SOME OBSERVATIONS OF ANTIFIBRILLATORY AGENTS ON VENTRICULAR FIBRILLATION UNDER HYPOTHERMIA

By

J. P. SAXENA

Department of Physiology, College of Medical Sciences, Banaras Hindu University, Varanasi

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Some antifibrillatory drugs viz., prostigmine, potassium chloride and pronestyl were tried to check ventricular fibrillation caused by complete inflow and outflow occlusion of the heart under hypothermia. Potassium chloride showed some beneficial effect while prostigmine and pronestyl did not show any improvement.

Ventricular fibrillation is a serious cardiac complication in induced hypothermia. A trial of many drugs to prevent fibrillation has been given from time to time. Hegnauer (1950) used intravenous procaine and adrenaline blocking agents without any success in preventing ventricular fibrillation. Lewis and Taufic (1953) and later Crookson *et al* (1953) obtained moderate success in preventing ventricular fibrillation by the use of electric shock, procaine, coramine, massage and other conventional agents and methods. Incidence of ventricular fibrillation is reported to be reduced to 50 per cent if prostigmine is administered in general circulation before occlusion is done (Swan *et al*, 1954). The same authors earlier have reported the efficacy of potassium chloride too. In the present article a study of few antifibrillatory drugs has been presented to see if they have any promising results.

METHODS

Healthy mongrel dogs, 19 males and 8 females weighing between 8 to 14 kg. were chosen for experiments. Animals were anaesthetised by intravenous injection of chloralose, 80 mg per kg body weight. Tracheal intubation was done and animals were hyperventilated throughout the experiment by means of a pump respirator at a rate of 28 per min, each time delivering 200 to 250 ml air per stroke. Hypothermia was induced by immersing the animal in ice cold water (1° to 5°C) till the rectal temperature reached to 26°C. The technique of performing intracardiac operation was same as described by Kapoor and Saxena (1960). Briefly stating, the chest was opened by a right lateral incision in the fourth intercostal space. The vena azygos was ligatured near its termination. The superior and inferior vena cava were isolated and rubber tapes were passed loosely twice around them. The pericar-

dium was cut in between the two stay sutures. The superior vena cava was occluded by tightening the rubber tapes and thirty seconds after inferior vena cava was occluded. The outflow occlusion was done one minute later by clamping the root of the aorta distal to the origin of the coronary arteries after removing the pad of fat on its surface.

In 27 dogs where fibrillation occurred prostigmine methyl sulfate (F. Hoffmann la Roche & Co. Ltd., Basle. 1 in 4000 solution 0·05 to 0·1 ml per kg body weight), potassium chloride (0·5 milli-equivalent per ml solution, 2 to 3 ml) and procaineamide hydrochloride (pronestyl, M/s E. R. Squibbs & sons, 100 to 250 mg) were given and their effect studied on fibrillation. All these drugs were injected into the aorta proximal to the clamp and cardiac massage was done to perfuse the drug through coronary circulation and rhythm was restored. Electro-cardiographic records were taken by Burdick Cardioscribe in standard lead II to observe ventricular fibrillation as well as to see the effect of restoration of the normal cardiac rhythm. The animals were rewarmed back to normal by immersion n warm water at 45°C.

RESULTS AND DISCUSSION

The results are shown in the tables I to III.

TABLE I

Effects of prostigmine on ventricular fibrillation.

Expt. No.	Weight of dog in kg	Rectal temp when V.F. appeared (centigrade)	Time when V.F. appeared after complete occlusion (min)	Amount of drug injected (ml)	V.F. stopped or not	Revival of rhythm	Result
1	10·0	24	1	0·5	yes	no	dog expired
2	9·25	26	2	0·5 & 0·5 intracardiac	no	no	„
3	6·75	25	V.F. appeared before occlusion	1·5	no	no	„
4	8·3	25	V.F. appeared during cooling	1·0	no	no	„
5	11·0	25	1	1·0	no	no	„
6	11·3	25	7	0·5	yes	no	„
7	9·5	23	5·5	2·0	yes	no	„
8	9·2	25	20	1·0	no	no	„
9	9·45	25	V.F. appeared during cooling	1·5	no	no	„
10	11.7	24	5	1·0	no	no	„

In experiment No. 4 & 9 where ventricular fibrillation appeared during cooling, the chest was opened hurriedly, occlusion was done and drug was injected.

V.F., Ventricular fibrillation.

TABLE II

Effect of potassium chloride on ventricular fibrillation. Resuscitation was done by injection of 0·2 ml of 2% calcium chloride followed by cardiac massage

Expt. No.	Weight of dog in kg	Rectal temp when V.F. appeared in centigrade	Time when V.F. appeared after complete occlussion (min)	V.F. stopped by drug or not	Revival rhythm	Result
1	8·0	24	20	yes	yes	dog revived
2	10·5	23	20	yes	temporarily	dog expired
3	11·4	25	1	yes	no	,,
4	8·35	25	7	yes	yes	dog revived
5	8·9	25	V.F. appeared during cooling	yes	no	dog expired
6	11·0	24	15	yes	no	,,
7	10·5	24	20	yes	yes	dog revived
8	11·7	25	11	yes	no	dog expired
9	13·7	24	11	yes	yes	dog revived
10	11·6	24	11	yes	no	dog expired
11	11·45	25	immediate	yes	yes	dog revived

In expt. No. 1 & 2 dog tolerated occlusion for 20 min. In those cases a mechanical stimulus was given to start fibrillation.

In expt. No. 5 where ventricular fibrillation appeared during cooling, the chest was opened hurriedly, occlusion was done and drug was injected.

V.F., Ventricular fibrillation.

TABLE III

Effect of pronestyl on ventricular fibrillation

Expt No.	Weight of dog in kl	Rectal temp when V.F. appeared centigrade	Time when V.F. appeared after complete occlusion (min)	Amount of drug injected (mg)	V.F. stopped or not	Revival of rhythm	Result
1	12·2	24	12·5	150	no	no	dog expired
2	12·5	25	12·0	100	yes	no	,,
3	12·25	24	10·5	200	yes	occasional vent. beats	,,
4	11·0	24	V.F. recorded just after cooling	200	no	no	,,
5	10·8	24	10·5	150	no	no	,,
6	9·8	24	7	200	no	no	,,

In expt. No. 4 where ventricular fibrillation appeared during cooling, the chest was opened hurriedly, occlusion was done and drug was injected.

In Table I, it was observed that prostigmine was able to check the ventricular fibrillation in 3 dogs out of 10. In those 3 dogs where fibrillation was checked, cardiac massage as a resuscitative method was of no use. The rhythm could not be restored. Swan *et al* (1954) have reported encouraging results with coronary perfusion of prostigmine. In their control series they reported that right ventriculotomy was a fibrillatory stimulus in hypothermic dogs. In 16 animals they gave the drugs after putting aortic clamp and later performed ventriculotomy. Their observations showed the absence of fibrillation. The period of inflow and outflow occlusion was for an average of eight minutes. It might be possible that this period of occlusion was less and prostigmine protected the heart against ventricular fibrillation due to ventriculotomy and not due to hypothermia. In the present work ventriculotomy was not done and the drug was used after ventricular fibrillation had started. Hence it can be presumed that prostigmine has no checking influence on ventricular fibrillation occurring under hypothermia in the absence of ventriculotomy.

Potassium chloride, on the other hand, checked fibrillation in all the cases (Table II). Resuscitation of cardiac rhythm by calcium chloride followed by massage was possible only in 5 dogs out of 11. The increased cardiac irritabilitycausing fibrillation was probably depressed by the potassium chloride as it directly acts on the myocardium. Swan *et al* (1954) tried potassium chloride in 7 dogs in the same manner and reported revival of rhythm in all the cases. In their series, complete occlusion was not done, moreover, it is not evident from the reports as for how long inflow occlusion was done. Outflow occlusion was done only after fibrillation had started. Probably in our series by complete occlusion the heart suffered from some irreversible injury which was more detrimental for the servival and that is why potassium chloride in the present experiments was efficacious in 45·45% of the cases.

In the third group of experiments pronestyl was administered in 6 dogs. The fibrillations were checked by this drug in two cases only, and in those two cases revival of the rhythm was not possible (Table III). In one case (Expt. No. 3), occasional ventricular beats were noticed but they were so feeble that the animal could not be revived.

Thus it may be concluded from the above studies that potassium chloride has got some beneficial effect in stopping fibrillation while the other two drugs have no effect at all.

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