EVALUATION OF RISK MARKERS FLUCTUATION DURING AN INITIAL THERAPY WITH ROSIGLITAZON IN PATIENTS SUFFERING FROM METABOLIC SYNDROME

Amra Macić-Džanković[1*], Fuad Džanković[2], Belma Pojskić[3], Zelija Velija- Ašimi[4]

[1] Department of Cardiology, General Hospital "Prim. dr. Abdulah Nakaš" 71000 Sarajevo, Bosnia and Herzegovina
[2] Clinic for Bone Surgery, University of Sarajevo, Clinics Centre Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina
[3] Cantonal Hospital Zenica, Crkvice 67, 72 000 Zenica, Bosnia and Herzegovina
[4] Clinic for endocrinology-University of Sarajevo Clinics Centre Bolnička 25, 71000 Sarajevo, Bosnia and Herzegovina

* Corresponding author

Abstract

The aim of this study was to examine the effects of hypoglycaemic drug-agonists of PPAR-gama receptors-rosiglitazone (Avandia,4 mg - Glaxo Smith Kline) on values of wide-spread risk-markers: fibrinogen, C-reactive protein and uric acid and glicolysated haemoglobin HbA1C as parameter of metabolic control. We examined forty patients who satisfied criteria for metabolic syndrome and distributed them into groups of diabetic and prediabetic patients according to criteria of IDF (International Diabetic Federation).

These risk markers and glicolysated haemoglobin HbA1C were observed at the beginning of therapy, then four, eight and twelve weeks into therapy and results were compared and statistically processed.

Three months initial therapy with rosiglitazone significantly reduced values of HbA1C, fibrinogen and CRP but not uric acid in prediabetic patients.

Rosiglitazone initial three months therapy significantly reduced HbA1C, fibrinogen and uric acid, but not CRP in diabetic patients.

KEY WORDS: metabolic syndrome, HbA1C, risk-markers, diabetics, prediabetics.

Introduction

The number of patients diagnosed with non-infectious diseases and the related mortality is alarmingly rising daily in all the world, especially in developing countries. These facts influence the accelerated manifestation of new risk-markers for cardiovascular diseases. The appearance of multiple risk-factors, known as metabolic syndrome, includes: central obesity, hypertension, increased triglycerides and low HDL-cholesterol, as well as increased fasting plasma glucose values. In pathophysiological base of this syndrome lies insulin resistance that, in the process of blood coagulation, leads to hypofibrinosis together with blood coagulation disorder in blood vessels. Major part of those effects in insulin resistance, as well as the changes in coagulation and in endothelium confirm the existence of inflammation (1, 2). Also, in insulin resistance, breakdown of nucleic acids accelerates the accumulation of uric acid and development of related consequences. Several factors are influenced by insulin resistance, such as change in contractility of smooth muscles of small blood vessels, changes in their endothelium, changes in blood coagulation and hypertension. All the mentioned factors lead to changes in cardio-vascular system, marking it the cause of the most massive mortality in persons with metabolic syndrome. It has already been accepted for years to regard C-reactive protein as an acute inflammation reactant, fibrinogen as a part of coagulant system, and, recently, the values of uric acid as important risk-markers and possible statistic predictors of cardiovascular incidents. C-reactive protein is an important newly identified potential risk factor, which provides a strong prediction of future risk for cardiovascular events (3,4). It has been demonstrated that reducing CRP levels causes a reduction in cardiovascular diseases (3,4,5). CRP in not only a marker of inflammation; this protein, itself, contributes to atherogenesis. It appears to help monocytes infiltrate the arterial wall, starting the process of plaque formation. Thiazolidinediones, metformin, aspirin and statins reduce CRP in varying degrees (5). Recent intervention studies have also demonstrated the distinct efficacy of different anti-diabetes treatments on the variety of cardiovascular risk markers. Treatment with peroxisome proliferator-activated receptor gamma has lead to substantial reduction of hsCRP and other cardiovascular risk markers in several comparative studies. Since this effect was shown to be independent of the degree of glycemic improvement, it can be regarded as a class-specific effect (6). Fibrinogen is an acute phase reactant with active participation in endothelial function, thrombosis and inflammation. It has proven to be an independent variable in cardiovascular risk together with its participation in resistance phenomena in different antithrombotic approaches. Reasons behind fibrinogen elevated levels in cardiovascular diseases and atherosclerosis are, in general, incompletely understood; but all cells involved in the atherogenetic process are able to produce cytokines, which induce an acute phase reaction that increases fibrinogen levels in plasma. Analyses of the retrospective studies suggest that fibrinogen is an important and independent cadiovascular risk marker and factor, clearly associated with conventional risk factor and genetic polymorphisms (7,8) . Uric acid is a final breakdown product of purine metabolism in man. There is a growing body of evidence which indicates that elevated uric acid levels increase the probability of developing hypertension and cardiovascular disease, especially coronary artery disease (7). Several studies have reported that changes in serum cholesterol follow the changes in serum uric acid both in order and magnitude. Most recently, hyperuricaemia has been added to the constellation of abnormalities that comprise metabolic syndrome. The patophysiology of hyperuricaemia and link between hyperuricaemia, hypertension and cardiovascular disease are poorly understood. It is entirely possible that hyperuricaemia is a part of pathologic process that underlies fundamental alterations in renal function, as well as other metabolic pathophysiologies that ultimately lead to hypertension and cardiovascular disease (9,10,11,12) . Given the increased cardiovascular risk associated with both types of diabetes mellitus and metabolic syndrome on one hand, and the convincing overall consistency of the reported findings and potential value of the additional information provided by determination of CRP about the chronic vascular inflammatory state before, during and after therapeutic interventions on the other hand, introduction of these markers into routine diagnostic procedures and guidelines for diagnosis and treatment of diabetes mellitus is recommended. While the diet and exercise are still the cheapest and most effective ways to reduce cardiovascular risk, different drugs, like statins and PPAR gamma agonists, have been demonstrated to effectively reduce CRP levels and other risk-markers (13-15).

Materials and Methods

Over the period of three months, the values of fibrinogen as well as C-reactive pro-

tein, HbA1C and uric acid were observed prospectively in patients with metabolic syndrome featured by at least four of the following six criteria:

- abdominal obesity (waist circumference more than 80 cm in women and 94 cm in men)
- atherogenic dyslipidemia (triglycerides > 1,75 mmol/l, HDL < 1,0 mmol/l)
- high blood pressure (>130/85 mmHg)
- insulin resistance + glucose intolerance (impaired glucose tolerance test-two hours after ingestion of 75 mg glucose, serum glucose level is more than 7,8 mmol/l)
- increased level of pro-inflammatory factors (mostly known serum inflammation markers are in excess)
- increased level of pro-thrombotic factors (coagulation system balance tends to excess of procoagulants)

Methods

Patients were divided into the group of 19 prediabetics according to IDF (International Diabetic Federation) criteria (fasting plasma glucose value between 6,1 and 7,0 mmol/l, impaired glucose tolerance test with postprandial glycaemia between 7,8 and 11,1 mmol/l), and the group of 21 diabetic patients (fasting plasma glucose value more than 7,0 mmol/l and postprandial hyperglycaemia more than 11,1 mmol/l). Initial laboratory values of the mentioned parameters were recorded. Therapy with 1 tablet of rosiglitazone 4 mg (Avandia, Glaxo Smith Klein, United Kingdom) was introduced in the morning, without any correction in former therapy. Mentioned parameters were observed 4, 8 and 12 weeks into therapy, and the obtained data statistically and graphically elaborated.

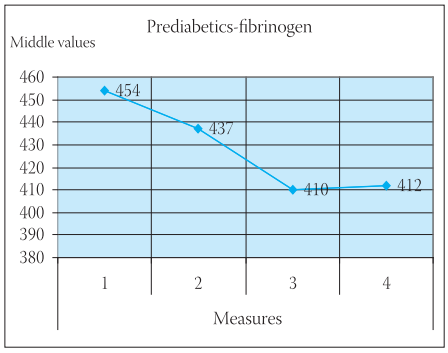
Statistical analysis

For statistical analysis we used tables and graphs (histogram and pie) and following statistical measures: mean, standard deviation, with average linear deviation, coefficient of variation, $\chi 2$ test for descriptive variables and Student`s test for quantitative variables. All data were analysed in SPSS 10.0 for Windows statistical program, and Microsoft Excel 2003 program.

RESULTS

The values of fibrinogen in the two groups of patients measured before the beginning of the therapy and 4, 8 and 12 weeks into therapy The values of C-reactive protein in the two groups of patients measured before the beginning of the therapy and 4, 8 and 12 weeks into therapy. The values of uric acid in the two groups of patients measured before the beginning of the therapy and 4, 8 and 12 weeks into therapy.

	Measures			
	1	2	3	4
Prediabetics-fibrinogen	454	437	410	412



Paired Samples Statistics

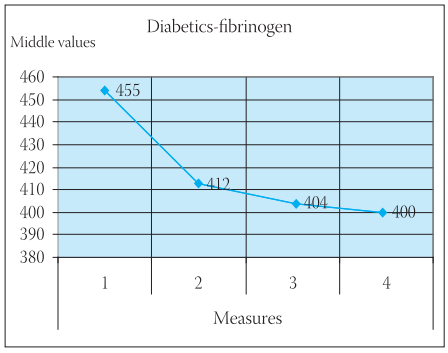
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	**fibrino 1**	4,5421	19	0,8840	0,2028
	fibrino 2	4,3711	19	0,7848	0,1800
Pair 2	**fibrino 2**	4,3711	19	0,7848	0,1800
	fibrino 3	4,1000	19	0,7789	0,1787
Pair 3	**fibrino 3**	4,1000	19	0,7789	0,1787
	fibrino 4	4,1237	19	0,8073	0,1852
Pair 4	**fibrino 1**	4,5421	19	0,8840	0,2028
	fibrino 4	4,1237	19	0,8073	0,1852

Paired Samples Test

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 FIBRINO1 -FIBR. 2	0,1711	0,3556	8,159E-02	-3,58E-04	0,3425	2,097	18	0,050
Pair 2 FIBRINO2 -FIBR. 3	0,2711	0,3679	8,441E-02	9,372E-02	0,4484	3,211	18	0,005
Pair 3 FIBRINO3 -FIBR. 4	-2,37E-02	0,2751	6,310E-02	-0,1563	0,1089	-0,375	18	0,712
Pair 4 FIBRINO1 -FIBR. 4	0,4184	0,4066	9,328E-02	0,2224	0,6144	4,485	18	0,000

TABLE 1. Group of prediabetics 001
The value of fibrinogen was considerably reduced in relation to its initial values (p<0,001).

	Measures			
	1	2	3	4
Diabetics-fibrinogen	455	412	404	400



Paired Samples Statistics

		Mean	N	Std. Deviation	Std.Error Mean
Pair 1	**Fibrino 1**	4,5524	21	1,13877	0,3028
	Fibrino 2	4,1238	21	0,8093	0,1766
Pair 2	**Fibrino 2**	4,1238	21	0,8093	0,1766
	Fibrino 3	4,0405	21	0,6848	0,1494
Pair 3	**Fibrino 3**	4,0405	21	0,6848	0,1494
	Fibrino 4	4,0010	21	0,7008	0,1529
Pair 4	**Fibrino 1**	4,5524	21	1,3877	0,3028
	Fibrino 4	4,0010	21	0,7008	0,1529

Paired Samples Test

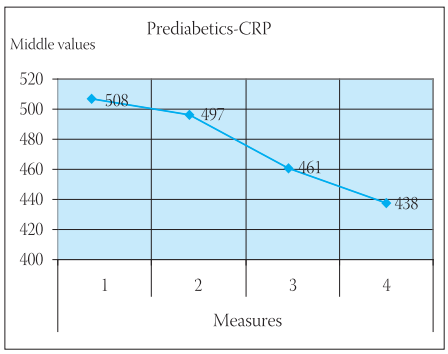
	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 FIBRINO1 -FIBR. 2	0,4286	0,6589	0,1438	0,1286	0,7285	2,981	20	0,007
Pair 2 FIBRINO2 -FIBR. 3	8,333E-03	0,3359	7,330E-02	-6,96E-02	0,2362	1,137	20	0,269
Pair 3 FIBRINO3 -FIBR. 4	-3,952E-02	0,1896	4,138E-02	-4,68E-02	0,1258	0,955	20	0,351
Pair 4 FIBRINO1 -FIBR. 4	0,5514	0,8198	0,1789	0,1783	0,9246	3,082	20	0,006

TABLE 2. Group of diabetics 002
Average value of fibrinogen showed a significant decrease (from 4,55 at the beginning of the research to 4,00 after 12 weeks)-p<0,006

The values of HbA1C in the two groups of patients measured before the beginning of the therapy and 4, 8 and 12 weeks into therapy. 10 of 19 prediabetic patients (52,63%) with HbA1C >6,0 % achieved HbA1c < 6,0 % after three initial months therapy of rosiglitazone 4 mg.

In total, 40 patients were screened, 19 prediabetics and 21 diabetic patients. All patients were already using therapy which was not changed during the study. Rosiglitazone was well tolerated and no patient showed significant side effects other than headache, dizziness and gastrointestinal complaints.

	Measures			
	1	2	3	4
Prediabetics-CRP	508	497	461	438



Paired Samples Statistics

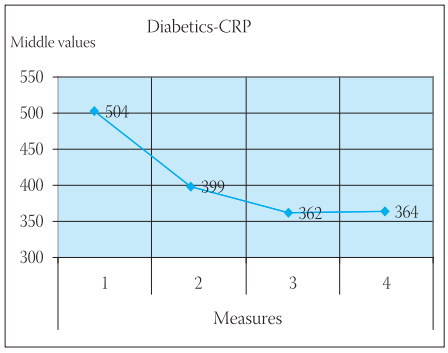
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	**CRP 1**	5,0842	19	2,7220	0,6245
	CRP 2	4,9684	19	2,5265	0,5796
Pair 2	**CRP 2**	4,9684	19	2,5265	0,5796
	CRP 3	4,6095	19	2,5695	0,5895
Pair 3	**CRP 3**	4,6095	19	2,5695	0,5895
	CRP 4	4,3789	19	2,3529	0,5398
Pair 4	**CRP 1**	5,0842	19	2,7220	0,6245
	CRP 4	4,3789	19	2,3529	0,5398

Paired Samples Test

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 CRP.1 - CRP.. 2	0,1158	0,6012	0,1379	-0,1740	0,4055	0,840	18	0,412
Pair 2 CRP.2 - CRP.. 3	0,3589	0,5440	0,1248	9,673E-02	0,6212	2,876	18	0,010
Pair 3 CRP.3 - CRP.. 4	0,2305	0,3438	7,888E-02	6,482E-02	0,3962	2,923	18	0,009
Pair 4 CRP.1 - CRP.. 4	0,7053	0,6553	0,1503	0,3894	1,0211	4,691	18	0,000

TABLE 3. Group of prediabetics 003
Value of CRP significantly decreased in relation to initial measuring in the group of prediabetics. P<0,0001.

	Measures			
	1	2	3	4
Diabetics-CRP	504	399	362	364



Paired Samples Statistics

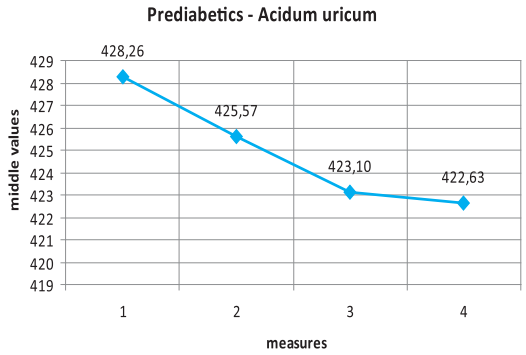
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	CRP 1	5,0362	21	7,1546	1,5613
	CRP 2	3,9924	21	3,4181	0,7459
Pair 2	CRP 2	3,9924	21	3,4181	0,7459
	CRP 3	3,6238	21	2,2914	0,5000
Pair 3	CRP 3	3,6238	21	2,2914	0,5000
	CRP 4	3,6376	21	2,4174	0,5269
Pair 4	CRP 1	5,0362	21	7,1546	1,5613
	CRP 4	3,6376	21	2,4147	0,5269

Paired Samples Test

	Paired Differences					t	df	Sig. (2-tailed)
	Mean	Std Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 CRP.1 - CRP.. 2	1,0438	3,7996	0,8291	-0,6857	2,7734	1,259	20	0,232
Pair 2 CRP.2 - CRP.. 3	0,3686	1,2143	0,2650	-0,1842	0,9213	1,391	20	0,180
Pair 3 CRP.3 - CRP.. 4	-1,38E-02	0,2644	5,770E-02	-0,1342	0,1066	-0,239	20	0,813
Pair 4 CRP.1 - CRP.. 4	1,3986	4,8250	1,0529	-0,7977	3,5949	1,328	20	0,199

TABLE 4. Group of diabetics 004
After 12 week therapy with Rosiglitazon the value of CRP did not significantly change in relation to the initial value in the group of diabetics (p=0,199).

In the prediabetic group, values of fibrinogen (Table 1) were slowly decreasing during the three months of initial therapy with Rosiglitazone, but the decrease was statistically significant, p<0,001. Significant decrease in fibrinogen values was also observed in the group of diabetics after treatment with rosiglitazone (Table 2). Average value of fibrinogen varied from 4,55 at the beginning of the study to 4,00 after 12 weeks p<0,006. Rosiglitazone significantly reduced CRP values in prediabetic group (Table 3). Value of CRP significantly decreased in relation to initial mea-



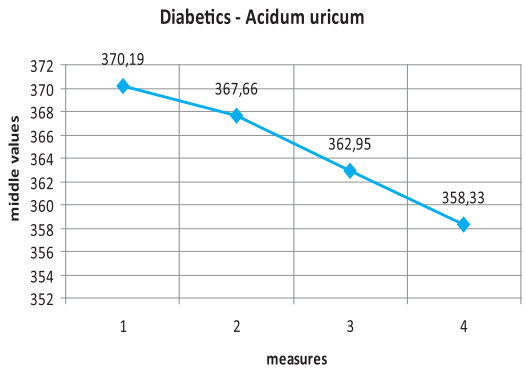
Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	ac.ur.1	428.2632	19	77.81805	17.85269
	ac.ur.2	425.5789	19	73.58843	16.88234
Pair 2	ac.ur.2	425.5789	19	73.58843	16.88234
	ac.ur.3	423.1053	19	67.00655	15.37236
Pair 3	ac.ur.3	423.1053	19	67.00655	15.37236
	ac.ur.4	422.6316	19	62.95961	14.44392
Pair 4	ac.ur.1	428.2632	19	77.81805	17.85269
	ac.ur.4	422.6316	19	62.95961	14.44392

Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	ac.ur.1 - ac.ur.2	2.68421	7.90255	1.81297	-1.12470	6.49312	1.481	18	.156
Pair 2	ac.ur.2 - ac.ur.3	2.47368	19.84767	4.55337	-7.09258	12.03995	.543	18	.594
Pair 3	ac.ur.3 - ac.ur.4	.47368	12.10311	2.77664	-5.35983	6.30720	.171	18	.866
Pair 4	ac.ur.1 - ac.ur.4	5.63158	38.08355	8.73697	-12.72410	23.98726	.645	18	.527

TABLE 5. Group of prediabetics 005
Values of uric acid did not significantly change after 12 week therapy in relation to initial values in the group of prediabetic (p=0,527).



Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	ac.ur1	370.1905	21	77.68244	16.95170
	ac.ur2	367.6667	21	76.89040	16.77886
Pair 2	ac.ur2	367.6667	21	76.89040	16.77886
	ac.ur3	362.9524	21	76.01939	16.58879
Pair 3	ac.ur3	362.9524	21	76.01939	16.58879
	ac.ur4	358.3333	21	75.84743	16.55127
Pair 4	ac.ur1	370.1905	21	77.68244	16.95170
	ac.ur4	358.3333	21	75.84743	16.55127

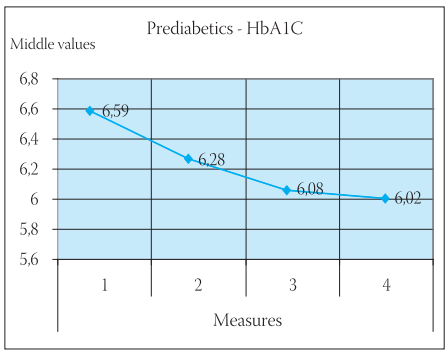
Paired Samples Test

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1	ac.ur1 - ac.ur2	2.52381	2.52228	.55041	1.37568	3.67194	4.585	20	.000
Pair 2	ac.ur2 - ac.ur3	4.71429	8.82691	1.92619	.69633	8.73225	2.447	20	.024
Pair 3	ac.ur3 - ac.ur4	4.61905	9.83095	2.14529	.14405	9.09404	2.153	20	.044
Pair 4	ac.ur1 - ac.ur4	11.85714	20.30588	4.43111	2.61402	21.10027	2.676	20	.015

TABLE 6. Group of diabetics 006
Value of uric acid significantly changed after 12 week therapy in relation to initial values in the group of diabetics (p=0,015).

suring in the group of prediabetics. P<0,0001. There was no significant reduction in CRP values in the group of diabetics after three months of initial therapy with Rosiglitazone (data shown in Table 4) p=0,199. During the first month of therapy CRP was significantly reduced, but later, during the following two months there was no significant difference compared with earlier results. Values of uric acid tended to be lower after treatment with Rosiglitazone in group of diabetic patients (data shown in Table 6), p<0,015 but there was no significant change after 12 week therapy in relation to initial

	Measures			
	1	2	3	4
Prediabetics - HbA1C	6,59	6,28	6,08	6,02



Paired Samples Statistics

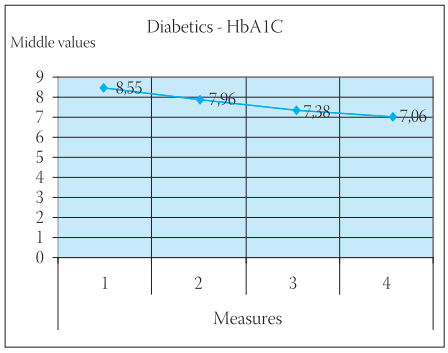
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	**HbA1C. 1**	6,5895	19	0,3406	9,879E-02
	HbA1C. 2	6,2842	19	0,3775	8,661E-02
Pair 2	**HbA1C. 2**	6,2842	19	0,3775	8,661E-02
	HbA1C3	6,0816	19	0,3006	6,895E-02
Pair 3	**HbA1C3**	6,0816	19	0,3006	6,895E-02
	HbA1C4	6,0168	19	0,3416	7,838E-02
Pair 4	**HbA1C1**	6,5895	19	0,4306	9,879E-02
	HbA1C4	6,0168	19	0,3416	7,838E-02

Paired Samples Test

	Paired Differences					T	df	Sig. (2-tailed)
	Mean	Std Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower	Upper			
Pair 1 HbA1C..1 - HbA1C... 2	0,3053	0,3472	7,965E-02	0,1379	0,4726	3,833	18	0,001
Pair 2 HbA1C..2 - HbA1C... 3	0,2026	0,2031	4,659E-02	0,1047	0,3005	4,349	18	0,000
Pair 3 HbA1C..3 - HbA1C... 4	6,474E-02	0,1448	3,321E-02	-5,04E-03	0,1345	1,949	18	0,067
Pair 4 HbA1C..1 - HbA1C... 4	0,5726	0,3989	9,151E-02	0,3804	0,7649	6,257	18	0,000

TABLE 7. Group of prediabetics 007
The values of HbA1 C was significantly reduced in relation of initial values(p<0,001).

	Measures			
	1	2	3	4
Diabetics - HbA1C	8,55	7,96	7,38	7,06



Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	**HbA1C. 1**	8,5476	21	1,9247	0,4200
	HbA1C. 2	7,9619	21	1,6794	0,3665
Pair 2	**HbA1C. 2**	7,9619	21	1,6794	0,3665
	HbA1C3	7,3762	21	0,9654	0,2107
Pair 3	**HbA1C3**	7,3762	21	0,9654	0,2107
	HbA1C4	7,0643	21	0,6639	0,1449
Pair 4	**HbA1C1**	8,5476	21	1,9247	0,4200
	HbA1C4	7,0643	21	0,6639	0,1449

Paired Samples Test

	Paired Differences					T	df	Sig. (2-tailed)
	Mean	Std Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower	Upper			
Pair 1 HbA1C..1 - HbA1C... 2	0,5857	0,3119	6,806E-02	0,4437	0,7277	8,605	20	0,000
Pair 2 HbA1C..2 - HbA1C... 3	0,5857	0,8248	0,1800	0,2103	0,9612	3,254	20	0,004
Pair 3 HbA1C..3 - HbA1C... 4	0,3119	0,5532	0,1207	6,011E-02	0,5637	2,584	20	0,018
Pair 4 HbA1C..1 - HbA1C... 4	1,4833	1,4573	0,3180	0,8200	2,1467	4,664	20	0,000

TABLE 8. Group of diabetics 008
Mean value of HbA1C at the start of therapy was 8,55 %. It showed decreasing tendency and after three months was significantly lower-7,06 % (p<0,001).

values in the group of prediabetics (Table 5), p<0,527. The most important parameter of metabolic control in this group of patients is glicolysated haemoglobin-HbA1C and we studied values of this parameter during this period (data shown in Table 7, and 8). This examination suggests very favourable effects of initial therapy of rosiglitazone on glycemic control in metabolic syndrome patients. Values of HbA1C were significantly reduced in both group of patients. In 52,63 % prediabetic patients with HbA1C more than 6,0 % achieved values lower than 6,0 % and tendency to normoglycaemia.

Discussion

The main result of the present study is the finding that three months initial therapy with Rosiglitazone caused significant reduction in fibrinogen and CRP values in the group of prediabetics. Fibrinogen values showed significant decrease after three months therapy with Rosiglitazone in the group of diabetics, but the values of CRP did not significantly change. Statistically, uric acid did not significantly change during three month initial therapy with rosiglitazone in the group of prediabetics. In the group of diabetics, uric acid showed statisticaly significant decrease during three month initial therapy with rosiglitazone, as opposed to the group of prediabetics where it was not noticed. This figure suggests the necessity of observing uric acid in diabetics with cardiovascular incidents, which can be a good predictor of further incidents. The goal of the research was to demonstrate possible effects of rosiglitazone on well-known risk-markers of cardiovascular events. As these markers are strong predictors of atherosclerosis, this may convey increased protection against cardiovascular disease in these patients. Early effects of treatment are especially important due to the fact that a great number of these patients, more precisely about two thirds, die of macrovascular diseases. In the present study, rosiglitazone has significant implications to the level of risk markers in patients with metabolic syndrome, and possibly influences also other pro-inflammatory components which are in excess during an acute cardiovascular incident. Increased hyperuricaemia is a common feature in diabetics as frequent as dyslipidaemia, and is associated with accelerated atherosclerosis and higher cardiovascular risk. Statistically significant decrease of uric acid in diabetics group (p<0,015) during initial three month therapy with Rosiglitazone was observed in this study. Whether these effects are sufficient to produce clinical benefit is an open issue. However, it is tempting to hypothesize that the antiatherosclerotic effects observed with Rosigitazone may involve the lowering of risk markers-fibrinogen, CRP and uric acid. These markers are well known predictors of acute cardiovascular events.

Another interesting aspect of the study is that the recorded effects of rosiglitazone succeed the effects of statin treatment, because our patients used statins before administration of rosiglitazone therapy. In our opinion, this is of interest because statins are used by majority of patients with type 2 diabetes, and they have been shown to improve risk markers It confirms the fact that this drug should be applied during acute cardiovascular incident to all patients with metabolic syndrome as soon as possible. And, probably, this drug should find its place among the drugs recommended for treatment of acute cardiovascular incidents in patients with centripetal obesity, but other large studies are needed to offer a definite confirmation for that. A change of life-style and diet is especially important for risk decreasing, but, surely, a significant help can be achieved through drug therapy, which should be combined. Function and the effect of this drug in the reduction of numerous essential risk factors in the very core of the obesity problem and insulin resistance offers indicates that this drug will surely be highly positioned in the combined therapy of acute vascular incidents, aiming at the reduction of cardiovascular mortality in patients with metabolic syndrome.

Conclusion

This study has demonstrated good tolerability and efficacy of rosiglitazone (Avandia, 4 mg, Glaxo Smith Cline) in the therapy of patients with metabolic syndrome.
Three months initial therapy with rosiglitazone significantly reduced values of HbA1C, fibrinogen and CRP but not uric acid in prediabetic patients with metabolic syndrome according to IDF criteria.
Three months initial therapy with rosiglitazone significantly reduced HbA1C, fibrinogen and uric acid, but not CRP in diabetic patients with criteria for metabolic syndrome.

List of Abbreviations

hs-CRP	-	high sensitive-C reactive protein
CRP	-	C reactive protein
HbA1C	-	glycosylated hemoglobin
IDF	-	International Diabetic Federation
HDL	-	high density lipoprotein
LDL	-	low density lipoprotein

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