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Kyoji Tasaki
Allen C. Norton

Department of Physiology,
Tohoku University School of Medicine,
Sendai, Japan.

Yoshiro Fukada

Technical Research Laboratories,
Japan Broadcasting Corporation (NHK),
Tokyo.

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PHARMACOLOGY

Post-mortem Increase of Potassium in Human Cerebrospinal Fluid

The composition of plasma and cerebrospinal fluid is similar so far as content of electrolytes is concerned. There is also evidence that cerebrospinal fluid can be used as a good medium for maintaining *in vitro* the activity of isolated organs: frog heart, for example. But if the cerebrospinal fluid of dead, instead of living, subjects is used, the frog heart stops working immediately. This will also occur with atropinized preparations. Potassium was supposed to be responsible for this effect.

Following this hypothesis, we examined the potassium content of cerebrospinal fluid from normal and dead subjects. Potassium was measured according to the standard flame spectrophotometric procedure.

Potassium-levels in the cerebrospinal fluid of normal subjects are about 70 mg/l., whereas those observed in the cerebrospinal fluid obtained from 5 different dead subjects were 1·12; 1·42; 1·48; 1·52; 1·58 g/l. The cerebrospinal fluid was obtained from bodies, kept at the Institute for Forensic Medicine, University of Milan, about 24 h after death.

The potassium in the cerebrospinal fluid of dead subjects may therefore become 20 times greater than in living subjects.

Later we examined how long the potassium takes to diffuse *post mortem* into the cerebrospinal fluid. For this, different samples of cerebrospinal fluid were taken from the same body 8, 12 and 24 h after death. The results were as follows: 228 mg at 8 h, 760 mg at 12 h, and 1·6 g at 24 h. These figures show that potassium moves into the cerebrospinal fluid progressively, and that the rate of this diffusion is greater between the eighth and the twenty-fourth hour after death than between the first and the eighth hour.

So far as sodium and calcium are concerned, their levels were similar in cerebrospinal fluids taken from living and dead subjects.

A Ringer medium having a potassium content similar to that of the post-mortem cerebrospinal fluid has an almost immediate paralysing effect on the frog heart. The functional alterations of frog heart-beats which appear when potassium-enriched Ringer diluted with normal Ringer is used or similarly diluted post-mortem cerebrospinal fluid are parallel.

In the last series of experiments we investigated the effects in dogs of the addition of potassium to the cerebrospinal fluid in order to reach comparable levels as observed 24 h *post mortem*.

In two dogs 1 ml. of cerebrospinal fluid was substituted through the sub-occipital way with 1 ml. of a solution containing 5 g/l. of potassium chloride. Preliminary investigations, carried out using dyes, showed that 1 ml. of solution substituted for 1 ml. of dog cerebrospinal fluid led to rapid mixing with a final dilution of about 1 : 5. The dogs showed a high degree of nervous excitation with unco-ordinated and generalized convulsions; in addition to this they struggled, stretching very rapidly their forelegs above and to the side of their heads. These symptoms lasted for about 15 min, then progressively decreased. The animals suffered from dyspnœa for about 30 min.

The conclusions which can be drawn from these experiments are as follows: after death there is a remarkable diffusion of potassium into the cerebrospinal fluid; potassium concentration in the 24-h post-mortem cerebrospinal fluid is about 20 times greater than that present in physiological conditions; the phenomenon is progressive with time and therefore may be used from the point of view of forensic medicine; there are no significant post-mortem variations in sodium- and calcium-levels; a potassium concentration in the cerebrospinal fluid of a living animal, of a comparable value to that found in cerebrospinal fluid *post mortem*, produces toxic symptoms characterized by a very strong and typical central nervous excitation.

F. Fraschini
E. Müller
A. Zanoboni

Department of Pharmacology,
University of Milan.

A Mechanism of Reflexogenic Bradycardia produced by Cardiac Glycosides

It has been accepted that the vagal factor is one of the most important factors concerning the production of bradycardia by cardiac glycosides[1,2]. However, the bradycardia produced by cardiac glycosides was not prevented completely by bilateral vagotomy or previous administration of atropine[3]. Gold *et al.*[4] called the latter factor the extravagal factor, which was considered to be a direct action of cardiac glycosides on the heart. On the other hand, cardiac glycosides did not exert a definite negative chronotropic action on the isolated mammalian heart[5,6]. In order to elucidate this discrepancy, the following experiments were carried out on cats using strospeside as the cardiac glycoside.

After severing vagus nerves, carotid sinus nerves or cervical cord, or extirpating stellate ganglia, one-tenth of the probable lethal dose of strospeside was administered intravenously every 5 min until cardiac arrest was confirmed. The electrocardiogram was recorded with standard limb lead II and the efferent discharges in sympathetic nerve fibres were recorded concomitantly throughout the experiments.

By denervation investigations of anæsthetized cats, it was observed that bradycardia by strospeside was prevented almost completely in the following cases: (1) severance of both vagi and both carotid sinus nerves; (2) severance of both vagi and cervical cord (C_{3-4}); (3) severing of both vagi and extirpation of both stellate ganglia. Bradycardia was not completely prevented in the following cases: (1) severance of both vagi; (2) severance of both carotid sinus nerves; (3) transection of cervical cord (C_{3-4}); (4) extirpation of both stellate ganglia.

From the foregoing results, the following hypothesis concerning the mechanism of bradycardia produced by cardiac glycosides may be postulated. There are two different pathways of impulses which are quite independent of each other in producing the bradycardia by cardiac glycosides: one is the vagal pathway, which exerts cardiac slowing by vago-vagal reflex, and the other is the carotid body–sympathetic nerve system, which exerts cardiac slowing by way of the sinus nerves, cervical cord, stellate ganglia and the heart (Fig. 1).

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