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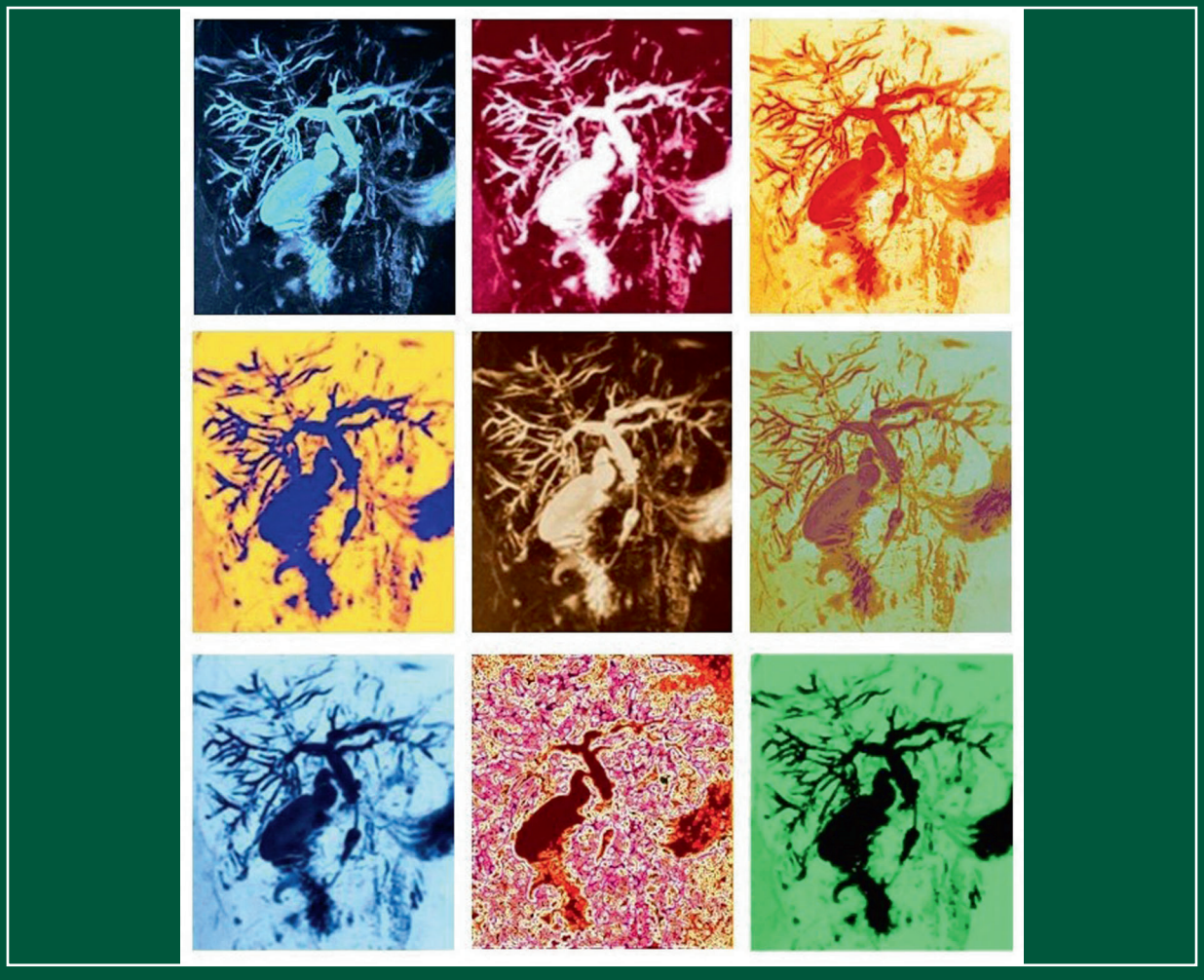
European Journal of Clinical Investigation

56TH ANNUAL SCIENTIFIC MEETING –
8–10 June 2022, Bari, Italy



Cholangiocarcinoma - 9 faces of the killer
It shows cholangiocarcinoma, an aggressive bile duct tumour with dismal prognosis,
It was captured during magnetic resonance cholangiopancreatography (MRCP)
Piotr Milkiewicz, Warsaw Poland

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ESCI EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

Official journal of the European Society for Clinical Investigation

European Journal of Clinical Investigation

THE JOURNAL OF THE EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

Aims & Scope

The European Journal of Clinical Investigation (EJCI), in publication since 1970, is a peer-reviewed general-interest biomedical journal with a broad readership. It is the official journal of the European Society for Clinical Investigation (ESCI) and it is published monthly by Wiley. It considers any original contribution from the most sophisticated basic molecular sciences to applied clinical and translational research and evidence-based medicine across a broad range of subspecialties. The EJCI publishes reports of high-quality research that pertain to the genetic, molecular, cellular, or physiological basis of human biology and disease, as well as research that addresses prevalence, diagnosis, course, treatment, and prevention of disease. We are primarily interested in studies directly pertinent to humans, but submission of robust in vitro and animal work is also encouraged. Interdisciplinary work and research using innovative methods and combinations of laboratory, clinical, and epidemiological methodologies and techniques is of great interest to the journal. Several categories of manuscripts (for detailed description see below) are considered: editorials, original articles (also including randomized clinical trials, systematic reviews and meta-analyses), reviews (narrative reviews), opinion articles (including debates, perspectives and commentaries); and letters to the Editor.

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THE JOURNAL OF THE EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

European Society for Clinical Investigation

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Officers and members of the ESCI Council 2020

Objectives

The objectives of the Society are the advancement of medical practice through science; the cultivation of clinical research by the methods of the natural sciences; the correlation of science with the art of medical practice; the fostering of high standards of ethical practice and investigation; and the diffusion of a spirit of fraternity and international co-operation among and through its members.

Membership

Any person who has been actively involved in medical research in Europe, for example by involvement in original investigations in clinical or allied sciences of medicine, can apply for membership of ESCI. Members will receive the *EJCI* monthly. Any company, corporation, organisation, or trust can apply for corporate membership in the Society.

Meetings

The Society holds one Annual Scientific Meeting each year, usually in April/May. Meetings are held in different cities in Europe. Other Society's activities include the sponsorship of Workshops and Postgraduate Courses and the encouragement of the exchange of Scientists between Laboratories.

Contact information ESCI

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Contents

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Results: During the recovery period, there was an increase of isolated heart LVP by 32.4% ($p < 0.05$), and decrease in heart rate by 6.3% and a decrease in CP by 39.4% ($p < 0.01$) compared with the 30- day hypodynamia.
Conclusions: Recovery after limitation of motor activity is accompanied by an increase in cardiac contraction force (LVP), and a decrease in heart rate and coronary flow. The results can be associated with recovery processes in the heart, since immediately after hypokinesia there was a general tendency to heart activity desadaptation, the force contraction decrease and increase of heart rate. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030)

56ASM-0009 | Influence of Alpha1(A)–adrenoreceptors stimulation on isolated rat heart coronary flow in ontogenesis

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Background: In the mammalian heart, alpha1-adrenergic receptors (α_1-AR) perform many functions: they participate in the regulation of myocardial contractility, heart chronotropy, coronary blood flow, as well as in various pathological processes. Earlier, we showed that non-selective stimulation of α_1-AR in adult rats reduces coronary circulation, and in 1-week-old rat pups it enhances it. According to scientists, the α_{1A}-AR can mediate a positive inotropic effect in stressful and pathological situations. In this regard, the study of the role of this receptor subtype in the regulation of the blood supply to the heart is gaining relevance. The aim of this study was to investigate the effect of α_{1A}-adrenoreceptors stimulation on coronary flow in isolated hearts of rats in ontogenesis
Materials and Methods: Isolated hearts were perfused in the Langendorff system (ADInstruments). The experiments we used selective agonist α_{1A}-AR A-61603 (10^{-9}mol/L). The degree of coronary circulation was evaluated using the indicator-coronary flow (CF), which was calculated by measuring the amount of perfusate flowing through the coronary vessels of the isolated heart for 1 minute. Statistical processing of the obtained results was performed using the Student's *t*-test.
Results: Perfusion of A-61603 10^{-9}mol/L caused an increase CF isolated heart of 20- and 6-week-old rats by 12% ($p < 0.01$), and 10% ($p < 0.05$), respectively. The speed of isolated heart CF in 3 and 1 week old rats did not change in response to A-61603.
Conclusions: Stimulation of α_{1A}-AR with A-61603 changed the CF in rats of 6 week-old, as well as in adult animals. The absence of changes in CF in 1-week and 3-week-old rats on the introduction of A-61603 is probably due to the lack of sympathetic innervation of the heart of animals at this period of postnatal development. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030)

56ASM-0010 | Stimulation of α2-adrenergic receptors change heart rate and coronary flow in the newborn rats isolated heart

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Background: Controversial data on the role of alpha2-adrenergic receptors (α_2-AR) in the regulation of coronary blood supply are presented in the modern literature. It was reported that α_2-AR agonists exert a vasoconstrictor effect. On the other hand, the results of the vasodilator effect on coronary vessels of the α_2-AR agonist clonidine hydrochloride are presented in the studies. It is known that α_2-AR is present on the myocardiocytes membranes, and in vascular smooth muscles. The aim was to investigate the effect of different concentrations of the α_2-AR agonist on coronary flow (CF) and heart rate (HR) in the isolated heart of newborn rats.
Materials and Methods: Experiments were performed on 28 newborn rat, they do not have adrenergic innervation of the heart. Isolated hearts were perfused in a Krebs-Henseleit solution - Langendorff (ADInstruments) installation. The CF and HR were calculated. The signals were recorded in a PowerLab system. 10^{-9}–10^{-6}M concentrations range of clonidine hydrochloride (Sigma) were used for the stimulated of α_2-AR. The data were processed statistically using Microsoft Excel software and Student's t test.
Results: Application to a perfuse solution of clonidine hydrochloride (10^{-9}M) decreased CF and causes tachycardia in the newborn rat isolated heart. The α_2-AR agonist (10^{-8}M) caused decreased CF and bradycardia was observed. Clonidine hydrochloride (10^{-7}M) had a different effects CF and HR. The α_2-AR agonist (10^{-6}M) had no effect on the CF, and caused a different effects HR.
Conclusions: Stimulation of alpha2-AR with low concentrations of clonidine hydrochloride (10-9, 10-8 M) leads to a decrease in coronary flow and bradycardia of the newborn rats isolated heart. High concentrations of the α2-AR agonist (10-7, 10-6 M) resulted in opposite

dynamics of heart rate and coronary flow in the newborn rats isolated heart. The study was supported by Russian Science Foundation (grant No. 21-15-00121, https://rscf.ru/ project/21-15-00121/)

56ASM-0011 | Influence of clonidine hydrochloride on the effect of if blockade on isolated rat heart

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Background: Sympathetic control of heart rate plays an important role in the pathophysiology of arrhythmias, hypertension, coronary heart disease, and chronic heart failure. Alpha$_2$-adrenergic receptors (α_2-AR) and hyperpolarization-activated currents (If) are involved in the regulation of heart function. The aim of this study was to investigate the effect of clonidine hydrochloride after of preliminary blockade of If-currents on isolated by Langendorff rat heart.
Materials and Methods: Experiments were carried out ex vivo on isolated hearts of 3-week-old rats ($n = 14$). This age is characterized by significant properties of the heart function associated with the formation of adrenergic innervation. During the experiment, an electrogram of the heart was recorded using atraumatic electrodes. Changes in heart rate (HR) and coronary flow (CF) were recorded after application of the If blocker ZD7288 (10^{-9}mol/L and 10^{-5}mol/L) and the α_2-AR agonist clonidine hydrochloride (10^{-6}mol/L).The data were statistically processed using Student's t-test.
Results: Stimulation of α_2-AR by clonidine hydrochloride after If blockade by ZD7288 (10^{-9}mol/L) in isolated heart of 3-week-old rats increased the HR decline by 20% ($p < 0.01$) and increased CF by 15% ($p < 0.01$). ZD7288 in concentration 10^{-5} mol/L decrease the effect of bradycardia after the application of clonidine hydrochloride by 12% ($p < 0.01$).
Conclusions: Thus, in experiments to studying the role of α_2-AR and If in regulation 3-week-old rats isolated heart was shown that preliminary If blockade enhanced the bradycardic effect and increased blood supply in the isolated heart. The study was supported by Russian Science Foundation (grant No. 21-15-00121, https://rscf.ru/ project/21-15-00121/)

56ASM-0012 | Isolated rat heart function after new cardioplegic solution perfusion

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Background: Cardioplegic heart failure is the most popular method of providing open-heart surgery. Negative changes of ischemia and reperfusion are reduced by quality cardioplegic protection. There is no consensus what types of cardioplegic solutions (CPS) is better. Unfortunately, studies of various cardioplegic solutions are carried out on different experimental models, which makes difficult comparison them with each other. The aim of our study was to evaluate the efficacy of created in Kazan Federal University new extracellular crystalloid CPS in the experiments on isolated rat heart model.
Materials and Methods: Isolated hearts were perfused on a Langendorff apparatus (ADInstruments) with an oxygenated Krebs-Henseleit solution (KH) (37°C, pH = 7.3–7.4) at a constant pressure of 80-82 mmHg. After stabilization of the heart activity, the initial values were recorded. The work was performed according to the following protocol: new solution was administered for 3 minutes, then ischemia was prolonged for 20 minutes, then the heart perfusion was resumed with KH solution. The heart rate was recorded during 40 minutes of reperfusion. The assessment of the contractility of the myocardium was carried out according to the indicator of left ventricular developed pressure (LVDP). The signals were recorded on the PowerLab 8/35 setup using the "LabChart Pro" program. Statistical processing of the obtained results was carried out using the Student's t-test.
Results: Asystole was achieved within 1 minute of CPS administration. Recovery of spontaneous cardiac activity after myocardial ischemia induced by the new CPS occurred within the first minute of reperfusion in 100% cases. Decrease in myocardial contractility compared to the initial values was not observed during the entire reperfusion period ($LVDP_{initial} = 52 \pm 5.2$ mmHg and $LVDP_{reperfusion} = 58 \pm 5.8$ mmHg), what allows us to conclude about the effectiveness of myocardial protection by the new CPS.
Conclusions: In our experiment on a model of an isolated rat heart, which is widely used for the study of various CPR, we showed that the new solution is able to quickly and effectively cause myocardial plegia, and also does not interfere with the rapid and full recovery of its function after the start of reperfusion. This paper has been supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).