References

1. Roper VL, Go AS, Lloyd Jones DM, Benjamin EJ, Berry JD, Borden WB, et al. On behalf of the American Association Statistics Committee and Stroke Statistics Subcommittee Heart Disease and Stroke Statistics-2012 Update: a report from the American Heart Association. Circulation 2012; 125: e2-e220. [CrossRef]
2. Arıkan İ, Metintaş S, Kalyoncu C, Yıldız Z. The cardiovascular disease risk factors knowledge level (CARRF-KL) Scale: a validity and reliability study. Turk Kardiyol Dern Ars 2009; 37: 35-40.
3. Oğuz S, Cesur K, Koç S. Coronary heart diseases risk factors in the determination of nursing students. Turk Soc Cardiol Turkish J Cardiol Nursing 2011; 1: 18-21.
4. Webb E, Ashton H, Kelly P, Kamali F. Patterns of alcohol consumption, smoking and illicit drug use in British university students: in faculty comparisons. Drug Alcohol Depend 1997; 47: 145-53. [CrossRef]
5. Global Recommendations on Physical Activity for Health. The World Health Organization; 2010.p.9-11.
6. Metintaş S, Buğrul N, Öztürk A, Kalyoncu C. Cardiovascular risk factors knowledge levels among high school students at Sivrihisar. 15. National Public Health Congress; 2-6.10.2012; Bursa; Accessed on: 31.10.2012. Available from: URL: htt///halksagligiokulu.org/anasayfa/components/com_booklibrary/ebooks/15.UHSK%20K%C4%B0TAP_14_10_12.pdf

Address for Correspondence/Yazışma Adresi: Dr. Hilal Uysal
İstanbul Üniversitesi, Florence Nightingale Hemşirelik Fakültesi, Tıbbi Hemşirelik Bölümü, Abide-i Hurriyet Cad. No.: 82 Şişli, İstanbul-*Türkiye*
Phone:+90 212 440 00 00 /27028
Fax: +90 212 224 49 90
E-mail: hilaluysal@gmail.com, hilaluysal@istanbul.edu.tr
Available Online Date/ Çevrimiçi Yayın Tarihi: 23.10.2013

doi:10.5152/akd.2013.249

Cardiohepatic interactions in heart failure

Kalp yetersizliğinde kardiyohepatik etkileşim

To the Editor,

Heart failure (HF) is a fatal and progressive disease, driven by cardiac dysfunction (1). The syndrome of HF is characterized by organ cross-talks, since, heart is central to hemodynamics of many organs both in the form of distributing the oxygenated blood and delivering deoxygenated blood in order to send it to lungs . Among many organ cross-talks in the syndrome of HF, interaction between heart and kidney is relatively well established and defined as "cardiorenal syndrome" (2). Hepatic involvement in the form of cardiohepatic interaction has also been described in patients with chronic HF (3, 4).

In the recent analysis of the SURVIVE database (5), cardiohepatic dysfunction was present in about a half of this cohort of patients with acute decompensated heart failure (ADHF). Furthermore, it seems liver function tests behave as surrogates of systemic hemodynamics. In the analysis, cholestasis associated biochemical markers were associated with signs of systemic congestion and elevated right-sided filling pressure, while biochemical markers of liver cytolysis were associated with clinical signs of hypoperfusion. Hence, there are two hypothetical modes of cardio-hepatic interaction proposed within the light of the recent paper: 1) in the form of either predominantly HF-induced cholestasis or 2) predominantly HF-induced liver cell cytolysis. In addition to these two discrete modes of involvements, cardiohepatic dysfunction was shown to be associated with poor long term outcome.

Elevated plasma alkaline phosphatase (AP), alone or in conjunction with abnormal transaminase levels was present in 20% of patients with ADHF at baseline. High basal AP levels were associated with systemic congestion and elevated right-sided filling pressure, including peripheral edema, ascites, tricuspid regurgitation and high plasma levels of creatinine and BNP. The results were confirmatory to the previous studies with pathophysiological background (3, 4). Although, the mechanism by which systemic congestion and elevated right-sided filling pressure causes release of biochemical markers of cholestasis remains uncertain, it is possible that in patients with ADHF, the markedly elevated right-sided filling pressure can possibly be transmitted to centrilobular liver sinusoids which could compress any collapsible structure within the lobule, including bile canaliculi and ductules (Fig. 1). Raised hydrostatic pressure in liver sinusoids can potentiate the compression along with enlargement of liver cells. Such pathophysiology could yield compression of bile ducts and change the direction of bile flow (including AP) towards the blood (5). Hence, AP stands as a biomarker of liver congestion and reflects the extent of right-sided filling pressure in ADHF patients. Along with this mechanism, elevated AP was not associated with poor short-term outcome in the study, since, decongestive therapy has the potential to decompress biliary tract and divert bile flow and hence causing normalization of AP without liver cell death.

In the study, a second discrete profile was characterized by elevated transaminase levels, which were associated with signs of hypoperfusion, including hypotension, tachycardia and cold extremities. Hepatic cytolysis, which yields elevations of alanine and aspartate transaminases (ALT/AST in the study), could potentially be driven by hypoperfusion and/or hypooxygenation of the liver cells of the centrilobular region ("nutmeg liver") that are known to be far away from the dual circulatory supply of the hepatic artery and portal veins. It seems liver ischemia, characterized by elevated liver enzymes, secondary to compromised perfusion, caused by rapid deterioration of cardiac function influenced the in-hospital outcome of the patients with ADHF negatively.

In conclusion, two discrete profiles of cardiohepatic interaction, identified in the study, seem to be critically important targets in order for physicians to tailor the therapy of patients with ADHF.

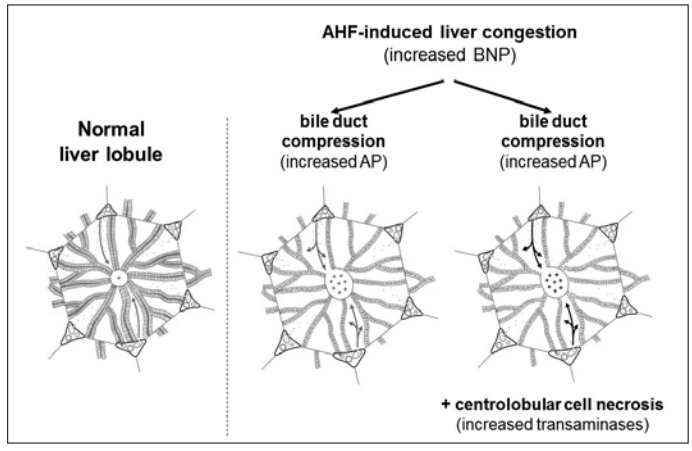

Figure 1. Hepatic microstructure
(Reproduced from Nikolau M, Parissis J, Yilmaz MB, Seronde MF, Kivikko M, Laribi S, et al. Liver function abnormalities, clinical profile, and outcome in acute decompensated heart failure. Eur Heart J 2013; 34: 742-9. with permission of Oxford University Press)

Mehmet Birhan Yılmaz[1,4], Maria Nikolaou[2,4], Alexandre Mebazaa[3, 4]
[1]Department of Cardiology, Faculty of Medicine, Cumhuriyet University, Sivas-*Turkey*
[2]Heart Failure Unit, 2nd Cardiology Department, Attikon University Hospital, University of Athens, Athens-*Greece*
[3]AP-HP, Department of Anesthesiology and Critical Care, Hôpitaux Universitaires Saint Louis Lariboisière, F-75475 Paris-*France*
[4]GREAT network

References

1. Dickstein K, Cohen-Solal A, Filippatos G, McMurray JJ, Ponikowski P, Poole-Wilson PA, et al. ESC Committee for Practice Guidelines (CPG). ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the diagnosis and treatment of acute and chronic heart failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). Eur J Heart Fail 2008; 10: 933-89. [CrossRef]
2. Ronco C, McCullough P, Anker SD, Anand I, Aspromonte N, Bagshaw SM, et al. Acute Dialysis Quality Initiative (ADQI) consensus group. Cardio-renal syndromes: report from the consensus conference of the acute dialysis quality initiative. Eur Heart J 2010; 31: 703-11. [CrossRef]
3. Naschitz JE, Slobodin G, Lewis RJ, Zuckerman E, Yeshurun D. Heart diseases affecting the liver and liver diseases affecting the heart. Am Heart J 2000; 140: 111-20. [CrossRef]
4. Lau GT, Tan HC, Kritharides L. Type of liver dysfunction in heart failure and its relation to the severity of tricuspid regurgitation. Am J Cardiol 2002; 90: 1405-9. [CrossRef]
5. Nikolaou M, Parissis J, Yılmaz MB, Seronde MF, Kivikko M, Laribi S, et al. Liver function abnormalities, clinical profile, and outcome in acute decompensated heart failure. Eur Heart J 2012; 34: 742-9. [CrossRef]

Address for Correspondence/Yazışma Adresi: Dr. Mehmet Birhan Yılmaz
Cumhuriyet Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, 58140, Sivas-*Türkiye*
Phone:+90 346 258 18 05
Fax: +90 346 219 12 68
E-mail: cardioceptor@gmail.com
Available Online Date/ Çevrimiçi Yayın Tarihi: 23.10.2013

doi:10.5152/akd.2013.250

Long-term prostaglandin E1 use in newborns with duct-dependent congenital heart diseases: one year experience of a tertiary neonatal intensive care unit in Turkey

Duktus-bağımlı konjenital kalp hastalıklı yenidoğanlarda uzun süreli prostaglandin E1 kullanımı: Türkiye'de üçüncü basamak bir yenidoğan yoğun bakım ünitesinin bir yıllık deneyimi

To the Editor,

Prostaglandin E1 (PGE1) is used in patients with duct-dependent congenital heart disease (CHD) to keep ductus open until intervention (1). Duration of infusion is often short but, sometimes prolonged therapy may be necessary (2). It has been reported that mostly observed complications of long term PGE1 therapy are cortical hyperostosis (CH), gastric outlet obstruction, fluid electrolyte disturbances, and platelet dysfunction (3-5).

In this retrospective case series, 21 newborns with duct-dependent CHD and received PGE1 infusion for longer than 2 weeks were evaluated (Table 1). The mean birth weight and gestational age of the patients were 2982±740 grams and 39.1±2.1 weeks, respectively. The median age of initial PGE1 infusion was three days (1-17). The mean initial dose of PGE1 was 0.022±0.05 mcg/kg/min, and modified accordingly to keep the oxygen saturation above 75%. Average and cumulative dose during treatment were 0.026±0.09 mcg/kg/min and 2219±567 mcg/kg, respectively. The median (min-max) length of the PGE1 therapy was 28 (17-115) days.

Observed complications during long-term PGE1 therapy were noted. The signs of gastric outlet obstruction developed in two patients; at 1st case, on 29th day of therapy (cumulative dose of 3474 mcg) and at 2nd case, on 32nd day of therapy (cumulative dose: 4285 mcg). Ultrasonography (USG) showed elongation of the antropyloric channel with increase in wall thickening (Fig. 1). Hypokalemia (serum K level <3.5 mEq/L) developed in 12 patients on 14-25 days of PGE1 therapy. Three patients on additional furosemide therapy had more prominent hypokalemia. Marked hypokalemia (serum K 1.9-2.7 mEq/L) and metabolic alkalosis (bicarbonate concentrations 28-32 mmol/L) developed in four patients with PGE1 dose of 0.035-0.056 mcg/kg/minute. In another patient, with the PGE1 dose of 0.05 mcg/kg/minute, persistent hyponatremia (serum sodium 120-129 mEq/L) with natriuresis (urine Na: 121.2 mmol/L) were observed after 24 days of PGE1 therapy. Polyuria (8 ml/kg/

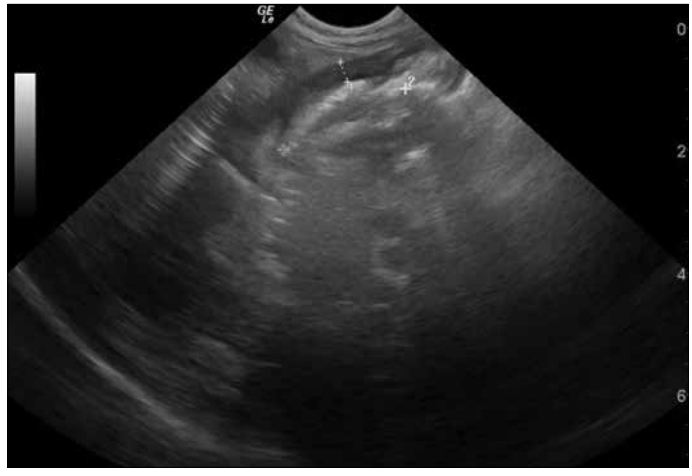

Figure 1. Abdominal ultrasonography of one of the patients showing elongation of the antropyloric channel with increase in wall thickening

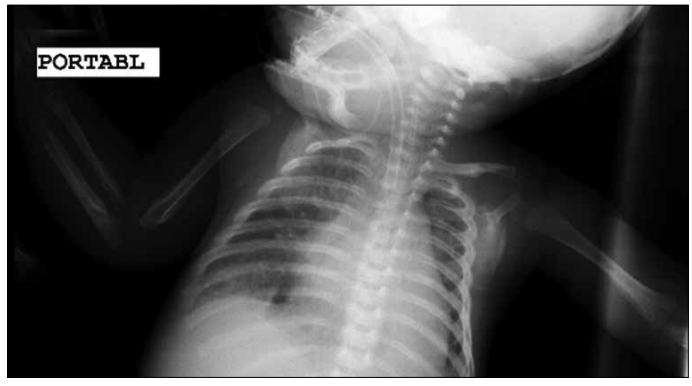

Figure 2. Cortical thickening (hyperostosis) and periosteal reaction on humerus bilaterally and right ulna and radius