

LETTER TO THE EDITOR

PUPILLARY CHANGES AFTER INSTILLATION OF ADRENALINE AND ADRENALINE WITH HYALURONIDASE IN RABBIT

Sir

Mydriasis is not readily produced in animals or man by adrenaline instilled into the conjunctival sac of normal eyes. However, adrenaline thus applied causes mydriasis after post-ganglionic sympathetic denervation of the pupil and also in patients with diabetic chronic renal hypertension and acute pancreatitis (1). This idea is contradicted by some other authors: the pupillary dilator muscle of the eye is contracted by adrenaline causing wider dilatation of the pupil (2). Adrenaline acts on the alpha receptors of dilator fibres (5), producing dilatation after instillation of the four drops of 1 in 1000 solution the instillation being repeated in five minutes (3). These reports prompted us to perform experiments with adrenaline on the eye of normal rabbits. Different dilutions of adrenaline and adrenaline with hyaluronidase at a concentration of 1 U per *ml* were used for the experiments. Hyaluronidase hydrolyses the mucopolysaccharides of hyaluronic acid class which are components of intercellular ground substance (4). This promotes diffusion of injected fluids and enhances the dispersion of other injected drugs.

Experiments were done in different rabbits which were selected at random. The different concentrations of adrenaline ranged from 1/100,000 to 1/2,000. The dilution of adrenaline with hyaluronidase was such that each dilution contained 1 U of hyaluronidase per *ml*. The third type of solution prepared contained only hyaluronidase at a concentration of 1 U per *ml*.

The initial diameter of pupil was measured (*vide infra*). To begin with 1 in 100,000 dilution of adrenaline was administered dropwise. The diameter was measured every 15 sec. The experiment for each of the concentrations was done for one hr and was repeated in eight different animals. Likewise experiments were carried out for all prepared concentrations.

The rabbit was placed on a level table. A half foot scale was used to measure the diameter. The measurements were carried out vertically by keeping the scale on the same plane. The diameter was measured in mm at the side of the rabbit's eye. The sensitivity of the scale was 1 mm. Error of parallax was avoided as far as possible. Utmost care was taken to avoid winking by the rabbit during the process of measurement.

It is generally accepted that adrenaline may produce an increase in pupillary diameter. The first set of experiments with various dilutions of adrenaline alone showed that the minimum concentration of adrenaline required to produce an increase in diameter of pupil in rabbits, was 1 in 25,000. As the concentration was increased the response also increased accordingly. With 1 in 2,000 solution the response was the quickest and maximum (Table I-A).

TABLE I : Effect of topical application of various concentrations of adrenaline on rabbits eye alone (A) and with 1 U/ml of hyaluronidase (B).

<i>Solutions used</i>	<i>Increase in pupillary diameter in mm</i>	<i>Time after which the response was obtained</i>
(A) 1 in 100,000	Nil	60 min
1 in 50,000	Nil	60 min
1 in 25,000	1	10 min 45 sec
1 in 10,000	1	5 min 45 sec
	2	15 min 30 sec
1 in 5,000	1	4 min 45 sec
	2	13 min 30 sec
	3	27 min 30 sec
1 in 2,000	1	2 min 15 sec
	2	12 min 45 sec
	3	23 min 15 sec
(B) 1 in 100,000	Nil	60 min
1 in 50,000	1	14 min 15 sec
1 in 25,000	1	9 min 15 sec
	2	21 min 45 sec
	3	27 min
1 in 10,000	1	4 min
	2	12 min
	3	19 min 45 sec
	4	26 min 45 sec
1 in 5,000	1	3 min 15 sec
	2	10 min 15 sec
	3	18 min 30 sec
	4	25 min 30 sec
1 in 2,000	1	2 min 30 sec
	2	9 min 30 sec
	3	17 min 30 sec
	4	24 min 15 sec

In the second set of experiments carried out with the same dilution of adrenaline but with hyaluronidase at the concentration of 1 U per ml, it was found that response was obtained even in lower concentration i.e. 1 in 50,000 solution (Table I-B). The possible

explanation for the efficiency of adrenaline in lower concentration may be that 1 in 50,000 dilution of adrenaline applied alone had very poor penetrating capacity or it was more diluted by the other secretions of the eye before it reached the site of action. The difficulty was probably overcome by the addition of hyaluronidase. It was also found that for subsequent higher concentrations, the response was more and quicker, for the same reason. The maximum dilatation attained was with 1 in 10,000 solution, at 26 min 45 sec. The increased concentration of adrenaline, only quickened the response. Thus the maximum increase in dilatation was 4 mm which was not altered by the addition of hyaluronidase.

In the third set of experiments, hyaluronidase alone at the concentration of 1 U per *ml* produced no increase in the initial diameter of the pupil.

Statistical analysis showed that for the addition of hyaluronidase *F* calculated (16.6) was greater than *F* tabulated (5.05) and for adrenaline *F* calculated (14.5) was greater than *F* tabulated (6.61) at 0.05 level of significance. Hence a significant difference existed both by the change of concentration and by addition of hyaluronidase.

G. MOHAN, G.M. YAHYA AND B.I. VURGHESE
*Department of Pharmacology,
Stanley Medical College, Madras-600 001*

REFERENCES

1. Goodman, L.S. and A. Gilman. Pharmacological Basis of Therapeutics, 5th edition, Macmillan Publishing Co. Inc., New York, pp.477-513 and 946-959, 1975.
2. Meyers, F.H., E. Jawatz and A. Goldfien. Review of Medical Pharmacology, 4th edition, Lange Medical Publications, Los Altos, California, pp.78-101, 1974.
3. Sir Stewart Duke-Elder. Parson's Diseases of the Eye, 15th edition. The English Language Book Society and J&A Churchill, London, pp. 29-41, 1970.
4. Mayer, K. and M.M. Rapport. Hyaluronidases. *Adv. Enzymol.*, **13** : pp. 199-236, 1952.
5. Brobeck, J.R. Function of adrenal glands. In : Physiological Basis of Medical Practice, Indian Edition, 9th edition, The Williams & Wilkins Company, Baltimore, S. Chand & Co. (Pvt) Ltd., New Delhi, p.7-75, 1973.