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Effects of diadenosine tetraphosphate on systemic and regional hemodynamics in dogs

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Abstract

Purpose. Diadenosine tetraphosphate (AP_4A) produces vasodilation and hypotension. If AP_4A is to be employed clinically, its influence on systemic and regional hemodynamics needs to be investigated. In this study, we observed systemic and regional hemodynamics during reduction of mean arterial pressure (MAP) induced by AP_4A in dogs.

Methods. Nineteen mongrel dogs were allocated to three groups: those given physiological saline (vehicle group) and dogs in which MAP was decreased either by 8% (8% group) or by 30% (30% group) by infusion of AP_4A. Systemic hemodynamics and microsphere-determined regional blood flow to vital organs were assessed before and during AP_4A infusion.

Results. In the 8% group, cardiac output (CO) increased, and systemic vascular resistance (SVR) decreased during AP_4A infusion. Although regional blood flow to myocardium and portal organs increased, hepatic blood flow decreased. In the 30% group, heart rate and SVR decreased, and stroke volume index increased without change in CO. Regional blood flow to myocardium, kidneys, and portal organs increased. In both groups, cerebral blood flow remained unchanged.

Conclusion. During the decrease in MAP induced by AP_4A, there were increases in regional blood flow distributed to the myocardium, kidneys, and portal organs, without change in the blood supply to the brain. This finding suggests that AP_4A may be clinically useful for reducing blood pressure without compromising blood flow to vital organs.

Key words: Diadenosine tetraphosphate, Regional blood flow, Microsphere method

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Introduction

Diadenosine tetraphosphate (AP_4A) is a bioactive substance that is stored in the dense granules found in human platelets [1] and in chromaffin granules [2]. It has a potent vasodilating action [3]. When continuously administered to dogs under enflurane anesthesia, AP_4A decreased mean arterial pressure (MAP) in a dose-dependent manner [4]. This effect was due to its vasodilating action on resistance vessels and occurred despite increased cardiac output (CO), with no change in heart rate (HR) when MAP was decreased by up to 40% [4]. However, to our knowledge, there are no reported investigations of the comparative changes in regional hemodynamics when MAP is reduced by varying degrees by AP_4A infusion. In the present study, therefore, in order to assess the possibility of clinical application, we examined regional hemodynamics during mild (target decrease in MAP of 8%) and moderate (target decrease in MAP of 30%) reduction in MAP induced by AP_4A.

Methods

Animals

Approval for the study was granted by the University Animal Care Committee, and we studied 19 mongrel dogs, weighing 10–14 kg. After induction with intravenous thiopental 20 $mg \cdot kg^{-1}$, anesthesia was maintained with oxygen/nitrous oxide (F_IO_2 0.4) and enflurane (1.5%). After muscle relaxation was achieved with pancuronium, ventilation was adjusted, using a mechanical ventilator, to maintain normocapnia ($PaCO_2$ 35–41 mmHg). Lactated Ringer's solution was infused at a rate of 5 $ml \cdot kg^{-1} \cdot h^{-1}$, and the rectal temperature was maintained at about 37°C. Both femoral arteries were catheterized, for blood pressure measurement and arterial blood gas analysis, and both femoral veins were

Table 1. Effects of diadenosine tetraphosphate (AP_4A) on arterial blood gas tensions

	Vehicle		8% group		30% group	
	Control	Vehicle	Control	AP_4A	Control	AP_4A
$PaCO_2$ (mmHg)	38.2 ± 0.7	38.9 ± 0.8	37.5 ± 0.8	37.0 ± 0.7	38.6 ± 0.5	38.0 ± 0.8
PaO_2 (mmHg)	265.3 ± 5.9	265.3 ± 6.5	268.5 ± 10.2	268.5 ± 22.8	272.1 ± 6.1	270.6 ± 7.6
pH	7.38 ± 0.01	7.37 ± 0.01	7.38 ± 0.01	7.38 ± 0.01	7.36 ± 0.01	7.37 ± 0.01
BE (mEq/l)	−1.3 ± 0.5	−1.6 ± 0.3	−1.4 ± 0.5	−1.8 ± 0.4	−1.6 ± 0.3	−1.6 ± 0.3

Values are given as means ± SEM.
BE, Base excess; $PaCO_2$, arterial carbon dioxide tension; PaO_2, arterial oxygen tension.

cannulated, for the administration of AP_4A and insertion of a 7-Fr balloon-tipped thermodilution pulmonary artery catheter. Another catheter was inserted from the right common carotid artery into the left ventricle for the injection of radionuclide-labeled microspheres.

Experimental protocol

The experimental animals were allocated to three groups: (1) those given physiological saline (vehicle group, $n = 6$), (2) dogs in which MAP was decreased by 8% of the pre-AP_4A value by low-dose AP_4A administration (25–30 $\mu g \cdot kg^{-1} \cdot min^{-1}$; 8% group, $n = 6$), and (3) dogs in which MAP was decreased by 30% of the pre-AP_4A value by higher-dose AP_4A administration (80–140 $\mu g \cdot kg^{-1} \cdot min^{-1}$; 30% group, $n = 7$). AP_4A was dissolved in physiological saline. Pre-AP_4A values for MAP, systolic arterial pressure (SAP), HR central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), CO, and arterial blood gas tensions were determined under steady state conditions. Then cardiac index (CI), stroke volume index (SI), and systemic vascular resistance (SVR) were calculated by routine methods. After the determination of pre-AP_4A hemodynamic measurement, the first microspheres bolus was administered via the left ventricular catheter, and then AP_4A or physiological saline was administered intravenously with an infusion pump. Each episode of decreased MAP was maintained for 30 min. At this point, the individual hemodynamic parameters were determined again and a second microspheres bolus was given. The microspheres used were ^{46}Sc- or ^{85}Sr-labeled spherical granules, 15 μm in diameter (185 MBq/g, New England Nuclear, Boston, MA, USA). Approximately 4×10^5 granules per dose were diluted with 5 ml of physiological saline and injected over a 30-s period into the left ventricle. After the second administration of microspheres, the animals were killed by exsanguination. Various organs and tissues, including brain, heart, liver, kidneys, adrenal glands, pancreas, stomach, duodenum, small intestine, large intestine, skeletal muscle (4% of body weight), and skin (500 cm^2), were then extracted. The extracted organ weight was measured and the radioactivity was determined with a Universal Gamma-Counter (JSM-R 17-3871; Aloka, Tokyo, Japan).

Calculation of percent distribution of CO to organs, and organ blood flow

The ratio of the γ-ray level for a given organ to the total γ-ray dose administered by way of the microspheres was determined. Then, the percentage of CO distributed to a given organ and the blood flow per 100 g of tissue were calculated with the equations below:

Percentage of CO to a given organ (%)
= γ-ray level in organ × 100/total γ-ray dose given
Blood flow per 100 g of tissue ($ml \cdot min^{-1} \cdot 100\,g^{-1}$)
= CO × percentage of CO to that organ
× 100/organ weight (g)

The stomach, duodenum, small and large intestines, spleen, and pancreas were grouped together as "the portal organs". The total weight of the skin was calculated according to the formula for body surface area [5]. The skeletal muscle sample used was taken as 4% of the body weight.

Statistical analysis

The experimental data values were expressed as means ± SEM. A paired Student's *t*-test was used for comparison within each group. Statistical comparison among groups was performed by analysis of variance. *P* values <0.05 were considered statistically significant.

Results

Vehicle group

No significant change was observed in arterial blood gas tensions (Table 1), hemodynamic variables (Table 2), regional blood flow (Table 3), or percent blood flow (distribution of CO) to each organ tested (Table 4).

Table 2. Effects of diadenosine tetraphosphate (AP_4A) on systemic hemodynamics

	Vehicle		8% Group		30% Group	
	Control	Vehicle	Control	AP_4A	Control	AP_4A
MAP (mmHg)	129 ± 6	129 ± 6	137 ± 8	125 ± 8**	124 ± 9	85 ± 6**
SAP (mmHg)	162 ± 3	165 ± 6	169 ± 6	157 ± 5**	159 ± 8	114 ± 7**
HR (beats/min)	141 ± 11	143 ± 10	140 ± 10	135 ± 10	140 ± 14	125 ± 7*
CO (l/min)	1.4 ± 0.2	1.4 ± 0.2	1.7 ± 0.2	2.1 ± 0.2**	1.6 ± 0.1	1.7 ± 0.2
CI ($l \cdot min^{-1} \cdot m^{-2}$)	2.8 ± 0.4	2.8 ± 0.3	2.8 ± 0.2	3.4 ± 0.3**	2.8 ± 0.2	2.9 ± 0.2
SI ($ml \cdot beat^{-1} \cdot m^{-2}$)	19.6 ± 1.6	19.2 ± 1.4	19.9 ± 1.1	25.2 ± 1.5**	20.7 ± 1.8	24.0 ± 2.3**
CVP (mmHg)	4 ± 0.6	4 ± 0.7	6 ± 0.2	6 ± 0.4	6 ± 0.4	6 ± 0.4
PCWP (mmHg)	8 ± 2	8 ± 1	9 ± 1	10 ± 2	9 ± 2	9 ± 3
SVR ($dynes \cdot s^{-1} \cdot cm^{-5}$)	7605 ± 911	7640 ± 868	6180 ± 320	4758 ± 341**	6066 ± 547	3938 ± 433**

* $P < 0.05$ vs control; ** $P < 0.01$ vs control.
Values are given as means ± SEM.
MAP, Mean arterial pressure; SAP, systolic arterial pressure; HR, heart rate; CO, cardiac output; CI, cardiac index; SI, stroke volume index; CVP, centrol venous pressure; PCWP, pulmonary capillary wedge pressure; SVR, systemic vascular resistance.

8% Group

During administration of AP_4A at 25–30 $\mu g \cdot kg^{-1} \cdot min^{-1}$, MAP decreased from 137 ± 8 to 125 ± 8 mmHg ($P < 0.01$). CO, CI, and SI increased ($P < 0.01$), while SVR decreased by 25 ± 4% of pre-AP_4A values ($P < 0.01$, Table 2).

Regional and percent blood flow to myocardium increased by 207 ± 48% and 150 ± 35%, respectively ($P < 0.05$, Tables 3 and 4) during AP_4A infusion. There was an increase in regional blood flow (26 ± 5%; $P < 0.01$), but not in percent blood flow to kidneys. Regional and percent blood flow to portal organs increased by 75 ± 14% and 44 ± 13%, respectively ($P < 0.01$), whereas regional and percent blood flow to liver via hepatic artery decreased by 53 ± 8% and 60 ± 7%, respectively ($P < 0.05$). Regional and percent blood flow to adrenal glands increased by 296 ± 66% and 223 ± 63%, respectively ($P < 0.01$). There were no changes in regional and percent blood flow to brain, skeletal muscle, and skin.

30% Group

During administration of AP_4A at 80–140 $\mu g \cdot kg^{-1} \cdot min^{-1}$, MAP decreased from 124 ± 9 mmHg to 85 ± 6 mmHg ($P < 0.01$). HR and SVR decreased by 9 ± 3% ($P < 0.05$) and 36 ± 3% ($P < 0.01$), respectively, while SI increased by 15 ± 2% of pre-AP_4A values ($P < 0.01$, Table 2).

Regional and percent blood flow to myocardium and kidneys increased by 199 ± 51% and 185 ± 51% ($P < 0.01$), and 46 ± 13% and 41 ± 15% ($P < 0.05$), respectively (Tables 3 and 4) during AP_4A infusion. Regional and percent blood flow to portal organs increased by 67 ± 11% and 60 ± 13%, respectively ($P < 0.01$), whereas regional and percent blood flow to the liver via hepatic artery and skeletal muscle decreased by 54 ± 8% and 58 ± 7% ($P < 0.05$), and 50 ± 7% and 47 ± 8% ($P < 0.01$), respectively. Regional and percent blood flow to adrenal glands increased by 356 ± 53% and 343 ± 64%, respectively ($P < 0.01$). There were no changes in regional and percent blood flow to brain and skin.

Intergroup comparisons

Regional blood flow to both pancreas and spleen was lower in the 30% group than in the 8% group ($P < 0.05$).

Discussion

When AP_4A is given as a single intravenous injection under physiological conditions, it is rapidly metabolized to adenosine. For this reason, its hypotensive effect is usually attributed primarily to the action of adenosine. However the actions of both AP_4A and adenosine, via the P_{2y} receptor [3] and the A_2 receptor [6], respectively, may account for the hypotensive effect of AP_4A.

In our 8% group, although there was no change in HR, there was a significant increase in CI, due to increased SI. The increased SI may have been caused by decreased SVR. In contrast, there was no significant change in CI in the 30% group, a finding that may be explained by the significant increase in SI being accompanied by a significant decrease in HR. The influence of AP_4A on HR observed in this study is in accord with a previous report that showed decreased HR response to high doses of AP_4A [4].

Table 3. Effects of diadenosine tetraphosphate (AP_4A) on regional blood flow

	Vehicle		8% Group		30% Group	
	Control ($ml \cdot min^{-1} \cdot 100^{-1} g$)	Vehicle ($ml \cdot min^{-1} \cdot 100^{-1} g$)	Control ($ml \cdot min^{-1} \cdot 100^{-1} g$)	AP_4A ($ml \cdot min^{-1} \cdot 100^{-1} g$)	Control ($ml \cdot min^{-1} \cdot 100^{-1} g$)	AP_4A ($ml \cdot min^{-1} \cdot 100^{-1} g$)
Brain	93.3 ± 14.6	74.8 ± 6.6	65.5 ± 16.9	62.5 ± 3.1	67.0 ± 17.7	69.3 ± 11.3
Myocardium	86.7 ± 15.5	89.3 ± 21.2	78.5 ± 13.8	246.5 ± 56.5*	96.1 ± 13.6	295.3 ± 58.3*††
Liver (hepatic artery)	60.2 ± 19.2	50.5 ± 14.5	37.8 ± 9.4	16.0 ± 2.8*†	23.9 ± 7.4	11.9 ± 4.5*†
Kidney	419.3 ± 71.4	385.0 ± 52.2	351.8 ± 34.7	435.8 ± 36.4**	278.1 ± 30.8	400.7 ± 50.3*
Adrenal gland	380.2 ± 100.7	282.7 ± 68.9	255.3 ± 60.9	848.3 ± 113.2**‡	245.3 ± 62.1	948.1 ± 133.8**‡
Skeletal muscle	8.8 ± 3.3	8.6 ± 2.3	7.6 ± 1.6	8.8 ± 1.5	11.0 ± 2.3	4.6 ± 0.7**
Skin	3.5 ± 0.7	3.8 ± 0.7	3.1 ± 0.7	5.3 ± 1.5	2.4 ± 0.7	3.9 ± 0.9
Portal organs	67.5 ± 8.2	62.8 ± 5.8	65.2 ± 8.4	111.3 ± 13.1**‡	60.7 ± 4.6	99.3 ± 7.1**†
Stomach	63.7 ± 13.8	56.7 ± 10.5	51.0 ± 9.4	100.2 ± 15.2*†	52.7 ± 11.1	57.1 ± 13.5†
Small intestine	61.0 ± 7.9	54.8 ± 7.2	56.5 ± 9.0	115.3 ± 18.8**†	56.0 ± 4.4	134.0 ± 12.7**‡
Large intestine	83.5 ± 15.2	82.7 ± 13.5	72.0 ± 13.7	121.5 ± 26.2*	67.9 ± 10.3	107.6 ± 17.2*
Pancreas	29.7 ± 5.3	30.0 ± 5.3	52.2 ± 15.2	54.7 ± 9.5†	17.3 ± 1.7	19.3 ± 2.9ss
Spleen	135.8 ± 13.3	141.8 ± 17.1	188.8 ± 29.1	168.2 ± 27.4	140.0 ± 19.6	89.0 ± 17.0*ss

* $P < 0.05$ vs control; ** $P < 0.01$ vs control; † $P < 0.05$ vs vehicle group; ‡ $P < 0.01$ vs vehicle group; ss $P < 0.05$ vs 8% group.
Values are given as means ± SEM.

Our finding that blood flow to myocardium increased during AP_4A infusion is in accordance with Pohl et al.'s report [7] that AP_4A dilated coronary resistance vessels for a longer period than adenosine triphosphate did in an isolated rabbit heart. To examine the myocardial oxygen balance before and after AP_4A administration in the two groups, we calculated the triple index (SAP × HR × PCWP). In the 8% group, the triple index value before AP_4A administration was 212940 and the myocardial blood flow was $79 ml \cdot min^{-1} \cdot 100 g^{-1}$. When the ratio of myocardial blood flow to the triple index before AP_4A administration (control) was taken to be 100%, the ratio after AP_4A administration was 314%, with a triple index value of 211950 and myocardial blood flow of $247 ml \cdot min^{-1} \cdot 100 g^{-1}$. In the 30% group, the ratio, calculated similarly, was 479% of control after AP_4A administration. Although there was no difference in the triple index before and after AP_4A administration in the 8% group, the increased ratio of myocardial blood flow to the triple index was exclusively due to the augmented myocardial blood flow after AP_4A administration. The further increased ratio in the 30% group was due to the decreased triple index value and increased myocardial blood flow during AP_4A administration. These results suggested that sufficient myocondial blood flow to meet the oxygen demand could be supplied during continuous administration of AP_4A.

Renal blood flow is not influenced by changes in systemic arterial blood pressure over a certain range, because of autoregulation. However, this autoregulation can be affected by drugs that influence vascular tone. After continuous administration of adenosine via the renal artery, it was shown that renal blood flow changed in a biphasic manner, decreasing briefly and then returning to the pretreatment level or above within 5–10 min [8–10]. In the present study, no intergroup differences were observed in renal blood flow. Since we determined blood flow 30 min after the start of AP_4A administration, we cannot say what changes in blood flow may have occurred immediately after the start of the administration. However, although our result does not conflict with previous reports on the effects of adenosine, it is possible that the action of AP_4A itself may have contributed to the observed large increase in renal blood flow.

The liver receives a double blood supply, from the hepatic artery and the portal vein. The portal blood flow is determined mainly by the CO and the volume of the perfused preportal region, while the blood flow in the hepatic artery changes to counteract the altered portal blood flow (the so-called hepatic arterial buffer response, HABR) [11]. In the present experiment, blood flow to portal organs increased, but blood flow to the

Table 4. Effects of diadenosine tetraphosphate (AP_4A) on percent distribution of cardiac output

	Vehicle		8% Group		30% Group	
	Control (%)	Vehicle (%)	Control (%)	AP_4A (%)	Control (%)	AP_4A (%)
Brain	4.1 ± 0.6	3.5 ± 0.3	2.7 ± 0.7	2.1 ± 0.2	2.8 ± 0.6	2.7 ± 0.4
Myocardium	5.2 ± 0.7	5.3 ± 1.0	4.5 ± 0.7	11.2 ± 2.2*	5.6 ± 0.7	16.6 ± 3.3**†
Liver (hepatic artery)	9.6 ± 1.9	8.1 ± 1.4	6.3 ± 1.5	2.3 ± 0.4*‡	4.5 ± 1.3	2.0 ± 0.6*‡
Kidney	13.6 ± 1.7	12.8 ± 1.3	12.6 ± 0.9	12.9 ± 0.9	9.2 ± 0.9	12.5 ± 1.2*
Adrenal gland	0.5 ± 0.1	0.3 ± 0.1	0.2 ± 0.1	0.5 ± 0.1**	0.2 ± 0.1	0.8 ± 0.1**
Skeletal muscle	21.8 ± 5.9	22.8 ± 4.1	22.7 ± 4.7	21.5 ± 2.9	33.3 ± 6.6	13.3 ± 2.5**
Skin	2.2 ± 0.4	2.4 ± 0.4	2.4 ± 0.5	3.3 ± 0.5	1.8 ± 0.4	2.9 ± 0.9
Portal organs	19.7 ± 2.1	18.5 ± 1.4	18.9 ± 3.0	25.8 ± 2.8*	19.3 ± 1.3	30.4 ± 2.6**‡
Stomach	4.8 ± 0.8	4.4 ± 0.6	4.5 ± 1.0	6.8 ± 0.8	4.8 ± 1.0	4.9 ± 1.1
Small intestine	8.5 ± 1.0	7.5 ± 0.4	7.4 ± 1.4	12.0 ± 1.8**	8.4 ± 0.8	19.5 ± 2.3**‡ˢˢ
Large intestine	3.3 ± 0.7	3.3 ± 0.7	2.5 ± 0.6	3.4 ± 0.8*	2.5 ± 0.3	3.8 ± 0.6*
Pancreas	0.4 ± 0.1	0.5 ± 0.1	0.7 ± 0.2	0.6 ± 0.1	0.3 ± 0.0	0.3 ± 0.0ˢˢ
Spleen	2.8 ± 0.3	2.9 ± 0.3	3.9 ± 0.4	3.0 ± 0.5*	3.3 ± 0.6	1.9 ± 0.4**

* $P < 0.05$ vs control; ** $P < 0.01$ vs control; † $P < 0.05$ vs vehicle group; ‡ $P < 0.01$ vs vehicle group; ˢˢ $P < 0.05$ vs 8% group.
Values are given as means ± SEM.

liver via the hepatic artery decreased in both AP_4A-treated groups. The increased portal blood flow in the 8% group was probably due to the significant increase in CO and in blood flow to the preportal region (stomach and small and large intestines), while the increased portal blood flow in the 30% group was probably due to the significantly increased blood flow in the preportal region (small and large intestines). This assumption seems to be supported by findings that the administration of adenosine produced a marked increase in portal blood flow, probably due to increased blood flow in the small and large intestines, spleen, and stomach [12]. The decrease in blood flow to the liver via the hepatic artery in the face of increased portal blood flow suggests that HABR may be functioning during AP_4A infusion

Since intravenous adenosine does not cross the blood-brain barrier, adenosine is thought to have no direct action on cerebrovascular smooth muscle [13]. AP_4A is also considered not to cross the blood-brain barrier, and changes in cerebral blood flow during AP_4A administration are more likely to result from alterations in cerebral perfusion pressure. However, in normal brain, the cerebral blood flow is maintained at a constant level through autoregulation. Our finding of no change in blood flow to the brain during AP_4A infusion supports this assumption.

In conclusion, regional blood flow to myocardium, kidneys, and portal organs increased, but the blood flow to brain remained unchanged during AP_4A-induced decreases in blood pressure. This finding suggests that AP_4A may be clinically useful as an agent for reducing systemic blood pressure without compromising the perfusion of vital organs.

References

1. Lüthje J (1989) Origin, metabolism and function of extracellular adenosine nucleotide in the blood. Klin Wochenschr 67:317–327
2. Rodriguez del Castillo A, Torres M, Delicado EG, Miras-Portugal MT (1988) Subcellular distribution studies of diadenosine polyphosphates—AP_4A and AP_5A—in bovine adrenal medulla: Presence in chromaffin granules. J Neurochem 51:1696–1703
3. Busse R, Ogilvie A, Pohl U (1988) Vasomotor activity of diadenosine triphosphate and diadenosine tetraphosphate in isolated arteries. Am J Physiol 254:H828–H832
4. Kikuta Y, Sekine A, Tezuka S, Okada K, Yamaura T, Nakajima H (1994) Intravenous diadenosine tetraphosphate in dogs. Cardiovascular effects and influence on blood gases. Acta Anaesthesiol Scand 38:284–288
5. Drabkin, DL, Cowgill GR (1927) Determination of a formula for surface area of the dog together with consideration of formulae available for other species. Am J Physiol 81:36–61
6. Burnstock G (1990) Purinergic mechanisms. Ann NY Acad Sci 603:1–17
7. Pohl U, Ogilvie A, Lamontagne D, Busse R (1991) Potent effect of AP_3A and AP_4A on coronary resistance and autacoid release of intact rabbit heart. Am J Physiol 260:H1692-H1697
8. Spielman WS, Thompson CI (1982) A proposed role for adenosine in the regulation of renal hemodynamics and renin release. Am J Physiol 242:F423–F435
9. Spielman WS, Britton SL, Fiksen-Olsen MJ (1980) Effect of adenosine on the distribution of renal blood flow in dogs. Circ Res 46:449–456
10. Zäll S, Edén E, Winsö I, Volkmann R, Sollevi A, Ricksten S-E (1990) Controlled hypotension with adenosine or sodium nitroprusside during cerebral aneurysm surgery: Effects on renal hemodynamics, excretory function, and renin release. Anesth Analg 71:631–636
11. Lautt WW (1983) Mechanism and role of intrinsic regulation of hepatic arterial blood flow: Hepatic arterial buffer response. Fed Proc 42:1662–1666
12. Orrego H, Carmichael FJ, Saldivia V, Giles HG, Sandrin S, Israel Y (1988) Ethanol-induced increase in portal blood flow: Role of adenosine. Am J Physiol 254:G495–G501
13. Kassell NF, Boarini DJ, Olin JJ, Sprowell JA (1983) Cerebral and systemic circulatory effects of arterial hypotension induced by adenosine. J Neurosurg 58:69–76