Acute hemodynamic effects of propranolol in the conscious spontaneously hypertensive rat (SHR)

T.G. COLEMAN[2], T.L. SMITH[2], J.F.M. SMITS[1] & H.A.J. STRUYKER-BOUDIER[1]

Dept. Pharmacology, Rijksuniversiteit Limburg, Beeldsnijdersdreef 101, Postbus 616, 6200 MD Maastricht, The Netherlands[1] and
Dept. Physiology and Biophysics, University of Mississippi Medical Centre, 2500 North State Street, Jackson, Miss. U.S.A.[2]

In conscious SHR we recently reported a 2–4 h delayed antihypertensive effect following acute subcutaneous (s.c.) propranolol in different doses (Struyker-Boudier, 1978). In this study we further characterized the hemodynamic effects of propranolol in this species using chronically implanted electromagnetic flow-probes for the measurement of cardiac output.

Male SHR (Blue Spruce Farms) weighing 250–300 g were used. Flow-probes (Carolina Medical Electronics EP 105) were placed around the ascending aorta according to the method of Smith & Hutchins (1977). A teflon catheter was positioned into the abdominal aorta via the left femoral artery for monitoring pulsatile and mean arterial blood pressure (MAP). Rats were allowed at least 3 days for recovery from surgery.

On the experimental day, after 1 h for stabilization of haemodynamics, rats were injected s.c. either with propranolol (5 mg/kg, $n = 8$) or vehicle (0.1 ml 0.9% NaCl, $n = 7$). Haemodynamic variables were measured continuously during the first 8 h and furthermore at 12 and 20 h after the injection. Cardiac index (CI, ml min^{-1} 100 g body $weight^{-1}$), total peripheral resistance (TPRI = MAP/CI; mm Hg min 100 g body weight ml^{-1}) and stroke volume (SVI = CI/heart rate; ml 100 g body $weight^{-1}$) were calculated.

The results, summarized in Table 1, indicate an immediate reduction of heart rate (HR) and CI following propranolol. However, TPRI increased, resulting in a net increase of MAP. At 2 h after injection all parameters were gradually returning to their control values, with the exception of MAP, which was then significantly lowered ($P < 0.05$) as compared to saline controls. HR and TPRI were back to control values at 4 h post-injection, whereas CI remained lowered for 12 hours. At 20 h post-injection MAP and TPRI were significantly below saline control values.

The results indicate that the haemodynamic effects of a single dose of propranolol in SHR resemble those in humans (Tarazi & Dustan, 1972), suggesting that this species is a suitable animal model for the study of the cardiovascular pharmacology of β-adrenoceptor blocking drugs.

This study was supported by a grant from the Dutch Heart Foundation.

References

SMITH, T.L. & HUTCHINS, P.M. (1977). Chronic measurement of hemodynamic changes in the spontaneously hypertensive rat prior to, during and after the development of hypertension. *Fed. Proc.*, **36**, 617.

STRUYKER-BOUDIER, H.A.J. (1978). Cardiovascular actions and pharmacokinetics of propranolol in the spontaneously hypertensive rat. *Naunyn Schmiedebergs Arch. Pharmac.*, **302** (suppl.), R40.

TARAZI, R.C. & DUSTAN, H.P. (1972). Beta-adrenergic blockade in hypertension. *Am. J. Cardiol.*, **29**, 633–640.

B.J.P. 68/1–H

Table 1 Haemodynamic changes produced by saline and propranolol

		Start values	*Δ at 0.5 h*	*2 h*	*4 h*	*12 h*	*20 h*
HR[1]	S[2]	403 ± 19	+10 ± 14	+7 ± 20	−4 ± 15	−9 ± 17	+10 ± 13
	P[3]	436 ± 18	−103 ± 16***	−83 ± 26***	−47 ± 17	−34 ± 14	0 ± 14
SVI[1] × 10^2	S	8.82 ± 0.68	−0.12 ± 0.21	−0.27 ± 0.22	−0.17 ± 0.46	−0.15 ± 0.19	+0.25 ± 0.35
	P	8.85 ± 0.62	−0.36 ± 0.30	−1.00 ± 0.29	−0.74 ± 0.25	−0.12 ± 0.38	−0.22 ± 0.25
CI[1]	S	34.9 ± 1.9	+0.3 ± 0.7	−0.6 ± 0.7	−1.4 ± 1.1	+0.7 ± 0.9	+0.8 ± 1.3
	P	37.5 ± 2.0	−10.0 ± 0.8***	−10.4 ± 1.3***	−6.7 ± 1.6*	−3.1 ± 1.0**	+0.2 ± 1.3
TPRI[1]	S	4.00 ± 0.07	+0.14 ± 0.08	+0.21 ± 0.13	+0.17 ± 0.14	0.00 ± 0.17	+0.21 ± 0.29
	P	3.78 ± 0.24	+1.95 ± 0.27**	+1.60 ± 0.37***	+0.57 ± 0.25	+0.08 ± 0.24	−0.46 ± 0.13*
MAP[1]	S	138 ± 6	+6 ± 2	+4 ± 2	−1 ± 2	+3 ± 3	+5 ± 3
	P	136 ± 7	+12 ± 4	−2 ± 2*	−11 ± 3*	−8 ± 5*	−15 ± 4**

[1] Units explained in the text. [2] S: Saline. [3] P: Propranolol.
All values are presented as means ± s.e. mean.
Significances in the difference between P and S: *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.