Experiment (1964)	Dosage of Drug (mg./kg.)	Eye	Recovery Rate of IOP (mm. Hg/min)		Inhibition (per cent.)	Equilibrium Value of IOP (mm. Hg)		Δ IOP (per cent.)	Venous Pressure (mm. Hg)		Mean Blood Pressure		
			Before	After		Before	After*		Before	After*	Before	After*	Δ B.P.
May 8	0.10	R L	1.0 2.0	0.1 0.6	90 70	16.0 21.0	9.8 16.5	38.7 21.4	1.0	1.0	90	130	40
May 14	0.13	R L	0.2 0.3	0.1 0.2	50 33	10.0 13.5	7.0 11.5	30.0 14.8	0.0	-1.0	70	120	50
May 20	0.075	R L	0.9 1.2	0.3 0.4	66 66	24.0 20.0	20.0 17.0	16.7 15.0	9.0	11.0	63	98	35
June 3	0.10	R L	— 0.2	— 0.2	— 0	— 14.5	— 10.5	— 27.6	1.5	—	136	140	4
June 10	0.10	R L	0.2 0.3	0.1 —	50 —	10.2 13.0	9.8 11.0	39.2 15.4	0.0	—	52	62	10
June 18	0.10	R L	0.7 0.7	0.7 0.4	0 43	11.0 14.2	10.5 14.5	4.5 +2.1	1.0	0.6	101	115	14
July 6	0.075	R L	0.4 0.6	0.2 0.2	50 66	13.5 14.0	13.5 14.0	0.0 0.0	1.5	0.2	72	80	8
Average			0.67	0.30	48.7	14.9	12.7	17.0	2.0	2.4	83.4	106.4	23.0
Standard Deviation			± 0.51	± 0.19	± 27.1	± 4.3	± 4.4	± 13.9					

* Readings taken 15 minutes after injection of digoxin.

TABLE II
EFFECT OF INTRAVENOUS ADMINISTRATION OF OUABAIN ON AQUEOUS HUMOUR
DYNAMICS IN THE CAT

Date of Experiment	Dosage of Drug (mg./kg.)	Recovery Rate of IOP (mm. Hg/min.)		Inhibition (per cent.)	Equilibrium Value of IOP (mm. Hg)		Δ IOP (per cent.)	Venous Pressure (mm. Hg)		Mean Blood Pressure (mm. Hg)		
		Before	After		Before	After*		Before	After	Before	After*	Δ B.P.
February 18	.10				23.0	19.5	15.2			126	135	9
February 19	.07	0.12	0.10	16.7	15.3	13.8	9.8			102	120	18
February 20†	.10	0.33	0.56	69.9	8.0	10.0	25.0			97	124	27
March 3	.05	0.47	0.18	61.7	28.0	24.4	12.8			120	160	40
March 4	.04	0.40	0.18	55.0	26.0	20.6	20.8			140	152	12
March 6	.05	0.84	0.38	50.5	17.5	14.2	18.8			98	126	28
Average		0.46	0.21	46.0	22.0	18.5	15.5			117.2	138.6	21.4
Standard Deviation		± 0.29	± 0.21	± 20.1	± 5.4	± 4.5	± 4.4					

* Readings taken 15 minutes after injection of ouabain.

† Results of experiment, February 20, not used in calculations of final totals, averages, and standard deviations because of variations in blood pressure during the initial recovery rate estimations.

Discussion

The results obtained were comparable to those obtained by Simon and others (1962). It was demonstrated that, with the administration of cardiac glycosides in the anaesthetized cat, there was a fall in the steady-state intra-ocular pressure with a fall in recovery rate of intra-ocular pressure and that this was accompanied by a rise in the mean blood pressure in the experimental series. The control series, without cardiac glycoside, showed that, in the anaesthetized cat, there is a decrease in the

TABLE III
AQUEOUS DYNAMICS OF THE CAT WITHOUT INTRAVENOUS ADMINISTRATION OF
CARDIAC GLYCOSIDES

Date of Experiment	Eye	Recovery Rate of IOP (mm. Hg/min.)		Inhibition (per cent.)	Equilibrium Value of IOP (mm. Hg)		Δ IOP (per cent.)	Venous Pressure (mm. Hg)		Mean Blood Pressure (mm. Hg)		
		Before	After		Before	After		Before	After	Before	After	Δ B.P.
September 2	R	1.11	0.53	52.3	22.5	12.5	44.4	4.5	1.0	84	86	+2
	L	0.94	1.05	11.7*	24.0	19.0	20.8					
September 4	R	2.49	1.90	23.7	32.0	23.0	28.1	1.5	-0.5	122	108	-14
	L	1.83	1.35	28.2	31.0	25.0	19.4					
September 8	R	0.44	0.33	25.0	20.5	15.0	26.8	2.5	1.5	66	68	+2
	L	0.63	0.38	39.3	22.5	18.5	17.7					
September 16	R	2.00	0.44	78.0	35.0	15.0	57.1	5.0	3.5	120	108	-12
	L	2.05	0.44	78.5	36.0	14.0	61.1					
September 17	R	0.61	0.25	59.0	20.0	14.0	30.0	3.0	2.0	108	132	+24
	L	0.96	0.25	73.8	26.0	19.0	26.9					
Average		1.31	0.69	50.9	27.0	17.5	33.2	3.3	1.5	100.0	100.4	+0.4
Standard Deviation		± 0.72	± 0.56	± 22.7	± 5.9	± 4.2	± 15.5					

* Not included in the calculation of the average and standard deviation.

recovery rate of the intra-ocular pressure and a decrease in the steady-state intra-ocular pressure, but that this is associated with a slight rise in blood pressure.

It would appear that the effect of intravenous cardiac glycosides in cats reported by Simon and others (1962), namely, a fall in intra-ocular pressure and in recovery rate of the intra-ocular pressure, cannot be attributed to cardiac glycosides alone. It has been demonstrated in control series in this investigation that the major part of the decrease in intra-ocular pressure and inflow rate could be attributed to the prolonged Nembutal anaesthesia, which is associated in cats with: (1) a minimal rise in the systolic blood pressure, (2) a fall in a steady-state intra-ocular pressure, and (3) a decrease in the recovery rate of intra-ocular pressure.

Summary

The alteration in the inflow rates of aqueous humour in the cat eye as a result of intravenous digoxin or ouabain were studied. *In vivo* experiments in the cat showed that the intravenous administration of digoxin, 0.075 to 0.13 mg./kg., caused an inhibition of aqueous inflow by 48 per cent. measured by the slope of the pressure recovery curve after aqueous drainage. Ouabain given in doses of 0.046 to 0.10 mg./kg. caused an inhibition of aqueous inflow by 45 per cent. It was shown in the control series, where no cardiac glycosides were used, that there was an inhibition of aqueous inflow under comparable circumstances of 50.9 per cent. Blood pressure and venous pressure were monitored throughout the experiments.

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