## EFFECT OF BRADYKININ ON CIRCULATION IN THE TERRITORY OF THE HUMAN CELIAC ARTERY

P. Ya. Gaponyuk, A. F. Tsyb, V. I. Strigunov, B. Ya. Drozdovskii, and I. S. Mannanov UDC 615.225.2.015.4: 612.138].031:611.136.4

By selective angiography and direct measurement of the blood pressure in the celiac artery, high sensitivity of the vessels was demonstrated to the action of bradykinin (0.1-10  $\mu$ g), a single injection of which into the celiac artery lowers the systolic and diastolic pressures, increases the velocity of the blood flow and the diameter of the arteries and veins and arteriovenous anastomoses, and increases the number of functioning capillaries. No organ-specific differences were found in the responses of the blood vessels of the celiac region to bradykinin.

KEY WORDS: bradykinin; celiac vessels; angiography.

The object of this investigation was to study the action of bradykinin on the regional circulation in the territory of the human celiac artery, knowledge of which is essential for the safe and effective use of the preparation for angiography.

## EXPERIMENTAL METHOD

The paper is based on the results of tests carried out on 24 patients suspected of primary or metastatic malignant growths in the organs of the gastrointestinal tract (the final diagnosis was negative). The preliminary testing of the sensitivity of the patient's blood vessels to the action of bradykinin was carried out by direct measurement of the regional pressure and its recording on the Mingograph 44-C apparatus. Puncture of the femoral artery and selective catheterization of the celiac trunk were carried out as described by Seldinger [6]. The tests were carried out with the Elema-Shenander angiographic apparatus with AOT seriographic attachment. The pressure in the celiac artery was recorded before and after injection of 0.1-10 µg bradykinin, dissolved in 5 ml sterile physiological saline, through the catheter. Each subsequent dose was injected after the pressure had returned to its initial level (interval between injections 2-3 min). During serial angiography, 76% solution of Verographin\* (0.6-0.8 ml/kg body weight) was injected into the trunk of the celiac artery under a pressure of 2.8 kg/cm<sup>2</sup> surface of the syringe plunger (rate of injection 10-12 ml/sec). From 15 to 20 min later 10 µg bradykinin was injected into the trunk of the celiac artery, followed 15-20 min later by injection of the contrast material from an automatic injecter. To estimate the velocity of the blood flow the same quantity of contrast material was injected before and after the injection of bradykinin. To study the diameter of the vessels after the injection of 10 µg bradykinin, the dose of Verographin was increased to 1-1.2 ml/kg and the rate of its injection was increased to 15-18 ml/sec (allowing for the increase in capacity of the blood vessels). Control tests showed that an increase in the dose of contrast substance and in the rate of its injection does not affect the diameter of the vessels, for the excess of Verographin is discharged into the aorta, where it is seen on the angiograms as a reflux. Serial films were taken after 1, 2, 3, 4, 7, 8, 12, and 17 sec. Photography began after injection of

Research Institute of Medical Radiology, Academy of Medical Sciences of the USSR, Obninsk. (Presented by Academician of the Academy of Medical Sciences of the USSR G. A. Zedgenidze.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 79, No. 6, pp. 14-16, June, 1975. Original article submitted April 8, 1974.

© 1975 Plenum Publishing Corporation, 227 West 17th Street, New York, N.Y. 10011. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, microfilming, recording or otherwise, without written permission of the publisher. A copy of this article is available from the publisher for \$15.00.

<sup>\*</sup>Sodium amidotrizoate - Translator.

TABLE 1. Effect of Injection of 10 µg Bradykinin into Celiac Artery on Diameter of Blood Vessels

Vessels (2, 4)	Diameter of vessels (in mm)	
	before injection of bradykinin	after injection of bradykinin*
Right branch of proper hepatic artery	5.44	6.27 (9)
Antero-inferior segmental artery	2.99	4.02 (8)
Postero-superior " "	1.95	3.28 (6)
Left branch of proper hepatic artery	4.14	5.29 (9)
Gastro-duodenal artery	4.75	<b>5.</b> 82 (6)
Right gastro-epiploic artery	3,71	<b>5.</b> 22 (8)
Supero-posterior pancreatico-duodenal artery	2.37	3,23 (6)
Left gastric artery	4.14	5.24 (8)
Gastric branch	2.46	3.18 (6)
Esophogeal "	2.00	2.66 (5)
Splenic artery	7.82	8.45 (9)
Splenic branch	4.56	5.30 (8)
Short gastric branch	2.08	2.87 (6)
Great pancreatic artery	2,30	2.86 (8)
Artery of tail of pancreas	1.66	2.16 (6)
Portal vein	15.36	16.93 (7)
Splenic vein	11.20	13.00 (5)
Gastro-epiploic vein	5.80	8.00 (5)

<sup>\*</sup>P < 0.05 compared with the control. Statistical analysis by difference method. Number of subjects tested shown in parentheses.

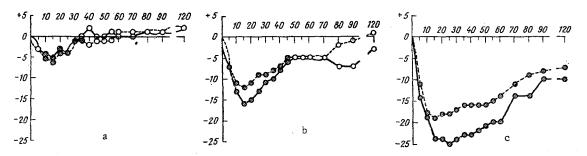


Fig. 1. Changes in blood pressure in human celiac artery during selective injection of bradykinin into it in doses of: a) 0.1  $\mu$ g, b) 1  $\mu$ g, c) 10  $\mu$ g. Abscissa, time (in sec); ordinate, change in pressure in celiac artery (in %). Continuous line — maximal pressure, broken line — minimal pressure; filled circles — values differing significantly (P < 0.05) from same before injection of bradykinin; empty circles — differences not significant. Each point reflects mean value of changes in 7-8 subjects.

the first 15 ml of the contrast material. The diameter of the vessels on the angiograms and the density of contrast of the organs were estimated by the method of Veniaminov and Strigunov [1].

## EXPERIMENTAL RESULTS

Small doses of bradykinin (0.1-1  $\mu$ g), injected into the trunk of the celiac artery, induced changes in the regional circulation. The greatest effect was observed after injection of 10  $\mu$ g bradykinin (Fig. 1). The hypotensive action reached a maximum after 15-20 sec. When repeated injections (4-5 times at intervals of 2 min) of the same dose of bradykinin were given, no sign of tachyphylaxis occurred.

Angiograms obtained from 18 subjects showed that injection of 10  $\mu$ g bradykinin causes dilatation of all arterial branches leaving the celiac trunk (Table 1). As a rule the vasodilator action of the drug was stronger in small arteries (1-3 mm in diameter). Bradykinin had its weakest action on large arterial trunks

9-12 mm in diameter. No organ-specificity in the action of bradykinin on the blood vessels was present.

On all angiograms a previously invisible network of small arteries could be seen after the injection of bradykinin. In some cases accessory arterio-venous anastomoses were found. The number of functioning capillaries was increased, as shown by the greater degree of contrast of the parenchyma of the liver, spleen, and pancreas. For instance, whereas the density of the liver (in % of the density of the wedge) was normally 12%, after injection of bradykinin it was 41%. A marked increase was found in the diameter of the splenic, portal, and gastro-epiploic veins, with the appearance of an accessory venous network. The capacity of the vascular bed after injection of bradykinin was increased by 50-70%.

The change in the velocity of blood flow was estimated from the time taken for contrast material to disappear from the arterial network before and after injection of bradykinin (nine patients). The time for the contrast material to disappear from the small arteries (1-3 mm) was reduced by 2 sec after the injection of 10  $\mu$ g bradykinin. The Verographin appeared earlier in the microvessels (parenchymatous phase). The contrast material also passed more quickly from the arterial part into the venous part of the vascular system. The observed acceleration of the blood flow and dilation of the arteries agree with data in the literature [3]. The conclusion regarding dilatation of the veins and arterio-venous anastomoses under the influence of bradykinin is particularly interesting, for the data on this question are contradictory [5, 7-9]. It can thus be concluded that bradykinin can advantageously be given in doses of 5-10  $\mu$ g for angiographic examination of the territory of the human celiac artery.

## LITERATURE CITED

- 1. L. A. Veniaminov and V. I. Strigunov, Abstracts of Proceedings of the First and Second All-Union Symposia on Modern Methods of Selective Angiography and Their Clinical Application [in Russian], Moscow (1973), p. 116.
- 2. A. P. Savchenko, G. P. Filimonov, and T. V. Privezentseva, Vestn. Rentgenol., No. 1, 50 (1971).
- 3. G. Boijsen and J. C. Redman, Invest. Radiol., 1, 422 (1966).
- 4. D. Luzsa, X-Ray Anatomy of the Vascular System [in Russian], Budapest (1973).
- 5. T. Ishioka, T. Matsumura, J. Honda, et al., Angiologica, 6, 255 (1969).
- 6. S. I. Seldinger, Acta Radiol. (Stockholm), 39, 368 (1953).
- 7. T. Shimamoto, H. Maezawa, H. Yamazaki, et al., Am. Heart J., 71, 297 (1966).
- 8. I. Sholtholt and T. Shiraishi, Pflig. Arch. ges. Physiol., 300, 189 (1968).
- 9. H. Takacs and K. Albert, Arch. Internat. Pharmacodyn., 155, 117 (1965).