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ABSTRACTS

The authors are solely responsible for the scientific content and linguistic presentation of the abstracts.

PHYSIOLOGICAL AND CLINICAL ASPECTS

AMBIVALENT EFFECTS OF CURCUMIN: MODEL OF EXTRAHEPATAL BILIARY ATRESIA AS AN EXAMPLE

A. Barta[1], P. Janega[1,2], P. Babál[2], E. Murár[3], O. Pechánová[1]
[1]Institute of Normal and Pathological Physiology and Centre of excellence for regulatory role of nitric oxide in civilization diseases, Slovak Academy of Sciences, Bratislava, [2]Department of Pathological Anatomy, Faculty of Medicine, Comenius University, Bratislava, [3]Pediatric Surgery Department, Children's University Hospital, Slovak Medical University, Banská Bystrica, Slovak Republic

Curcumin, like different polyphenolic compounds (1,2) belongs among effective scavengers of reactive oxygen species. In addition to direct antioxidant activity, curcumin may function indirectly as an antioxidant by inhibiting the activity of inflammatory enzymes or by enhancing the synthesis of glutathione, an important intracellular antioxidant. However, side – prooxidative effect of curcumin was described as well.

We aimed to determine effects of curcumin on liver fibrosis and to clarify the role of NF-κB and iNOS in the model of extrahepatal biliary atresia. Male Wistar rats, 12-week-old, were divided into six groups (n=8, each): sham operated rats; rats that received curcumin (200 mg/kg/day); biliary duct ligated group (BDL); biliary duct ligated group that received curcumin (BDL curc). After 3 weeks of the treatment the animals were sacrified and the liver, kidney and blood samples were analysed.

Curcumin treatment did not modify blood plasma markers like alkaline phosphatase and aspartat aminotransferase activities, total protein, albumin, total bilirubin and conjugated bilirubin concentrations as well as iNOS and p65 NF-κB expressions in the liver species of sham group. Interestingly, there were significant increase in both liver and kidney fibrosis extents. On the other hand, despite decrease in iNOS and p65 NF-κB expressions, cucrcumin treatment did not affect fibrosis enlargement elevated due to bile duct ligation in the liver. In BDL, curcumin treatment also decreased the levels of blood plasma markers.

In conclusion, curcumin treatment was able to improve functional properties of hepatocytes and to inhibit both NF-κB and iNOS upregulations in BDL, however, without beneficial effect on the liver fibrosis developed in this model of cholestasis. Thus, in our conditions other factors, different from NF-κB and iNOS are responsible for fibrotic process in the liver.

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CARDIAC ARREST AND CARDIOPULMONARY RESUSCITATION: NEW PERSPECTIVES OF NITRIC OXIDE DONORS

P.Kružliak[1,2], O.Pecháňová[1]
[1]Institute of Normal and Pathological Physiology and Centre of Excellence for Regulatory Role of Nitric Oxide in Civilization Diseases, Slovak Academy of Sciences, Bratislava, Slovak Republic, [2]International Clinical Research Center, Brno, Czech Republic

Research of over two decades has shown nitric oxide (NO) to be a central and peripheral modulator of biological phenomena from cell signal to effector and from physiology to pathophysiology (1–3). The involvement of NO in neurophysiology and cardiovascular biology has contributed significantly to our understanding of complex disease states including atherosclerosis, systemic and pulmonary hypertension, myocardial infarction, Alzheimer and Parkinson diseases.

Nitric oxide is often used to treat heart failure accompanied with pulmonary edema. According to present knowledge, however, NO donors are contraindicated when systolic blood pressure is less than 90 mmHg. Based on recent findings and our own clinical experience, we formulated a hypothesis about the new breakthrough complex life-saving effects of NO donors in patients with cardiac arrest and cardiopulmonary resuscitation therapy. It includes a direct haemodynamic effect of NO donors mediated through vasodilation of coronary arteries in cooperation with improvement of cardiac function and cardiac output through reversible inhibition of mitochondrial complex I and mitochondrial NO synthase, followed by reduction of reactive oxygen species and correction of myocardial stunning. Simultaneously, an increase in vascular sensitivity to sympathetic stimulation could lead to an increase in diastolic blood pressure.

Confirmation of this hypothesis in clinical practice would mean a milestone in the treatment of cardiac arrest and cardiopulmonary resuscitation.

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ANGIOTENSIN CONVERTING ENZYME INHIBITORS: DRUG DESIGN EFFECTS IN THE SPONTANEOUS HYPERTENSION

O. Pecháňová, S. Vranková, L. Paulis
Institute of Normal and Pathological Physiology and Centre of Excellence for Nitric Oxide Research, Slovak Academy of Sciences, Bratislava, Slovak Republic

A balance between angiotensin II and nitric oxide (NO) production in both peripheral and central nervous systems may play a significant role in the development of hyperten-

sion (1,2). We aimed to compare the effect of angiotensin converting enzyme (ACE) inhibitors captopril (containing thiol group), enalapril and ramipril (without thiol group) on the development of spontaneous hypertension and to analyze molecular mechanisms of their actions in the aorta and kidney.

Six-week-old SHR were divided into four groups: controls, group receiving captopril, or enalapril, or ramipril (each 50 mg/kg/day for 6 weeks). At the end of experiment, systolic blood pressure (SBP) increased by 41 % in controls. All ACE inhibitors used prevented blood pressure increase, however, SBP in the captopril group (121±-5 mmHg) was significantly lower than that in the enalapril (138±6 mmHg) or ramipril group (141±5 mmHg). All ACE inhibitors increased renal and aortal NO synthase activity to the comparable level. Any of the inhibitors used was, however, able to increase expression of eNOS or nNOS. Captopril, on distance to enalapril and ramipril, increased the level of nitrosothiols, cGMP concentration and antioxidant activity measured by TEAC assay. Captopril decreased the level of superoxides and expression of nuclear factor kappaB subunits.

In conclusion, captopril, beside inhibition of ACE, increased NO synthase activity and nitrosothiols with simultaneous decrease of oxidative stress. This together resulted in increase of cGMP concentration in the tissues, including the vessels, and contributed to the prevention of blood pressure increase in SHR.

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IRREGULAR LIGHT-DARK CYCLES AND LIGHT CONTAMINATION AS RISK FACTORS OF CIVILIZATION DISEASES

M. Zeman, L. Molčan, A. Veselá, M. Okuliarová, I. Herichová, P. Hanuliak, J. Hraška
Faculty of Natural Sciences, Department of Animal Physiology and Ethology, Comenius University, Bratislava, Faculty of Civic Engineering, Department of Building Structures, Slovak Technical University, Bratislava, Slovakia

Disturbances of natural light/cycles in ambient environment are a wide spread phenomenon in the modern society. It is related to high prevalence of shift work in developed countries and light contamination in environment. Subsequent disturbances of circadian rhythms arise as a significant problem especially for people used to spend most time indoor. It is true especially for autumn and winter periods when problems with entrainment of circadian rhythms in physiological and behavioural processes most frequently occur. From this point of view optimal lighting of houses, offices and buildings is strongly required.

Artificial lighting has been designed to reach an optimum visual comfort and performance. However, recently new type of photoreceptors was discovered in retinal ganglion cells which are involved in entrainment of circadian rhythms. They contain a new photopigment – melanopsin which is sensitive for blue light and most efficiently suppresses melatonin production. On the basis of spectral sensitivity a new area of light measurement has been established – circadian photometry, which monitors ability of ambient light to entrain circadian oscillations in human beings. A new device – Daysimeter was designed which enables us to define internal daylight environment from the point of circadian spectral quality and identify conditions of "biological darkness" which do not allow adequate synchronization of the circadian system. Moreover, we can monitor "light smog" arising mainly from aggressive advertisements which can supper endogenous melatonin production, negatively influence circadian rhythmicity and participate in progression of civilization diseases.

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AGE-DEPENDENT CHANGES OF ADIPOCYTE SIZE AND GLUCOSE TOLERANCE IN OBESE ZUCKER RATS

S. Zorad, L. Gajdosechova, K. Krskova
Institute of Experimental Endocrinology, SAS, Bratislava, Slovakia

Obese (fa/fa) Zucker rats develop obesity, insulin resistance, hyperleptinemia and hyperlipidemia but display only impaired glucose tolerance (IGT) with normoglycemia making them useful for studies of pre-diabetic state, a critical period appropriate for pharmacological treatment. In order to elucidate the development of obesity and insulin resistance we studied selected morphometric and metabolic parameters with focus on adipose tissue of 12-week-old (young) lean and obese Zucker rats and compared with 33-week-old (old) animals.

Adiposity index showed high degree of obesity in both young and old obese rats. The obesity was mostly of hypertrophic type as suggested by significantly increased adipocyte cell size in both young and old obese animals in comparison to their lean littermates, respectively. In addition, there was a significant increase in adipocyte cell size between old obese and young obese Zucker rats. The obese animals were hyperinsulinemic with significantly higher blood insulin in old animals when comparing with young ones. Intraperitoneal glucose tolerance test showed that only old obese Zucker rats display IGT. In addition, only the old obese group of Zucker rats displayed significantly increased expression of TNFalpha, an inflammatory marker, in epididymal adipose tissue.

Our data suggest relationship between degree of adipose tissue hypertrophy and metabolic status of animals. In the model of obese Zucker rats the adipocyte hypertrophy clearly relates to IGT and adipose tissue inflammation.

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