GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Analysis of Central Blood Pressure during Diphtheria Intoxication in Rabbits

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Diphtheria intoxication was induced in rabbits by a single intravenous injection of native diphtheria toxin in dose of 0.3 MLD/kg, preliminary titrated on guinea pigs. Significant decrease in diastolic and systolic blood pressure and in intraventricular pressure in the left ventricle was established to take place during intoxication. Pulse wave propagation time was prolonged, likely due to prolongation of pressure wave, while the reflection wave appeared at the same time. Reduction of central blood pressure was concluded to result from changes in biomechanical characteristics of the left ventricle, and not to be associated with changes in elastic properties of the arterial wall.

Key Words: *diphtheria intoxication; central blood pressure; pulse wave; vascular wave rigidity; left ventricle*

Recently, increased attention is paid by clinicians to investigations of central pulse wave, characteristics of which are tightly bound with a degree of rigidity and tonus of vascular wave. Changes in elastic properties of central arteries, assessed by the pulse wave velocity, may be used as a predictor of unfavorable outcomes of various cardiac and vascular pathologies, and also of non-cardiac diseases [2,4-6]. Pulse wave analysis in experimental studies may be employed for of pathophysiological mechanisms of systemic hemodynamic changes in various pathological processes. Apart from marked decrease in left ventricle contractility, marked drop of diastolic blood pressure (BP) and similar (but non-significant) changes in systolic BP were found during intoxication with diphtheria toxin in rabbits [3]. In this study we attempted to determine whether it results from reduction in left ventricle contraction force or from changes in elastic properties of central arteries.

The aim of this study was to investigate experimentally the pathophysiological mechanisms of systemic hemodynamic changes during diphtheria intoxication.

MATERIALS AND METHODS

Experiments were carried out on 20 male chinchilla rabbits weighting 3.0-3.5 kg. The animals were divided into 4 groups: 3 experimental and 1 control groups, 5 animals in each. Rabbits from experimental groups were injected intravenously with a single dose of native diphtheria toxin in dose of 0.3 MLD/kg of body weight (MLD, minimum lethal dose). The amount of the toxin, which after intraperitoneally injection to guinea pigs caused more than 50% mortality due to adrenal apoplexy within 3 days, was accounted as 1 MLD. Experiments were carried out 1, 3, and 5 days after the onset of diphtheria intoxication. Control group consisted of intact animals.

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At mentioned time points, registration of hemodynamic parameters was performed using hardware-software complex Mikard consisting of an analog-to-digital converter with electromagnetic transducer for blood pressure and intraventricular pressure measurements, coupled with a personal computer. The common carotid artery was isolated under local anesthesia and a transducer catheter filled with 0.9% NaCl was injected into its central end. Registration of BP curve was carried out during several minutes. On the basis of data obtained, the systolic (SBP), diastolic (DBP) BP and actual intraventricular pressure in the left ventricle (IPLV) were determined.

Pulse wave analysis was performed by measuring parameters, indirectly reflecting vascular wall rigidity (Fig. 1): reflection wave amplitude, which is the wave occurring as a result of pressure wave reflection at bifurcations of conductive arteries and smaller muscle arteries; time of reflection wave appearance (time between peaks of pressure and reflection waves); propagation time of pressure wave (time from the origin of the pressure wave to its complete decay), which is the sum of pressure wave and reflection wave [1].

All quantitative data was statistically analyzed using the software developed at the Department of General Pathology and Pathological Physiology, People's Friendship University of Russia, and program Biostat. Assessment of the differences was performed using Student's *t* test. The differences considered to be significant at $p \leq 0.05$.

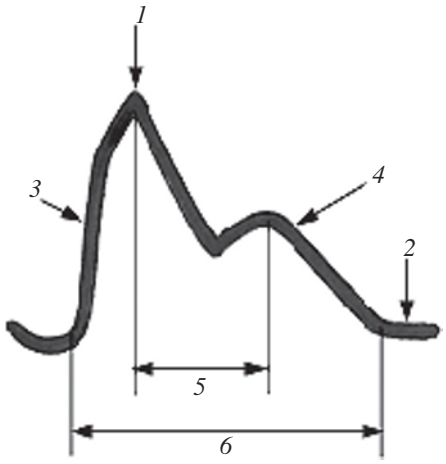

Fig. 1. Single cycle of pulse wave travel. *1* — SBP; *2* — DBP; *3* — pressure wave; *4* — reflection wave; *5* — time of reflection wave appearance; *6* — propagation time of pulse wave.

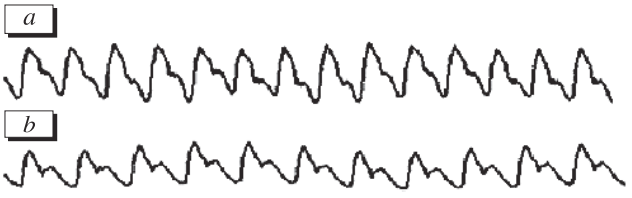

Fig. 2. Fragments of central BP curves in normal animals (*a*) and 5 days after injection of diphtheria toxin (*b*).

RESULTS

At the end of first 24 hours after diphtheria toxin injection, a significant decrease in SBP and DBP occurred (Table 1). On day 3, SBP continued to decrease, and DBP remained at the level of day 1. On day 5, both parameters slightly increased, but still were significantly below the normal values. Thus, marked and statistically significant decrease in both SBP and DBP is characteristic of this process.

Reflection wave amplitude changed in parallel to SBP and DBP, and was below the control value at all terms of the study.

Time of reflection wave appearance remained unchanged.

Propagation time of pressure wave significantly increased on day 3 and remained at this level up to day 5 (Fig. 2).

TABLE 1. Characteristics of Central BP and Left Ventricle Contraction in Rabbits During Diphtheria Intoxication (*M*±*m*)

Parameter	Control	Day after injection		
		1	3	5
SBP, mm Hg	142.8±1.8	124.4±3.7*	116.8±0.6*	131.8±3.3*
DBP, mm Hg	119.4±1.4	105.6±3.5*	105.2±0.5*	110.2±3.0*
RW, mm Hg	130.4±1.6	115.2±3.8*	111.2±0.4*	121.3±3.2*
TRWA, msec	40.2±1.3	36.4±1.6	39.2±1.1	39.7±2.8*
PTPW, msec	107.9±2.1	109.4±2.8	116.5±3.4*	117.6±3.8*
IPLV, mmHg	139.6±1.3	113.7±1.5*	114.2±1.7*	123.4±2.1*

Note. RW — amplitude of reflection wave; TRWA — time of reflection wave appearance; PTPW — propagation time of pulse wave. *$p \leq 0.05$.

IPLV significantly and steadily decreased on days 1 and 3. This parameter tended to increase at later terms, but still remained significantly below the normal.

Thus, propagation time of pressure wave increased in time, what might indicate a decrease in arterial wall rigidity in central vessels. At the same time, the time of reflection wall appearance was not affected, what suggests that deceleration of the pressure wave is not associated with changes in vessel wall properties and is most likely determined by prolongation of pressure wave due to significant decrease in contraction force of the left ventricle.

The decrease in amplitude of the reflection wave was also probably associated with a decrease in the amplitude of the pressure wave.

Thus, diphtheria intoxication in rabbits is associated with a decrease in central BP due to impaired biomechanical properties of the left ventricle. Significant changes in elastic properties of central arteries seem not to appear after exposure to diphtheria toxin.

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