Effect of Baseline Vasodilation on Adrenergic Reactions of Systemic Hemodynamics

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Systemic vasodilation produced by sodium nitroprusside in various concentrations and accompanied by a decrease in baseline blood pressure was followed by progressive reduction in pressor responses to α-adrenoceptor agonist phenylephrine (mesatone) in rats. In a blood pressure range of below the physiological level (80-100 mm Hg), a positive linear correlation was revealed between the decrease in baseline blood pressure and pressor effect of phenylephrine.

Key Words: *blood pressure; baseline vascular tone; cardiac output; sodium nitroprusside; phenylephrine*

The law of baseline levels suggests that changes in activity of functional systems depend on their initial (prestimulation) activity.

Our previous studies revealed a negative correlation between pressor reactions to α-adrenoceptor agonist phenylephrine (mesatone) and the rise in baseline blood pressure (BP) in response to the increase in arterial tone in rats produced by angiotensin-II [14]. Moreover, the pressor effect of phenylephrine directly depended on the decrease in baseline BP during orthostasis or papaverine infusion [8].

Here we evaluated whether the decrease in baseline BP during systemic vasodilation produced by NO donor sodium nitroprusside (SNP) modulates the vasoconstrictor effect of phenylephrine.

The interest in the model of hypotension caused by vasodilation produced by SNP and NO stems from abundant experimental studies of endothelium-derived relaxing factor acting similarly to NO on vascular smooth muscle cells [10,11], in particular, during exposure of blood vessels to mechanical factors — increased blood flow rate, amplitude of pulse pressure, and degree of vasodilation [2,4,13]. SNP was used for modeling of arterial hypertension and study NO-dependent regulation of blood flow [5].

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MATERIALS AND METHODS

Experiments were performed on 10 adult male Wistar rats (250-350 g) narcotized with 1.2-1.5 g/kg urethane and receiving 500 U/kg heparin. Artificial ventilation was performed on a Vita device. Systolic (BP_S), diastolic (BP_D), and mean BP (BP_M) were recorded in the femoral artery using a PDP-400 detector. Cardiac output was measured with a RKE-2 electromagnetic flow meter. This value was determined by blood flow velocity in the ascending aorta estimated with a 2-mm detector. The total peripheral resistance was calculated as the ratio between BP_M and cardiac output in the same time interval.

SNP was infused into the femoral artery using a NP-1M pump (flow rate 0.25 ml/min). SNP in concentrations of 1.9, 3.8, 7.6, 15, and 30 μg/ml was used to produce baseline hypotension of different step values. Phenylephrine (10^{-6} g/ml) in 0.1 ml polyglucin per 100 g body weight was administered into the femoral vein. Infusion of SNP in each concentration was accompanied by injection of phenylephrine ($BP_{M.B.}$).

The results were analyzed by Student's *t* test. The method for collection and processing of the data was described previously [6].

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Correlation analysis was performed to determine the relationship between $BP_{M.B.}$ and changes in BP_S, BP_D, cardiac output, and total peripheral resistance produced by phenylephrine. The regression curve was constructed by the least-square method. The strength of correlations was evaluated by the correlation coefficient.

RESULTS

$BP_{M.B.}$ and cardiac output were 86.9±4.7 mm Hg and 103.9±8.5 ml/min, respectively.

SNP in various concentrations decreased $BP_{M.B.}$ to a level varying from 22.7±4.4 to 58.0±2.3 mm Hg. After infusion of SNP the maximum rise in BP_S and BP_D produced by phenylephrine (55.7±4.5 and 44.5± 3.8 mm Hg, respectively) decreased to 16.6±2.3 and 10.5±1.5 mm Hg, respectively. Moreover, a shift in total peripheral resistance decreased from 1.335±0.159 to 0.462± 0.043 mm Hg/ml/min, respectively (Fig. 1). Cardiac output remained practically unchanged (6.2± 1.9 ml/min).

We evaluated the relationship between maximum effects of phenylephrine and changes in $BP_{M.B.}$ during infusion of SNP (Fig. 2). A direct linear correlation was revealed between the pressor response to phenylephrine and decrease in $BP_{M.B.}$. This relationship was moderate for BP_S (r=0.43±0.13) and significant for BP_D (r=0.56±0.11). The correlation coefficient for the total peripheral resistance was 0.80±0.06. These data reflect a strong correlation between the constrictor response to phenylephrine and $BP_{M.B.}$. Changes in cardiac output did not depend on $BP_{M.B.}$ (r=0.04±0.16).

In the present study we compared pressor responses to phenylephrine during SNP-induced arterial hypotension of different degrees and evaluated the relationship between these values. The pressor response to phenylephrine progressively decreased under these conditions. A correlation was revealed for phenylephrine-produced changes in BP_D and total peripheral resistance, but not for cardiac output. Therefore, these relationships concern only the vascular effect of phenylephrine and serve as a criterion for reactivity of the arterial system.

These results are consistent with our previous data on changes in the relationships during experimental hypotension under orthostatic conditions or papaverine-produced vasodilation. A direct correlation was

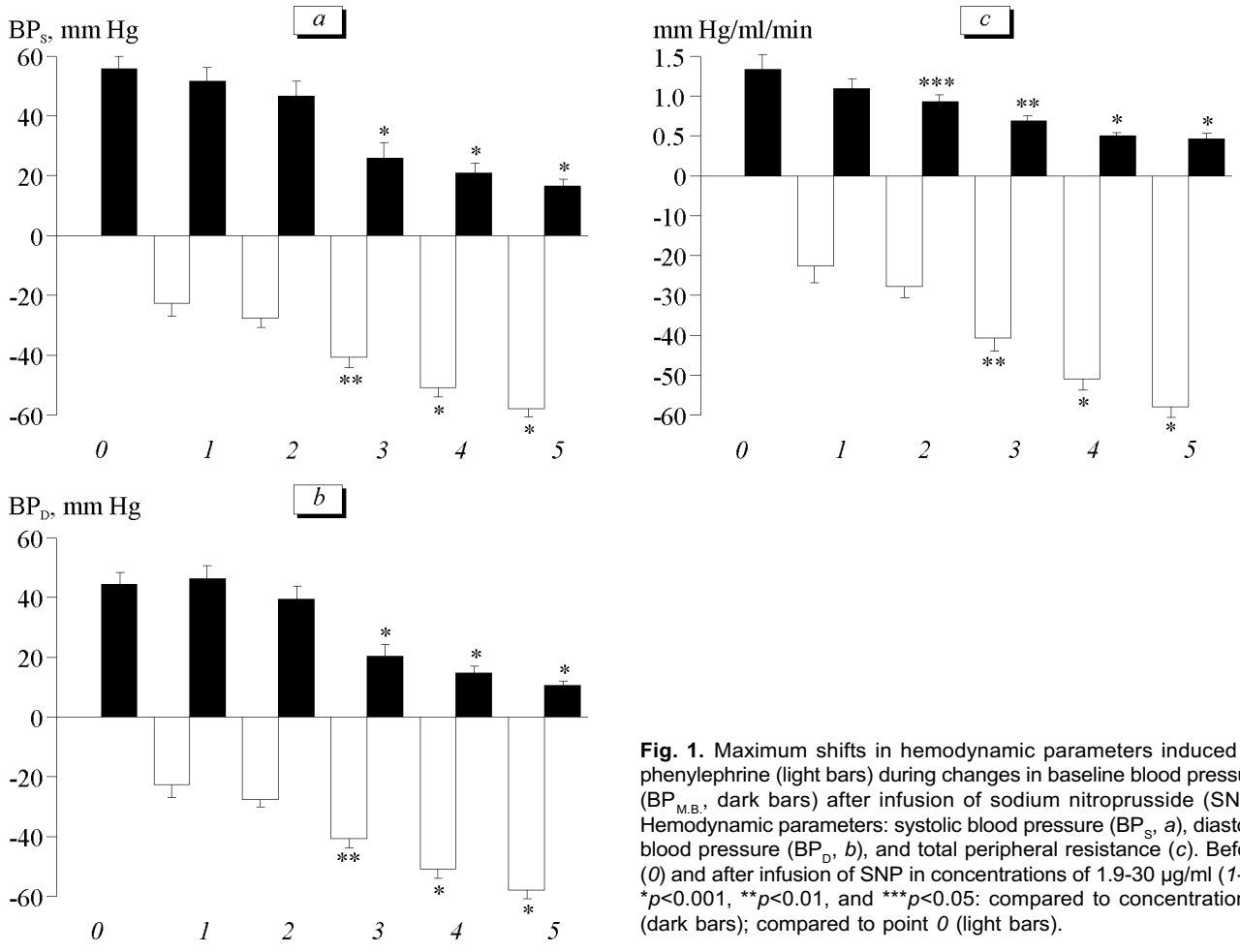

Fig. 1. Maximum shifts in hemodynamic parameters induced by phenylephrine (light bars) during changes in baseline blood pressure ($BP_{M.B.}$, dark bars) after infusion of sodium nitroprusside (SNP). Hemodynamic parameters: systolic blood pressure (BP_S, *a*), diastolic blood pressure (BP_D, *b*), and total peripheral resistance (*c*). Before (*0*) and after infusion of SNP in concentrations of 1.9-30 μg/ml (*1-5*). **p*<0.001, ***p*<0.01, and ****p*<0.05: compared to concentration *1* (dark bars); compared to point *0* (light bars).

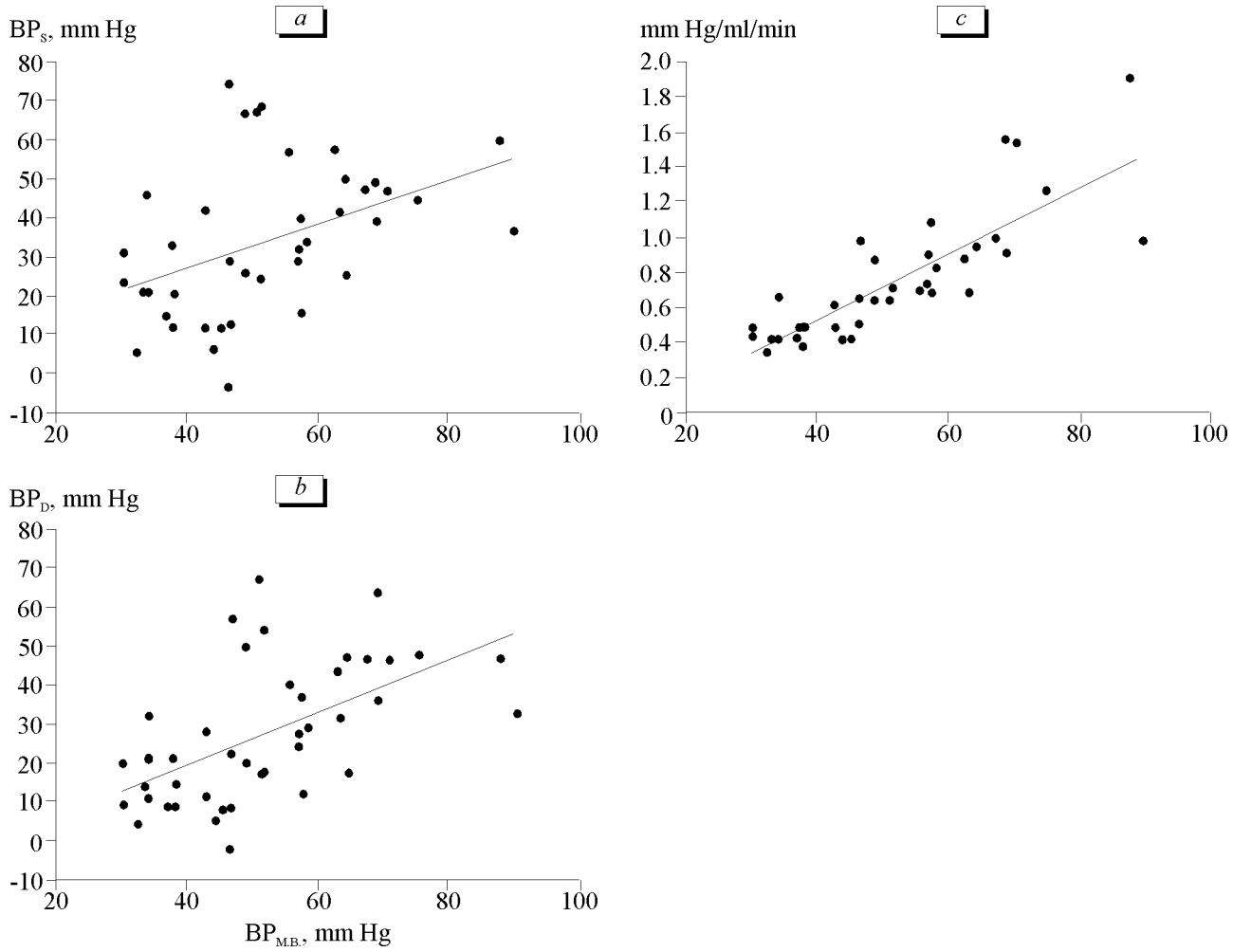

Fig. 2. Maximum changes in BP_S (*a*), BP_D (*b*), and total peripheral resistance (*c*) induced by phenylephrine in a concentration of 10^{-6} g/ml as a function of mean baseline blood pressure during infusion of SNP. Straight line: regression curve. Regression equation: *y*=0.5617x+4.5759 (*a*), *y*=0.6738x-7.3142 (*b*), *y*=0.0186x-0.2204 (*c*).

found between the pressor response to phenylephrine and degree of baseline hypotension [8].

Probably, the mechanism of a decrease in myogenic arterial tone does not determine the relationship between vasoconstrictor response to α-adrenoceptor stimulation and initial tone of arteries during hypotension. These relationships are observed at the reduced baseline tone of arterial smooth muscles resulting from the decrease in their passive tension (orthostasis) and vascular relaxation induced by papaverine or NO donor SNP.

This type of relationships is similar to the parabolic dependence of adrenergic reactions in skeletal muscles on baseline perfusion pressure [2]. Moreover, they resemble the dependence of arterial segment reactivity to electrical stimulation and norepinephrine on the degree of tension [9].

It should be emphasized that reactivity of arteries depends not only on the direct effect of vasoactive agents on smooth muscles, but also on the degree of tension in the vascular wall [12]. Vascular tension depends on the degree of preactivation with vasoactive agents (catecholamines and blockers of α- and β-adrenoceptors) [15].

The pressor response to phenylephrine was most pronounced at $BP_{M.B.}$ close to a normal physiological level (85-90 mm Hg in narcotized rats, Fig. 1). Our results are consistent with published data that the response to humoral and neurogenic factors is most pronounced in the physiological range of BP (80-110 mm Hg).

We found that the dilatory response to β-adrenoceptor agonist isopropyl norepinephrine directly depends on baseline BP. The degree of vasodilation was maximum at BP of 80-90 mm Hg, which agrees with published data on the effect of phenylephrine [7]. It remains unclear why the optimal vascular response is associated with the physiological range of baseline BP. Probably, in this range of BP the vasomotor response corresponds to the maximum in length-tension curves for vascular smooth muscles.

Our results show that reserve constrictor reactions to phenylephrine decrease at baseline BP of above [14] or below the physiological level. These findings and previous data [5] indicate that the reactivity of the arterial system to adrenergic stimulation is determined by its prestimulation activity and its correspondence to the physiological range of BP.

REFERENCES

1. G. E. Galustyan and K. E. Gavrikov, *Usp. Fiziol. Nauk*, **30**, No. 4, 67-79 (1999).
2. D. P. Dvoretskii and V. P. Nedoshivin, *Fiziol. Zh.*, **79**, No. 8, 50-57 (1993).
3. D. P. Dvoretskii, A. T. Matchanov, and N. Ya. Shustova, *Ibid*., **81**, No. 12, 81-87 (1995).
4. D. P. Dvoretskii and L. I. Osadchii, *Izv. Akad. Nauk. Ser. Biol*., No. **2**, 221-229 (2000).
5. O. S. Medvedev, *Aviokosm. Ekol. Med*., **33**, No. 6, 42-46 (1999).
6. L. I. Osadchii, T. V. Balueva, and I. V. Sergeev, *Fiziol. Zh*., **81**, No. 9, 111-126 (1995).
7. L. I. Osadchii, T. V. Balueva, and I. V. Sergeev, *Ros. Fiziol. Zh*., **84**, No. 11, 1231-1241 (1998).
8. L. I. Osadchii, T. V. Balueva, and I. V. Sergeev, *Ibid*., **86**, No. 11, 1521-1530 (2000).
9. D. P. Dvoretskii, V. N. Yartsev, O. V. Karachentseva, and M. P. Granstrem, *Acta Physiol. Scand*., **169**, No. 1, 13-19 (2000).
10. T. M. Griffith, *Exp. Physiol*., **79**, No. 3, 873-913 (1994).
11. L. J. Ignarro, *Proc. Natl. Acad. Sci. USA*, **184**, 9265-9269 (1987).
12. V. V. Machkov, O. S. Tarasova, E. M. Timin, and I. M. Rodionov, *Acta Physiol. Scand*., **161**, No. 1, 41-46 (1997).
13. T. Nacano, R. Tominaga, and I. Nagano, *Am. J. Physiol*., **278**, No. 4, Pt. 2, H1098-H1103 (2000).
14. L. I. Osadchii, T. V. Balueva, and I. V. Sergeev, *Acta Physiol. Hung*., **87**, No. 1, 77-86 (2000).
15. R. N. Speden and D. M. Warren, *J. Physiol*., **375**, No. 1, 283-302 (1986).