Acute Bradyarrhythmia Induced by Occlusion of the Posterior Interventricular Branch of the Right Coronary Artery

I. Yu. Luk'yanova, V. V. Ruksin, and Sh. Larbi

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 131, No. 3, pp. 268-271, March 2001
Original article submitted August 28, 2000

Ligation of the posterior interventricular branch of the right coronary artery in rats induced bradyarrhythmia similar by its pathophysiological mechanisms to bradyarrhythmias developed in humans during acute ischemia of the posterior cardiac wall. The type and severity of arrhythmia and conduction disturbances, their latency and duration, and correlation with the volume of damaged myocardial tissue were determined. The efficacy and safety of the use of methylxanthines during acute myocardial ischemia was proved.

Key Words: *posterior interventricular branch*; *atrioventricular node*; *sinoatrial node*; *atrioventricular block*; *sinoatrial block*

Until the present time experimental studies of cardiac rhythm disturbances were carried out on the model of acute ischemia of the anterior wall of the left ventricle produced by ligation of the anterior interventricular branch of the left coronary artery [5,13].

By contrast, disturbances of the heart rate and conduction induced by ligation of the posterior interventricular branch (PIVB) of the right coronary artery were not investigated. Blood supply to the atrioventricular (AV) and sinoatrial (SA) nodes is provided by the right coronary artery in 90% and 54% cases, respectively [6], therefore rhythm and conductance disturbances due to dysfunction of the AV and SA nodes most often accompany posterodiaphragmatic myocardial infarction [1,4,7,11]. Early bradyarrhythmias can result from transient vagotonia [3,8,15] or acute ischemia in the heart conduction system [12]. There is evidence on the relationship between the size of infarction zone and the incidence of AV blocks II and III [4,9,14].

Our aim was to study the particularities of cardiac rhythm and conduction disturbances induced by PIVB ligation, to determine their relation to the size of infarction zone, and to evaluate the efficiency and safety of cholinergic antagonists and methylxanthines.

MATERIALS AND METHODS

Experiments were carried out on 39 outbred male rats weighing 260-300 g anesthetized with nembutal (50 mg/kg, intraperitoneally) and artificially ventilated. Ligation of PIVB was performed by the method proposed by I. Yu. Luk'yanova and A. G. Miroshnichenko (1999). The preparations were administered via catheterized right femoral vein. Cardiac rhythm and conduction disturbances were assessed by ECG recorded in the standard lead II and by the right atrial electrogram (RAEG) recorded with an intracardiac electrode inserted through the jugular vein.

ECG monitoring was performed from minute 1 to minute 30 after PIVB ligation, then 9 rats were intravenously injected with 0.3 ml isotonic NaCl, 8 rats were given 5 mg/kg metacin, and 8 rats received 3.5 mg/kg aminophylline. ECG monitoring was performed from minute 30 to minute 60. Finally, the size of ischemic damage to the myocardium was determined by planimetry of serial sections of heart ventricles. To this end, the hearts were perfused with 5% Evans blue at a rate of 5 ml/sec for 1 min, frozen in a cryostat (-20°C, 30 min), and 10 cross-sections of the heart

Medical Academy of Postgraduate Education, St. Petersburg. ***Address for correspondence:*** mapo@actor.ru. Luk'yanova I. Yu.

0007-4888/03/1313-0223$25.00

TABLE 1. Heart Rate and Conduction Disturbances during the First 30 min after Ligation of PIVB of the Right Coronary Artery

Disturbances in heart rate and conduction	The number of rats with arrhythmia		Arrhythmia duration, sec
	abs.	%	
Sinus bradycardia	12	30.7	378.7±139.5
Sinus arrhythmia	6	15.3	41.0±3.5
SA block II	3	7.6	28.3±7.2
Migration of pacemaker	1	2.5	29.0
Lower atrial rhythm	2	5.1	145.0±55.0
Junction rhythm	1	2.5	540.0
AV block I degree	16	41.0	476.2±167.97
II degree	13	33.3	343.5±132.1
III degree	9	23.0	154.1±65.0
Atrial tachycardia	1	2.5	48.0
Ventricular extrasystoles	3	7.6	—

were prepared. The first section was made at a distance of 250 μ from the apex and others were made with 1000-μ intervals. The ischemic zone was identified by the absence of staining. The volume of ischemic myocardium was determined by summing the products of unstained area by section thickness (1000 μ). The volume of cardiac muscle in both ventricles was determined in the same way. The volume ratio of ischemic (unstained) to total ventricular myocardium was calculated in percents [10].

RESULTS

During the first 30 min after PIVB ligation, disturbances of atrioventricular conduction developed in 97.4% rats (Table 1). Early (within 1 min after PIVB ligation) disturbances of AV conduction were recorded in 44.7% cases: AV block III (66.6%), AV block II (38.4%) and AV block I (37.5%). All AV blocks II and III were transient (Table 1). AV block I was persistent in 18.7% and transient in 31.5% cases.

Dysfunction of the SA node manifested in sinus bradycardia, sinus arrhythmia, and SA block II was observed in 53.8% rats (Table 1). One minute after PIVB ligation, these disturbances of cardiac rhythm and conduction appeared in 52.3% rats. In these cases, sinus arrhythmia (66.6%), sinus bradycardia (50.0%), and SA block II (33.3%) were observed. Sinus arrhythmia and SA block II were transient (Table 1). During the first 30 min after ligation of PIVB, sinus bradycardia was transient or intermittent in 41.6% and 16.6% cases, respectively.

Ectopic atrial rhythms recorded in 3 rats (2 lower atrial rhythms, and junction rhythm) appeared on minutes 4, 5, and 20 after PIVB (Table 1).

Migration of supraventricular pacemaker was recorded in one rat on minute 3, while atrial tachycardia was observed on minute 1 after PIVB ligation (1 rat). In 7.6% rats singe infranodal extrasystoles were observed on the first minute after ligation.

Thirty minutes after PIVB ligation, sinus rhythm with heart rate of 301.6±7.1 bpm was recorded in all rats, the duration of *P—R* interval being 0.064± 0.001 sec.

No cardiac rhythm and conduction disturbances were recorded after injection of isotonic NaCl and aminophylline, *i. e.* from 30th to 60th minute of the experiment. Transient SA block developed in 1 rat 20 sec after metacin injection, it was followed by AV junction rhythm 20 min postinjection, which persisted to the end of recordings. In other rat, transient SA block II developed 4 min postinjection and was followed by AV block II from the 20th min to the end of recordings. In all subgroups, *P—R* interval did not significantly change from minute 30 to minute 60.

In rats receiving isotonic NaCl, the maximum increase in *P—R* interval observed between minutes 30 and 60 was 3% relatively to its value on minute 30.

TABLE 2. Volume of Ischemic Damage to Myocardium (%) in Subgroups of Rats

Volume of ischemic myocardium	Control (*n*=9)	Aminophylline (*n*=8)	Methacin (*n*=8)
Extensive	60.2±5.6	66.2±3.1	53.6±3.6
Minor	22.3±1.4	22.3±1.4	21.8±2.2

Note. All differences between the subgroups with minor and extensive ischemic lesions are significant.

TABLE 3. Cardiac Rhythm and Conduction Disturbances in Rats with Minor and Extensive Ischemic Lesions during the First 30 Minutes after Ligation of PIVB of the Right Coronary Artery

Disturbances in cardiac rhythm and conduction	Extensive ischemic lesion (n=10)			Minor ischemic lesion (n=16)		
	number of rats with arrhythmia		arrhythmia duration, sec	number of rats with arrhythmia		arrhythmia duration, sec
	abs.	%		abs.	%	
Sinus bradycardia	3	30	920.0±341.7	6	37.5	640.0±302.2
Sinus arrhythmia	2	20	47.5±2.5	2	12.5	55.0±5.1
SA block II	1	10	18	0	—	—
AV block I	4	40	660.0±396.5	6	37.5	680±295
AV block II	4	40	720.0±136.4	5	31.2	81.0±16.5
AV block III	4	40	285.0±59.2	0	—	—
Extrasystoles	0	—	—	1	6.2	—

Metacin increased the duration of *P—R* interval by 19% as soon as on 1 min postinjection (without taking into account the change in *P—R* interval in one rat with AV block). The maximum increase in *P—R* interval (by 28.5% initial value) was recorded after 45 min of the experiment and after 60 min the duration of *P—R* interval remained increased by 15.8% compared to the initial value.

One minute after injection of aminophylline the duration *P—R* interval decreased by 13.1% (p<0.02), but then this parameter gradually increased and by the 60th min surpassed the initial value by 6.5%.

The significant differences in the duration of *P—R* interval compared to its initial value were observed only 1 min after injection of aminophylline; significant differences between the control and aminophylline-treated group was observed on minute 31, while differences between methacin- and aminophylline-treated groups were significant on minutes 31, 32, 35, and 40.

Since no significant correlation between the heart rate and the duration of *P-R* interval was revealed in methacin- and aminophylline-treated groups (r=-0.29 and r=-0.43, respectively), the observed changes in *P—R* interval can be explained by the effect of these preparations.

Morphometric data showed that the same procedure of PIVB ligation produced two subgroups characterized by extensive and minor ischemic lesion (Table 2). These differences are probably due to different type of blood supply.

Rats with minor ischemic lesions never developed AV block III, although this conduction disturbance was observed in 40% rats with extensive ischemic le-

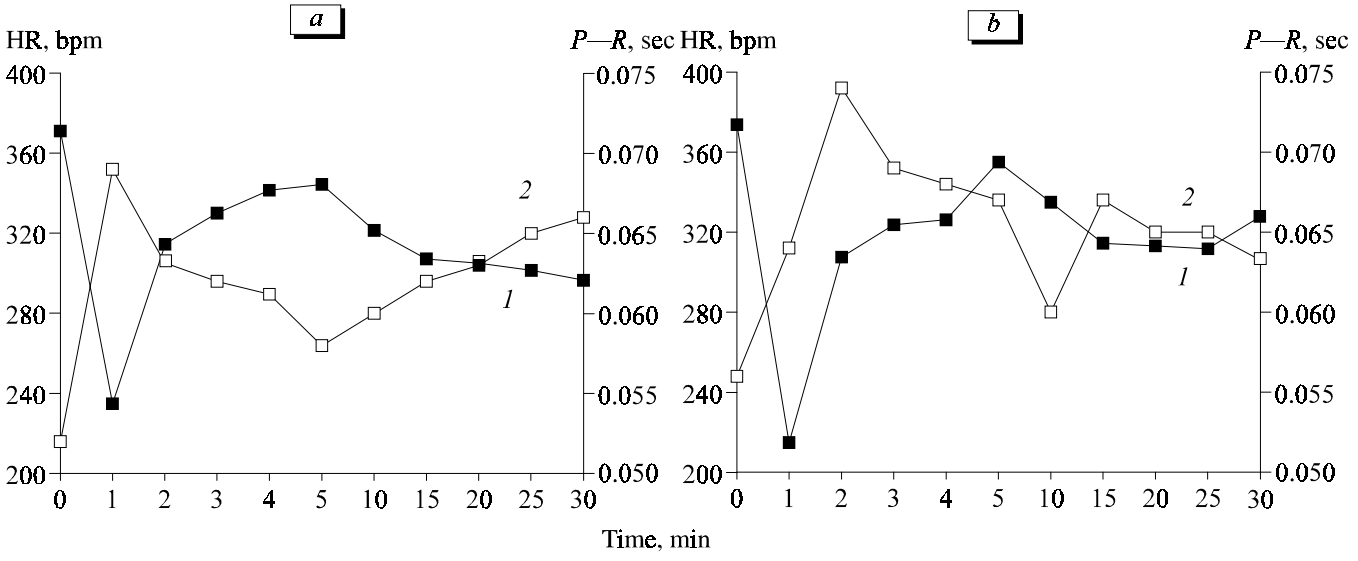

Fig. 1. Changes in heart rate (HR, *1*) and duration of *P—R* interval (*2*) during the first 30 minutes after ligation of the posterior interventricular branch of the right coronary artery in rats with minor (*a*) and extensive (*b*) ischemic lesions.

sions ($p<0.03$, Table 3). The incidence of AV blocks II was similar in these two subgroups, but the duration of AV block differed significantly ($p<0.04$, Table 3).

In rats with minor ischemic lesions heart rate decreased by 36.7% and *P—R* interval increased by 32.6% compared to the initial values (Fig. 1, *a*). On minutes 2-5 of the experiment, the heart rate decreased by 7.2%, while *P—R* interval increased by 11.5% compared to the initial values. Then the heart rate gradually decreased and *P—R* interval increased during 25 min. On minute 30 of the experiment, the heart rate decreased by 20.1%, and *P—R* interval increased by 26.9% compared to the initial values. It should be emphasized that in rats with minor ischemic lesion, the changes in the duration of *P—R* interval and the heart rate were closely correlated ($r=-0.92$, $p<0.05$).

In the rats with extensive ischemic lesions, the maximum decrease in the heart rate (by 42.5% initial value) was observed 1 min after ligation of PIVB, while the maximum increase of *P—R* interval (by 32.1% initial value) occurred on minute 2 (Fig. 1, *b*). Then the heart rate increased and peaked on 5th min, but remained below the initial value by 5%. The maximum decrease in *P—R* interval was observed only 10 min after ligation, but this parameter still surpassed the initial value by 7.2%. Hence, in rats with extensive ischemic lesions the correlation between the heart rate and the duration of *P—R* interval was disturbed ($r=-0.25$; $p>0.05$).

Thus, disturbances in cardiac rhythm and conduction during the first 30 min after ligation of PIVB manifested themselves by transient dysfunction of AV and SA nodes. The incidence, duration, and severity of disturbances of cardiac rhythm and AV directly correlate with the size of ischemic damage to the heart. Aminophylline produces positive chronotropic and dromotropic effects in acute ischemia of the posterior wall of the heart, without provoking ectopic activity. Finally, both methacin and aminophylline did not significantly increase the size of ischemic zone in subgroups with minor and extensive ischemic lesions to the heart.

REFERENCES

1. A. L. Syrkin, *Myocardial Infarction* [in Russian], Moscow (1998).
2. P. Albony, G. F. Baggioni, S. Scarfo, *et al*., *Am. J. Cardiol.*, **67**, 1180-1184 (1991).
3. D. Feigl, J. Ashkenasy, and Y. Kishon, *J. Am. Coll. Cardiol.*, **4**, 35-38 (1984).
4. P. K. Gupta, E. Lichstein, and K. D. Chadda, *Chest*, **69**, 599-604 (1976).
5. A. S. Harris, *Circ. Res*., **7**, 1318-1328 (1950).
6. T. N. James, *Progr. Cardiovasc. Dis.*, **10**, 410-416 (1968).
7. D. Jewit, *Progr. Cardiol.*, **1**, 61-70 (1972).
8. M. Kyriakidis, J. Barbetseas, A. Antonopoulos, *et al*., *Chest*, **101**, 944-947 (1992).
9. A. Melgarejo-Moreno, J. Galcera-Tomas, A. Garcia-Alberola, *et al*., *Rev. Exp. Cardiol*., **50**, 397-405 (1997).
10. L. G. T. Riberio, W. M. Cheng, and P. R. Maroko, *Circulation*, **66**, No. 1, 181-186 (1982).
11. M. Rotman, G. S. Wagner, and A. G. Wallage, *Ibid*., **45**, 703-722 (1972).
12. S. Sclarovsky, B. Strasberg, A. Hirshberg, *et al*., *Am. Heart J*., **108**, 19-24 (1984).
13. H. Selye, E. Bajusz, S. Grasso, and P. Mendell, *Angiologie*, **11**, 398-407 (1960).
14. A. C. Tans, K. I. Lie, and D. Durrer, *Am. Heart J*., **99**, 4-8 (1980).
15. G. C. Timnis, D. C. Westveer, A. M. Hauser, *et al*., *Arch. Intern. Med*., **145**, 2188-2199 (1985).