ZBORNÍK ABSTRAKTOV

ROZŠÍRENÉ ABSTRAKTY PRÁC, PREZENTOVANÉ NA KARDIOLOGICKÝCH PODUJATIACH V ZAHRANIČÍ, FINANČNE PODPORENÉ SLOVENSKOU KARDIOLOGICKOU SPOLOČNOSŤOU

2006/2007

Hakacova N, Zahorec M, Laluhova-Striezencova Z.
Coagulation factor abnormalities in neonates with single ventricle physiology precede surgery.
Presented by: 10th Annual Meeting Cardiology 2007, Orlando, Florida, USA (21. – 25. February 2007)

Skrak P, Kovacikova L, Zahorec M.
Long-term outcome of pediatric cardiosurgical patients requiring prolonged mechanical ventilation.
Presented by: 10th Annual Update on Pediatric Cardiovascular Disease, Disney's Yacht and Beach Club Resort, Lake Buena Vista, Florida, USA (21. – 25. February 2007)

Zahorec M, Hakacova N, Skrak P, Kovacikova L, Nosal M.
Ductus arteriosus closure during the modified Blalock-Taussig shunt operation: influence on early postoperatrive hemodynamics.
Presented by: 10th Annual Update on Pediatric Cardiovascular Disease, Disney's Yacht and Beach Club Resort, Lake Buena Vista, Florida, USA (21. – 25. February 2007)

Penesova A, Koska J, Cizmarova E, Radikova Z, Belan V, Vigas M.
Decreased insulin sensitivity in young lean hypertensive men is not associated with increased visceral fat and changes in plasma adipocytokines.
Presented by: 9th European Congress of Endocrinology, Budapest, Hungary (28. April – 2. May 2007)

Goncalvesova E, Jurkovicova D, Sedlakova B, Hudecova S, Luknar M, Krizanova O.
ApoE polymorphism and heart failure caused by dilated cardiomyopathy.
Presented by: Heart Failure 2007, Hamburg, Germany (9. – 12. June 2007)

Jurko A, Jurko A jr., Krupickova S.
Doppler derived myocardial performance index in the healthy children.
Presented by: Heart Failure 2007, Hamburg, Germany (9. – 12. June 2007)

Klimas J, Štrbová J, Kyselovič J, Uhliar R.
Antihypertenzívna terapia zlyháva v redukcii pulzného tlaku napriek primeranej kontrole tlaku krvi u hypertenzných osôb.
Presented by: XV. Scientific Congress on Hypertension, Milan, Italy (15. – 19. June 2007)

Klimas J, Krošláková M, Gažová A, Kučerová D, Plandorová J, Štrbová J, Bajuszová Z, Kmecová J, Křenek P, Kyselovič J.
Inhibícia ACE normalizuje endotelovú dysfunkciu u potkanov medikovaných daunorubicínom.
Presented by: XV. Scientific Congress on Hypertension, Milan, Italy (15. – 19. June 2007)

Klimas J, Stankovičová T, Kyselovič J, Bachárová L.
Nárast trvania QT intervalu súvisí so zvýšeným tlakom krvi skôr ako so zvýšenou hmotnosťou ľavej komory u spontánne hypertenzných potkanov.
Presented by: XV. Scientific Congress on Hypertension, Milan, Italy (15. – 19. June 2007)

Adameova A, Kuzelova M, Andelova E, Faberova V, Pancza D, Svec P, Ziegelhoffer A, Ravingerova T.
Hypercholesterolemia abrogates an increased resistance of diabetic rat hearts to ischemia-reperfusion injury.
Presented by: XIX. World Congress of the International Society of Heart Research, Bologna, Italy (22. – 26. June 2007)

Ravingerova T, Matejikova J, Neckar J, Andelova E, Kolar F.
Differential role of PI3K/Akt pathway in the infarct size limitation and antiarrhythmic protection in the rat heart.
Presented by: XIX World Congress of the International Society for Heart Research, Bologna, Italy (22. – 26. June 2007)

Kováčiková L, Škrak P, Doboš D, Záhorec M, Dakkak K.
Použitie amiodarónu a hypotermie v liečbe pooperačnej junkčnej ektopickej tachykardie.
Presented by: 5th World Congress on Pediatric Critical Care, Geneva, Switzerland (24. – 28. June 2007)

Bordacova L, Kaldararova M, Tittel P, Masura J.
Experiences with fenestration closure in patients after Fontan operation.
Presented by: PIC Symposium. Pediatric and Adult Interventional therapies for Congenital and Valvular Heart Diseases, Las Vegas, USA (22. – 25. July 2007)

Kamensky G, Avdicova M, Gerova Z, Egnerova A, Krak J, Murin J, Sidlo R.
The effects of socio-economic status on the prevalence of cardiovascular risk factors in healthy individuals in western and eastern parts of Slovakia.
Presented by: ESC Congress 2007, Vienna, Austria (1. – 5. September 2007)

Madaric J, Vulev I, Mistrik A, Vozar M, Lederer P, Gocar M, Riecansky I, De Bruyne B, Bartunek J.
Ultrasound guided percutaneous thrombin injection as a treatment of choice in 140 iatrogenic femoral artery pseudoaneurysms after heart catheterization.
Presented by: ESC Congress 2007, Vienna, Austria (1. – 5. September 2007)

Mitro P, Mudráková K, Mičková H, Dudáš J.
Génové polymorfizmy renín-angiotenzínového systému u pacientov s vazovagálnou synkopou.
Presented by: ESC Congress 2007, Vienna, Austria (1. – 5. September 2007)

Paulis L, Matuskova J, Adamcova M, Pelouch V, Pechanova O, Simko F.
Effect of L-arginine and spironolactone in NO-deficient hypertensive rats: Asynchronous regression of left ventricular and aortic hypertrophy.
Presented by: ESC Congress 2007, Vienna, Austria (1. – 5. September 2007)

Penz P, Vachulova A, Teren A, Caprnda M, Blazicek P, Atalay M, Hanninen O, Lietava J.
Homocysteine and vitamins of class B are associated with metabolism of lipoproteins.
Presented by: ESC Congress 2007, Vienna, Austria (1. – 5. September 2007)

Vachulova A, Bukovinova P, Penz P, Janoska D, Vohnout B.
Can we influence manifestation of metabolic syndrome by using antipsychotic drugs in patients with schizophrenia?
Presented by: ESC Congress 2007, Vienna, Austria (1. – 5. September 2007)

Šimko F, Paulis Ľ.
Melatonín ako potenciálna antihypertenzívna terapia.
Published by: J Pineal Res 2007;42:319–322.

Kristek F, Koprdova R, Cebova M.
Long-term effects of early administered sildenafil and NO donor on the cardiovascular system of SHR.
Published by: Journal of Physiology and Pharmacology 2007;58:33–43.

COAGULATION FACTOR ABNORMALITIES IN NEONATES WITH SINGLE VENTRICLE PHYSIOLOGY PRECEDE SURGERY

[1]Hakacova N, [1]Zahorec M, [2]Laluhova-Striezencova Z.

[1]Cardiac Intensive Care Unit, Dept. of Pediatric Cardiology, Children's Cardiac Center, Bratislava,
[2]Dept. of Clinical Hematology, Children's University Hospital, Bratislava

Cardiology in the Young 2007;17(Suppl.):1–24.

Introduction: Thromboembolic complications are major factors contributing to morbidity and mortality in patients with single ventricle physiology (1, 2). Abnormal coagulation parameters have recently been described in patients after second and third stage of single ventricle repair (3, 4, 5). However, to date there was no study, which evaluated hemocoagulation factors neonates before surgery.

Aim of the study: The aim of the study is to test the hypothesis that coagulation factor abnormalities are present in neonatal age, before the staged surgery and are associated with hemocoagulation disturbances.

Patients and methods: After obtaining institutional ethical committee approval and informed parental consent, twenty neonates with single ventricle physiology admitted to Children's Cardiac Center in Slovakia were included into the study. Twenty healthy neonates were assessed as age-matched controls.

Demographic data were collected from medical records. Groups did not differ significantly in demographic characteristics.

Central venous blood was taken for the purpose of hematological screening tests, biochemical blood tests and coagulation studies. Concentration of factor (F) II, FV, FVII, FVIII, protein (P) C, PS and antithrombin (AT), were measured before the surgical procedure and evaluated as possible predictors of hemocoagulation state disturbances. Laboratory signs of hemocoagulation state disturbance, were assessed by measuring of plasminogen concentration, FDP, D-dimer, prothrombin time (PT) and activated partial thromboplastin time (APTT).

Controls and single ventricle patients were compared using the 2-sample Student t-test. Statistical analysis was conducted using the JMP software package. Values are given as mean ± SD. Significance was set at $P < 0.05$.

Results: Procoagulation factor (F) II ($p < 0.001$), FVII ($p < 0.01$), FVIII ($p < 0.001$) reached significantly lower values in single ventricle (SV) group compared with Control group (**Figure 1**). Anticoagulation protein (P) C ($p < 0.001$), PS ($p < 0.01$) and antithrombin III ($p < 0.001$) were significantly lower in SV patients (**Figure 2**). Both pro- and anticoagulation factors were under the low limit for age in the single ventricle group.

SV group had significantly higher levels of D-dimer ($p < 0.0001$) and FDP ($p < 0.0001$) and significantly lower leves of plasminogen ($p < 0.0001$) in comparison with Control group.

Discussion: Several authors have previously described coagulation factor abnormalities as a cause of a hypercoagulable state in children who have undergone Fontan operation. Specific emphasis was given on low levels of coagulation inhibitors: protein C, protein S and, ATIII (3, 4, 5). The early identification of subsets of patients who are at increased risk of thrombosis is necessary to predict risk more accurately and increase the scope for targeted prevention. To date, no study was undertaken to assess hemocoagulation factor abnormalities in neoates with single ventricle physiology. In the presented study, altered levels of both pro- and anticoagulation factors were evident in neonates before the course of staged single ventricle repair and were associated with laboratory signs of thrombolysis.

The reason of decreased hemocoagulation factor levels may be because of decreased synthesis in the liver or increased consumption after the initiation of thrombosis and subsequent thrombolysis (6). There were no signs of hepatic synthetic dysfunction (e. g. reduced albumin) or evidence of hepatocellular dysfunction (e. g. increased bilirubin or transaminase levels) in our patients. Decreased coagulation factors correlated with signs of thrombolysis (positive FDP and high D-dimmer levels and decrease plasminogen levels), which suggest initiation of coagulation and subsequent thrombolytic process.

It has been emphasized, that many studies evaluating coagulation factors did not assess both pro- and anticoagulant part of coagulation system and did not employ age-matched control subjects (7). In our study, healthy neonates were assessed as age matched controls and both pro- and anticoagulant factors were studied.

A significant elevation in factor VIII has been shown in patients who underwent third stage of single ventricle repair and suggested a reason of prothrombotic state (8). In our study group of neonates, concentration of factor VIII reached significantly lower values compared with control group. The time onset of elevation of FVIII is still discutable and prospective evaluation of coagulation factor development.

Conclusion: In the presented study, altered levels of both pro- and anticoagulation factors were shown in SV neonates before surgery. Moreover, patients had laboratory signs of thrombolysis. The prospective longitudinal study of coagulation factors and hemostatic state will clarify the developmental hemostasis of SV patients and answer the question, whether abnormalities of coagulation reporterd in neonates are predictive of coagulation abnormalities during the second and third stage of single ventricle.

Acknowledgement: I wish to thank Assoc. prof. Ljuba Bacharova, MD, PhD, MBA for outstanding education in biomedical research field and members of Cardiological Intensive Care Unit in Children's Cardiac Center for providing excellent teaching, enthusiasm and cooperation in blood samples taking.

The study is supported by Grant UK 41/2007.

References

1. Monagle P. Thrombosis in pediatric cardiac patients. Semin Thromb Hemost 2003;29:547–555.
2. Monagle P, Cochrane A. Thromboembolic complications after Fontan procedures – the role of prophylactic anticoagulation. J Thorac Cardiovasc Surg 1998;115:493–498.
3. Cromme-Dijkhuis AH, Henkens CMA, et al. Coagulation factor abnormalities as possible thrombotic risk factors after Fontan operations. Lancet 1990;336:1087–1090.
4. Cromme-Dijkhuis AH, Hess J, Hahlen K, et al. Specific sequelae after Fontan operation at mid- and long-term follow-up. J Thorac Cardiovasc Surg 1993;106:1126–1132.
5. Jahangiri M, Shore D, et al. Coagulation factor abnormalities after the Fontan procedure and its modifications. J Thorac Cardiovasc Surg 1997;113:989–992.
6. Perry D, Passy K, et al. Methods in molecular medicine: hemostasis and thrombosis protocols. Totowa press, 2006.
7. Monagle P, Andrew M. Coagulation abnormaities after Fontan procedure (letter). J Thorac Cardiovasc Surg 1998;115:732–733.
8. Odegard KC, McGowan Jr FX, Zurakowski D, et al. Procoagulant and anticoagulant factor abnormalities following the Fontan procedure: increased factor VIII may predispose to thrombosis. J Thorac Cardiovasc Surg. 2003;125:1260–1267.

Presented at the 10th Annual Meeting Cardiology 2007, Orlando, Florida
Published in supplement: Hakacova N, Zahorec M, Striezencova Z. Hemocoagulation factor abnormalities in neonates with single ventricle physiology precede surgery. Cardiology in the Young 2007;(Suppl.):17(abstract).

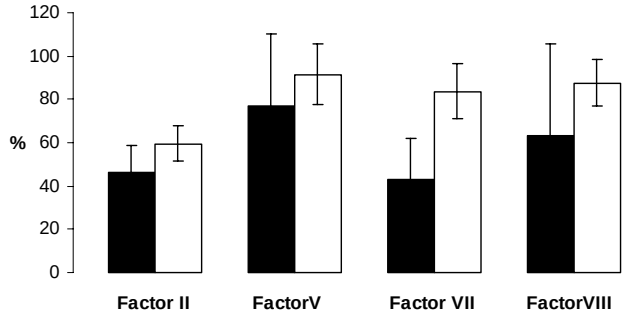


Figure 1 Comparison of particular procoagulation foactors in SV group (black) and Control group (white)

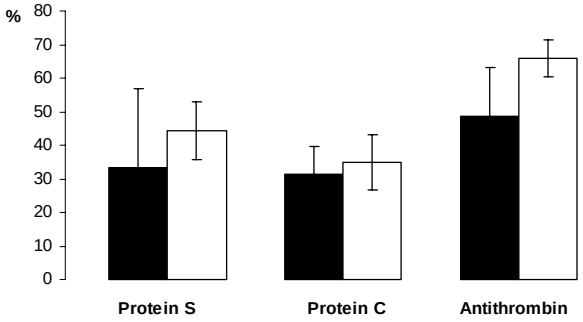


Figure 2 Comparison of anticoagulation factors in SV group (black) and Control group (white)

Cardiol 2007;16(Suppl. 1):35S–36S

LONG-TERM OUTCOME OF PEDIATRIC CARDIOSURGICAL PATIENTS REQUIRING PROLONGED MECHANICAL VENTILATION

Skrak P, Kovacikova L, Zahorec M.

Pediatric Cardiac Intensive Care Unit, Pediatric Cardiac Center, Bratislava

Cardiology in the Young 2007;17(E – Suppl. 1):23.

Introduction: Improvement in perioperative care of cardiosurgical patients leads to survival of patients even after complex surgery with severe postoperative complications. Part of these patients requires prolonged mechanical ventilation (PMV). These patients become resources outliers with poor prognosis and represent huge burden for family and health care providers. According to consensus conference (1) PMV is defined as 21 days or more of mechanical ventilation for 6 hours/day or more and one-year survival is considered as the most relevant outcome of PMV. Aim of the study was to assess one-year survival and risk factors for mortality in patients requiring PMV after pediatric cardiac surgery.

Methods: 41/1 372 (3%) patients admitted to Cardiac ICU between 2001 – 2005 requiring PMV for 20 days or more were evaluated in retrospective analysis. Reasons for PMV were: low cardiac output (n = 29 resulting from transient myocardial dysfunction, correctable cardiac defect or intractable heart failure), chronic lung disease (n = 2), diaphragm paralysis (n = 11), upper airway obstruction (n = 7), bronchomalatia (n = 6), recurrent bronchospasms (n = 3), plastic bronchitis (n = 1), sepsis (n = 17), neurological complications (n = 3: apalic syndrome, spinal lesion, cerebral edema following cardiopulmonary resuscitation), pulmonary hypertension (n = 4). Primary outcome was one-year survival after cardiac surgery. Univariate analysis was performed to assess risk factors for mortality.

Results: One-year survival of patients was 51%. Twenty (48%) patients died within period of one year after cardiac surgery. Causes of death during CICU stay (n = 12) were: sepsis (n = 4), heart failure (n = 4), sudden death (n = 1), cessation of life-sustaining therapy (n = 3). Causes of death after discharge from CICU (n = 8): bronchopneumonia (n = 4), ileus after abdominal surgery (n = 1), sudden death (n = 1), acute respiratory failure (n = 1) and central vein thrombosis (n = 1). Median follow up was 3.2 (1.4 – 5.6) years. There were two deaths during the second year after surgery due to therapy resistant atrial flutter (n = 1), bronchopneumonia (n = 1). Sixteen survivors were in good condition, one patient has apalic syndrome, another one has delayed psychomotoric development and one patient has desaturation. Perioperative characteristics of patients are presented in **Table 1**. Risk factors for mortality are presented in **Table 2**.

Discussion: Our study showed that prognosis is influenced mainly by functional capacity of the heart. Intractable heart failure is associated with poor prognosis, especially in the situation when vailability of heart transplantation is limited due to lack of donor hearts. The need for tracheotomy is also a risk factor for mortality, but can be a contributing factor as six of seven patients with tracheotomy were suffering of intractable heart failure. Correctable cardiac defect is associated with favorable outcome as well as diaphragmatic paresis. Patients with diaphragmatic paresis require PMV until diaphragm plication is performed or phrenic nerve recovers; afterwards good hemodynamic condition allows early recovery.

Conclusion: Prognosis of pediatric cardiosurgical patients requiring prolonged mechanical ventilation is unfavorable. Only 51% of them are surviving one year after surgery. Correctable cardiovascular defect and diaphragm paralysis are associated with survival. Intractable cardiovascular defect is a predictor of mortality.

Table 1 Perioperative characteristics of patients

Factor	Nonsurvivors (N = 20)	Survivors (N = 21)	
Age (d – day, y – year)	72d (1d – 6y)	82d (1d – 15y)	p = 0.82
ICU stay (days)	53 (20 – 181)	44 (20 – 308)	p = 0.55
Hospital stay (days)	72 (20 – 181)	59 (20 – 308)	p = 0.4
Weight (kg)	4 (1.6 – 19)	3.9 (1.4 – 39)	p = 0.82
Mechanical ventilation before surgery	11	6	p = 0.08
ICU immediately before surgery	11	9	p = 0.43
Genetic syndrome	9	7	p = 0.44
Down syndrome	4	3	p = 0.73
Complexity of surgery (ABCS)	8.5 (5 – 14.5)	9 (6 – 14.5)	p = 0.88
Need for reoperation	10	11	p = 0.87
Functional single ventricle	8	12	p = 0.27
Duration of PMV (days)	34 (20 – 180)	30 (20 – 308)	p = 0.36
Tracheotomy	**6**	**1**	**p = 0.03**
Cardiopulmonary resuscitation	7	6	p = 0.65
Inotrope support (days)	29 (5 – 81)	17 (4 – 35)	p = 0.08
Peritoneal dialysis	9	7	p = 0.44
Chylothorax	13	15	p = 0.65

ICU – Intensive care unit, ABCS – Aristotle basic complexity score2, PMV – Prolonged mechanical ventilation

Table 2 Reasons for prolonged mechanical ventilation

Factor	Nonsurvivors (N = 20)	Survivors (N = 21)	
Correctable cardiac effect	**4**	**12**	**p = 0.024**
Intractable heart failure	**13**	**0**	**p < 0.001**
Sepsis	8	9	p = 0.85
Neurological impairment	2	1	p = 0.51
Diaphragm paresis	**1**	**10**	**p = 0.003**
Pulmonary hypertension	2	2	p = 0.97
Bronchomalatia	4	2	p = 0.40
Upper airway obstruction	3	4	p = 0.73
Bronchospasm	1	2	p = 0.57
Plastic bronchitis	0	1	p = 0.84
Cardiopulmonary resuscitation	2	4	p = 0.41
Multiorgan dysfunction	7	8	p = 0.83
N. of factors in one patient	3 (1 – 4)	3 (1 – 4)	p = 0.46

References

1. MacIntyre NR, Epstein SK, Carson S, et al. Management of patients requiring prolonged mechanical ventilation: report of NAMDRC consensus conference. Chest 2005;128:3937–3954.

2. Lacour-Gayet F, Clarke D, Jacobs J, et al. The Aristotle score: a complexity-adjusted method to evaluate surgical results. Eur J of Cardio-thorac Surg 2004;25:911–924.

DUCTUS ARTERIOSUS CLOSURE DURING THE MODIFIED BLALOCK – TAUSSIG SHUNT OPERATION: INFLUENCE ON EARLY POSTOPERATIVE HEMODYNAMICS

Zahorec M, Hakacova N, Skrak P, Kovacikova L, Nosal M.

Cardiac Intensive Care Unit, Pediatric Cardiac Center, Bratislava, Slovakia

Cardiol Young 2007;17(E – Suppl 1):24.

Background: The modified Blalock-Taussig (MBT) shunt is a procedure of choice for neonates with single ventricle physiology and ductus dependent pulmonary blood flow.

The policy of closing vs. not closing patent ductus arteriosus (PDA) during MBT shunt surgery differs between institutions. The patency of PDA is potentially life-saving in case of early shunt obstruction. On the other hand, patency of PDA may adversely influence the early postoperative hemodynamics by excessive pulmonary blood flow. The objective of this study was to compare the early postoperative hemodynamic status of newborns with and without ductal closure during MBT shunt procedure.

Methods: Retrospective observational study. During the period from January 1997 to November 2006, 74 newborns (1 – 30 days) with complex cyanotic congenital heart lesions underwent primary MBT shunt operations at Pediatric Cardiac Center, Bratislava, Slovakia.

PDA was surgically closed in 27 patients (group 1) and was not closed during operation in 47 patients (group 2). The closure of PDA was decided by actual center policy and/or surgeons decision. Preoperative prostaglandin E infusion was discontinued during operation in all patients. The preoperative and operative variables were analyzed as baseline characteristics of both groups. There were significantly more patients with pulmonary atresia in group 2 (p = 0.03). The early postoperative period was defined as first 24 hours after surgery. Mean arterial pressure (MAP), diastolic arterial pressure (DAP), central venous pressure, heart rate, arterial oxygen saturations, arteriovenous saturation difference, inotropic support, urinary output, blood losses and fluid balance were recorded during the study period (divided into four equal periods: hours 1 – 6, 7 – 12, 13 – 18, 19 – 24).

Early mortality was defined as death during 30 days after surgery. Early shunt failure was defined as the need to return to the operating room for a second shunt during the same hospitalization period because of complete occlusion of the shunt.

Analysis was performed using the statistical software package JMP 5.0.1a (SAS Institute, Inc.). Differences were considered statistically significant at a P value of ≤ 0.05.

Results: Compared to group 2, significantly less positive fluid balance during first 6 postoperative hours, lower heart rate during first 18 postoperative hours (**Figure 1**) and higher MAP and higher DAP during first 12 postoperative hours (**Figure 2**), were recorded in group 1. Data analysis did not reveal significant differences in remaining outcome measures during the whole study period.

Multivariate analysis of variables determining pulmonary blood flow early after MBT shunt surgery (PDA closed/not closed, PA/PS, normalized MBT shunt area) confirmed PDA closure as the only significant factor, which affects early hemodynamic status.

Number of patients with pulmonary atresia was lower in group 1 than in group 2 (P < 0.03). Early mortality was 3.7% in group 1 and 8.5% in group 2 (P = 0.42). Early shunt failure did not occur in group 1 and was diagnosed in 5 patients in group 2 (P = 0.08). There were no differences in length of mechanical ventilation and ICU stay between both groups (p = 0.32 and 0.71).

Conclusion: PDA closure during MBT shunt procedure affects positively hemodynamic status in very early postoperative period without adversely affecting early mortality. Nevertheless, the length of mechanical ventilation and ICU stay were not influenced by ductal closure.

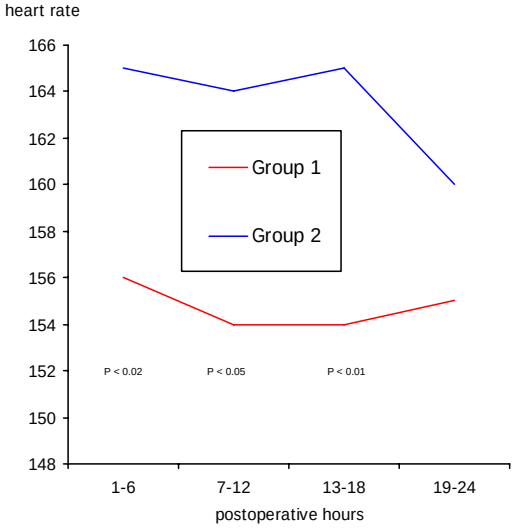


Figure 1 Heart rate

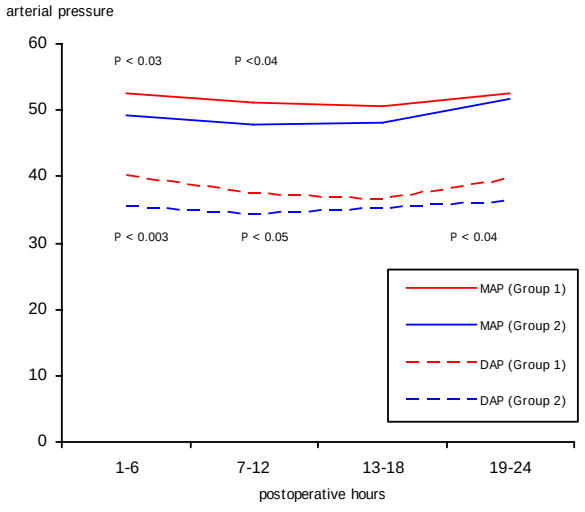


Figure 2 Mean and diastolic arterial pressure

DECREASED INSULIN SENSITIVITY IN YOUNG LEAN HYPERTENSIVE MEN IS NOT ASSOCIATED WITH INCREASED VISCERAL FAT AND CHANGES IN PLASMA ADIPOCYTOKINES

[1]Penesova A, [1]Koska J, [2]Cízmarova E, [1]Radikova Z, [3]Belan V, [1]Vigas M.

[1]Institute of Experimental Endocrinology,
Slovak Academy of Sciences, Bratislava,
[2]Department of Pediatric Cardiology,
Out-patients Clinic Karlova Ves, Bratislava,
[3]Clinic of Radiology, Comenius University, Bratislava

Endocrine Abstracts 2007;14(Presentation: poster).

Insulin resistance in hypertensive patients is often associated with obesity and/or accumulation of adipose tissue (AT) in abdominal region (1). Previous studies showed controversial findings on changes in circulating levels of adipocytokines. Kazumi, et al. (2) found lower and Mallamaci, et al. (3) higher circulating levels of adiponectin, and Narkiewicz, et al. (4) reported about higher concentrations of leptin in patients with hypertension.

The aim of our study was to investigate the association of insulin sensitivity with the amount of abdominal AT and plasma levels of adipocytokines in young, lean, non-treated males with recently diagnosed high normal blood pressure or hypertension (HT) grade 1 (5).

Subjects and methods: A total of 21 male subjects with HT (age 20.3 ± 0.6 years, BMI 22.4 ± 0.5 kg/m^2, systolic BP 141 ± 2 mmHg, diastolic BP 73 ± 2 mmHg, mean ± SE) and 19 matched normotensive controls (NT; age 23.1 ± 1.0 years, BMI 22.1 ± 1.4 kg/m^2, systolic BP 117 ± 3 mmHg, diastolic BP 67 ± 2 mmHg) underwent a standard 75 g oral glucose tolerance test (oGTT). Magnetic resonance imaging was used for measurement of total, visceral and subcutaneous abdominal adipose tissue. Areas were evaluated from a single slice scan at the level between the L4 and L5 vertebral body using image analysis freeware (ImageJ, Bethesda, MD). Fasting concentrations of leptin and adiponectin, and fasting and post load concentrations of glucose and insulin were measured in plasma. Indices of insulin sensitivity Cederholm (ISI_{CED}) (6), Matsuda (ISI_{MAT}) (7), and index of insulin resistance (IR HOMA) (8) were also calculated.

Results: All subjects had normal fasting glucose levels and normal glucose tolerance. HT patients had higher IR HOMA (2.4 ± 0.4 vs. 1.2 ± 0.1, p = 0.007) and lower ISI_{CED} and ISI_{MAT} (58 ± 3 vs. 77 ± 4, p = 0.0001 and 5.1 ± 0.6 vs. 9.0 ± 0.8, p = 0.001, respectively) than NT subjects. The two study groups did not differed in amount of visceral AT (31.80 ± 8.63 vs. 47.35 ± 6.78 cm^2, NS); and subcutaneous AT (93.58 ± 15.66 vs. 111.05 ± 10.80 cm^2, NS), and in plasma levels of leptin (3.82 ± 0.52 vs. 3.45 ± 0.49 ng/ml; NS) and adiponectin (1.71 ± 0.40 vs. 1.40 ± 0.21 mg/ml, NS).

Conclusions: These results demonstrate that even lean subjects with recently established higher blood pressure and with normal fasting and post-load glucose levels display signs of insulin resistance. These changes were however not related to higher amount of abdominal adipose tissue or levels of circulating leptin and adiponectin.

References

1. Toft I, Bonora KH, Jenssen T. Insulin resistance in hypertension is associated with body fat rather than blood pressure. Hypertension 1998;32:115–122.
2. Kazumi T, Kawaguchi A, Sakai K, et al. Young men with high-normal blood pressure have lower serum adiponectin, smaller LDL size, and higher elevated heart rate than those with optimal blood pressure. Diabetes Care 2002;25:971–976.
3. Mallamaci F, Zoccali C, Cuzzola F, et al. Adiponectin in essential hypertension. J Nephrol 2002;15:507–511.
4. Narkiewicz K, Somers VK, Mos L, et al. An independent relationship between plasma leptin and heart rate in untreated patients with essential hypertension. J Hypertens 1999;17:245–249.
5. ESH/ECS 2003 – European Society of Hypertension/European Society of Cardiology guidelines for the management of arterial hypertension. Journal of Hypertension 2003;21:1011–1053.
6. Cederholm J, Wibell L. Insulin release and peripheral sensitivity at the oral glucose tolerance test. Diabetes Res Clin Pract 1990;10:167–175.
7. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes care 1999;22:1462–1470.
8. Mathews DR, Hosker JP, Rudenski AS, et al. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–419.

Acknowledgement: This study was supported by the grant SP51/0280800/0280/802.

APOE POLYMORPHISM AND HEART FAILURE CAUSED BY DILATED CARDIOMYOPATHY

Goncalvesova E, [1]Jurkovicova D, [1]Sedlakova B, [1]Hudecova S, Luknar M, [1]Krizanova O.

National Institute of Cardiovascular Diseases, Bratislava, [1]Institute of Molecular Physiology and Genetics, Bratislava

Europ J Heart Failure 2007;6(Suppl. 1):27.

Background: Besides its effect on cholesterol metabolism, apolipoprotein E (ApoE) plays an important role in the downregulation of inflammatory response. It has recently been shown that ApoE4 is less effective in suppressing the neuroinflammatory activation than ApoE2 and ApoE3.

Aim: To describe ApoE polymorphism in patients with heart failure caused by dilated cardiomyopathy (DMC) and to evaluate the relation of ApoE polymorphism to selected clinical/laboratory variables.

Patients and methods: Caucasian pts with advanced heart failure caused by DCM were included. Basic patients characteristics are presented in **Table 1**. Diagnosis of DCM was based on echocardiography, the coronary angiogram was normal in all pts. CVS StripAssay (ViennaLab, Labordiagnostika, GmbH), using polymerase chain reaction and subsequent reverse hybridization, was used to identify the ApoE gene polymorphism. Association between ApoE polymorphism and lymphocyte count (LC) and blood leveis of hemoglobin (HB), total cholesterol (TC), C-reactive protein (CRP), and uric acid (UA) were determined. Obtained values were compared between individuals with ApoE4 allele-containing genotype, i. e. ε2/4 or ε3/4 (ApoE4+, n = 37), and individuals without ApoE4, i. e. ε2/3 or ε3/3 (ApoE-, n = 13).

Table 1 Patients characterisctics

Total number of pts (males)	50 (43)
Age (yrs ± SD)	49.7 ± 6.1
Left ventricular ejection fraction (% ± SD)	24.7 ± 7
NYHA class (± SD)	2.9 ± 0.6
ApoE4+ (individuals with ApoE4 allele)	37
ApoE4- (individuals without ApoE4 allele)	13

Results: Frequency of the ApoE4 allele was 40%. Prevalence of the ApoE4 allele in the common local population is 10.9% (Hubacek et al., 2003). Frequency of ε2/4 was 58% and ε3/4 22%. There was no patient carrying ε4/4 or ε2/2 genotype. ApoE4+ patients showed significantly higher levels of CRP and lower levels of UA than the ApoE4- pts (**Figures 1 and 2**, resp.). Differences in LC, HB, and TC were not significant.

Conclusion: 1. Frequency of the ApoE4 allele in pts with heart failure due to DCM is unexpectably high in comparison to common population. 2. Presence of the ApoE4 allele appears to be associated with signs of a higher inflammatory activity. 3. Physiological and clinical significance of these findings remains to be clarified yet.

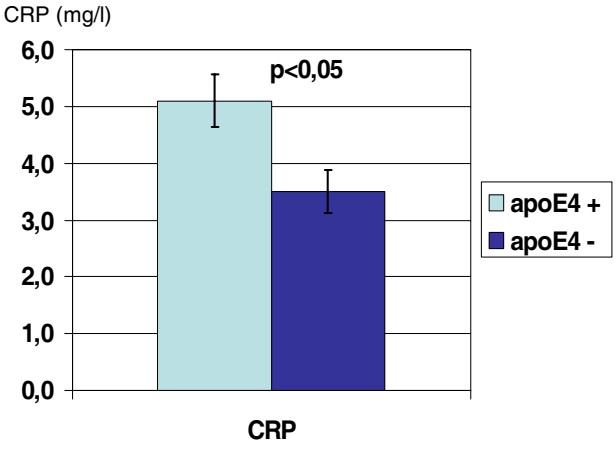


Figure 1 C-reactive protein in the apoE4+ and apoE4- groups

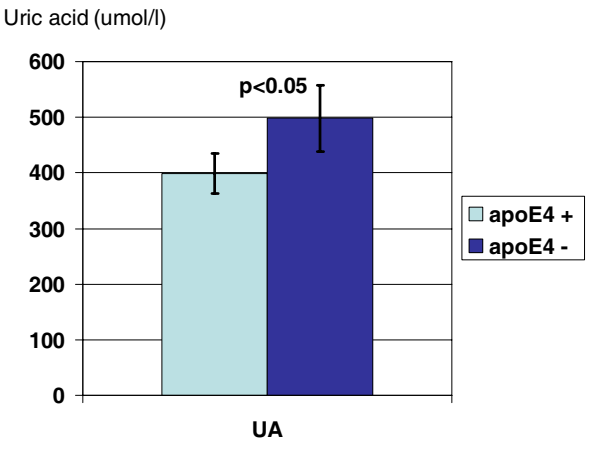


Figure 2 Uric acid in the apoE4+ and apoE4- groups

DOPPLER DERIVED MYOCARDIAL PERFORMANCE INDEX IN HEALTHY CHILDREN

Jurko A, Jurko A jr., Krupickova S.

Pediatrics department, Comenius University, Martin

Europ J Heart Failure 2007;6(Suppl. 1):166.

The development of 2 dimensional (2-D) echocardiography has raised new expectations and hopes for improving the accuracy of echocardiography in quantitating left ventricular (LV) function. The myocardial function is determined by preload, afterload, contractility, heart rate and rhytm. The myocardial performance index is a simple quantitative non geometric index of ventricular function and is readily applicable to studying the functions of right and left ventricle. The aim of study was to assess PMI in a healthy children in various age groups.

Patients and methods: We studied 38 healthy children from 2 years to 18 year of age. They had no structural cardiovascular diseases and had normal physical examination. All data analysis was performed by one clinician on online measurement system. The following Doppler time interval were measured (**Figure 1**). The interval: a – from the cessation to the onset of mitral or tricuspid inflow was equal to the sum of the isovolumetric contraction time (ICT), ejection time (ET) and isovolumetric relaxation time (IRT). The interval: b – was measured as a of ventricular ejection flow from the onset to the end of ejection. Thus the sum of ICT and IRT was obtained by subtracing interval – b from interval – a. The Doppler derived Tei-index, combining systolic and diastolic functions, was then calculated using following: a – b/b.

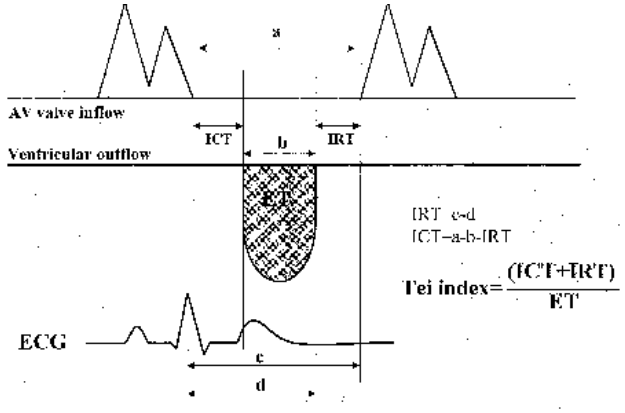


Figure 1

Statistical analysis: Data analysis were performed by using t-test. A – $p < 0.05$ was considered significant.

Results: In our study the normal value of LV and RV Tei-indices were 0.32 ± 0.07 and 0.27 ± 0.09 with mean confidence interval of 0.31 – 0.33 and 0.25 – 0.29.

No correlation was found between Doppler index and age, heart rate and left ventricular dimensions. Echocardiographic data are summarized in **Table 1**.

Discussion: Since the results obtained from the Tei-index correspond to those of invasive methods it would be preferable to the available invasive techniques.

We determined the average of normal values for RV and LV Tei-indices as presented in **Table 1**. These values are consistent with those of other studies (**Table 2**).

Our study presented LV and RV Tei-indices in normal children. The Tei-index is a simple, sensitive and accurate tool for quantitative assessment of functions of RV and LV. Because the Tei-index is easy and highly reproducible, it could be considered as a valuable technique in a comprehensive hemodynamic workup, especially when other indices of myocardial performance are within.

Table 1 Echocardiographic measurements

Measurement	Mean ± SD
EDV (ml)	64.3 ± 33.2
ESV (ml)	25.1 ± 1.2
SV (ml)	40.8 ± 30.8
LVIDs (cm)	2.5 ± 0.7
LVIDd (cm)	3.8 ± 0.9
RVTei index	0.27 ± 0.09
LVTei index	0.32 ± 0.07

Table 2 MPI in different studies in a healthy children

Study	No pat.	RV MPI	LV MPI
Kim	26	–	0.38 ± 0.04
Eidem	152	–	0.35 ± 0.03
Dujardin	75	–	0.37 ± 0.05
Williams	30	–	0.32 ± 0.1
Bruch	35	–	0.39 ± 0.31
Ishii	150	0.24 ± 0.04	–
Tei	37	0.24 ± 0.04	–
Borzoee	108	0.25 ± 0.09	0.36 ± 0.11
Our study	38	0.27 ± 0.09	0.32 ± 0.0

References

1. Borzoee M, Kheirandish Z. Doppler-derived myocardial performance index in healthy children in Shiraz. Iran J Med Sci 2004;29:85–89.
2. Lakoumentas JA, Panou FK, Kotseroglou VK, et al. The Tei-index of myocardial performance: applications in cardiology. Hellenic J Cardiol 2005;46:52–58.
3. Galderisi M, Vitale G, D'Errico A, et al. Usefulness of pulsed tissue Doppler for the assessment of left ventricular myocardial function in overt hypothyroidism. Ital Heart J 2004;5:257–264.
4. Ishi M, Tei C, Tsutsumi T, et al. Quantitation of global right ventriculart function in children with normal heart and congenital heart disease: a right ventricular myocardial performance index. Pediatr Cardiol 2000;1:416–421.
5. Tei C, Nishimura RA, Seward JB, et al. Non invasive doppler-derived myocardial performance index: correlation with simultaneous measurements. J Am Soc Echocardiogr 1997;1:169–178.
6. Ishi M, Tsutsumi T, Himeno E, et al. Sequential evaluation of left ventricular myocardial performnce in children after anthracycline therapy. Am J Cardiol 2000;86:1279–1281.
7. Jurko A, Jurko A jr., Krupickova S. Doppler derived myocardial performance index in healthy children. Europ J Heart Failure 2007;6(Suppl. 1):166.

ANTIHYPERTENZÍVNA TERAPIA ZLYHÁVA V REDUKCII PULZNÉHO TLAKU NAPRIEK PRIMERANEJ KONTROLE TLAKU KRVI U HYPERTENZNÝCH OSÔB

[1]Klimas J, [2]Štrbová J, [1]Kyselovič J, [2]Uhliar R.

[1]Katedra farmakológie a toxikológie, Farmaceutická fakulta, Univerzita Komenského, Bratislava,
[2]Nemocnica s poliklinikou Ministerstva vnútra SR, Bratislava

Journal of Hypertension 2007;25:S174.

Úvod: Zvýšený brachiálny pulzný tlak (PP) definovaný ako rozdiel medzi systolickým (sTK) a diastolickým (dTK) arteriálnym tlakom krvi je silným prediktorom kardiovaskulárnej a cerebrovaskulárnej mortality (1). Jeho zvýšenie sa dáva do súvisu so zvýšenou tuhosťou artérií (2). Antihypertenzívna terapia redukuje riziko súvisiace so zvýšeným PP (3). V tejto práci sme sledovali, či antihypertenzívna terapia rozdielne ovplyvňuje PP a sTK, resp. dTK.

Materiál a metódy: Retrospektívne sme analyzovali 24-hodinové merania sTK, dTK a PP u neliečených kontrolných osôb (Untreated), pacientov liečených na hypertenziu (Treated) a liečených hypertenzných pacientov s prítomnosťou prídavných rizikových faktorov ako diabetes mellitus a/alebo ischemická choroba srdca a/alebo infarkt myokardu (High-risk treated). Za zvýšený tlak krvi boli považované hodnoty ≥140 a/alebo ≥ 90 mmHg, za zvýšený PP ≥ 55 mmHg (4).

Výsledky: Antihypertenzívna terapia účinne kontrolovala sTK aj dTK u liečených pacientov bez prídavnej komplikácie (**tabuľka 1**). Táto skupina však mala signifikantne vyššie hodnoty PP ako kontrolná populácia. V tejto skupine bola aj signifikantne zvýšená incidencia hodnôt PP ≥ 55 mmHg ($p < 0,05$). Pacienti s vysokým rizikom mali signifikantne vyššie hodnoty sTK, PP aj incidenciu zvýšeného PP ako ostatné skupiny ($p < 0,05$). Analýza závislostí ukázala signifikantne pozitívny vzťah medzi PP a sTK, ale nie dTK u všetkých sledovaných skupín (**tabuľka 2**).

Záver: Antihypertenzívna terapia zlyhala v normalizácii sTK u hypertenzných osôb s prídavným rizikom. Rovnako nebola dostatočne účinná v redukcii pulzného tlaku v oboch liečených skupinách. Pulzný tlak pozitívne závisel od sTK, ale nie od dTK. Tieto výsledky ukázali, že PP poskytuje prídavnú informáciu v hodnotení antihypertenzív aj v prípade, že je závislý od systolického tlaku krvi.

Literatúra

1. Vaccarino V, Holford TR, Krumholz HM. Pulse pressure and risk for myocardial infarction and heart failure in the elderly. J Am Coll Cardiol 2000;36:130–138.
2. Safar ME, Levy BI, Struijker-Boudier H. Current perspectives on arterial stiffness and pulse pressure in hypertension and cardiovascular diseases. Circulation 2003;107:2864–2869.
3. Fyhrquist F, Dahlof B, Devereux RB, et al. Pulse pressure and effects of losartan or atenolol in patients with hypertension and left ventricular hypertrophy. Hypertension 2005;45:580–585.
4. Voors AA, Petrie CJ, Petrie MC, et al. Low pulse pressure is independently related to elevated natriuretic peptides and increased mortality in advanced chronic heart failure. Eur Heart J 2005;26:1759–1764.

Tabuľka 1 Základná charakteristika (*p < 0,05 vs. Untreated, †p < 0,05 vs. Treated)

24 h priemer	Vek (roky)	BMI (kg/m²)	sTK (mmHg)	dTK (mmHg)	PP (mmHg)
Untreated (n = 20)	45 ± 2	27 ± 1	123 ± 2	76 ± 1	47 ± 2
Treated (59)	49 ± 1	29 ± 1	127 ± 2	75 ± 1	52 ± 1*
High-risk treated (35)	64 ± 2*†	30 ± 1*	138 ± 3*†	73 ± 2	65 ± 3*†

Tabuľka 2 Analýza korelácií medzi pulzným tlakom a tlakom krvi

	PP – sTK	PP – dTK
Untreated (n = 20)	0,7316 ($p < 0,001$)	0,2701 (NS)
Treated (59)	0,7365 ($p < 0,001$)	0,0823 (NS)
High-risk treated (35)	0,8697 ($p < 0,001$)	0,0757 (NS)

INHIBÍCIA ACE NORMALIZUJE ENDOTELOVÚ DYSFUNKCIU U POTKANOV MEDIKOVANÝCH DAUNORUBICÍNOM

[1]Klimas J, [1]Krošláková M, [2]Gažová A, [1]Kučerová D, [1]Plandorová J, [3]Štrbová J, [1]Bajuszová Z, [1]Kmecová J, [1]Křenek P, [1]Kyselovič J.

[1]Katedra farmakológie a toxikológie, Farmaceutická fakulta, Univerzita Komenského, Bratislava,
[2]Farmakologický ústav, Lekárska fakulta, Univerzita Komenského, Bratislava,
[3]Nemocnica s poliklinikou Ministerstva vnútra SR, Bratislava

Journal of Hypertension 2007;25:S325.

Úvod: V klinických prácach boli prezentované pozitívne účinky inhibítorov angiotenzín-konvertujúceho enzýmu u pacientov s poškodením funkcie srdca po antracyklínovej chemoterapii (1, 2). Antracyklíny spôsobujú endotelovú dysfunkciu (3), inhibítory ACE sú známe svojím pozitívnym účinkom na relaxáciu závislú od endotelu (4). V tejto štúdii sme sledovali, či súčasné podávanie iACE zabráni endotelovej dysfunkcii aj poškodeniu srdca po antracyklíne.

Materiál a metódy: Použili sme potkanov Wistar vo veku 10 – 12 týždňov. Zvieratám sme aplikovali 2 týždne daunorubicín (DAU, 3 mg/kg, 6 cyklov, každých 48 hodín), enalaprilát (ENA, 5 mg/kg, každých 12 hodín) a obe látky (DAU + ENA). Kontrolám (CON) bolo podávané vehikulum. Invazívne sme merali arteriálny tlak krvi v a. carotis a funkciu srdca ľavokomorovou katéterizáciou v tribrómetanolovej anestéze. Endotelovú relaxáciu na acetylcholín sme hodnotili na izolovaných krúžkoch aorty prekontrahovaných noradrenalínom.

Výsledky: Aplikácia daunorubicínu viedla k poklesu hmotnosti zvierat, rovnako ako aj k poklesu hmotnosti srdca (**tabuľka**). Enalaprilát viedol k očakávanému poklesu tlaku krvi. Daunorubicín spôsobil pokles ľavokomorového systolického tlaku (LVP), rýchlosti kontrakcie (dP/dtmax) a relaxácie (dP/dtmin), ktorému enalaprilát nezabránil. Enalaprilát však zabránil zhoršeniu od endotelu závislej relaxácie po daunorubicíne (**obrázok**).

Záver: Simultánna aplikácia enalaprilátu nezabránila poškodeniu funkcie ľavej komory navodenej daunorubicínom, ale zabránila rozvoju endotelovej dysfunkcie. Predpokladáme, že inhibícia ACE môže mať pozitívny vplyv v chronickom štádiu poškodenia srdca po antracyklínoch cestou normalizácie endotelovej funkcie, resp. poklesom afterloadu.

Výsledky boli získané s finančnou podporou z grantu SKS 2007.

Literatúra

1. Jensen BV, Nielsen SL, Skovsgaard T. Treatment with angiotensin-converting-enzyme inhibitor for epirubicin-induced dilated cardiomyopathy. Lancet 1996;347:297–299.

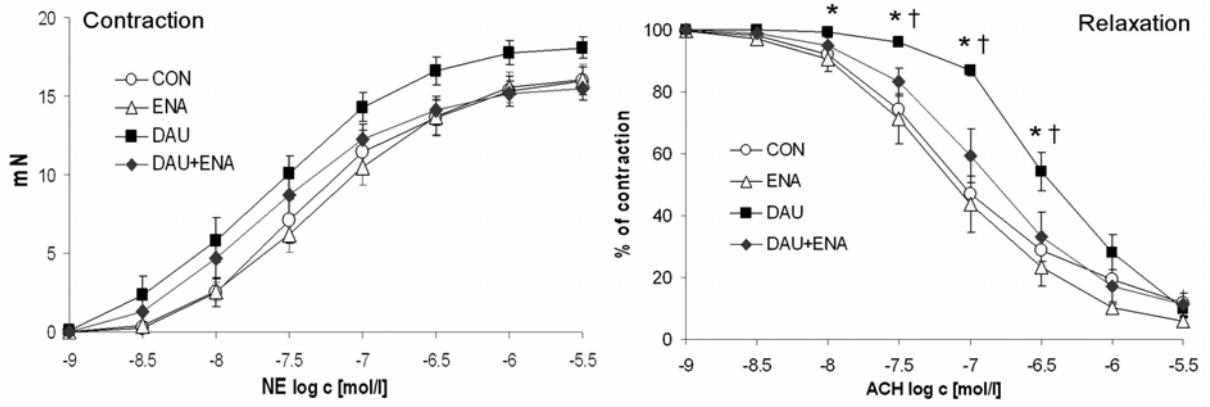
2. Cardinale D, Colombo A, Sandri MT, et al. Prevention of high-dose chemotherapy-induced cardiotoxicity in high-risk patients by angiotensin-converting enzyme inhibition. Circulation 2006;114:2474–2481.

3. Murata T, Yamawaki H, Yoshimoto R, et al. Chronic effect of doxorubicin on vascular endothelium assessed by organ culture study. Life Sci 2001;69:2685–2695.

4. Hoshino J, Sakamaki T, Nakamura T, et al. Exaggerated vascular response due to endothelial dysfunction and role of the renin-angiotensin system at early stage of renal hypertension in rats. Circ Res 1994;74:130–138.

Tabuľka Základná charakteristika zvierat (*p < 0,05 vs. CON)

	CON	ENA	DAU	DAU + ENA
n	9	9	8	8
Telo (g)	277 ± 11	270 ± 5	199 ± 5*	211 ± 8*
Srdce (mg)	857 ± 20	784 ± 19*	600 ± 14*	607 ± 9*
Srdce/Telo (mg/g)	3,04 ± 0,09	2,88 ± 0,05*	3,00 ± 0,11	2,91 ± 0,10
sTK (mmHg)	120 ± 4	102 ± 6*	112 ± 5	100 ± 7*
dTK (mmHg)	89 ± 4	66 ± 8*	81 ± 6	67 ± 7*
LVP (mmHg)	137 ± 5	116 ± 7*	113 ± 8*	110 ± 5*
dP/dtmax (mmHg)	4970 ± 445	4160 ± 797	2795 ± 502*	3242 ± 213*
dP/dtmix (mmHg)	4265 ± 295	3443 ± 653	2842 ± 350*	2928 ± 197*



Obrázok Kontrakcia izolovaných krúžkov aorty na noradrenalín a relaxácia po acetylcholíne (*p < 0,05 vs. CON, †p < 0,05 vs. DAU)

NÁRAST TRVANIA QT INTERVALU SÚVISÍ SO ZVÝŠENÝM TLAKOM KRVI SKÔR AKO SO ZVÝŠENOU HMOTNOSŤOU ĽAVEJ KOMORY U SPONTÁNNE HYPERTENZNÝCH POTKANOV

[1]Klimas J, [1]Stankovičová T, [1]Kyselovič J, [2]Bachárová L.

[1]Katedra farmakológie a toxikológie, Farmeceutická fakulta, Univerzita Komenského, Bratislava,
[2]Medzinárodné laserové centrum, Bratislava

Journal of Hypertension 2007;25:S311.

Úvod: Nárast trvania QT intervalu u hypertenzných pacientov sa dáva do súvislosti s hypertrofiou ľavej komory (HĽK) diagnostikovanej na základe hmotnosti ľavej komory (MĽK) (1). Na druhej strane, v podmienkach hypertenzie sú aktívne aj iné faktory – samotný zvýšený tlak krvi, či zvýšená aktivita sympatikového nervového systému. Ich vplyv na elektrokardiografické parametre je však obtiažne oddeliť od vplyvu hypertrofie myokardu, keďže sa vyskytujú súčasne. Klinické štúdie ukázali signifikantný vzťah medzi tlakom krvi a trvaním QT (2, 3), dokonca silnejší ako medzi trvaním QT a MĽK (4). Cieľom štúdie bolo sledovať, ktorý z týchto faktorov je dôležitejší pre nárast trvania QT v štádiu rozvoja hypertenzie a HĽK v experimentálnom modeli spontánne hypertenzného potkana (SHR).

Materiál a metódy: Použili sme samce SHR vo veku 12 a 20 týždňov (SHR12 a SHR20) a normotenzné kontroly Wistar-Kyoto (WKY) rovnakého veku a pohlavia (WKY12 a WKY20). Zvieratám sme merali arteriálny systolický tlak krvi (sTK) pletyzmografickou metódou na chvoste. Registrovali sme ortogonálne elektrokardiogramy podľa Franka u zvierat v tiopentalovej anestéze. Hodnotili sme trvanie RR a QT. Zároveň sme merali in vitro EKG u izolovaných sŕdc podľa Langedorffa.

Výsledky: U SHR sme zaznamenali progresívny nárast sTK aj MĽK (**tabuľka 1**). U WKY bol signifikantný vzťah medzi MĽK a sTK (Pearson $r = 0{,}6043$, $p < 0{,}01$), naopak u SHR sme nezanamenali vzťah medzi týmito parametrami ($r = 0{,}1728$, NS). Zároveň sme zaznamenali progresívny nárast trvania QT u SHR, ktorý signifikantne pozitívne koreloval s tlakom krvi v oboch vekových skupinách, ale nie s MĽK (**tabuľka 2**). U izolovaných sŕdc z SHR sme nezaznamenali signifikantné zmeny trvania QT v porovnaní s WKY (SHR20: 220 ± 55 ms, WKY20: 196 ± 39 ms, NS), napriek signifikantne predĺženému trvaniu RR (SHR20: 388 ± 69 ms, WKY20: 279 ± 38 ms, $p < 0{,}05$).

Záver: SHR v sledovanom období ukázali progresívny, ale navzájom nezávislý nárast sTK a MĽK. Rovnako ukázali progresívny nárast trvania QT počas rozvoja hypertenzie a HĽK. Tento nárast signifikantne pozitívne koreloval s sTK, ale nie s MĽK. U izolovaných sŕdc sme nezaznamenali nárast trvania QT. Tieto nálezy indikujú, že v období rozvoja hypertenzie a HĽK je zvýšený tlak krvi silnejším prediktorom predĺženia QT ako nárast MĽK.

Literatúra

1. Chapman N, Mayet J, Ozkor M, et al. QT intervals and QT dispersion as measures of left ventricular hypertrophy in an unselected hypertensive population. Am J Hypertens 2001;14:455–462.

2. Matsumura K, Takata Y, Ansai T, et al. Association of QT interval with blood pressure in 80-year-old subjects. Hypertens Res 2004;27:387–391.

3. Peng S, Yu Y, Hao K, et al. Heart rate-corrected QT interval duration is significantly associated with blood pressure in Chinese hypertensives. J Electrocardiol 2006;39:206–210.

4. Passino C, Franzoni F, Gabutti A, et al. Abnormal ventricular repolarization in hypertensive patients: role of sympatho-vagal imbalance and left ventricular hypertrophy. Int J Cardiol 2004;97:57–62.

Tabuľka 1 Progresia hypertenzie, hypertrofie ľavej komory a predĺženia QT u SHR (*p < 0,05 vs. WKY12, †p < 0,05 vs. SHR12, #p < 0,05 vs. WKY20)

	WKY12	WKY20	SHR12	SHR20
n	12	11	15	20
sTK (mmHg)	123 ± 7	131 ± 7	182 ± 6*	207 ± 13*†#
MĽK (mg)	645 ± 68	729 ± 50*	821 ± 58*	888 ± 105*†#
RR (ms)	155 ± 9	148 ± 20	150 ± 13	155 ± 11
QT (ms)	82 ± 9	81 ± 9	88 ± 15	100 ± 10*†#

Tabuľka 2 Pozitívne korelácie medzi trvaním QT a sTK u oboch vekových skupín SHR

	QT – MĽK	QT – sTK
WKY12 (n = 12)	0,4245 (NS)	- 0,0755 (NS)
WKY20 (11)	0,3684 (NS)	0,1632 (NS)
SHR12 (15)	0,5240 (p = 0,0450)	0,6644 (p = 0,0069)
SHR20 (20)	0,0804 (NS)	0,6842 (p = 0,0009)

HYPERCHOLESTEROLEMIA ABROGATES AN INCREASED RESISTANCE OF DIABETIC RAT HEARTS TO ISCHEMIA-REPERFUSION INJURY

[1]Adameova A, [1]Kuzelova M, [2]Andelova E,
[3]Faberova V, [2]Pancza D, [1]Svec P, [2]Ziegelhoffer A, [2]Ravingerova T.

[1] Department of Pharmacology and Toxicology, Faculty of Pharmacy, Comenius University, Bratislava,
[2]Institute for Heart Research, Slovak Academy of Sciences, Bratislava,
[3]Department of Experimental Pharmacology, VULM a. s., Modra

Molecular and Cellular Biochemistry 2007;295:129–136.

Although, diabetes mellitus (DM) and hypercholesterolemia (HCH) are known as risk factors of ischemic heart disease, the effects of experimental DM, as well as of HCH, on ischemia/reperfusion-induced myocardial injury are not unequivocal. In our previous study we demonstrated an enhanced tolerance to ischemia-induced arrhythmias in rat hearts in the acute phase of DM (1). These findings indicated that early period of the disease are associated with activation of adaptive mechanisms, which successfully counteract metabolic disorders leading to irreversible cell damage and arrhythmias (2). The aims of this study were to extend our knowledge on how DM in combination with another risk factor, such as HCH, a model that is relevant to diabetic patients with altered lipid metabolism, may affect the susceptibility to arrhythmias and the size of myocardial infarction. A combination of streptozotocin (STZ; 80 mg/kg, i. p.) and the fat-cholesterol diet (1% cholesterol, 1% coconut oil; FCHD) was used as a double-disease model mimicking DM and HCH simultaneously occurring in humans. Following 5 days, anesthetized open-chest diabetic, diabetic-hypercholesterolemic (DM-HCH) and age-matched control rats were subjected to 6-min ischemia (occlusion of LAD coronary artery) followed by 10 reperfusion to test susceptibility to ventricular arrhythmias in the *in vivo* experiments and to 30-min ischemia and subsequent 2-h reperfusion for the evaluation of the infarct size in the Langendorff-perfused hearts. The incidence of the most life-threatening ventricular arrhythmia, ventricular fibrillation (VF), was significantly increased in the DM-HCH rats as compared with the non-diabetic control animals (100% vs. 50%; $P < 0.05$; **Figure 1A**). Indeed, the severity of injury expressed by arrhythmia score (AS) was significantly higher in the DM-HCH rats than in the controls (4.9 ± 0.2 vs. 3.5 ± 0.5; $P < 0.05$), but was not increased in the diabetic animals (AS 3.7 ± 0.9; $P > 0.05$ vs. controls; **Figure 1B**). In the *in vitro* experiments focused on the infarct size determination, diabetic hearts exhibited a reduced infarct size ($15.1 \pm 3.0\%$ of the area at risk vs. $37.6 \pm 2.8\%$ in the control hearts; $P < 0.05$), however, a combination of DM and HCH increased the size of myocardial infarction to that observed in the controls (**Figure 2**). It seems that the differences in the pathogenesis of arrhythmias and myocardial infarction, as well as between the experimental protocols may account for the above-mentioned discrepancy. Further studies are required to explore the specific mechanisms of this phenomenon, which indicated that HCH abrogates enhanced resistance to ischemia-reperfusion injury in the diabetic rat heart.

References

1. Ravingerova T, Stetka R, Volkovova K, et al. Acute diabetes modulates response to ischemia in isolated rat heart. Mol Cell Biochem 2000;210:143–151.

2. Feuvray D, Lopaschuk GD. Controversies on the sensitivity of the diabetic heart to ischemic injury: the sensitivity of the diabetic heart to ischemic injury is decreased. Cardiovasc Res 1997;34:113–120.

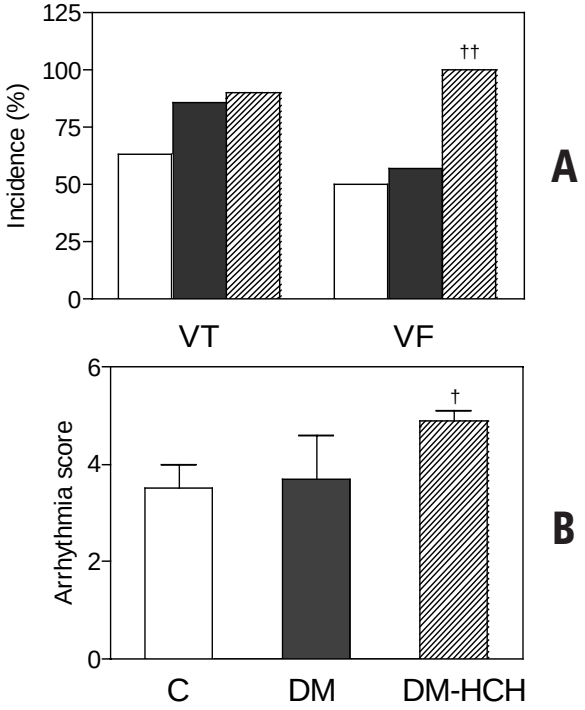


Figure 1 A and 1 B Effect of simultaneously occurring acute diabetes mellitus and hypercholesterolemia on the incidence of ventricular arrhythmias and arrhythmia severity score in the open-chest rats, †$P < 0.05$, ††$P < 0.01$ diabetic-hypercholesterolemic animals vs. controls

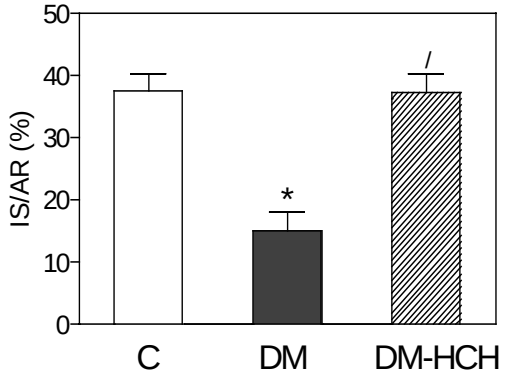


Figure 2 Effect of simultaneously occurring acute diabetes mellitus and hypercholesterolemia on the size of myocardial infarction, *$P < 0.05$ diabetic animals vs. controls, /$P < 0.05$; diabetic-hypercholesterolemic animals vs. diabetics

DIFFERENTIAL ROLE OF PI3K/AKT PATHWAY IN THE INFARCT SIZE LIMITATION AND ANTIARRHYTHMIC PROTECTION IN THE RAT HEART

Ravingerova T, Matejikova J, [1]Neckar J, Andelova E, [1]Kolar F.

Institute for Heart Research, Centre of Excellence for Cardiovascular Research of the Slovak Academy of Sciences, Bratislava, [1]Institute of Physiology, Academy of Sciences of the Czech Republic & Centre for Cardiovascular Research, Prague, Czech Republic

Mol Cell Biochem 2007;297(1–2):111–120.

Background: Cardiac protection against prolonged ischemia can be achieved by repeated episodes of brief ischemia (hypoxia), a phenomenon known as ischemic preconditioning (IP), or by long-term cardiac adaptation to chronic hypoxia, however, the role of pro-survival cascades underlying protective mechanisms of both adaptive phenomena is not completely elucidated. Phosphatidylinositol 3-kinase (PI3K) and its downstream effector, protein kinase Akt, is a key signaling enzyme system implicated in cell survival and metabolic control in various cell types including cardiomyocytes (1). Recent observations indicate that acute activation of PI3K/Akt occurring during IP (2) may mediate antiapoptotic effects (3), however, its role in overall cardiac salvage including clinically relevant end-points such as myocardial infarction and malignant ventricular arrhythmias remains obscure. Moreover, chronic Akt activation is also involved in hypertrophic cardiomyocyte growth (4) and in transition from compensated hypertrophy to heart failure (5).

Objectives: Rats exposed to chronic intermittent hypobaric hypoxia (IHH) become more tolerant to ischemia (6) and exhibit cardiac hypertrophy, increased myocardial levels of phosphatidylinositol (7) and phosphorylated (activated) Akt (8). Therefore, we have hypothesized that activation of PI3K/Akt might represent a potential common pathway in both, short-term and long-term cardioprotective mechanisms of the infarct size-limiting effect in the rat heart. Our further goal was to address the role of PI3K/Akt in susceptibility to ischemia-induced ventricular arrhythmias that has not been sufficiently characterized so far.

Methods: Step-wise adaptation of the in vivo rats to IHH was induced in hypobaric chamber simulating the altitude of 7000 m (8 h/day, 25 – 30 exposures, PO2 = 64 mmHg), while acute IP (2 cycles of I/R, 5 min each) was performed in the setting of Langendorff-perfused isolated hearts. In both settings, regional test ischemia was induced by LAD coronary artery occlusion (20 – 30 min) followed by reperfusion (3 – 2 h) with or without prior administration of a selective inhibitor of PI3-kinase LY294002 (LY). In the open-chest rats, LY (0.3 mg/kg) given 5 min before I/R partially attenuated infarct size-limiting effect of IHH: infarct size (IS) normalized to the size of area at risk (AR) was increased to 59.7 ± 4.1% vs. IS/AR 51.8 ± 4.4% in the non-treated hypoxic animals compared to IS/AR 64.9 ± 5.1% in the normoxic ones ($P < 0.05$). In the isolated hearts, LY (5 μM) applied 15 min prior to I/R completely abolished anti-infarct protection conferred by IP (IS/AR 55.0 ± 4.9% vs. 15.2 ± 1.2% in the non-treated hearts and 42.0 ± 5.5% in the non-preconditioned controls; $P < 0.05$). In the non-adapted controls in both settings, PI3K/Akt inhibition did not modify the size of infarction (**Figure 1**). On the other hand, it markedly suppressed arrhythmias in the LY-treated isolated hearts, where the total number of ventricular premature beats (VPB) and the incidence of ventricular tachycardia was reduced from 518 ± 71 and 100% in the controls to 155 ± 15 and 12.5%, respectively ($P < 0.05$).

Importantly, bracketing of IP with LY did not reverse antiarrhythmic effect of IP (**Figure 2**). These results suggest that activation of PI3K/Akt cascade plays a role in the infarct size-limiting mechanism in the rat heart, however, it is not involved in the mechanisms of antiarrhythmic protection. Negative role of PI3K/Akt in arrhythmogenesis and its divergent effects shown in this study may be related to different pathway of PI3K signaling and isoforms specifity of Akt mediating both, anti-infarct protection and proarrrhythmic mechanisms (9).

Supported by VEGA SR grants No 2/5110/25, APVT 51-027404 and GACR grant No 305/04/0465.

References

1. Matsui T, Rosenzweig A. J Mol Cell Cardiol 2005;38:63–71.
2. Mocanu MM, Bell RM, Yellon DM. J Mol Cell Cardiol 2002;34:661–668.
3. Mockridge JW, Marber MS, Heads RJ. Biochem Biophys Res Commun 2000;270:947–952.
4. Naga Prasad SV, Esposito G, Mao L, et al. J Biol Chem 2000;275:4693–4698.
5. Haq S, Choukroun G, Lim H, et al. Circulation 2001;103:670–677.
6. Kolar F, Ostadal B. Physiol Res 2004;53:S3–S13
7. Jezkova J, Novakova O, Kolar F, et al. Mol Cell Biochem 2002;232:49–56.
8. Strniskova M, Ravingerova T, Neckar J, et al. Gen Physiol Biophys 2006;25:25–41.
9. Oudit GY, Sun H, Kerfant B-G, et al. J Mol Cell Cardiol 2004;37:449–471.

Published in: Mol Cell Biochem 2007;(297):1–2, 111–120. Presented at the XIX World Congress of the International Society for Heart Research, Bologna (Italy), 22. – 26. June 2007.

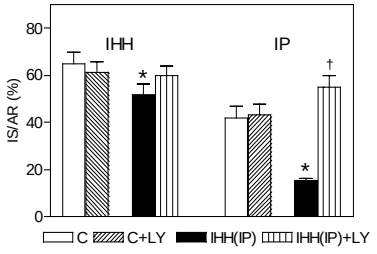


Figure 1 Myocardical infarction
* - $P < 0.05$ vs. non-adapted controls; † - $P < 0.05$ vs. non-treated group

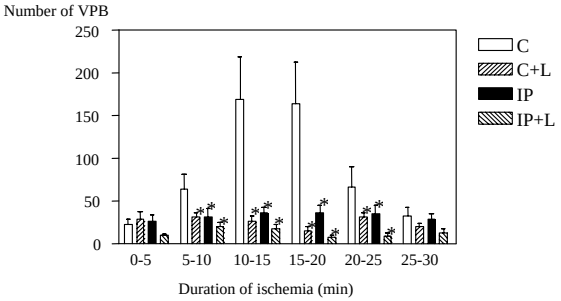


Figure 2 Ventricular arrhythmias
* - $P < 0.05$ vs. non-adapted controls; † - $P < 0.05$ vs. non-treated group

POUŽITIE AMIODARÓNU A HYPOTERMIE V LIEČBE POOPERAČNEJ JUNKČNEJ EKTOPICKEJ TACHYKARDIE

Kováčiková L, Škrak P, Doboš D, Záhorec M, Dakkak K.

OAIM, Detské kardiocentrum, Bratislava

Ped Crit Care Med 2007;8(Suppl.):A3.

Úvod: Junkčná ektopická tachykardia (JET) je po operáciách vrodených srdcových chýb život ohrozujúcou arytmiou. JET vyvoláva hemodynamickú instabilitu, a preto vyžaduje agresívnu liečbu. Liečebné protokoly sa medzi jednotlivými pracoviskami odlišujú. Niektoré uprednostňujú liečbu celkovým chladením, iné používajú antiarytmiká (1 – 4).

Cieľom práce je vyhodnotenie nášho liečebného protokolu zahŕňajúceho intravenózne podanie amiodarónu v prvej línii liečby a použitie celkovej hypotermie v prípade neúspechu liečby amiodarónom. Práca tiež zisťuje rizikové faktory spojené s potrebou použitia hypotermie.

Pacienti a metodika: Protokol liečby JET sa hodnotil u 39 pediatrických pacientov po operácii vrodenej srdcovej chyby. Protokol zahŕňal amiodarón: a) vo forme intravenóznych bolusov 2 mg/kg počas 10 minút, s maximálnou celkovou dávkou 10 mg/kg, b) podľa potreby kontinuálnu infúziu v dávke 10 – 15 mg/kg/min. V prípade neúspechu liečby amiodarónom sa použilo aktívne celkové chladenie spolu so sedáciou a svalovou relaxáciou.

Výsledky: V rokoch 1998 – 2007 sa junkčná ektopická tachykardia zaznamenala u 39 pediatrických kardiochirurgických pacientov, čo predstavuje 2 % všetkých operovaných pacientov. Intravenózny bolus amiodarónu 10 mg/kg (2 – 10 mg/kg) viedol k spomaleniu frekvencie srdca zo 185 (170 – 230) úderov za minútu na 145 (108 – 210) úderov za minútu. Kontinuálnu infúziu amiodarónu sme použili u 25 (65 %) pacientov v trvaní 48 (8 – 132) hodín. Vedľajšími účinkami liečby bola u 28 (72 %) pacientov hypotenzia vyžadujúca podanie kalcia (28 pacientov), objemu (23 pacientov) a zvýšenie inotropie (4 pacienti). Liečba amiodarónom bola úspešná v 18 (46,2 %) prípadoch. U ostatných 21 (53,8 %) pacientov bolo potrebné použiť liečbu celkovým chladením na centrálnu telesnú teplotu 33 °C (31 – 35,5 °C) v trvaní 34 (4 – 168) hodín.

Univariantná analýza ukázala, že s potrebou celkovej hypotermie bol spojený typ chirurgického riešenia, mladší vek, nižšia hmotnosť, skorý začiatok JET, nižšia telesná teplota a vyšší rozdiel medzi arteriálnou a venóznou saturáciou kyslíka. V multivariantnej analýze bol pre potrebu hypotermie rizikový skorý začiatok JET a vyšší rozdiel medzi arteriálnou a venóznou saturáciou kyslíka.

Počas iniciálnych bolusov amiodarónu došlo ku konverzii JET na sínusový rytmus u 12 pacientov. V celom súbore pacientov došlo k trvalému návratu sínusového rytmu 30 (0,5 – 264) hodín od začatia liečby.

Záver: Naše skúsenosti ukazujú, že intravenózny amiodarón je účinný u polovice pacientov s pooperačnou junkčnou ektopickou tachykardiou. Hypotenzia je častým vedľajším účinkom liečby a zvyčajne reaguje na podanie kalcia a objemu. U polovice pacientov je potrebné okrem intravenózneho amiodarónu použiť aj celkovú hypotermiu, a to hlavne u pacientov so včasným začiatkom pooperačnej tachykardie a s vyšším rozdielom medzi arteriálnou a venóznou saturáciou kyslíka.

Literatúra

1. Walsh EP, Saul JP, Sholler GF, et al. Evaluation of a staged treatment protocol for rapid automatic junctional tachycardia after operation for congenital heart disease. J Am Coll Cariol 1997;29:1046–1053.

2. Perry JC, Fenrich AL, Hulse JE, et al. Pediatric use of intravenous amiodarone: efficacy and safety in critically ill patients from a multicenter protocol. J Am Coll Cardiol 1996;27:1246–1250.

3. Laird WP, Snyder CS, Kertesz NJ, et al. Use of intravenous amiodarone for postoperative junctional ectopic tachycardia in children. Pediatr Cardiol 2003;24:133–137.

4. Saul JP, Scott WA, Brown S, et al. Intravenous amiodarone for incessant tachyarrhythmias in children: a randomized, double-blind, antiarrhythmic drug trial. Circulation 2005;112:3470–3477.

Práca bola prezentovaná vo forme prednášky na 5th World Congress on Pediatric Critical Care v Ženeve, Švajčiarsko (24. – 28. jún 2007).

Abstrakt bol publikovaný v Pediatric Critical Care Medicine: Kovacikova L, Skrak P, Dobos D, Zahorec M, Dakkak K. Evaluation of a staged therapy with amiodarone and hypothermia for postoperative junctional ectopic tachycardia. Ped Crit Care Med 2007;8(Suppl):A3.

EXPERIENCES WITH FENESTRATION CLOSURE IN PATIENTS AFTER FONTAN OPERATION

Bordacova L, Kaldararova M, Tittel P, [1]Masura J.

Dept. of Pediatric Cardiology, Bratislava,
[1]Head of Dept., Children's Cardiac Center, Bratislava

Catheterization and Cardiovascular Intervention 2007;70(Abstract):31.

Introduction: Fontan procedure and its modifications, with the presence of surgically created fenestration improves hemodynamic changes by maintaining cardiac output and limitation of atrial pressures. Role of opened fenestration by increasing cardiac index and maintaining oxygen delivery is connected with mild arterial O_2 desaturation. Despite of hemodynamic advantages of fenestration, presence of right-to-left shunting is risk factor of systemic embolization and with chronic cyanosis for impairment of following neurological outcome. Decision and timing of fenestration closure has been discussed. By occlusion it is expected the enhance of O_2 saturation and exercise capability, by overloading of single ventricle might lead to ventricle depression and its residual findings.

Patients and methods: In this study we review our experiences with transcatheter occlusion of fenestration or residual baffle leak using Amplatzer septal occluder in 38 patients, during the period of November 1997 – June 2007. Demographic data of study population shows **Table 1.** Included to study were patients with previous Fontan procedure with fenestration (19 patients with lateral tunnel – LT and 19 patients with extracardiac conduict – EC modifications) and the presence of clinically important cyanosis, desaturation less < 88%, previously described leak by echocardiography, impaired exercise capability, absence of effusions and appropriate hemodynamic parameters. There were included 2 adult patients, operated and nowadays followed up in Childrens Cardiac Center. A cross-sectional study was approved by the single institutional review board of Children's Cardiac Center of Slovak republic in Bratislava. Values and variables were assessed and expressed as mean ± SD, or range as appropriate. Informed consent for cath lab was obtained from the parents of patients. For analysis of cohort we used one sample t-test. A p value < 0.05 was considered significant. Analysis was performed using standard, commercially available software package (JMP 4.0.2, SAS).

Results: Mean age at time of closure was 10 ± 6 years (range: 3 – 27 years), with mean time of follow-up after Fontan operation of 22 ± 6 months (range: 1 – 111 months). There were realized totally 40 procedures including closure of fenestration in 37 patients and baffle leak in 3 patients. The most frequent group of patients was that with double inlet left ventricle (DILV) (21%), hypoplastic left heart syndrome (HLHS) (18%), tricuspidal valve atresia (TA) (16%) and the same numerous groups of pulmonary valve atresia/stenosis (PA/PS), double outlet right ventricle (DORV) and L-type of transposition of great arteries (L-TGA) (all of them 13%). Subsequently closure of fenester or leak resulted in enhance of arterial O_2 saturation from 82.9 ± 4.6% (median: 84.0%, range: 72.0 – 90.0%) to 91.8 ± 3.1% (median: 92.0%, range: 85.0 – 98.0%) ($p < 0.001$) for whole population, as well as significant enhance for all types of diagnoses separately (**Table 2**). Type of transcatheter approach in patients were throught v. femoralis in 35 and v. jugularis int. in 5 procedures. There were no deaths in the study period, from complications were present in early period temporary episodes of fever in 2 patients, rhytm disturbances in 2 patients and fluidothorax with cardiac decompensation in 1 patients within 1 week after closure. From late complications bacterial endocarditis in 1 patient was present within three months after catheterization. Residual leaks, as forms of residual findings were present from early post-cath period in 2 patients of the study. No more significant complications in early and late period were detected and patients were discharged with uneventful follow-up (**Table 3**).

Discussion: Elimination of right-to-left shunting resulting to significant clinical cyanosis, led to increase of arterial O_2 saturation of 9.1%, this value is comparable with other published data of 9% enhance in foreign centers (Mavroudis et al., 1992, Goff et al., 2000). In 1 patient desaturation was caused by pulmonary AV fistulae, therefore closure of these malformations and other collaterals, was done using plugs and Amplatzer occluder, resulting in increase of O_2 saturation from 74.8% to 85%. Comparing groups of surgical modifications (LT vs. EC) and groups of diagnoses, we have not found significant difference in post-closure arterial O_2 saturation, or presence or types of complications. By closure of fenestration and following volume overloading of ventricle we expected higher amount of complications resulting from ventricular depression (2.5%), elsewhere totally percentage of complications/residual findings in early and late period reached 20%.

Conclusions: We support important role of fenestration presence in high risk patients and in our study population assessed individually the necessity of closure in presence of serious grade of prolonged desaturation and exercise intolerance. Our results confirm that after adjusting of risk hemodynamic parameters, transcatheter fenestration closure in high risk patients might be safe method to significantly increase arterial O_2 saturation. The long term benefits of closure are yet to be shown – by prospective study focusing on continuous pulse oxymetry, exercise capability and possibility of arrhythmia development.

Table 1 Demographic data

Gender (n)	Male	23
	Female	15
Age (years)	Mean ± SD	9.9 ± 5.8
	Range	3 – 27
Post-FF (months)	Mean ± SEM	22 ± 6
	Range	1 – 111
Closure (n)	Fen ester	37
	Leak	3
Modification (n)	Lateral tunnel (LT)	19
	Extra cardiac conduit (EC)	19
Diagnoses	HLHS	7
	PA/PS, SV	5
	TA	6
	DORV/MA	5
	DILV	8
	L-TGA	5
	AVSDC	2

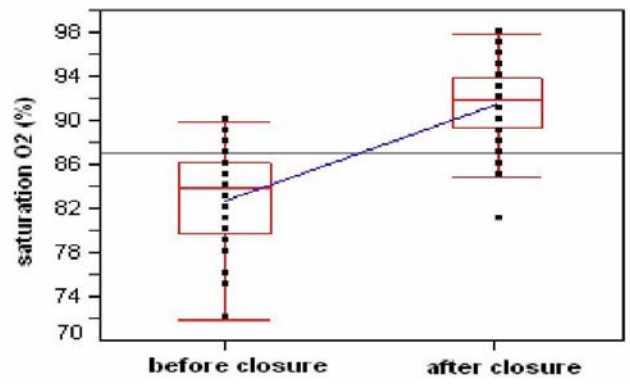
HLHS – Hypoplastic left heart syndrome, PA/PS – Pulmonary atresia/pulmonary stenosis, SV – Single ventricle, TA – Tricuspidal atresia, DORV/MA – Double outlet right ventricle/mitral atresia, DILV – Double inlet left ventricle, L-TGA – L-transposition of great vessels, AVSDC – Complete atrioventricle septal defect

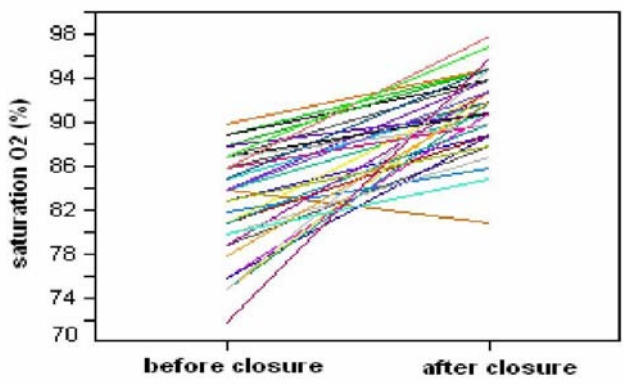
Table 2 Transcatheter closure resulting in increasing of O_2 sat in whole group ($p < 0.001$**)

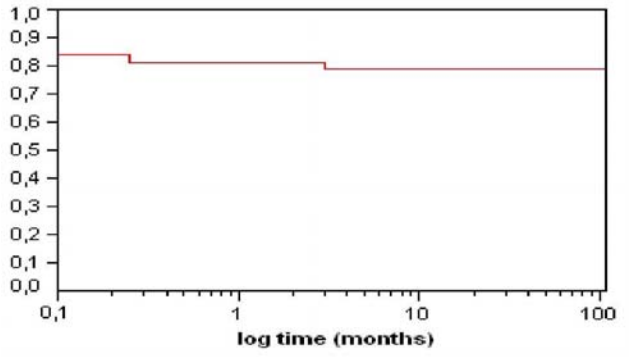
Sat O_2 (%)	Mean ± SD	Median	Range
Before closure	82.9 ± 4.6	84.0	72.0 – 90.0
After closure	91.8 ± 3.1	92.0	85.0 – 98.0

Table 3 Type of complications/residual findings after closure

Complication/residual findings	Time	n
Residual leak	post-cath	2
Fluid thorax, cardiac decompensation	1 week	1
Bacterial endocarditis	3 months	1
Fever	post-cath	2
Rhythm disturbances	post-cath	2


saturation O2 (%)
98
94
90
86
82
78
74
70
before closure
after closure


saturation O2 (%)
98
94
90
86
82
78
74
70
before closure
after closure


1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
0,1
1
10
100
log time (months)

THE EFFECTS OF SOCIO-ECONOMIC STATUS ON THE PREVALENCE OF CARDIOVASCULAR RISK FACTORS IN HEALTHY INDIVIDUALS IN WESTERN AND EASTERN PARTS OF SLOVAKIA

[1]Kamensky G, [2]Avdicova M, [3]Gerova Z, [4]Egnerova A, [5]Krak J, [6]Murin J, [7]Sidlo R.

[1]University Hospital Ruzinov, Bratislava, [2]Regional Public Health Authority, Banska Bystrica, [3]Regional Public Health Authority, Bratislava, [4]Slovak Health University, Bratislava, [5]Regional Public Health Authority, Poprad, [6]University Hospital, Bratislava, [7]Economic University, Bratislava

European Heart Journal 2004;28(Abstract Supplement):146.

Background: Socioeconomical status has been related with the prevalence and incidence of cardiovascular (CV) disease. However, there is still controversy regarding inverse association between socioeconomic status and obesity indices, which has been confirmed in most univariate analyses, but not after udjusting for other covariates in multivariant analyses.

Objective: The goal of the study was to compare the socio-economic status with prevalence of CV risk factors in healthy persons in two Slovakian counties: Bratislava county with the highest GDP and the lowest unemployment rate and Presov county, with one of the lowest GDP and highest unemployment rates in Slovakia.

Methods: During the period of 1995 – 2005, 27 797 healthy volunteers from Bratislava and Presov counties were examined in Counselling centers. For the purposes of statistical comparison all examined persons from both counties were matched by age, gender and the year of examination. Finally, 12 024 persons (mean age 46.9 ± 12.7 yrs, 3 458 men, 8 566 women) were entered into the retrospective analysis. Trends in established and emerging cardiovascular risk factors were examined accross the participants socio-economic status.

Results: Persons from Presov county had significantly higher systolic blood pressure, heart rate, BMI, waist circumference, total and LDL cholesterol, triglycerides (all $p < 0.0001$) and lower HDL cholesterol ($p < 0.0001$) compared to volunteers from Bratislava county in univariate analysis (**Table 1, 2**).

Table 1 Univariate comparison of main risk factors in persons living in Presov and Bratislava

Parameter	County	Mean	P
Age (years)	BA	46.88	0.9994
	PRE	46.88	
Systolic BP (mmHg)	BA	127.08	0.0000
	PRE	130.95	
Diastolic BP (mmHg)	BA	82.64	0.9806
	PRE	82.65	
Heart rate (beats/min)	BA	70.80	0.0001
	PRE	72.13	
BMI	BA	25.44	0.0000
	PRE	26.77	
Waist circumference (cm)	BA	84.37	0.0000
	PRE	87.63	
Hip circumference (cm)	BA	101.85	0.0000
	PRE	104.50	

BA – Bratislava county, PRE – Presov county

Table 2 Univariate comparison of lipids and glycaemia in persons living in Presov and Bratislava county

Parameter	County	Mean	P
Total-CH	BA	5.17	0.0000
	PRE	5.43	
Triglycerides	BA	1.35	0.0000
	PRE	1.44	
HDL-CH	BA	1.34	0.0000
	PRE	1.28	
LDL-CH	BA	3.22	0.0000
	PRE	3.47	
Glycaemia	BA	5.43	0.0000
	PRE	5.29	

BA – Bratislava county, PRE – Presov county

Systolic blood pressure as well as BMI and waist circumference were in Presov county significantly and constantly higher compared with those in Bratislava county (**Figure 1, 2**). The lower the social class the higher the proportion of obesity. Simultaneously they were significantly more physically inactive, they preferred less healthy food and were much less educated regarding their risk factors (all $p < 0.01$). Using stepwise adjusted multivariate logistic regression analysis, age (OR 1.061, 95% CI 1.047 – 1.075, $P < 0.0001$), socio-economic status (manual versus nonmanual work: OR 2.09, CI 1.52 – 2.86, $P < 0.0001$), low leisure time physical activity (OR 1.90, CI 1.44 – 2.52, $P < 0.0001$), and unhealthy food (OR 1.91, CI 1.44 – 2.54, $P < 0.0001$), all were independent predictors of obesity in this cohort.

Conclusions: Lifestyle factors including low socio-economical class, were strongly associated with obesity and other conventional cardiovascular risk factors. Socio-economic disparities have persisted and in former eastern European countries have even widened in some populations, which underlines the need to improve preventive care among the lower socioeconomic groups.

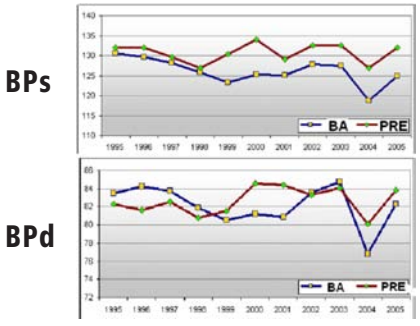


Figure 1 Differences in BP during 10 years in Bratislava and Presov county

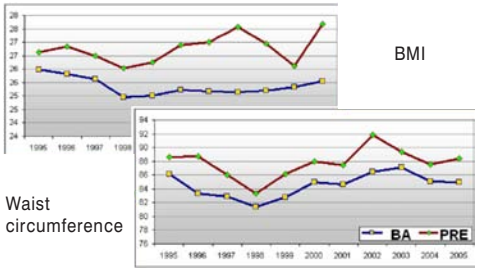


Figure 2 Differences in BMI and waist circumference during 10 years in Bratislava and Presov county

ULTRASOUND GUIDED PERCUTANEOUS THROMBIN INJECTION AS A TREATMENT OF CHOICE IN 140 IATROGENIC FEMORAL ARTERY PSEUDOANEURYSMS AFTER HEART CATHETERIZATION

[1, 2]Madaric J, [1]Vulev I, [1]Mistrik A, [1]Vozar M, [1]Lederer P, [1]Gocar M, [1]Riecansky I, [2]De Bruyne B, [2]Bartunek J.

[1]National Cardiovascular Institute, Bratislava, [2]Cardiovascular Center Aalst, Belgium

European Heart Journal 2007;28(Abstract Supplement):75.

Introduction: The incidence of iatrogenic femoral artery pseudoaneurysm after heart catheterization ranges from 0.3% to 2% and has increased over recent years with intensified antiagregation therapy and as a result of the use of larger-size catheters for interventional procedures (1 – 4). Of note, even the use of closure system devices didn't decrease their incidence as compare to conventional compressive management (4 – 5). Ultrasound guided thrombin injection is rapid, minimally invasive and highly successful treatment of post-catheterization pseudoaneurysm.

The aim of the study was to evaluate efficacy of this technique and to assess the risk factors associated with recurrence of femoral pseudoaneurysm after occlusion by thrombin injection.

Methods: From February 2002 to September 2006, 140 patients (pts, male/female: 39/101) aged 76 years (range 62 – 83) presented with femoral artery pseudoaneurysm after heart catheterization were treated by percutaneous ultrasound guided thrombin injection (500 IU/ml solution of activated human thrombin). The mean pseudoaneurysm diameter was 2.1 x 1.4 cm. Very small cavities (less then 1.5 x 1.5 cm) suitable for local compressive therapy, and very big cavities (5 x 5 cm) scheduled for surgery, were excluded from the study. The factors associated with recurrence of pseudoaneurysm were retrospectively analyzed.

Colour-duplex ultrasound (CDUS): The CDUS image of femoral artery pseudoaneurysm is characterised by arterial flow through a narrow neck arising from the puncture place in femoral artery (**Figure**). Typical "to-and-from" Doppler waveform in the pseudoaneurysm neck is essential criterion for proper diagnosis. Under 2-D ultrasound control the 20-gauge needle is positioned in the middle of the pseudoaneurysm cavity. Exact position of needle tip has to be properly identified before thrombin injection. Injection of thrombin is characterized by sudden thrill as a sign of fast blood thrombotisation in the cavity. Complete thrombotisation of the cavity is confirmed by the absence of the flow in the pseudoaneurysm after thrombin injection.

Results: Immediate success rate of thrombin occlusion was 85% (119/140). One hundred nineteen pts were successfully treated by one injection of activated thrombin (average amount 0.4 ± 0.2 ml). In 20 pts (14%), immediate short local compression (2 min) following injection was needed for complete occlusion. In one case, progression of pseudoaneurysm required conversion to surgical repair (0.8%). The procedure was well tolerated and no thrombotic complications occurred. During the 30-days follow-up recurrence of pseudoaneurysm occurred in 10 pts (7%), exclusively the second and the third day after the first injection. All of them were successfully treated by the second thrombin application. The recurrence of pseudoaneurysm was associated with obesity (BMI > 30, r = 0.42, 95% CI 0.26 – 0.56, p < 0.0001), and with extensive combination of antiagregation and anticoagulation therapy (ASA, thienopyridins, LMWH), (r = 0.64, 95% CI 0.53 – 0.73, p < 0.0001).

Conclusion: Ultrasound-guided thrombin injection is a safe and effective treatment of iatrogenic femoral artery pseudoaneurysm. It should be considered as a method of choice in suitable patients. Low rates of recurrence are associated with obesity and extensive use of combined antiagregation and anticoagulation therapy.

References

1. Olsen DM, Rodriguez JA, Vranic M, et al. A prospective study of ultrasound scan-guided thrombin injection of femoral pseudoaneurysm: a trend toward minimal medication. J Vasc Surg 2002;36:779–782.
2. Ates M, Sahin S, Konuralp C, et al. Evaluation of risk factors associated with femoral pseudoaneurysms after cardiac catheterization. J Vasc Surg 2006;43:520–524.
3. La Perna L, Olin JW, Goines D, et al. Ultrasound-guided thrombin injection for the treatment of postcatheterization pseudoaneurysms. Circulation 2000;102:2391–2395.
4. Applegate RJ, Grabarczyk MA, Little WC, et al. Vascular closure devices in patients treated with anticoagulation and IIb/IIIa receptor inhibitors during percutaneous revascularization. J Am Coll Cardiol 2002;40:78–83.
5. Dangas G, Mehran R, Kokolis S, et al. Vascular complications after percutaneous coronary interventions following hemostasis with manual compression versus arteriotomy closure devices. J Am Coll Cardiol. 2001;38:638–641.

Table 1 Baseline characteristics

Total number of heart catheterization (diagnostic/interventions)	13 890 (9943/3947)
Total incidence of femoral pseudoaneurysm	204 (1.5%)
Femoral pseudoaneurysm – thrombin inj.	140
M/F	39/101
Age (years)	76 (62 – 83)
Pseudoaneurysm location (AFC/AFS/APF)	59/52/29
Nu of cavities	1.4 ± 0.8 (1 – 4)
Diameter (cm)	2.1 x 1.4
Amount of thrombin inj. (ml)	0.4 ± 0.2

Table 2 Results of thrombin occlusion

Immediate success rate	119 (85%)
Occlusion with additional short local compression (2 min)	20 (14%)
Overall success rate	139 (99%)
Conversion to surgery	1 (0.8%)
30-days recurrence	10 (7%)

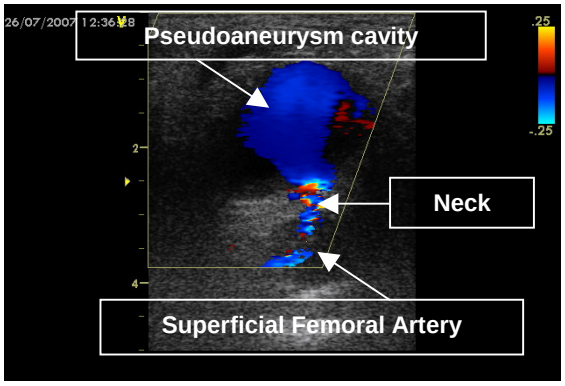


Figure CDUS image of pseudoaneurysm
Arterial flow through a narrow neck arising from the puncture place in femoral artery

GÉNOVÉ POLYMORFIZMY RENÍN-ANGIOTENZÍNOVÉHO SYSTÉMU U PACIENTOV S VAZOVAGÁLNOU SYNKOPOU

[1]Mitro P, [1]Mudráková K, [2]Mičková H, [2]Dudáš J.

[1]III. interná klinika LF UPJŠ a FN LP, Košice,
[2]Ústav lekárskej biológie LF UPJŠ, Košice

European Heart Journal 2007;28(Abstract Supplement):640.

Úvod: V literatúre bolo popísaných viacero prípadov familiárneho výskytu vazovagálnej synkopy (1 – 7). Preto sa predpokladá, že by jej výskyt mohol mať genetickú predispozíciu. Presná povaha tejto genetickej predispozície nie je známa. Gény, ktoré by mohli súvisieť s genetickým pozadím výskytu vazovagálnej synkopy, zatiaľ nie sú identifikované.

Patomechanizmus vazovagálnej synkopy nie je objasnený do všetkých podrobností. Ide o reflexne mediovanú hypotenziu v dôsledku náhlej inhibície sympatikovej aktivity. Okrem odchýliek v autonómne nervovej regulácii sa uvažuje tiež o humorálnych mechanizmoch, predovšetkým v oblasti adrenalínu, endogénnych opiátov a serotonínu. Intracerebrálne podanie serotonínu v experimente znižuje aktivitu sympatika, predpokladá sa teda, že vzostup hladín serotonínu v CNS môže spúšťať vazovagálnu reakciu. Dlhodobé podávanie inhibítorov spätného vychytávania serotonínu (SSRI) vedie k down-regulácii serotonínových receptorov v CNS, čím sa vysvetľuje priaznivý efekt podávania týchto farmák v prevencii recidív VVS (8).

Existujú doklady o tom, že patogenéza vazovagálnej synkopy môže súvisieť s poruchou regulácie extracelulárneho sodíka a jeho vylučovania. Pacienti s VVS majú nízku exkréciu sodíka za 24 hodín v moči (9) a exkrécia sodíka koreluje so stupňom klinickej závažnosti a symptomatológiou VVS (10). Zvýšený príjem sodíka v potrave zlepšuje symptómy u pacientov s VVS (11).

Renín-angiotenzínový systém (RAS) je jedným z primárnych mechanizmov, ktorý sa podieľa na regulácii homeostázy sodíka v organizme, ovplyvňuje reguláciu krvného tlaku a ovplyvňuje tiež aktivitu sympatikového nervového systému. Vzhľadom na to bol vyslovený predpoklad o asociácii génových polymorfizmov RAS s predispozíciou k VVS (12). Rovnako by bolo možné predpokladať aj asociáciu s polymorfizmom génu pre serotonínový transportér, ktorý ovplyvňuje intrasynaptickú koncentráciu serotonínu.

Cieľom práce bolo porovnať výskyt génových polymorfizmov RAS a serotonínu u pacientov s vazovagálnou synkopu a kontrolnou skupinou pacientov so synkopou inej etiológie. Sledované boli nasledovné génové polymorfizmy: inzerčný/delečný polymorfiznus v géne pre angiotenzín konvertujúceho enzýmu (ACE I/D), génový polymorfizmus M235T v géne pre angiotenzinogén, génový polymorfizmus A1166C v géne pre receptor angiotenzínu II typu 1 a S/L polymorfizmus génu pre serotonínový transportér (SERT).

Súbor pacientov a metodika: Do štúdie bolo zaradených 116 pacientov (33 mužov, 83 žien, s priemerným vekom 40 ± 10 rokov) s anamnézou synkopálnych stavov. U pacientov bol v rámci diferenciálnej diagnostiky realizovaný head-up tilt test (HUT) podľa tzv. Talianskeho protokolu (60-stupňový sklon, 20 minút pasívna fáza, 15 min stimulácia nitroglycerínom). Pred začatím HUT bola pacientom odobratá vzorka (4 ml) venóznej krvi na vyšetrenie génových polymorfizmov. Na stanovenie génových polymorfizmov bola použitá polymerázová reťazová reakcia.

Výsledky: Head-up tilt test bol pozitívny u 68 pacientov (20 mužov, 47 žien, priemerný vek 39 ± 10 rokov) a negatívny u 48 pacientov (13 mužov, 35 žien, priemerný vek 42 ± 12 rokov).

U 48 pacientov s negatívnym HUT bola zistená nasledovná etiológia synkopy: dysfunkcia sinoatriálneho uzla u 10 pacientov, AV blokáda III. stupňa u 2 pacientov, AV blokáda II. stupňa u 7 pacientov, komorová tachykardia u 1 pacienta, supraventrikulárna tachykardia u 13 pacientov, reflexná synkopa u 3 pacientov, ortostatická hypotenzia u 3 pacientov a synkopa nejasnej etiológie u 9 pacientov.

Medzi skupinami HUT pozitívnych a HUT negatívnych synkopálnych pacientov sa nezistili signifikantné rozdiely vo výskyte jednotlivých polymorfizmov. Výskyt jednotlivých genotypov bol nasledujúci (HUT pozitívni versus HUT negatívni pacienti). Výskyt génového polymorfizmu I/D v géne pre angiotenzín konvertujúci enzým (ACE) bol nasledovný: ID 43 % vs. 48 % pacientov, DD 34 % vs. 40 % pacientov a II 23 % vs. 12 % pacientov (n. s.). Génový polymorfizmus M235T v géne pre angiotenzín: MT 51 % vs. 43 % pacientov, MM 23 % vs. 27 % pacientov, TT 26 % vs. 30 % pacientov (n. s.). Génový polymorfizmus A1166C v géne pre AT1 receptor: AA 44 % vs. 32 % pacientov, AC 51 % vs. 60 % pacientov, CC 4 % vs. 8 % pacientov (n. s.). Polymorfizmus SERT: SL 44 % vs. 38 % pacientov, LL 41 % vs. 44 % pacientov, SS 15 % vs. 18 pacientov (n. s.).

Záver: Génové polymorfizmy renín-angiotenzínového systému a serotonínového transportéra nie sú podľa našich zistení asociované s predispozíciou k vazovagálnej synkope.

Literatúra

1. Márquez MF, Urias KI, Hermosillo AG, et al. Familial Vasovagal Syncope. Europace 2005;7:472–474.
2. Cooper CJ, Ridker P, Shea J, et al. Familial occurrence of neurocardiogenic syncope. N Engl J Med 1994;331:205.
3. Campfield PR, Campfield CS. Syncope in childhood: a case control clinical study of the family tendency to faint. Can J Neurol Sci 1990;17:306–308.
4. Mathias C, Deguchi K, Bleasdale-Barr K, et al. Familial vasovagal syncope and pseudosyncope: observations in case with both natural and adoptal siblings. Clin Aut Res 2000;10:43–45.
5. Mathias C, Deguchi K, Bleasdale-Barr K, et al. Frequency of family history in vasovagal syncope. Lancet 1998;352:33–34.
6. Newton JL, Kenny R, Lawson J, et al. Prevalence of family history in vasovagal syncope and haemodynamic response to head up tilt in first degree relatives:preliminary data for the Newcastle cohort. Clin Auton Res 2003;13:22–26.
7. Serletis A, Rose S, Sheldon AG, et al. Vasovagal syncope in medical students and their first-degree relatives. Eur Heart J 2006;27:1965–1970.
8. Di Girolamo E, Di Iorio C, Sabatini P, et al. Effects of paroxetine hydrochloride, a selective serotonin reuptake inhibitor, on refractory vasovagal syncope: a randomized, double-blind, placebo-controlled study. J Am Coll Cardiol 1999;33:1227–1230.
9. Cooper VL, Hainsworth R. Effects of dietary salt on orthostatic tolerance, blood pressure and baroreceptor sensitivity in patients with syncope. Clin Auton Res 2002;12:236–241.
10. Hampton JL, Parry SW, Kenny RA, et al. Lower 24-hour urinary sodium concentrations are associated with more severe symptoms in subjects with vasovagal syncope. Heart 2004;90:687–688.
11. El-Sayed H, Hainsworth R. Slat supplement increases plasma volume and orthostatic tolerance in patients with unexplained syncope. Heart 1996;75:134–140.
12. Newton JL, Donaldson P, Parry S, et al. Angiotensin converting enzyme insertion/deletion polymorphisms in vasovagal syncope. Europace 2005;7:396–399.

EFFECT OF L-ARGININE AND SPIRONOLACTONE IN NO-DEFICIENT HYPERTENSIVE RATS: ASYNCHRONOUS REGRESSION OF LEFT VENTRICULAR AND AORTIC HYPERTROPHY

[1,2]Paulis L, [1]Matuskova J, [3]Adamcova M, [4]Pelouch V, [2]Pechanova O, [1]Simko F.

[1]Institute of Pathophysiology, School of Medicine, Comenius University, Bratislava, [2]Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, [3]Department of Physiology, School of Medicine, Hradec Kralove, Charles University, Czech Republic, [4]Second School of Medicine, Charles University, Prague, Czech Republic

European Heart Journal 2007;27(Abstract Supplement):864.

Introduction: Left ventricular hypertrophy (LVH) represents an independent risk factor of cardiovascular morbidity and mortality. An especially important scope of antihypertensive treatment is the achievement of LVH regression along with reversion of myocardial fibrosis (1). The N^G-nitro-L-arginine methyl ester (L-NAME)-induced hypertension represents an attractive model for investigation of both increased blood pressure (BP) and concomitant LVH. Spironolactone was reported to reduce myocardial fibrosis and BP (2). L-arginine, the precursor of NO production, was also shown to lower BP and to reverse the remodeling of the left ventricle (LV) in spontaneously hypertensive rats (3). In this study we investigated whether spironolactone and/or L-arginine were able to reverse structural remodeling of the LV and aorta in L-NAME hypertension. We also investigated how the reversion of structural alterations is related to BP changes and NO-synthase (NOS) activity alterations.

Methods: Six groups of male adult Wistar rats (n = 9 each) were investigated: controls after 4 (Ctr-4) and 7 (Ctr-7) weeks of experiment, L-NAME (LN-4, 40 mg/kg/day L-NAME for 4 weeks), spontaneous recovery (SR, 4-week L-NAME + 3 weeks placebo), L-arginine-induced recovery (Arg, 4-week L-NAME + 1 500 mg/kg/day L-arginine for 3 weeks) and spironolactone-induced recovery (Spi, 4-week L-NAME + 200 mg/kg/day spironolactone for 3 weeks). BP was measured weekly by tail-cuff plethysmography. After the experiment the left ventricle weight (LVW) and body weight (BW) were determined and LVW/BW was calculated. Hydroxyproline (Hyp) concentration (indicating the level of fibrosis) was determined in myocardial tissue homogenates by measuring absorbance of chromophore developed after oxidation (initiated by chloramine-T reagent and stopped after 50 min by Ehrlich's aldehyde reagent) (4). NOS activity was determined in fresh crude homogenates form the LV and aorta by measuring the conversion of [^{3}H]-citrulline to [^{3}H]-L-arginine and expressed per g of protein (5). In aortic sections embedded in paraffin and stained with haematoxylin/eosin the *media + intima* thickness and inner perimeter were measured and cross-sectional area (CSA) was calculated. The results are expressed as mean ± SEM. Differences were considered significant if $P < 0.05$ (ANOVA-Bonferroni).

Results: L-NAME administration induced hypertension and LVH (**Figure 1**), fibrosis of the LV, and hypertrophy of the aorta (**Figure 2**) and attenuated NOS activity in the LV and aorta (not shown). The reduction of BP and regression of LVH were observed in all recovery groups (SR, Arg, Spi) (**Figure 1**), yet reduction of left ventricular fibrosis and aortic hypertrophy were not observed in any recovery group (**Figure 2**). NOS activity was restored only in the L-arginine and spironolactone group (not shown).

Discussion: Regressive experiments in L-NAME-induced hypertension are rarely accomplished, despite the fact that design of these experi-

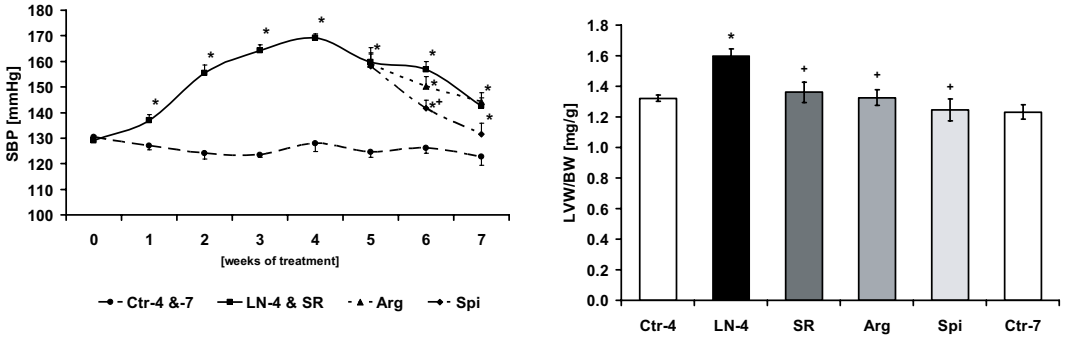


Figure 1 The influence of L-NAME administration, spontaneous recovery after the cessation of L-NAME (in the 4th week) and recovery induced by L-arginine or spironolactone administration on systolic blood pressure (SBP) and relative LV weight (LVW/BW)

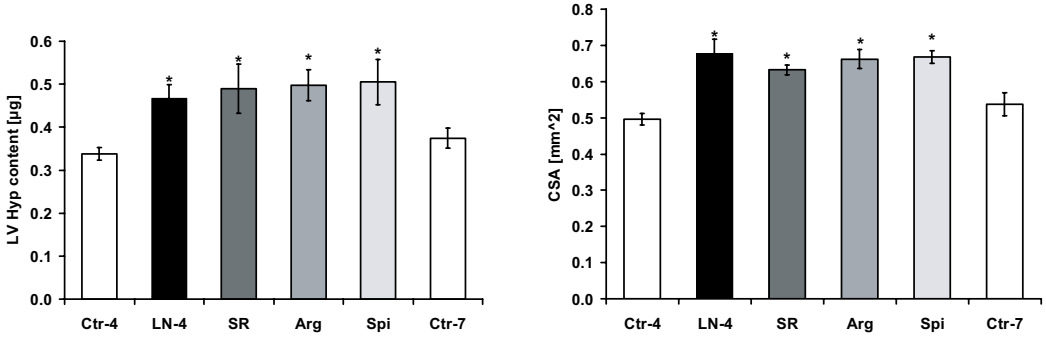


Figure 2 The influence of L-NAME administration, spontaneous recovery after the cessation of L-NAME (in the 4th week) and recovery induced by L-arginine or spironolactone administration on left ventricular Hyp concentration and aortic cross-sectional area (CSA)

ments is similar to a clinical setting. In this experiment, we compared the effect of three week lasting pure cessation of L-NAME administration with additional pharmacological interventions by spironolactone and L-arginine. In spontaneously hypertensive rats L-arginine attenuated already developed LVH (2) and spironolactone reduced fibrosis of the LV (6).

In our study on NO-deficient hypertension, the BP decreased in all recovery groups: spontaneous, L-arginine-induced and spironolactone-induced although the NOS activity in the heart and aorta was only restored in L-arginine and spironolactone groups. It seems that L-NAME is firmly bound in tissues thus blocking the NOS activity for a certain period even after the cessation of L-NAME treatment. Moreover it was shown that various regulatory systems affected by L-NAME-treatment, may be differently modified by spontaneous, L-arginine and spironolactone-induced recovery. The uniform reversal of hypertension and LVH despite different behavior of NOS activity in reversal groups supports the idea that haemodynamic alterations are decisive for LVH maintenance while neurohumoral changes play rather a modulating role.

Interestingly, while LVH regressed in all recovery groups, fibrosis of the LV and hypertrophy of aorta was not reversed in either group. These results are in agreement in L-NAME hypertension where captopril reversed hypertension and LVH, yet the concentrations of collagen, contractile and metabolic proteins of the LV remained increased (7). It seems that the fibrosis of the LV and hypertrophy of aorta are more resistant to conditions inducing regression of pathologic changes and they may need more time to reverse. Preserved level of fibrosis in the regressed heart may result in loss of structural homogeneity leading to increased stiffness of the LV or increased electrical instability during regression of hypertrophy, at least in its initial period. Our results suggest the level of BP is the decisive factor in the process of LVH regression and fibrosis of the LV ventricle and hypertrophy of aorta seem to be more resistant to conditions resulting in regression of LVH.

References

1. Diamond JA, Phillips RA. Hypertensive heart disease. Hypertens Res 2005;28:191–202.
2. Brilla CG, Pick R, Tan LB, et al. Remodeling of the rat right and left ventricles in experimental hypertension. Circulation Res 1990;67:1355–1364.
3. Matsuoka H, Nakata M, Kohno K, et al. Chronic L-arginine administration attenuates cardiac hypertrophy in spontaneously hypertensive rats. Hypertension 1996;27:14–18.
4. Reddy GK, Enwemeka CS. A simlified method for the analysis of hydroxyproline in biological tissues. Clin Biochem 1996;29:225–229.
5. Bernatova I, Pechanova O, Simko F. Effect of captopril in L-NAME-induced hypertension on the rat myocardium, aorta, brain and kidney. Exp Physiol 1999;84:1095–1105.
6. Mandarim-de-Lacerda CA, Pereira LM. The effects of spironolactone monotherapy on blood pressure and myocardial remodeling in spontaneously hypertensive rats: a stereological study. J Biomed Sci 2003;10:50–57.
7. Bernatova I, Pechanova O, Pelouch V, et al. Regression of chronic L-NAME treatment-induced left ventricular hypertrophy: Effect of captopril. J Mol Cell Cardiol 2000;32:177–185.

Acknowledgement: Supported by VEGA 1/3429/06 and APVT 51-027404 grant.

HOMOCYSTEINE AND VITAMINS OF CLASS B ARE ASSOCIATED WITH METABOLISM OF LIPOPROTEINS

[1]Penz P, [1]Vachulová A, [1]Teren A, [1]Čaprnda M,
[2]Blažíček P, [3]Atalay M, [3]Hänninen O, [1]Lietava J.

[1]2nd Internal Department, University Hospital, Bratislava,
[2]Department of Clinical Biochemy,
Hospital of Ministry of Defence, Bratislava,
[3]Department of Physiology of University of Kuopio, Kuopio, Finland

European Heart Journal 2007;28(Abstract Supplement):212.

Introduction: Elevated level of total plasma homocysteine are associated with increased risk of coronary events, stroke and venous thromboembolism (1). Most of the data indicate that hyperhomocysteinemia (HHcy) is not associated with change of plasma total cholesterol but is negatively associated with HDL cholesterol (2). This association could be clinically important because HDL protects from vascular disease by facilitating reverse cholesterol transport and also through its direct antiinflamatory properties (3). Many animal models of hyperhomocysteinemia were developed to examine pathological consequences in vivo. Like HHcy humans, HHcy animals developed endothelial dysfunction, hepatic lipid accumulation and decreased plasma HDL cholesterol with minimal changes in total cholesterol (4).

Methods: Consecutive, unselected Caucasian subjects were included the human study. Subjects were randomly recruited from cardiology ambulance register and control subject were taken from census and were invited by letter to participate. Patients on hypolipidemic medications were excluded from statistical analysis. Analysis of total cholesterol (TC) and triglycerides were realized by enzymatic method. ApoB and apoA1 were measured imunoturbidimetry. HDL cholesterol (HDL) was assessed directly by commercial kit. LDL cholesterol (LDL) was measured directly (Randox, UK). Homocysteine was done with high performance liquid. Serum leves of vitamin B12 and folic acid were measured ELISA method.

Results: Patient with CAD had significantly higher age, were more obese, waist circumference, fasting glucose, systolic blood pressure, homocysteine and lower HDL cholesterol and apolipoprotein A1. We confirmed negative association between homocysteine and apolipoprotein A1 ($r = - 0.119$; $p = 0.023$) and observed positive association with triglycerides ($r = 0.104$; $p = 0,044$). Also assessment of small dense LDL by rate of LDL cholesterol to apolipoprotein showed significant correlation with homocysteine ($r = - 0.145$; 0.005). I further sex specific survey we found, in female population, significant correlation of lipid parameter with homocysteine (Apolipoprotein B100 $r = 0.197$; $p = 0.005$; LDL cholesterol $r = 0.165$; 0.018; Triglycerides $r = 0.191$; 0.006). Group with decreased level of vitamin B12 have significantly decreased apoA1 (1.07 ± 0.137 vs. 1.13 ± 0.185; $p = 0.011$) a non significantly decreased HDL-CH (1.26 ± 0.29 vs. 1.34 ± 0.36; $p = 0.13$). We observed positive correlation between Hcy and waist ($r = 0.159$; $p = 0.002$), negative between Hcy and apoA1 ($r = - 0.13$; $p = 0.013$). Vitamin B12 positively correlated with cholesterol ($r = 0.154$; $p = 0.003$), HDL cholesterol ($r = 0.138$; $p = 0.008$), LDL cholesterol ($r = 0.158$; $p = 0.003$), ApoA1 ($r = 0.193$; $p < 0.0005$). Level o folate negatively correlated with circumference of waist ($r = - 0.119$; 0.023). There was also strong positive correlation between vitamin B6 and level of triglycerides ($r = 0.269$; $p = 0.001$). Patients with hyperhomocysteinemia had elevated systolic (157.03 ± 29.57 vs. 147.03 ± 27.63; $p = 0.01$) and diastolic (95.03 ± 13.08 vs. 90.03 ± 13.75; $p = 0.013$) pressures (in mmHg). Risk of cardiovascular event in 10 years period calculated according to ESC-SCORE was elevated in HHcy group [5.87 ± 5.03 vs. 3.73 ± 3.86 (%); $p < 0.0005$] also in patients with decreased level of vitamin B12 (6.2 ± 5.5 vs. 3.9 ± 3.9; $p = 0.004$). In further analysis elevated levels of homocysteine ameliorate protective effect of apolipoprotein A1 on risk of cardiovascular event in 10 years (**Figure 1**).

Discussion: Several potential mechanisms for the observed relationship between hyperhomocysteinemia and altered lipid metabolism have been proposed. Transcriptional upregulation of cholesterol synthesis attributable to effects of homocysteine on hepatic endoplasmatic reticulum (ER) stress and activation of sterol regulatory binding proteins (SREBP) (4). Increased levels of plasma very low density lipoproteins (VLDL) thought to be result of diminished VLDL lipolysis rather than increased hepatic secretion of VLDL (5). Decreased hepatic and serum lecithin-cholesterol acyltansferase (LCAT) activity (5), which could contribute to reduced HDL cholesterol land diminished VLDL lipolysis. Resent work by Mikael showed that MTHFR mice have altered lipid metabolism including apolipopotein A-I (ApoA-I), apolipoprotein A-IV (ApoA-IV) and cholesterol 7αzhyroxylase (CYP7A1). Hcy reduces the protective lipoprotein ApoA-I, the major protein component of HDL (6). In one study were observed decreased mRNA for ApoA-I in liver and decreased ApoA-I in liver and plasma in MTHFR deficient mice. Finding of reduced ApoA-I expression also in another murine model CBS-deficient mice suggest that it is the elevation of homocysteine, rather than the disturbance in folate metabolism that regulate apolipoprotein A-I. Beyond direct effect on Hcy on apoA1 we observed its additional deleterious effect on total risk of cardiovascular events.

References

1. Homocysteine Studies Collaboration. Homocysteine and risk of ischemic heart disease and stroke: a meta-analysis. J Am Med Assoc 2002;288:2015–2022.
2. Stampfer MJ, Malinow MR, Willet WC, et al. A prospective study of plasma homocyst(e)ine and risk of myocardial infarction in U.S. physicians. J Am Med Assoc 1992;268:877–881.
3. Navab M, Anantharamaiah GM, Fogelman AM. The role of high-density lipoprotein in inflammation. Trends Cardiovasc Med 2005;15:158–161.
4. Werstuck GH, Lentz SR, Dayal S, et al. Homocysteine induced endoplasmic reticulum stress causes dysregulation of the cholesterol and fatty acid biosynthetic pathways. J Clin Invest 2001;107:1263–1273.
5. Namekata K, Enokido Y, Ishii I, et al. Abnormal lipid metabolism in cystathionine-synthase-deficient mice, an animal model for hyperhomocysteinemia. J Biol Chem 2004;51:52961–52969.
6. Devlin AM, Lentz SR. ApoA-I A Missing Link Between Homocysteine and Lipid Metabolism? Circ Res 2006;98:431–433.

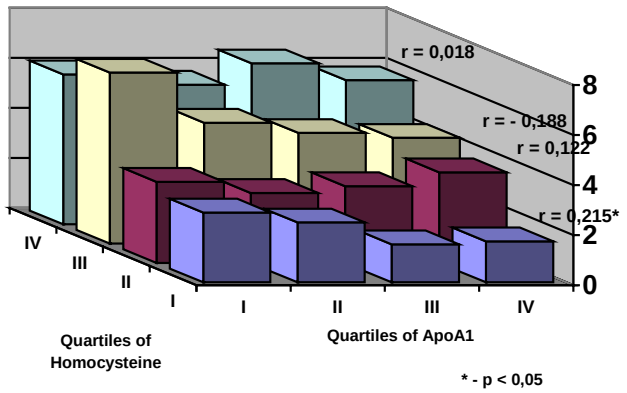


Figure 1 Mutual effect of apolipoproteinA1 and homocysteine on 10 years ESC risk

CAN WE INFLUENCE MANIFESTATION OF METABOLIC SYNDROME BY USING ANTIPSYCHOTIC DRUGS IN PATIENTS WITH SCHIZOPHRENIA?

[1]Vachulova A, [1]Bukovinova P, [1]Penz P, [2]Janoska D, [1]Vohnout B.

[1]2nd Dept. of Internal Medicine, Comenius University, Bratislava,
[2]Dept. of Psychiatry, Pinnel' Hospital, Pezinok

European Heart Journal 2007;28(Abstract Supplement):347.

The metabolic syndrome is clustering of metabolic abnormalities within a single induvidual that is associated with an increased risk of cardiovascular disease. Comorbid metabolic disorders in patients with schizophrenia are underrecognized by many health care professionals and patients. The lack of awarness can contribute to serious morbidity and mortality in patiens with schizophrenia. Although the use of atypical antipsychotics in the treatment of schizophrenia offers many positive benefits and may reduce some of the factors related to the morbidity and mortality of the disorder, these drugs appear to be associated with varying degrees of comorbid metabolic disorder, such as metabolic syndrome and more serious concequences, such as cardiovascular disease. More recently the psychiatric comunity has focused on the propensity that some atypical antipsychotics have to prolong corrected QT (QTc) interval. Current information suggests that concerns regarding the risk of QTc prolongation with the atypical antipsychotics now marketed are minimal. The effect of schizophrenia and antipsychotics on metabolic syndrome are just beginning to be investigated.

The aim of the study was to investigate relationship between pharmacological treatment with olanzapine vs alternative treatment and metabolic syndrome.

We have examined 452 subjects (18 – 87 years old) treated with antipsychotic treatment involved in a cross-sectional multicentric screening in Slovakia aimed to describe prevalence of metabolic syndrome in patients with psychotic disorders. Inclusion criteria – all adult pharmacologically treated patients with schizophrenia. We obtained short structured anamnesis including risk factors (lipids, DM, arterial hypertension, smoking), drug anamnesis – antipsychotic drugs- age of onset, duration of therapy, dosis, presence of side effects. Plasma levels of lipids and blood glucose were measured using standard methods. Blood pressure was measured in sitting position after resting for 15 minutes. Waist circumference was measured using standard method. Metabolic syndrome was defined according to Berlin's modification of NCEP ATP III criteria. Logistic regression model with binary outcome was used to evaluate effect of olanzapine on metabolic syndrome (adjusted to sex and age). Risk is reported as OR and 95% confidence interval.

Results: Baseline assessments for the metabolic syndrome were obtained from 452 patiens with schizophrenia, the average age 40.1 ± 13.0 years, males vs. females 45.8% vs. 54.2%. 115 patients were treated with olanzapine, 337 patients were treated with alternative treatment (ziprasidone, clozapine, chlorpromazine, levomeprazine, perferazine, thioridazine, haloperidol, zuclopentixole, quetiapin, sulpiridum, tiapridal, amisulpride, lithium, zotepine, risperidone, aripiprazole). Basic characteristics of subjects according to olanzapine treatment is in the **table**. The two groups differed in waist circumference, systolic and diastolic blood pressure and mean blood glucose but not in cholesterol, triglycerides, LDL and HDL. Prevalence of metabolic syndrome was significantly higher in olanzapine users (59% vs. 35%). An odds ratio of OR 2.67 (95% CI: 1.7 – 4.2) was found for olanzapine users versus users of other types of antipsychotic drugs.

Conclusion: In our study treatment with olanzapine is related with higher waist circumference, higher systolic and diastolic blood pressure and glycemia and metabolic syndrome. Many psychiatric medications adversely affect body weight and may adversely affect plasma lipid and glucose regulation. Recognizing that some antipsychotics may carry a metabolic liability requires that clinicians consider the metabolic risk before starting therapy with these agents, as well as conduct regular monitoring when patients do require these medications.

Table 1

	Olanzapine +	Olanzapine -	Sign
Age (years)	41.3 ± 12.1	39.8 ± 13.3	NS
Waist circum. Males (cm)	99.4 ± 13.9	93.2 ± 16.6	p < 0.02
Waist circum. Females (cm)	89.6 ± 14.4	83.6 ± 17.8	p < 0.02
SBP	130.57 ± 12.9	124.26 ± 11.7	p < 0.0001
DBP	82.19 ± 9.5	78.92 ± 8.9	p < 0.005
Tchol (mmol/l)	5.06 ± 0.9	4.85 ± 1.1	NS
Triglycerides	1.89 ± 1.3	1.76 ± 0.6	NS
HDL cholesterol	1.10 ± 0.2	1.08 ± 0.3	NS
LDL cholesterol	2.5 ± 0.6	2.45 ± 0.7	NS
Glycemia (mmol/l)	5.24 ± 1.1	5.05 ± 0.9	p < 0.05

MELATONÍN AKO POTENCIÁLNA ANTIHYPERTENZÍVNA TERAPIA

Šimko F, Paulis Ľ.

Ústav patologickej fyziológie, LFUK, Bratislava

J Pineal Res 2007;42:319–322.

Napriek obrovskému pokroku v diagnostike a kontrole hypertenzie adherencia k antihypertenzívnej terapii a dosiahnutie želateľnej úrovne krvného tlaku je v celosvetových podmienkach alarmujúco nízka. Táto skutočnosť stimuluje kardiológiu hľadať nové cesty liečby vysokého tlaku.

Existuje niekoľko úrovní dôkazov, že melatonín sa podieľa na regulácii krvného tlaku. Zistilo sa, že nočná produkcia melatonínu je znížená u hypertenzných pacientov. Na druhej strane podávanie melatonínu znížilo krvný tlak pri niekoľkých animálnych modeloch hypertenzie, u zdravých mužov a žien a u pacientov s arteriálnou hypertenziou. Najsľubnejšie výsledky sa dosiahli u pacientov bez adekvátneho poklesu nočného tlaku krvi (non–diperov), u ktorých je narušený cirkadiárny rytmus variácie krvného tlaku. Melatonín môže ovpyvniť krvný tlak niekoľkými potenciálnymi cestami. Svojím skevendžerovým a antioxidačným efektom zlepšuje melatonín endoteliálnu funkciu, a tým bioaktivitu hlavného vazodilatačného a hypotenzívneho faktora nitric oxidu. Zdá sa, že melatonín interferuje s periférnym aj centrálnym autonómnym nervovým systémom, čoho výsledkom je zoslabenie tonusu adrenergného systému a absolútna alebo relatívna dominancia cholinergného systému. Okrem toho melatonín môže ovplyvňovať krvný tlak aj cestou špecifických melatonínových receptorov lokalizovaných v periférnych cievach, alebo v špecifických oblastiach CNS podieľajúcich sa na udržiavaní cievneho tonusu. Veľká klinická štúdia s melatonínom u hypertenzných pacientov môže dať odpoveď na celý rad otázok, ako je terapeutická dávka a spôsob aplikácie, optimálny výber pacientov s najväčším potenciálnym benefitom, zistenie protektívnych vlastností na remodelované srdce a cievy a interakcie melatonínu s inými antihypertenzívami.

LONG-TERM EFFECTS OF EARLY ADMINISTERED SILDENAFIL AND NO DONOR ON THE CARDIOVASCULAR SYSTEM OF SHR

Kristek F, Koprdova R, Cebova M.

Institute of Normal and Pathological Physiology,
Slovak Academy of Sciences, Bratislava

Journal of Physiology and Pharmacology 2007;58:33–43.

The relation between nitric oxide (NO) and cyclic guanosine monophosphate (cGMP) plays an important role in the regulation of blood pressure. NO induces the formation of intracellular cGMP. cGMP represents a keystone on the way to relaxation not only for the NO, but also for other regulatory systems. Thus an increased level of cGMP may have a preventive effect against hypertension. Sildenafil (Sild), which selectively inhibits phosphodiesterase 5 (PDE5), effectively blocks the degradation of cGMP and thereby increases its level. The beneficial long-term effect of Sild in pulmonary hypertension has been generally accepted. Nevertheless, there is no information concerning long-term effects of Sild on the heart and the geometry of conduit arteries in SHR (an animal model of human essential hypertension). Considering the fact that the pathological changes in the cardiovascular system evoked by hypertension are more difficult to be influenced once the condition has stabilized, our study sought to determine whether a treatment with an NO donor (pentaerythrityl tetranitrate – Petn) and/or inhibitor of PDE5 – Sild, individually or together, started from pre-hypertensive period through to adulthood, could delay the development of pathological changes in the cardiovascular system of SHR. So far, no data about the effect of NO donor and/or Sild administration on the cardiovascular system of young SHR have come to our attention.

Petn (100 mg/kg/day) and Sild (10 mg/kg/day) were administered to SHR individually or together from week 4 (pre-hypertensive period) to week 9 of age. BP was measured in vivo by plethysmographic method. Finally the rats were perfused with a glutaraldehyde fixative (120 mmHg). Carotid (AC) and coronary artery (RS) were processed for electron microscopy (1).

BP of four weeks old SHR did not differ from that of age-matched control normotensive Wistar rats. Rise of BP was observed from week 5 of age. At week 9 of age increase of BP and accompanying cardiac hypertrophy was found. Administration of Petn and Sild individually or together did not affect BP (**Table 1**). Similar effect we observed when Petn was administered to adult SHR (2). These results support the suggestion that in SHR NO-deficiency is not the pivotal stimulus for BP increase either in the pre-hypertensive period or in the stabilized period of hypertension. No literary data are available for comparison with our results regarding a long-term Sild administration to SHR. A modest effect of Sild on blood pressure when administered alone or combined with antihypertensive drugs was observed in humans (3). A mild or negligible effect of Sild on systemic BP was also reported in frequently studied cases of pulmonary hypertension (4). Surprisingly in spite of unchanged BP, administration of Petn and Sild resulted in a preventive effect against cardiac hypertrophy (heart weight to body weight ratio) (**Table 1**). The preventive effect of Sild and Petn on cardiac hypertrophy (restoring certain parameters even to control levels) seems to be more interesting, because BP was not changed and the myocardium still had to surmount increased peripheral resistance. Moreover, it was showed that PDE5 inhibition had no effect on cardiac contractility in humans (3). In light of these findings arose the doubt whether decreased cardiac hypertrophy does not lead to untimely beginning of heart insufficiency. Since Das, et al. (5) observed enhanced mRNA and protein content of inducible and endothelial NO synthase in mouse myocytes after Sild administration, we suggest that the decrease of cardiac hypertrophy could be coupled with antiproliferative effect of increased NO level in myocardium. We did not evaluate the weight of the left and right ventricle individually and cannot exclude that the reduction of cardiac hypertrophy after Sild treatment could also be influenced by reduction of the right ventricle mass due to decrease of pulmonary vascular resistance index as shown in humans and in chronically hypoxic rats (4, 6). Contrary to young SHR, administration of Petn to adult SHR (from 10 to 17 weeks) did not exert any effect on cardiac hypertrophy (2).

Table 1

	BP (mmHg)	BW (g)	HW (g)	HW/BW (mg/g)
Wistar	107 ± 1.0	220 ± 8.4	1.06 ± 0.025	4.60 ± 0.14
SHR	154 ± 1.4**	190 ± 4.5**	1.08 ± 0.028	5.80 ± 0.08**
SHR + PETN	165 ± 5.0**	185 ± 4.9**	0.96 ± 0.026^{+}	4.80 ± 0.14^{++}
SHR + Sildenafil	145 ± 7.5**	191 ± 5.0**	0.95 ± 0.046^{+}	4.37 ± 0.25^{++}
SHR + PETN + Sildenafil	162 ± 6.6**	191 ± 5.0**	0.94 ± 0.023^{+}	4.43 ± 0.20^{++}

BP – Blood pressure, BW – Body weight, HW – Heart weight, HW/BW – Ratio at the end of experiment. Data are means ± SEM. **$P < 0.01$ vs. Wistar rats, $^{+}P < 0.05$, $^{++}P < 0.01$ vs. SHR.

In SHR increase of wall thickness (WT), cross sectional area (CSA) and WT/inner diameter (ID) ratio was found in both arteries. ID and circumferential stress was not changed. Administration of Petn and Sild affected the arteries differently. Increase of CSAs was found in both arteries but in RS, increase of ID without an increase of WT resulted in increased WT/ID and circumferential stress. In AC, increase in ID were accompanied by appropriate increase of WT and, thereby, WT/ID ratio and circumferential stress remained unchanged. Taking into account the evidence that decrease of circumferential stress inhibits experimental atherogenesis (7), we suppose that the opposite could aggravate the pathological processes in the arterial wall of RS.

Summarising: In the light of the above-mentioned findings, we suggest that administration of Petn and Sild to SHR from the pre-hypertensive period through adulthood did not result in a beneficial effect either on the myocardium or on the geometry of the carotid and coronary artery.

References

1. Kristek F. Brit J Pharmacol 2000;130:450–456.
2. Kristek F, et al. Physiol Res 2003;52:709–717.
3. Brindis RG, Kloner RA. Am J Cardiol 2003;92:26M–36M.
4. Michelakis ED, et al. Circulation 2003;108:2066–2069.
5. Das A, et al. J Biol Chem 2005;280:12944–12955.
6. Andersen CU, et al. Europ J Pharmacol 2005;510:87–96.
7. Thubrikar MJ, Robicsek F. Ann Thorac Surg 1995;59:1594–1603.

Poznámka redakcie: Súhrny z prednášok z vedeckých podujatí neprechádzajú jazykovou ani obsahovou korektúrou, preto za ich správnosť redakcia nezodpovedá.