EFFECT OF TAURINE AND THE DIPEPTIDE Tyr-Tyr ON VENTRICULAR DEFIBRILLATION OF THE HEART

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The list of new therapeutic substances with a cardioprotective effect includes taurine and the dipeptide Tyr-Tyr [1, 5], whose use in emergency cardiology is indicated on several counts. For instance, the important role of disturbances of ionic homeostasis in the generation of reperfusion damage [3, 7], and an increase in the intracellular calcium concentration during ventricular fibrillation have now been established. With these facts in mind, the study of the effect of these substances on the efficacy and safety of electric shock therapy was carried out.

The aim of this investigation was to study the effect of taurine and Tyr-Tyr on the functional injury threshold of the myocardium during defibrillation of the heart.

EXPERIMENTAL METHOD

Experiments were carried out on 27 anesthetized mongrel dogs weighing from 12 to 30 kg. Defibrillation with a "Lifepak-7" apparatus (USA), generating a dc shock of Edmark type, was carried out on the heart 18 ± 5 sec after the onset of ventricular fibrillation (VF), which was induced by application of an ac current (127 V) from the supply system. Defibrillation was carried out in the expiration phase. The functional injury threshold (IT) and the defibrillation threshold (DT) were determined and the electrotherapeutic index (ETI) was calculated as the ratio of IT to DT [2]. IT was taken to be the appearance of two or three ventricular extrasystoles or a transient conduction disturbance. The control group consisted of 14 experiments in which IT and DT were estimated over a period of observation of 3 h. Group 1 consisted of six experiments in which values of IT, DT, and ETI were estimated 1 h before and during the 2 h after intravenous injection of taurine (in a dose of 100 mg/kg). In group 2 (seven experiments) the parameters studied were analyzed 1 h before and during 2.5 h after intravenous injection of Tyr-Tyr (in a dose of 25 mg/kg).

EXPERIMENTAL RESULTS

The control group of experiments showed that repeated episodes of electrical fibrillation–defibrillation, applied in the course of 3 h, caused no significant changes in values of IT, DT, and ETI. Fluctuations of the average values of these parameters observed in these experiments did not exceed 7-20%. Although in some cases deviations of IT and DT were greater, the values of ETI remained sufficiently stable (Table 1).

In group 1 the mean values of the parameters in the initial state were: ETI 1.65 ± 0.23 relative unit, IT 18.7 ± 2.8 A, DT 11.3 ± 1.6 A. No significant changes in the values of IT and DT were found after injection of taurine. The value of ETI by the end of the first hour showed a tendency to fall (by 9%). In group 2, in the initial state, IT was 17.8 ± 2.4 A, DT 9.7 ± 0.9 A, and ETI 1.84 ± 0.30 relative unit. A significant increase in IT by 27% and in DT by 29%

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TABLE 1. Changes in IT, DT, and ETI after Administration of Taurine (Group 1) and of Dipeptide Tyr-Tyr (Group 2), M ± m

Parameter	Group	Time of observation, h		
		initially	1–1,5	2–2,5
IT, A	Control (n=14)	19,1±1,6	19,0±1,5	17,8±1,7
DT, A		10,7±1,6	10,2±1,4	9,7±1,3
ETI, rel. units		1,78±0,12	1,83±0,17	1,75±0,18
IT, A	1 (n=6)	18,7±2,8	18,0±1,8	20,0±1,7
DT, A		11,3±1,6	12,1±1,4	12,3±1,5
ETI, rel. units		1,65±0,23	1,51±0,19	1,60±0,25
IT, A	2 (n=7)	17,8±2,4	22,6±1,3*	28,8±3,2*
DT, A		9,7±0,9	12,5±1,0*	12,8±1,8
ETI, rel. units		1,84±0,30	1,87±0,12	2,31±0,25

Legend. *$p < 0.05$ compared with control group.

was observed 1 h after injection of Tyr-Tyr, rising to 62 and 32% respectively after 2 h. A tendency was noted for values of ETI to increase (by 26%) 2 h after injection of the preparation.

Injection of taurine thus had no significant effect on the functional injury threshold of the myocardium during defibrillation. The use of Tyr-Tyr caused an increase in both IT and DT, and the increase in IT was greater. These changes corresponded to the tendency for values of ETI to rise. The positive effect of Tyr-Tyr was most likely connected with its rapid breakdown into two molecules of Tyr and subsequent uptake by the sympathetic endings of the heart as a precursor or noradrenalin [6]. It can be tentatively suggested that the higher noradrenalin content in the sympathetic terminals of the heart is a factor increasing both the injury threshold of the myocardium and the defibrillation threshold. In turn, this suggests that the use of Tyr-Tyr may be indicated in the combination of measures aimed at abolishing VF, but this is a matter for further study.

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