SERUM IGF–1 LEVELS OF PATIENTS UNDERWENT TO PERCUTAN TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA)

Oktay SARI[1], Ümit AYDOĞAN[1], İnci ÇELİKKOL[1], Halil AKBULUT[1], Cemal SAĞ[2], Mehmet YOKUŞOĞLU[2], Kenan SAĞLAM[1], Kurtuluş ÖNGEL[3],

[1] Gülhane Military Medical Academy, Department of Family Medicine, Ankara, Turkiye; [2] Gülhane Military Medical Academy, Department of Cardiology, Ankara, Türkiye; [3] Tepecik Research and Implamentation Hospital, Department of Family Medicine, İzmir, Türkiye

Rezumat

Introducere. *Obiectivul studiului este de a determina relaţia dintre factorii de creştere similari insulinei (IGF-1) şi ateroscleroza coronariană.*

Materiale şi metode. *În studiu au fost incluşi 30 de pacienţi cu angiografie coronariană normală şi 43 de pacienţi supuşi angioplastiei coronariene transluminale percutanate (PTCA). Grupurile de studiu au fost formate din bolnavi care s-au adresat la Departamentul de Cardiologie al Facultăţii de Medicină din cadrul GATA. Probele de sânge au fost recoltate din artera coronariană în prima etapă a angiografiei, înainte de introducerea substanţei de contrast.*

Rezultate. *Nivelurile medii ale IGF-1 în primul grup cu angiografie coronariană normală şi în al doilea grup supus PTCA au fost 222,05, respectiv 686,15. Rezultatele erau semnificative sub aspect statistic. O creştere semnificativă din punct de vedere statistic în nivelurile IGF-1 a fost determinată în cel de-al doilea grup (p=0,000). De asemenea, variaţiile din rezultatele electrocardiografice (ECG) au fost semnificative în cadrul aceluiaşi grup (p=0,002).*

Concluzii: *Nivelurile IGF-1 ale pacienţilor supuşi PTCA au fost mai mari decât rezultatele studiilor similare precedente, acest lucru fiind determinat de modul în care am recoltat probele de sânge, adică direct din artera coronariană. Considerăm că această creştere a nivelurilor IGF-1 este generată de mecanismul de compensare locală, declanşat în inima afectată de ischemie.*

Cuvinte-cheie: *factori de creştere similari insulinei (IGF-1), angioplastie coronariană transluminală percutanată (PTCA), insuficienţă coronariană.*

Introduction

Several factors play role in the physiopathology of coronary aterosclerosis and endohelium dysfunction, lipids, genetic factors, environmental and metabolic factors plays mediator role. Experimental and clinical studies indicate that growth hormone (GH) and insulin like growth factor–1 (IGF–1) play a role in the development of the cardiovascular system [1–3].

IGF–1 has a similar structure as proinsulin, it is a polypeptide consisting of 70 amino acids. IGF–1 and its receptors are found in various tissues, such as myocard, vessel endothelium and vessel smooth muscles. It has been demonstrated that IGF–1 has endocrine, paracrine and otocrine effects via a complex system [1].

It is known that IGF–1 has a positive effect over the development of cardiac structures and function of contraction and fraction of ejection. According to previously done experimental studies revealed that IGF–1 has increased cardiac contraction and performance, at the same time decreasing cardiac wall stress [2].

IGF–1 is a primary mediator which demonstrates the effects of growth hormone (GH) and has a regulatory function of cellular proliferation, differentiation, and apopytosis. It is also known that deficiencies of GH and IGF–1 are closely related with early atherosclerosis and high cardiovascular disease mortality rate [1].

It is also apparent that hypopituitarism with GH and IGF–1 deficiencies causes endothelial dysfunction and premature atherosclerosis and these cases are reversible with GH replacement [4]. Cardiovascular diseases' mortality is doubled in GH/IGF–1 deficiencies [5]. Furthermore, recent epidemiologic studies demonstrate that subnormal IGF–1 levels increase the risk of acute myocardial infarct (AMI) and carotid atherosclerosis. It is thought that IGF1's cardiovascular disease protection effect is because of its effect over myocyte survival, atherosclerotic plaque stability and endothelial function [6].

While insulin and GH stimulate IGF–1 secretion, interleukin–1 (IL–1) and cortisol inhibit it [7–8]. Additionally, IGF–1 regulates glucose metabolism by lowering insulin levels and increasing insulin sensitivity and it effects lipid profiles in a positive way [9].

According to studies completed since 1992, GH and IGF–1 are in series of events related with heart development and hypertrophism, which are related to cardiovascular diseases and risk factors (hypertrygliseridemia, obesity and glucose intolerance[10–11].

Both IGF–1 and IGF–2 take a role in cardiac protein synthesis stimulation, in the level of plasma stability and act like a buffer in the protein synthesis [12].

Purpose of this study is to determine the increase in the blood levels of IGF–1 due to coronary artery disease.

Material and Method

Elective coronary angiography was administered in this study to 73 participants suspect of having coronary artery disease and not undergoing any medical treatment. There are two categories of participants, participants who had some type of coronary artery lesions (atherosclerosis) and participants who were completely normal. According to this, 30 participants were in group 1, or the completely normal group and group 2 was composed of 43 participants who had atherosclerosis.

According to the JNC–7 (The Seventh Report of the Joint National Committee) guide, participants who had artery blood pressure of more than 140/90 mm/Hg. and ADA (American Diabetes Association) the diagnosis of diabetes mellitus which is accepted as a hunger blood sugar level of over 126 mg/dl were not included to our study.

The blood samples were collected in the first phase of angiography and just before contrast substance delivery, and after PTCA guiding catheter was placed to coronary artery. A blood sample of approximately 5.0 mL was placed into sterile preservative-free test tubes. The blood was centrifuged at a speed of 2.500 rpm for 45 minutes. The serums obtained were stored in -80C deep-freeze conditions until the study day. The samples obtained in one month were used in a maximum of 40 days.

Serum levels of IGF–1 were determined by IRMA techniques and Nonextraction IGF–1 IRMA (Diagnostic Systems Laboratories-USA) in consecutive groups. Serum glucose level has been calculated from these serum samples the day they were taken with the help of photometric-colorimetric kit.

In statistitical analyses continuous variables were presented with mean-standard deviation and other variables with percentage. Chi-square test and Mann Whitney U test for transient variables and continuous variables were used, respectively.

Results

16 female (21,9%) and 57 male (78,1%) individuals were included to the study No significant difference was observed between groups in terms of sex (p=0,1666) (Table 1). Age disturbances of groups were shown in (table 2).

Table 1

Comparison of groups according to gender

GROUPS	*gender*				*Total*		*p*
	female		*male*				
	n	%	n	%	n	%	
Normal	9	30,0	21	70,0	30	100	0,163
PTCA	7	16,3	36	83,7	43		
Total	16	21,9	57	78,1	73	100	

Table 2

Comparison of groups according to age disturbance

Groups		*AGE SUBGROUPS*			*Total*	*p*
		Under 45 year	*45-65 year*	*Over 65 year*		
Normal	n	8	13	9	30	0.035
PTCA	%	26,7	43,3	30,0	100,0	
	n	4	18	21	43	
Total	%	9,3	41,9	48,8	100,0	
	n	12	31	30	73	
	%	16,4	42,5	41,1	100,0	

Also no significant difference was observed between groups according to kidney(urea, creatinine), liver function tests (AST, ALT) and lipid profile (cholesterole, triglyceride, HDL, LDL) (table 3).

Table 3

Comparison of renal functions, hepatik functions tests, lipid profile among the groups

Groups		*n*	*Mean*	*Standart deviation*	*p*
Urea	Normal	30	33,00	10,31	0.231
	PTCA	43	36,40	13,70	
Creatin	Normal	30	,9967	,1866	0.735
	PTCA	43	1,0140	,2479	
AST	Normal	30	20,37	6,40	0.219
	PTCA	43	26,91	33,56	
ALT	Normal	30	22,03	11,81	0.454
	PTCA	43	24,28	13,48	
Cholesterol	Normal	30	184,77	40,57	0.582
	PTCA	43	190,07	39,97	
Triglyceride	Normal	30	147,70	58,70	0.600
	PTCA	43	140,23	60,67	
HDL	Normal	30	44,27	10,65	0.696
	PTCA	43	43,30	9,86	
LDL	Normal	30	106,92	33,33	0.060
	PTCA	43	121,51	29,99	

Average levels of IGF–1 were 496.66+/-376.70; ıt was 225.05+/-203.25 in group 1 686,15+/-353,95 in group 2. Levels of IGF–1 were significantly higher in group 2 (table 4).

Table 4
Comparison of IGF–1 levels

GROUPS	*n*	*mean*	*Standart deviation*	*mini-mum*	*maxi-mum*	*p*
Normal	30	225.05	203.25	9.10	868.50	
PTCA	43	686.15	353.95	79.90	1415.00	<0.001
TOTAL	73	496.66	376.70	9.10	1415.00	

According to ischemic alterations in electrocardiographic examination, findings were significantly apparent in group 2 (table 5).

Table 5
Comparison of the groups in the view of ischemic changes at EKG

Groups		*Ischemia*		*Total*	*p*
		+	-		
Normal	n	6	24	30	0.002
PTCA	%	20,0%	80,0%	100,0%	
	n	24	19	43	
Total	%	55,8%	44,2%	100,0%	
	n	30	43	73	
	%	41,1%	58,9%	100,0%	

Discussion

Recent epidemiologic studies concluded that IGF-1 levels in patients with a diagnois of MI is found to be lower due to the control group in two cross-sectional studies. IGF–1 levels of patients with a diagnose of acute coronary artery disease found to be lower than the control group.

In two similar evidence based studies IGF–1 levels of patients who were hospitalized with a diagnose of AMI is our found to be lower than the control group [8–13]. In the results of these studies the levels of IGF binding protein 3 is found to be significantly higher in AMI cases [14,15]. In Dan Monika study which is the only prospective study, the relative risk of coronary heart disease onset is found 1.65 in patients with a low IGF–1 level. According to Dan Monica study results, the partial risk of coronary artery disease has been determined as 4.07 for IGF–1 level of low 25% and IGF-binding protein 3 high 25% [16]. IGF–1 induces vasculary smooth muscle proliferation and migration. In study models after vascular amate intimal hiperplazi develops due to decreased IGF–1 levels [17, 18]. IGF–1 and other sonata staton analog G Factors causes restenosis after angioplasty [19–20]. Its known that growth hormone realizes its effects such as mitogenic effect true IGF–1 [6]. Its an excellent indicator to determine GH level indirectly due to its long half life and diurnal stability compared to GH. Serum IGF–1 levels decreased by age and for people over age of 65, ıts levels are 50% less than the young adults [21].

Mean level of IGF is 560.27 for patients between age of 45–65 years. Patients older than 55 years, mean level turns out to be 489.87. However it is insignificant and our result is discordant with the previous reports mentioning to decrease in the levels of IGF–1 by aging. This may be related to insufficient number of participants in our study.

The receptors of myocardial cells can express GH and IGF–1 therefore GH realize its effects on the heart directly both local and systemic IGF–1 induction [3].

In a study group consisting of 87 patients with a diagnosis of coronary artery disease both blood and cardiac IGF–1 levels were examined. The cardiac IGF–1 levels were found to be increasing and the blood IGF–1 levels were found to be decreasing. A negative correlation between ejection fraction and cardiac IGF–1 levels is determined. Due to these results, the compensator mechanism which regulates the left ventrical dysfunction also led cardiac IGF–1 [22].

In Dan-Monika Cohort Study IGF–1 levels were examined before the coronary event. Even though at first the risk decreased, it was later found in this study that as IGF–1 levels decreased, the risk increased [16].

In our study, coronary levels of IGF in patients underwent to PTCA were significantly higher than that of previous reports. Difference may related to our way of blood sample collection directly from the coronary vessels. Due to our results, we can conclude that the heart may develop local compensatory mechanisms to increase IGF–1 levels in ischemic cardiac events. IGF–1 levels may increase in heart and related vessels to regulate the heart function.

In conclusion, a comprehensive, long-term study with a large number of participants is required. to establish the function of IGF–1 in patients with coronary artery disease.

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