EFFECT OF THE β-ADRENOBLOCKER PROPRANOLOL ON ADRENALIN LIPOLYSIS IN ADIPOSE TISSUE OF RATS WITH SPONTANEOUS GENETIC HYPERTENSION

G. M. Boriskina, P. V. Gulak
and Yu. V. Postnov

UDC 616.12-008.331.1-092.9-085.
217.24-07:616-008.939.15-074

The action of the β-adrenoblocker propranolol on adrenalin lipolysis was studied in adipose tissue of rats with spontaneous hypertension and of control rats. The degree of lipolysis was judged from the accumulation of glycerol in the incubation medium *in vitro*. The maximal response of adipose tissue to adrenalin was found to be the same in rats with hypertension and control animals. The adrenalin concentration evoking half the maximal response (K_A) in rats with hypertension was found to be half that observed in control rats. In the presence of propranolol this parameter increased more in SHR rats than in the controls. The results indicate increased sensitivity of the adipose tissue of SHR rats to propranolol, possibly in connection with changes in the properties of the β-adrenoreceptor in this form of hypertension.

KEY WORDS: hypertension; adrenalin; propranolol; adipose tissue.

The object of this investigation was to study activation of lipolysis by adrenalin in the adipose tissue of rats with spontaneous hypertension and also the inhibition of this process by the β-adrenoblocker propranolol, which has antihypertensive properties. The study of the effect of this drug on adrenalin lipolysis enables the state of the β-adrenoreceptors in hypertension to be evaluated.

METHOD

Spontaneously hypertensive (SHR) Kyoto-Wistar rats aged 10-12 weeks, weighing 120-140 g and with a systolic pressure of 180 ± 10 mm Hg were used. Inbred male Wistar rats with similar body weight and age, and with an arterial pressure of 80 ± 10 mm Hg served as the control. The pressure was measured in the unanesthetized animal by means of a plethysmograph (Nihon Kohden).

Rats deprived of food for 24 h but receiving water ad lib. were decapitated, the epididymal adipose tissue was removed, and its distal part (about 80 mg) placed in incubation medium. The adipose tissue was incubated in Krebs–Ringer phosphate buffer, pH 7.4 (2.0 ml), containing increasing concentrations of adrenalin (0.54-8.64 M, from Calbiochem, USA), in the presence of DL-propranolol (1.0 μM, from Sigma, USA) or without propranolol. The samples were incubated for 1 h at 37°C with continuous shaking. After the end of incubation the samples were placed in ice, the tissue was weighed, and the quantity of free glycerol accumulating in the incubation medium was determined by an enzymic method [5]. The significance of the difference between the means was determined by Student's t-test at the $P < 0.05$ level of significance.

RESULTS

The lipolytic action of adrenalin was determined from the rate of accumulation of free glycerol in the incubation medium. The level of spontaneous lipolysis in the adipose tissue of the SHR and control rats was the same (1.92 μmoles substrate/h/g tissue). Kinetic parameters were calculated from reciprocal Lineweaver–Burk plots. By this method the maximal effect of adrenalin (E_{max}) and also the adrenalin concentration evoking half the maximal re-

Central Research Laboratory, Fourth Main Board, Ministry of Health of the USSR. Department of Pathomorphology, Moscow. (Presented by Academician of the Academy of Sciences of the USSR E. I. Chazov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 88, No. 11, pp. 553-555, November, 1979. Original article submitted September 6, 1978.

0007-4888/79/8811-1285$07.50

TABLE 1. Kinetic Parameters of Action of Propranolol on Adrenalin Lipolysis in Adipose Tissue of Spontaneously Hypertensive and Control Rats (M ± m)

Group of animals	Variant of experiment	K_A, μM	E_{max}, μmoles substrate/h/g wet weight of tissue
Spontaneously hypertensive rats (n = 6)	Adrenalin	0,40±0,05	4,7±0,30
	Adrenalin + propranolol (10^{-6} M)	1,63±0,20	4,25±0,60
Control (n = 6)	Adrenalin	0,78±0,09	5,19±0,42
	Adrenalin + propranolol (10^{-6} M)	1,34±0,37	4,96±0,98

sponse, i.e., the "apparent" affinity of the hormone (K_A) [4], could be determined. As Table 1 shows, the maximal effect of adrenalin on SHR rats was the same as its effect on the control rats. Conversely, the adrenalin concentration evoking half the maximal lipolytic response (K_A) was significantly lower (by half) in SHR rats ($P < 0.001$).

The results thus indicate increased "affinity" of adipose tissue for adrenalin in hypertensive animals.

Propranolol is known as a β-adrenoreceptor blocker which, because of its structural similarity with catecholamines, competitively inhibits the action of adrenalin. Inhibition of adrenalin lipolysis by propranolol takes place at the β-adrenoreceptor level and is expressed kinetically as an increase in K_A; the maximal response is unchanged under these circumstances. Preliminary experiments showed that propranolol does not affect the level of spontaneous lipolysis in adipose tissue. Under the influence of propranolol (1.0 μM) K_A for adrenalin in the adipose tissue of the control rats was increased by 1.7 times (Table 1), whereas in SHR rats the increase in K_A was much greater (by 4.6 times; $P < 0.01$). As Table 1 shows, propranolol increased K_A for adrenalin in SHR rats approximately to the value of K_A for the normotensive control.

The greater change in K_A for adrenalin in the adipose tissue of SHR rats suggests increased sensitivity of these animals to β-blockers compared with control animals. Increased sensitivity of SHR rats to β-blockers has also been found during the study of the action of propranolol and timolol in vivo after peroral administration of these drugs to rats. In the case cited, renin activity was reduced in the blood plasma of SHR rats whereas renin activity of the control animals remained unchanged [7].

Analysis of differences between the kinetic parameters of action of adrenalin in SHR and control rats (a lower value of K_A, a greater change in K_A in the presence of propranolol, identical maximal response) suggests a change in the properties of the β-adrenoreceptors in the adipose tissue of SHR rats.

Besides with the change in the sensitivity of the adipose tissue of SHR rats to adrenalin observed previously in adrenalectomized animals [3] and also a disturbance of passive permeability of cell membranes or monovalent cations [2, 6], and a change in the phosphoinositide content in the erythrocyte membrane [1], the changes in adrenalin lipolysis detected under the influence of propranolol provide additional confirmation of a widespread alteration of cell membranes in rats with spontaneous hypertension.

LITERATURE CITED

1. P. V. Gulak, G. M. Boriskina, and Yu. V. Postnov, Byull. Éksp. Biol. Med., No. 8, 155 (1977).
2. Yu. V. Postnov, S. N. Orlov, and A. S. Shevchenko, Kardiologiya, No. 10, 88 (1975).
3. Yu. V. Postnov and M. B. Reznikova, Byull. Éksp. Biol. Med., No. 12, 672 (1978).
4. A. Aulich, K. Stock, and E. Westermann, Life Sci., 6, 926 (1967).
5. P. B. Garland and P. J. Randle, Nature, 196, 987 (1962).
6. A. W. Jones, Circulat. Res., 33, 563 (1973).
7. R. L. Riley, A. Scriabine, and L. S. Watson, Proc. Soc. Exp. Biol. (New York), 153, 454 (1976).