3. Yu. P. Kozlov, R. B. Ritov, V. E. Kagan, et al., Free-Radical Oxidation of Lipids in Biomembranes [in Russian], Moscow (1972).
4. F. Z. Meerson, Adaptation, Stress, and Prophylaxis [in Russian], Moscow (1981).
5. F. Z. Meerson, V. E. Kagan, Yu. P. Kozlov, et al., Kardiologiya, No. 2, 81 (1982).
6. F. Z. Meerson and V. T. Dolgikh, Kardiologiya, No. 10, 38 (1982).
7. T. A. Yakovleva and P. N. Eskunov, Probl. Tuberk., No. 6, 70 (1982).
8. D. E. Atkinson, Biochemistry (Washington), 7, 4030 (1968).
9. A. S. Csallany and K. L. Ayaz, Lipids, 11, 412 (1976).
10. E. T. Fallen, W. Elliott, and G. H. S. Gorlin, J. Appl. Physiol., 22, 836 (1967).
11. J. Folch, M. Lee, and G. H. S. Stanly, J. Biol. Chem., 226, 497 (1957).
12. D. J. Hearse, S. M. Humphrey, and E. B. Chain, J. Mol. Cell. Cardiol., 5, 395 (1973).
13. T. J. Player and H. O. Hultin, Biochem. J., 48, 1 (1948).
14. S. Reutman and S. Frankel, Am. J. Clin. Pathol., 28, 56 (1957).

EFFECT OF PRELIMINARY ADMINISTRATION OF THE α-ADRENOBLOCKER PHENTOLAMINE AND THE β-ADRENOBLOCKER INDERAL ON STRESS-INDUCED FALL OF PORTAL VEIN RESPONSE TO NORADRENALIN

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KEY WORDS: stress; α-adrenoblocker phentolamine; β-adrenoblocker inderal.

Profound depression of spontaneous contractile activity of the smooth muscle of the portal vein and a sharp fall in its adrenoreactivity are known to occur as a result of previous severe emotional-painful stress (EPS), and they may play an important role in the pathogenesis of arterial hypovolemia and of states resembling collapse [2, 4]. At the same time, it has been shown that stress-induced damage to heart muscle can be effectively prevented by means of the β-adrenoblocker inderal [3, 5].

Since the adrenoreceptor apparatus in the smooth muscles of blood vessels consists of two types of receptors [6], the aim of this investigation was to study the effect of preliminary administration of the α-adrenoblocker phentolamine and the β-adrenoblocker inderal on contractility and adrenoreactivity of the isolated portal vein after EPS.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 200-220 g. Six groups of rats were used: 1) control, 2) control receiving inderal, 3) control receiving phentolamine, 4) exposed to EPS, 5) receiving inderal before the beginning of exposure to EPS, 6) receiving phentolamine before the beginning of EPS.

The α-adrenoblocker phentolamine and the β-adrenoblocker inderal were injected intraperitoneally in doses of 5 and 1 mg/kg respectively, 1 h before the beginning of exposure to stress.

EPS was produced by Desiderato's method [7] in the course of 6 h. The animals were decapitated 2 h after the end of exposure to stress and the portal veins were removed and placed in thermostatically controlled working chambers perfused with oxygenated Krebs' solution at a temperature of 32°C and with a load of 400 mg [4]. Spontaneous contractile activity was recorded on a two-channel system (Ugo Basile, Italy).

The following parameters of contractile activity were calculated: the developed tension, the frequency of phasic contractions per minute, the intensity of functioning of structures (IFS), equal to the product of the developed tension and frequency of contractions, calcula-

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TABLE 1. Effect of Preliminary Administration of Phentolamine and Inderal on Contractile Function of Portal Vein after EPS (M ± m)

Parameter studied	Control	EPS	EPS + inderal	EPS + phentolamine
Developed tension, mg	149±24	17±2,1	20±2,5	132±32*
Frequency of contractions (per minute)	7,9±0,6	11±1,0	11±1,5	6,5±0,6*
IFS, mg/mg·min	410±52	67±12	88±14	303±46*
Velocity of contraction, mg/sec	91±12	15±1,8	17±3,0	77±10*
Velocity of relaxation, mg/sec	141±24	21±1,9	19±3,5	135±27*

Legend. Here and in Table 2, *P < 0.05 compared with control.

TABLE 2. Effect of Preliminary Administration of Phentolamine and Inderal on Reactivity of Portal Vein to Noradrenalin after EPS (M ± m)

Experimental conditions	K, g/ml	
	inderal	phentolamine
Control	$4,4\cdot10^{-7}\pm0,8\cdot10^{-7}$	$4,0\cdot10^{-7}\pm0,9\cdot10^{-7}$
Control + blocker	$4,4\cdot10^{-7}\pm1,3\cdot10^{-7}$	$12\cdot10^{-7}\pm3,8\cdot10^{-7}$*
EPS	$50\cdot10^{-7}\pm13\cdot10^{-7}$	$53\cdot10^{-7}\pm7,0\cdot10^{-7}$
EPS + blocker	$47\cdot10^{-7}\pm14\cdot10^{-7}$	$13\cdot10^{-7}\pm3,2\cdot10^{-7}$*

ted per unit weight of the portal vein, the velocity of relaxation of the smooth muscle.

To study adrenoreactivity of the portal vein the effect of successively increasing concentrations of noradrenalin was studied: 10^{-7}, $3\cdot10^{-7}$, $6\cdot10^{-7}$, and 10^{-6} g/ml. The reaction was estimated according to the degree of tonic contraction of the smooth muscle.

To describe adrenoreactivity of the portal vein quantitatively, the value of the apparent dissociation constants (K) of the noradrenalin–adrenoreceptor complex was calculated. Numerically, the value of K is equal to the concentration of the substance causing a reaction equal to half of the maximal reaction [1].

EXPERIMENTAL RESULTS

The study of the effect of adrenoblockers on contractile function of the smooth muscle of the portal vein of the control animals showed that neither phentolamine nor inderal caused any significant changes in the parameters tested. Accordingly, intact animals were used as the control.

It was found that exposure to EPS caused a considerable decrease in the parameters of contractility of the portal vein studied (Table 1). The developed tension was reduced by more than eight times, and IFS and the velocities of contraction and relaxation were reduced by approximately six times. Depression of this kind may be due to disturbance of Ca^{++} transport in the vascular myocytes by stress or to a disturbance of the energy supply for the contractile system of the smooth-muscle cells [3, 4].

Preliminary injection of the α-adrenoblocker phentolamine to animals exposed to stress largely prevented the disturbances of contractile function of the vein caused by stress: the values of the principal parameters averaged about 85% of the control level. Preliminary administration of the β-adrenoblocker inderal had no protective action (Table 1).

Injection of phentolamine into the control animals caused adrenoreceptor sensitivity to fall by two-thirds (Table 2). Consequently, both intact animals and animals receiving the drug served as the control.

Because of exposure to EPS the adrenoreactivity of the smooth muscle was reduced by more than 12 times (Table 2), in agreement with data obtained previously [2]. Preliminary injection of phentolamine increased the adrenoreactivity of the portal vein by four times; the value of K under these circumstances almost reached the control level. Administration of inderal had no significant effect on sensitivity of the smooth-muscle adrenoreceptors of both control and stressed animals.

One result of exposure to severe stress is known to be catecholamine-induced damage to myocytes, due to excessively strong and prolonged activation of the sympathicoadrenal system [3]. Since in the present experiments disturbances of the contractile function and adrenoreactivity of the portal vein were prevented only by the α-adrenoblocker phentolamine, it can be postulated that the damaging effect of high concentrations of catecholamines is realized in stress through α-adrenoreceptors which, according to data obtained by other workers [8, 9], predominate in the receptor apparatus of the portal vein.

Preliminary injection of the α-adrenoblocker phentolamine thus largely abolishes the damaging effect of high concentrations of catecholamines arising as a result of previous exposure to stress on spontaneous contractility and adrenoreactivity of the smooth muscle of the portal vein.

LITERATURE CITED

1. B. N. Manukhin, Physiology of Adrenoreceptors [in Russian], Moscow (1968).
2. E. B. Manukhina, Byull. Éksp. Biol. Med., No. 2, 5 (1983).
3. F. Z. Meerson, Adaptation, Stress, and Prophylaxis [in Russian], Moscow (1981).
4. F. Z. Meerson, E. B. Manukhina, and V. G. Pinelis, Kardiologiya, (1983) (in press).
5. E. E. Ustinova, Kardiologiya (1983) (in press).
6. B. Folkov and E. Neil, The Circulation, Oxford Univ. Press (1971).
7. O. Desiderato and J. R. MacKinnon, J. Comp. Physiol. Psychol., 87, 208 (1974).
8. K. M. Hanson, Angiologica, 10, 65 (1973).
9. P. D. I. Richardson and P. G. Withrington, Br. J. Pharmacol., 57, 581 (1976).

EFFECT OF β-ADRENOBLOCKERS ON PROSTAGLANDIN-INDUCED OCULAR HYPERTENSION IN RABBITS

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Prostaglandins (PG) of various groups (E_1, E_2, F_2), if instilled into the conjunctival sac or injected subconjunctivally, cause an acute rise of intraocular pressure (IOP) in rabbits and monkeys — prostaglandin-induced ocular hypertension [1, 2, 9, 12]. There is reason to suppose that PG participate in the pathogenesis of acute increases of IOP in man.

Reports of the hypotensive action of β-adrenoblockers on normal and raised IOP under experimental and clinical conditions have recently been published [4, 6-8, 11, 13, 15]. Propranolol and Timolol have found wide application as drugs lowering IOP in glaucoma.

The problem of the effect of β-adrenoblockers on ocular hypertension induced by PG has received little study. Only Waitzman [14] and Green and Kim [10] have shown that propranolol

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