EFFECT OF DRUGS ON THE NICTITATING MEMBRANE OF DOG

By

G.V. JOGLEKAR AND J. H. BALWANI

From the Department of Pharmacology, B.J. Medical College, Poona

(Received October 18, 1961)

Effects of adrenaline and noradrenaline on the nictitating membrane of dog were studied. The nictitating membrane was more sensitive to adrenaline than to noradrenaline. Priscol caused partial blockade of adrenaline and noradrenaline though by itself it also caused sustained contraction of nictitating membrane.

In the literature there are many references regarding the action of adrenaline and noradrenaline on the nictitating membrane of cat. In Bradley (1948) is mentioned of the third eyelid (Palpebra tertia) or the nictitating membrane of the dog. Looking to the nictitating membrane of dog it appeared that it cannot be merely a vestigeal structure since such structures are usually atrophic and rudimentary in size. We have not come across any reference in literature regarding the action of drugs on the nictitating membrane of dog. Just through interest this work was undertaken to see if this membrane responded to drug action. This work is mainly a preliminary communication.

METHODS

Ten dogs of either sex weighing between 3.6 kg and 12 kg were used. Phenobarbitone sodium (150 mg/kg) was given intraperitoneally to anaesthetize the animal. After 10 min cocaine hydrochloride (8 mg/kg) was given intramuscularly. After the animal was well under anaesthesia usual arrangements were made to inject the drug intravenously through femoral vein. The head of the animal was held rigidly with a head holder. By means of a fine needle a silk thread was passed through the centre of the edge of the right nictitating membrane and tied. The silk was then taken outward and forward so as to be at an angle of about 40° with the axis of the dog then round a pulley (set in horizontal axis) to a pulley (set in vertical axis) up to a lever writting on a drum with a frontal writing point.

Each contraction was recorded for one minute and the interval between two successive doses was kept 10 min.

RESULTS

Dose-response curve with adrenaline and noradrenaline was studied (Fig. 1). In addition adrenaline and noradrenaline was given in doses of 6, 8, and 10 μg per kg alternately at an interval of 10 min. Again contractions with 8 μg of adrenaline and noradrenaline were recorded being the submaximal dose. Then priscol (tolazoline) was given in two doses (total dose 2.5 mg/kg at an interval of 5 min. Adrenaline and noradrenaline (8 μg per kg), were repeated 15 min after the first dose of priscol and again after an interval of 35 min (Fig. 2 & 3).

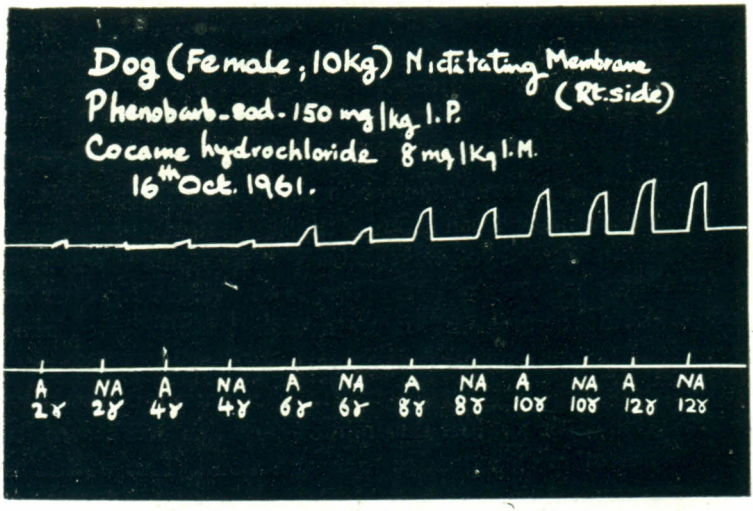

Fig. 1. Contractions of the nictitating membrane. Dose response courve with adrenaline and noradrenaline.

In a few experiments blood pressure tracing was taken also along with the contractions of nictitating membrane. It was noticed that the nictitating membrane started contracting only after the peak rise in blood pressure due to adrenaline and noradrenaline had reached. However, in the work on the nictitating membrane of cat by Bülbring and Burn (1949) it appears that the contraction of nictitating membrane starts with the increase in blood pressure there being no time lag. The contraction of the nictitating membrane of dog lasted for about one min and then the membrane relaxed gradually. From the plotting of log effect against log dose (Fig. 4) it is obvious that the log of contractions in mm of the nictitating membrane bore a linear relationship with the dose of adrenaline and noradrenaline. The

contractions due to noradrenaline were less than those due to equal dose of adrenaline.

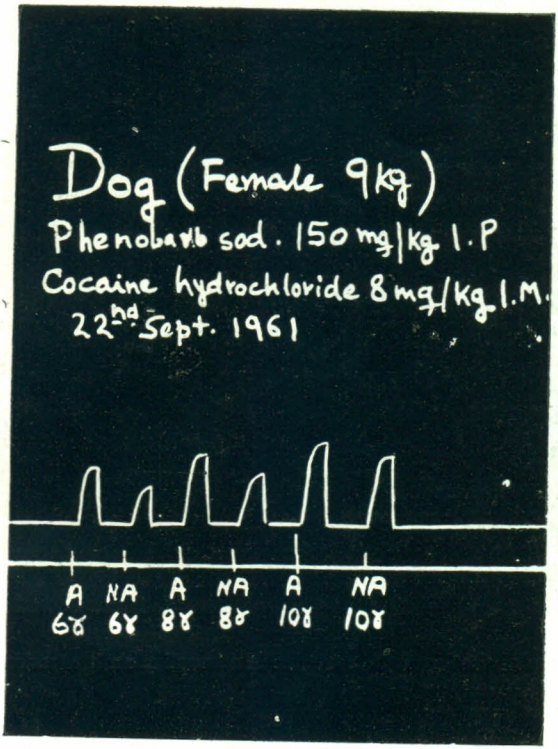

Fig. 2. Contractions of nictitating membrane with adrenaline and noradrenaline (6,8, and 10 μg/kg)

First dose of priscol caused a sustained contraction of the nictitating membrane. The second dose given after 5 min produced further increase in height. The membrane remained in the contracted state for a long time. Even after 35 min of interval (i. e., about 60 min after the first dose of priscol) the nictitating membrane did not relax completely (raised base line) adrenaline and noradrenaline repeated after priscol showed diminished contraction of the membrane.

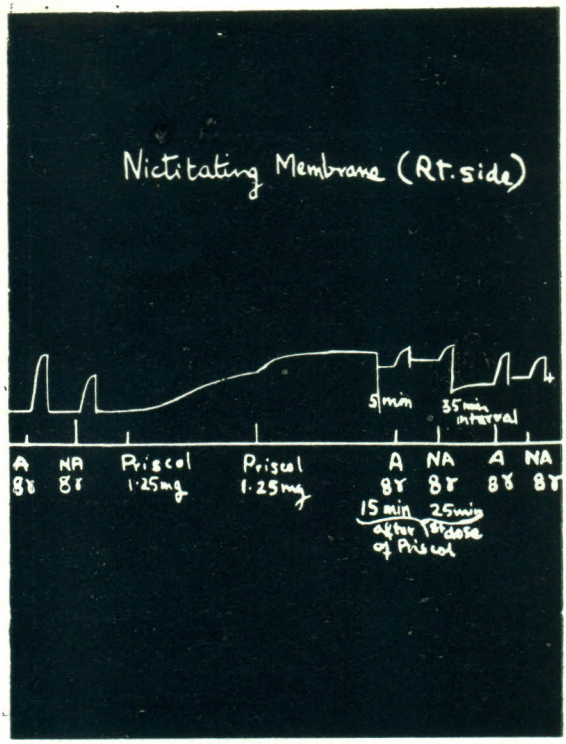

Fig. 3. Contractions of nictitating membrane due to adrenaline and noradrenaline before and after Priscol (given in two doses)

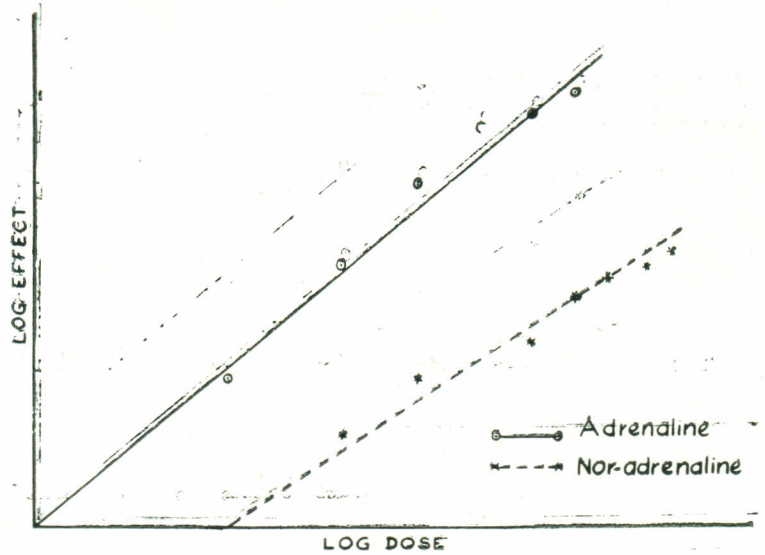

Fig. 4. Plotting of log effect against log dose.

DISCUSSION

Bülbring and Burn (1938, 1949) and Cannon and Rosenblueth (1933) have studied the effects of drugs on the nictitating membrane of cat, both in normal and denervated membranes. The difference in the contractions of the normal and denervated membranes after adrenaline and noradrenaline is used for assaying a mixture of these catecholamines, by using a spinal cat (Burn, 1950). The pressor response to adrenaline in atropinised dog is used as an official U. S P method for assaying adrenaline.

Cats are not very easily available locally and also the spinal cat preparation is a comparatively difficult procedure. It was decided to make efforts to use and modify this U. S. P. assay method for the purpose of assaying a mixture of adrenaline and noradrenaline. Preliminary studies regarding the behaviour of the nictitating membrane of dog towards adrenaline and noradrenaline were thus necessary. This short work is an outcome of these preliminary studies.

From the pilot experiments, it became obvious that some procedure will have to be used to increase the sensitivity of nictating membrane. Cocaine hydrochloride (8 mg/kg) which is used to sensitize the spinal cat (Euler, 1950) was tried with success.

The log of contraction in mm of nictitating membrane bore a linear relationship with the log dose of adrenaline and noradrenaline. Equal doses of adrenaline and noradrenaline showed that the contractions of membrane were smaller with the noradrenaline. Thus, the sensitivity of the normal membrane was more to adrenaline than to noradrenaline, a fact similarly noticed in case of normal nictitating membrane in a spinal cat.

Priscol was tried in order to block the effects of adrenaline and noradrenaline. Priscol in itself produced a considerable sustained contraction of the membrane. Adrenaline and noradrenaline after priscol (60 min after 1st dose) showed lesser contraction of nictitating membrane. Since the base line was raised after priscol action which showed that the membrane remained in a contracted state; one could not say with certainty that the action of adrenaline and noradrenaline was partially blocked. However, during the experiment one could see that the membrane had enough margin to contract further even though it was not fully relaxed. This meant that certain amount of adrenergic blockade was produced. Had there been no adrenergic blockade due to priscol action, adrenaline and noradrenaline should have shown an augmented response. In one dog the dose of priscol was reduced to only 1 mg/kg in order to get only 50 per cent reduction in response to adrenaline and noradrenaline. After 40 min interval, instead of

blockade, higher contractions of membrane were recorded with the same dose of adrenaline and noradrenaline. Potentiating effect of adrenergic blocking agents has been cited in literature (Jang, 1941; Holzbauer and Vogt, 1955).

REFERENCES

Bradley, O.C., and Crahame, T. (1948). *Topographical anatomy of the dog*, 5th edition, p. 242, London, Oliver and Boyd.

Bülbring, E. and Burn, J.H. (1938). *J. Physiol.*, **91**, 459.

Bülbring, E. and Burn, J.H. (1949). *Brit. J. Pharmacol.*, **4**, 202.

Burn, J.H. (1950). *Biological standardisation*, 2nd Edi. p. 229, London, Oxford Medical Publication.

Cannon, W.B. and Rosenblueth, A. (1933). *Amer. J. Physiol.*, **104**, 557.

Jang, C.S. (1941). *J. Pharmacol.*, **71**, 87.

Holzbauer, M. and Vogt, M. (1955). *Brit. J. Pharmacol.*, **10**, 186.

Euler, U.S.V. (1950). *Methods in medical research*, Vol. 3 p. 137, Chicago, Year Book Publishers.