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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]

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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/

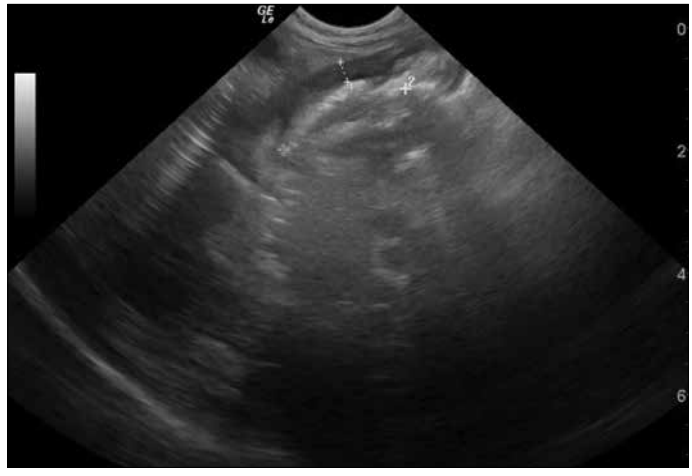

Figure 1. Abdominal ultrasonography of one of the patients showing elongation of the antropyloric channel with increase in wall thickening

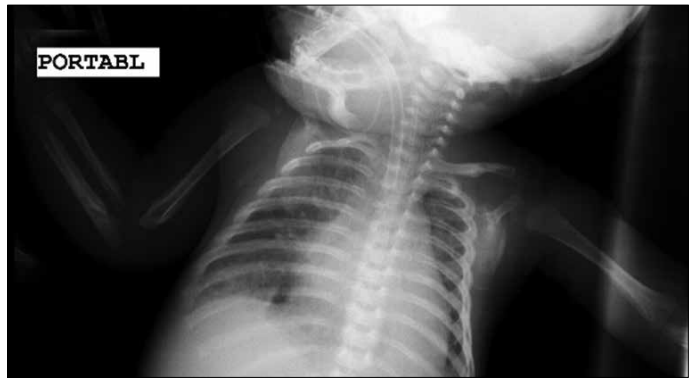

Figure 2. Cortical thickening (hyperostosis) and periosteal reaction on humerus bilaterally and right ulna and radius

Table 1. Clinical characteristics of the patients

Patient Number	Diagnosis	Average PGE1 dose, mcg/kg/ minute	Duration, day	Cumulative PGE1 dose µg/kg	Side effects	Intervention	Mortality
Duct-dependent pulmonary blood flow (n=15)							
1	P Atr,VSD	0.026	30	1125	Fever, hypokalemia, gastric outlet obstr.	Mod B-T shunt	Died postop
2	Critical PS, hypo RV	0.027	18	699	Fever	Mod B-T shunt	Well at 1 year
3	ToF, APCA	0.050	27	1943	Apnea, rash, CH, pseudoBartter synd.	Mod B-T shunt	Well at 6- month
4	PAtr,VSD	0.026	38	1422	Fever, hypokalemia,	Mod B-T shunt	Died postop
5	PAtr, ASD, VSD	0.017	19	465	(-)	Mod B-T shunt	Well at-month
6	ToF, PAtr, PAPVC	0.056	33	2375	Apnea, convulsion hypokalemia, CH	Died preop	
7	PS, hypo RV	0.021	27	777	(-)	Mod B-T shunt	Well at 12-month
8	PS, DORV	0.023	28	927	Fever, hypokalemia	Mod B-T shunt	Died postop
9	P Atr,VSD, double aortic arcus	0.018	18	466	(-)	Mod B-T shunt	Died postop
10	P Atr, MAPCA	0.040	41	2361	Apnea, jitteriness, hypokalemia, CH	Died preop	
11	P Atr,Tri. Atr, DORV,VSD	0.030	47	2030	Fever, hypokalemia, CH	Died preop	
12	ToF, ASD	0.026	24	1218	(-)	Clinical follow up	Well at 6 mo
13	P Atr, DORV	0.020	20	616	(-)	Mod B-T shunt	Well at 12 mo
14	P Atr, AVSD	0.021	110	3167	Fever, CH	Stent implant.	Well at 6 mo
15	P Atr, Tri. Atr, Hypo PA, VSD	0.040	35	2016	Apnea, fever,	Hypokalemia	Died preop
Duct-dependent systemic blood flow (n=6)							
16	DIRV, Hypo LV, Ao coarc, VSD	0 .030	39	1740	Fever, gastric outlet obst, hypokalemia	Died preop	
17	HLHS	0.029	26	1088	Fever, jitteriness, hypokalemia	Norwood Stage 1	Died postop
18	Ao coarc,VSD, isthmic hypoplasia	0.010	18	259	(-)	Coarc repair, PB, PDA lig.	Well at 16 mo
19	HLHS	0.037	30	1636	Fever, rash, hypokalemia	Norwood Stage 1	Died postop
20	HLHS	0.035	90	3515	Fever, jitteriness, hypokalemia, CH	Norwood Stage 1	Died postop
21	Ao int, DORV, VSD	0.025	115	3000	Fever	Clinial follow up	Well at 6 mo

*Ao int - aortic interruption, APCA - aorticopulmonary collateral artery, ASD - atrial septal defect, CH - cortical hyperostosis, Coarc - coarctation, DIRV - double inlet right ventricle, DORV - double outlet right ventricle, HLHS - hypoplastic left heart syndrome, Hypo LV - hypoplastic left ventricle, Hypo RV - hypoplastic right ventricle, MAPCA - multiple aorticopulmonary collateral artery, Mod B - T shunt- modified Blalock-Taussig shunt, Lig - ligation, P Atr - pulmonary atresia, PAPVC - partial anomalous pulmonary venous connection, PB - pulmonary banding, PS - pulmonary stenosis, ToF - tetralogy of Fallot, Tri. Atr - tricuspid atresia, VSD - ventricular septal defect

hours) and hypercalciuria (1.3 µmol/mmol creatinine) were also noted. Renal USG showed increased parenchymal echogenicity. We found a significant negative correlation between average PGE1 dose and serum K levels (r=-0.710, p=0.01) and positive correlation between average PGE1 dose and bicarbonate levels (r=0.496, p=0.04).

Symptoms of CH were observed in eight patients with swelling and tenderness in limbs. Direct X ray showed cortical thickening (hyperostosis) and periosteal reaction on humerus bilaterally, right ulna and radius (Fig. 2). These findings emerged at 25-55 days of PGE1 therapy. At these time points, alkaline phosphatase levels of these six patients were high in range of 525-1659 U/L.

White blood cell counts and average PGE1 dose were positively correlated on day 10 and 20 of the infusion; r=0.58, p=0.01 and r=0.54, p=0.04, respectively. Platelet counts were negatively correlated with average PGE1 dose (day 10; r=-0.46 p=0.03, day 20; r=-0.52 p=0.03, day 30; r=-0.29 p=0.44).

In conclusion, although PGE1 is a life-saving drug in patients with duct dependent CHD, it has many side effects especially when used for longer periods. The physicians should monitor the patients accordingly. If possible, early surgical intervention or transfer to another multidisciplinary centre of the patients with duct-dependent CHD seems to be essential for early discontinuation of PGE1 infusion.

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References

1. Caballero S, Torre I, Arias B, Blanco D, Zabala JI, Sanchez Luna M. Secondary effects of prostaglandin E1 on the management of hypoplastic left heart syndrome while waiting for heart transplantation. An Esp Pediatr 1998; 48: 505-9.
2. Teixeria OH, Carpenter B, McMurray S, Vlad P. Long term prostaglandin E1 therapy in congenital heart defects. J Am Coll Cardiol 1984; 3: 838-43. [CrossRef]
3. Kosiak W, Swieton D, Fryze I, Aleszewicz-Baranowska J, Duklas M, Chojnicki M. Gastric outlet obstruction due to an iatrogenic cause in a neonatal period - report of two cases. Ultraschall Med 2009; 30: 401-3. [CrossRef]
4. Talosi G, Katona M, Turi S. Side effects of long term prostaglandin E (1) treatment in neonates. Pediatr Int 2007; 49: 335-40. [CrossRef]
5. Iyú D, Jüttner M, Glenn JR, White AE, Johnson AJ, Fox SC, et al. PGE1 and PGE2 modify platelet function through different prostanoid receptors. Prostaglandins Other Lipid Mediat 2011; 94: 9-16. [CrossRef]

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Adult overweight and cardiovascular system: risk or disease?

Yetişkin kilolu ve kardiyovasküler sistem: Risk veya hastalık mı?

To the Editor,

Obesity is a major health problem of modern civilization that presents high risk for development of cardiometabolic diseases. Effects of adiposity are mediated through conventional risk factors and also act as independent predictor for tissue and organ damages. However, it is not clear whether overweight persons with body mass index from 25 to 29.99 kg/m^2 have the same risk for development of diseases as obese persons with body mass index above 30 kg/m^2. Both conditions are marked with increased volume of adipose tissue with altered value of adipokines and activated inflammation and most studies included obese persons. Not so long ago, being overweight was considered as a sign of good social status and health, today attitudes are changing dramatically due to new insights into the adipose tissue as an endocrine organ. Therefore, it is necessary to conduct research including overweight persons to find out the level of these pathologic mediators, the changes they induce and the level of risk for development of cardiovascular diseases in order to know what to recommend to our patients.

According to latest studies, the number of overweight and obese people is growing progressively in all age groups and the number of overweight persons has increased in comparison to the number of obese persons. Obesity is not only associated with development of conventional risk factors for cardiovascular diseases, it is also an independent predictor of heart failure in general population (1).

While it has been confirmed that a number of diseases and conditions are obesity-related, health consequences of being mildly to moderately overweight remain controversial and need thorough investigation. For example, only few existing evidence indicate that overweight also carries increased risk for heart failure (2). In overweight persons increased volume of adipose tissue as well as its distribution directly affect cardiac structure and function through neurohumoral factors associated with changes in preload and afterload, hyperdynamic circulation, chronic volume overload, peripheral vascular resistance, adipokines related hypertrophic effect and myocardial matrix remodeling and result in left ventricular mass growth (3). Left ventricular diastolic dysfunction and subclinical right ventricular dysfunction, represent impairment in the filling properties of the heart as a result overweight/obesity related cardiovascular risk factors and cardiac structural changes, that becomes more pronounced with the increase in body weight (4-6).

It can be concluded that being overweight is a condition where changes in adipose tissue composition and biochemical activity occur and it present risk for early cardiovascular changes. Due to high rates of morbidity and mortality from cardiovascular disease and the epidemic proportion of overweight in population, it is important to conduct further investigations in this area to clarify pathophysiologic processes in this pre-obesity stage and to prepare effective prevention and treatment strategies.

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References

1. Contaldo F, Pasanisi F, Finelli C, de Simone G. Obesity, heart failure and sudden death. Nutr Metab Cardiovasc Dis 2002; 12: 190-7.
2. Loehr LR, Rosamond WD, Poole C, McNeill AM, Chang PP, Folsom AR, et al. Association of multiple anthropometrics of overweight and obesity with incident heart failure: the Atherosclerosis Risk in Communities study. Circ Heart Fail 2009; 2: 18-24. [CrossRef]
3. Selthofer-Relatic K. Obesity and cardiomyopathy. Cardiol Croat 2012; 4: 204-8.
4. Russo C, Jin Z, Homma S, Rundek T, Elkind MS, Sacco RL, et al. Effect of Obesity and overweight on the left ventricular diastolic function: a community-based study in an elderly cohort. J Am Coll Cardiol 2011; 57: 1368-74. [CrossRef]
5. Turkbey EB, McClelland RL, Kronmall RA, Burke GL, Bild DE, Tracy RP, et al. The impact of obesity on the left ventricle: the Multi-Ethnic Study of Atherosclerosis (MESA). JACC Cardiovasc Imaging 2010; 3: 266-74. [CrossRef]
6. Wong CY, O'Moore Sulivan T, Leano R, Hukins C, Jenkins C, et al. Association of subcliical right ventricular function with obesity. J Am Coll Cardiol 2006; 47: 611-6. [CrossRef]

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