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Effects of Glucose Control on Hematological Indices in Patients with Diabetes Mellitus

Ceyhun Varım*, Tezcan Kaya, Ahmet Nalbant, Ayşenur Uçar, Ali Tamer

Sakarya University Medical Faculty - Internal Medicine, Adnan Menderes st. Sağlık Sok. No: 195, Adapazarı, Sakarya 54000, Turkey

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Key words: Diabetes Mellitus; hemogram; insulin; oral antidiabetics.

***Correspondence:** Ceyhun Varım, assistant professor. Sakarya University Medicine Faculty, Sakarya. Phone: +90 532 7005090. Fax: +90 264 444 54 00.
E-mail: ceyhunvarim@yahoo.com

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Abstract

Aim: We aimed to investigate the effects of diabetes treatment modalities on haematological parameters and leukocyte formula in patients with type 2 diabetes mellitus.

Materials and Methods: The study included 102 patients with type 2 diabetes, out of which 51 receiving insulin treatment and 51 receiving oral antidiabetics (OAD). Hemogram data of insulin and OAD treated groups were compared**.**

Results HbA1c levels were 11.12 ± 2.09 mg/dl in insulin group and 7.94 ± 2.1 mg/dl in OAD group p=0.001. Platelet counts were 27866.67 ± 77693 10^9/L before treatment and 258941.18 ± 69068.2 10^9/L in OAD group at six months, p: 0.015 whereas; 293011.76 ± 73711.21 10^9/L before treatment and 289492.86 ± 82631.49 10^9/L in insulin group at six months p: 0.821. Monocyte counts were 0.47 ± 0.12 10^9/L before the treatment and 0.57 ± 0.12 10^9/L in mix insulin therapy subgroup at six months, p:0.004; monocyte percentage was % 6.11 ± 1.74 before the treatment and %7.51 ± 2.57 in mix insulin subgroup at six months p:0.039; Basophiles counts were 0.1 ± 0.02 10^9/L before treatment and 0.09 ± 0.04 10^9/L in intensive insulin therapy subgroup at six months, p: 0.005; Lymphocyte and basophils counts were significantly decreased at six months insulin treatment as compared to the pretreatment values.

Conclusion: This study showed that, glucose control effects; blood indices HbA1C, basophiles, eosinophils, platelets and lymphocytes counts.

Introduction

Diabetes Mellitus (DM), is a multisystemic disease characterized by high blood sugar levels causing acute and chronic complications. High blood sugar levels caueses these complications. Diabetes mellitus is known to cause anemia of chronic disease, erythrocyte, leukocyte and platelet dysfunction [1-4]. Oral antidiabetics and insulins are used for the treatment of type 2 DM for many years. These treatment models can be applied separately or in combination. The aim of the treatment is reduction of diabetic complications by providing blood sugar regulation and suppression of chronic inflammatory process.

The effects of the various medical treatment modalities for patients with type 2 DM upon the hematological parameters have been analyzed, showing mainly no significant side effects, the most common side effects being allergic reactions. The increase in the peripheral blood eosinophils, basophils, and leukocyte counts seen in allergic reactions is also seen in chronic inflammatory processes, but the latter can be improved by regulation of blood sugar. This regulation also reduces the number of inflammatory cells in the peripheral blood.

The aim of our study was to evaluate the effects of glucose control on the hematological parameters in the study population.

Materials and Methods

We have performed a retrospective analysis of the data of 102 patients with type 2 diabetes mellitus, which have been followed-up at the Diabetes Polyclinic of our hospital for at least 6 months. The diagnosis of type 2 diabetes was based upon the diagnostic criteria of the American Diabetes

Association (ADA) from 2010. Venous blood samples were obtained from subjects for hemogram studies. The patients treated with insulin were divided into three subgroups: patients receiving conventional insulin therapy regime (short/intermediate acting insulin mixture 2 times a day), patients on intensive insulin regime (short-acting insulin 3 times a day and basal long-acting insulin) and patients using OAD in combination with basal insulin. The patients using oral antidiabetic therapy were also divided into 3 subgroups: patients using metformin, patients using metformin and sulfonylurea and patients using metformin and DPP4 analogues. Haematologic parameters and HbA1c levels were measured at the initiation of the therapy and after 3 and 6 months

Table 1: Distributions of the demographic and hematological parameters according to insulin and OAD groups.

		Insulin (n=51)	OAD (n=51)	[1]p
Age (year)		55.10 ± 10.86	53.51 ± 10.10	0.446
Gender (male)		22 (43.1)	26 (51.0)	0.552
DM duration (month)		117.45 ± 84.94	43.31 ± 45.96	**<0.001**
Hba1c	Pre-Treatment	11.12 ± 2.09	7.94 ± 2.11	**<0.001**
	Post-Treat. 3rd Month	9.17 ± 2.01	6.78 ± 1.25	**<0.001**
	Post-Treat. 6th Month	8.68 ± 1.95	7.13 ± 1.10	**<0.001**
	[2]p	**<0.001** [a,b]	**0.001** [a,b]	
	[3]p	**<0.001**		
WBC	Pre-Treatment	8072.55 ± 2050.76	8200.00 ± 2068.82	0.755
	Post-Treat. 3rd Month	8410.00 ± 2033.62	8050.98 ± 2034.44	0.377
	Post-Treat. 6th Month	8442.86 ± 2460.14	7805.88 ± 1728.86	0.147
	[2]p	0.192	0.320	
	[3]p	0.444		
Hb	Pre-Treatment	13.02 ± 1.75	13.36 ± 1.63	0.312
	Post-Treat. 3rd Month	12.98 ± 1.53	13.30 ± 1.57	0.305
	Post-Treat. 6th Month	12.85 ± 1.56	13.21 ± 1.39	0.256
	[2]p	0.985	0.663	
	[3]p	0.166		
Plt	Pre-Treatment	293011.76 ± 73711.21	278666.67 ± 77693.93	0.341
	Post-Treat. 3rd Month	285706.00 ± 72484.48	276352.94 ± 75820.00	0.528
	Post-Treat. 6th Month	289492.86 ± 82631.49	258941.18 ± 69068.20 [a,b]	0.055
	[2]p	0.821	**0.015** [a,c]	
	[3]p	0.287		
MCV	Pre-Treatment	85.12 ± 6.64	85.12 ± 6.34	1.000
	Post-Treat. 3rd Month	84.88 ± 5.99	84.70 ± 5.90	0.883
	Post-Treat. 6th Month	84.31 ± 6.32	85.37 ± 5.69	0.398
	[2]p	0.074	0.124	
	[3]p	0.864		
MPV	Pre-Treatment	9.59 ± 11.4	8.05 ± 1.27	0.341
	Post-Treat. 3rd Month	9.50 ± 11.59	7.84 ± 1.12	0.311
	Post-Treat. 6th Month	7.87 ± 1.21	8.06 ± 1.17	0.461
	[2]p	0.291	0.236	
	[3]p	0.312		

Data were shown as mean ± standard deviation and n (%). [1]: Results of the comparison between insulin and OAD groups. [2]: Results of the comparison among pre-treatment, post-treatment 3rd month and post-treatment 6th month measures. [3]: Results of the comparison among two groups according to alterations of hematologic parameters. [a]: There was statistically significant difference between pre-treatment and post-treatment 3rd month. [b]: There was statistically significant difference between pre-treatment and post-treatment 6th month. [c]: There was statistically significant difference between post-treatment 3rd month and post-treatment 6th month.

In the study we investigated the effect of the decrease in HbA1c levels to blood count and leukocyte formula in the 6-month treatment period for insulin and OAD using groups and also for the subgroups Patients are started on insulin therapy compared with patients are using oral antidiabetics. We investigate the effect of decrease in HbA1c levels to blood count and leukocyte formula in 6-month treatment period for insulin and OAD using groups and also for subgrups.

All patients were informed for the study and signed an informed consent forms for the study. Ethics committee approval was taken for the study.

Statistical analysis was made using computer software (SPSS version 15.0, SPSS Inc. Chicago, IL, USA). The results of all the parameters of insulin and OAD group are given as mean ± standard deviation. Samples T test was used to compare the data between the two groups. Level of statistical significance of the data interpreted with the 'p' value. p <0.05 was considered statistically significant.

Results

Patients were divided into two groups according to using OAD therapy and using insulin therapy. The average age of the insulin using group is 55.1 years, and 53.5 years of OAD using group. The distribution of gender is, 22 male/33 female patients (n = 55) in insulin using group and 26 male/29 female patients (n = 55) in OAD using group.. Duration of diabetes was found 117.45 ± 84.94 months in insulin using group and 43.31 ± 45.96 months in OAD using group (Table 1).

Table 2: Distributions of the hematological parameters according to the insulin and OAD groups.

		Insulin (n=51)	OAD (n=51)	[1]p
Neu %	Pre-Treatment	57.59 ± 9.65	58.23 ± 8.65	0.724
	Post-Treat. 3rd Month	57.79 ± 8.76	58.68 ± 7.64	0.590
	Post-Treat. 6th Month	58.79 ± 9.27	57.54 ± 7.2	0.466
	[2]p	0.465	0.548	
	[3]p	0.895		
Neu	Pre-Treatment	4.68 ± 1.45	4.78 ± 1.46	0.730
	Post-Treat. 3rd Month	4.91 ± 1.63	4.76 ± 1.50	0.624
	Post-Treat. 6th Month	4.99 ± 1.77	4.52 ± 1.23	0.143
	[2]p	0.220	0.413	
	[3]p	0.518		
Lym %	Pre-Treatment	32.56 ± 9.12	32.04 ± 7.26	0.753
	Post-Treat. 3rd Month	32.73 ± 8.41	31.64 ± 7.25	0.486
	Post-Treat. 6th Month	31.35 ± 8.35	32.82 ± 7.18	0.365
	[2]p	0.807	0.438	
	[3]p	0.959		
Lym	Pre-Treatment	2.72 ± 0.99	2.69 ± 1.01	0.905
	Post-Treat. 3rd Month	2.74 ± 0.92	2.61 ± 0.98	0.486
	Post-Treat. 6th Month	2.60 ± 0.98	2.62 ± 0.88	0.935
	[2]p	0.597	0.631	
	[3]p	0.816		
Mono %	Pre-Treatment	6.57 ± 2.35	7.01 ± 2.33	0.343
	Post-Treat. 3rd Month	6.55 ± 2.34	6.70 ± 2.62	0.756
	Post-Treat. 6th Month	6.92 ± 2.56	6.75 ± 1.87	0.710
	[2]p	0.719	0.496	
	[3]p	0.906		
Mono	Pre-Treatment	0.50 ± 0.16	0.58 ± 0.24	0.069
	Post-Treat. 3rd Month	0.54 ± 0.19	0.52 ± 0.2	0.601
	Post-Treat. 6th Month	0.55 ± 0.16	0.53 ± 0.19	0.507
	[2]p	0.206	0.165	
	[3]p	0.985		
Eos %	Pre-Treatment	2.24 ± 1.6	2.38 ± 2.08	0.876
	Post-Treat. 3rd Month	2.10 ± 1.28	1.93 ± 1.27	0.508
	Post-Treat. 6th Month	2.10 ± 1.44	2.04 ± 1.35	0.831
	[2]p	0.400	0.277	
	[3]p	0.550		
Eos	Pre-Treatment	0.18 ± 0.13	0.20 ± 0.22	0.870
	Post-Treat. 3rd Month	0.18 ± 0.12	0.16 ± 0.12	0.479
	Post-Treat. 6th Month	0.18 ± 0.12	0.17 ± 0.12	0.496
	[2]p	0.913	0.327	
	[3]p	0.468		
Baso%	Pre-Treatment	0.90 ± 0.38	0.88 ± 0.39	0.776
	Post-Treat. 3rd Month	0.83 ± 0.29	0.9 ± 0.41	0.328
	Post-Treat. 6th Month	0.84 ± 0.28	0.88 ± 0.34	0.611
	[2]p	0.266	0.843	
	[3]p	0.667		
Baso	Pre-Treatment	0.08 ± 0.04	0.08 ± 0.06	0.551
	Post-Treat. 3rd Month	0.07 ± 0.05	0.08 ± 0.06	0.535
	Post-Treat. 6th Month	0.08 ± 0.04	0.07 ± 0.05	0.348
	[2]p	0.225	0.741	
	[3]p	0.733		

Data were shown as mean ±standard deviation. [1]: Results of the comparison between insulin and OAD groups. [2]: Results of the comparison among pre-treatment, post-treatment 3rd month and post-treatment 6th month measures. [3]: Results of the comparison among two groups according to alterations of hematologic parameters.

Hematological parameters such as platelet and white blood cell count, hemoglobin, hematocrite, mean corpuscular volume (MCV), mean platelet volume (MPV), white blood cell formulas (neutrophils, lymphocytes, eosinophils, basophils, monocytes percentages) and HbA1c levels were examined in

both groups. The start of study, 3 and 6 months, these parameters and HbA1c levels were recorded. Changes in these parameters and HbA1c levels were assessed between insulin and OAD using group and as well as its subgroups. HbA1c levels were %11.12 ± 2.09 mg/dl in insulin group and %7.94 ± 2.1 in OAD group p = 0.001. Platelet counts were 27866.67 ± 77693 10^9/L before treatment and 258941.18 ± 69068.2 10^9/L in OAD using group at six months, p: 0.015 whereas; 293011.76 ± 73711.21 109/L before treatment and 289492.86 ± 82631.49 10^9/L, in insulin theraphy group at six months p: 0.821 (Table 1 and 2).

Table 3: Distributions of the demographic and hematological parameters according to the insulin subgroups.

		Mix insulin (n=20)	Intensive insulin (n=19)	OAD+Basal insulin (n=12)	[1]p
Age (year)		55.5 ± 8.38	53.37 ± 13.01	57.17 ± 11.3	0.633
Gender (male)		9 (45)	8 (42.1)	5 (41.7)	0.977
DM duration (month)		126 ± 76.94	110 ± 106.26	115 ± 62.14	0.841
Hba1c	Pre-Treatment	11.16 ± 1.86	11.68 ± 2.04	10.15 ± 2,35	0.137
	Post-Treat. 3rd Month	9.31 ± 2.05	9.55 ± 2.27	8.34 ± 1.31	0.279
	Post-Treat. 6th Month	8.45 ± 1.6	9.49 ± 2.28	7.88 ± 1.52	0.106
	[2]p	**0.010** [b]	**0.024** [b]	**0.005** [b]	
	[3]p		0.100		
WBC	Pre-Treatment	7970 ± 1522.84	8810.53 ± 2459.43	7075 ± 1779.75	0.066
	Post-Treat. 3rd Month	8705 ± 2425.41	8678.95 ± 1617.12	7409.09 ± 1722.47	0.183
	Post-Treat. 6th Month	8131.25 ± 2448.6	9426.67 ± 2449.92	7554.55 ± 2223.23	0.129
	[2]p	0.161	0.298	0.631	
	[3]p		0.079		
Hb	Pre-Treatment	12.86 ± 1.67	13.25 ± 1.91	12,.3 ± 1.75	0.778
	Post-Treat. 3rd Month	12.91 ± 1.27	13.15 ± 1.95	12.84 ± 1.22	0.836
	Post-Treat. 6th Month	12.41±1.5	13.39 ± 1.8	12.72 ± 1.13	0.217
	[2]p	0.567	0.630	0.801	
	[3]p		0.451		
Plt	Pre-Treatment	294000 ± 62839	300263.2 ± 72371.6	279883.3 ± 95000.8	0.760
	Post-Treat. 3rd Month	284300 ± 65384	294789.5 ± 72900.7	272572.7 ± 87780.5	0.725
	Post-Treat. 6th Month	290375 ± 54585.6	305600 ± 92041.8	266245.5 ± 103344.2	0.497
	[2]p	0.781	0.199	0.406	
	[3]p		0.806		
MCV	Pre-Treatment	85.81 ± 7.59	85.05 ± 5.52	84.07 ± 7.01	0.779
	Post-Treat. 3rd Month	84.97 ± 7.05	84.83 ± 5.79	84.78 ± 4.57	0.996
	Post-Treat. 6th Month	84.38 ± 6.56	84.23 ± 7.45	84.32 ± 4.65	0.998
	[2]p	**0.037** [a]	0.279	0.758	
	[3]p		0.933		
MPV	Pre-Treatment	8.21 ± 1.29	11.74 ± 18.58	8.49 ± 3.2	0.591
	Post-Treat. 3rd Month	7.88 ± 0.96	11.81 ± 18.77	8.46 ± 2.5	0.550
	Post-Treat. 6th Month	7.76 ± 0.99	7.78 ± 1.26	8.16 ± 1.46	0.661
	[2]p	0.056	0.350	0.775	
	[3]p		0.556		

Data were shown as mean ±standard deviation and n (%). [1]: Results of the comparison among groups. [2]: Results of the comparison among pre-treatment, post-treatment 3rd month and post-treatment 6th month measures. [3]: Results of the comparison among three groups according to alterations of hematologic parameters. [a]: There was statistically significant difference between pre-treatment and post-treatment 3rd month.. [b]: There was statistically significant difference between pre-treatment and post-treatment 6th month.

Insulin treatment group was divided into 3 subgroups. These subgroups consisted of patients initiated on mixed insulin therapy, patients started on intensive insulin therapy and patients using OAD therapy in combination with basal insulin. Hematological parameters, white blood cell formulas and HbA1c levels were examined in both subgroups. HbA1c levels were %11.16 ± 1.86 before treatment and % 8.45 ± 1.6 in mix insulin therapy subgroup at six months p: 0.010; HbA1c levels were %11.68 ± 2.04 before treatment and %9.49 ± 2.28 in intensive insulin therapy subgroup at six months p = 0.024; HbA1c levels were %10.15 ± 2.35 before treatment and % 7.88 ± 1.52 in OAD therapy and added basal insulin subgroup at six months p = 0.005.

Table 4: Distributions of the hematological parameters according to the insulin subgroups.

		Mix insulin (n=20)	Intensive insulin (n=19)	OAD+Basal insulin (n=12)	[1]p
Neu %	Pre-Treatment	57.17 ± 10.78	56.74 ± 10.03	59.65 ± 7.19	0.701
	Post-Treat. 3rd Month	56.98 ± 9.82	57.53 ± 7.31	59.73 ± 9.54	0.703
	Post-Treat. 6th Month	55.58 ± 10.32	59.27 ± 8.03	62.81 ± 8.24	0.133
	[2]p	0.839	0.162	0.195	
	[3]p		0.428		
Neu	Pre-Treatment	4.63 ± 1.38	5.04 ± 1.66	4.21 ± 1.15	0.301
	Post-Treat. 3rd Month	5.07 ± 2.15	5.01 ± 1.17	4.45 ± 1.19	0.568
	Post-Treat. 6th Month	4.53 ± 1.79	5.6 ± 1.68	4.82 ± 1.79	0.230
	[2]p	0.303	0.125	0.354	
	[3]p		0.389		
Lym %	Pre-Treatment	33.99 ± 9.08	32.86 ± 9.82	29.73 ± 8.15	0.443
	Post-Treat. 3rd Month	33.74 ± 8.67	33.36 ± 6.95	29.83 ± 10.26	0.436
	Post-Treat. 6th Month	33.63 ± 7.72	32.05 ± 8.68	27.09 ± 7.85	0.124
	[2]p	0.993	0.984	0.226	
	[3]p		0.209		
Lym	Pre-Treatment	2.68 ± 0.82	3.14 ± 1.14	2.13 ± 0.73	**0.020** [f]
	Post-Treat. 3rd Month	2.88 ± 0.94	2.91 ± 0.88	2.22 ± 0.83	0.099
	Post-Treat. 6th Month	2.59 ± 0.71	3.03 ± 1.22	2.02 ± 0.66	**0.029** [f]
	[2]p	0.108	0.336	0.385	
	[3]p		**0.019** [i]		
Mono %	Pre-Treatment	6.11 ± 1.74	6.57 ± 3.08	7.3 ± 1.78	0.394
	Post-Treat. 3rd Month	6.49 ± 1.89	6.15 ± 2.6	7.35 ± 2.64	0.409
	Post-Treat. 6th Month	7.51 ± 2.57	5.95 ± 2	7.38 ± 3.03	0.188
	[2]p	**0.039** [b]	0.178	0.991	
	[3]p		0.571		
Mono	Pre-Treatment	0.47 ± 0.12	0.54 ± 0.21	0.49 ± 0.11	0.403
	Post-Treat. 3rd Month	0.56 ± 0.17	0.52 ± 0.2	0.54 ± 0.2	0.857
	Post-Treat. 6th Month	0.57 ± 0.12	0.55 ± 0.15	0.53 ± 0.23	0.810
	[2]p	**0.004** [a,b]	0.868	0.735	
	[3]p		0.865		
Eos %	Pre-Treatment	2.15 ± 1.76	2.27 ± 1.6	2.33 ± 1.44	0.949
	Post-Treat. 3rd Month	1.94 ± 0.94	2.23 ± 1.5	2.17 ± 1.5	0.774
	Post-Treat. 6th Month	2.27 ± 1.89	1.99 ± 1.18	1.99 ± 0.99	0.828
	[2]p	0.605	**0.042** [c]	0.687	
	[3]p		0.944		
Eos	Pre-Treatment	0.16 ± 0.12	0.2 ± 0.13	0.18 ± 0.14	0.635
	Post-Treat. 3rd Month	0.17 ± 0.08	0.18 ± 0.11	0.16 ± 0.15	0.830
	Post-Treat. 6th Month	0.19 ± 0.13	0.19 ± 0.12	0.15 ± 0.09	0.550
	[2]p	0.691	0.685	0.574	
	[3]p		0.645		
Baso %	Pre-Treatment	0.89 ± 0.38	0.85 ± 0.34	0.99 ± 0.44	0.601
	Post-Treat. 3rd Month	0.85 ± 0.3	0.76 ± 0.3	0.92 ± 0.26	0.331
	Post-Treat. 6th Month	0.91 ± 0.24	0.83 ± 0.3	0.76±0.33	0.446
	[2]p	0.737	0.239	0.143	
	[3]p		0.759		
Baso	Pre-Treatment	0.08 ± 0.04	0.1 ± 0.02	0.08 ± 0.05	0.212
	Post-Treat. 3rd Month	0.08 ± 0.04	0.06 ± 0.05	0.08 ± 0.04	0.525
	Post-Treat. 6th Month	0.09 ± 0.03	0.09 ± 0.04	0.06 ± 0.05	**0.029** [e,f]
	[2]p	0.167	**0.005** [a,c]	0.092	
	[3]p		0.554		

Data were shown as mean ±standard deviation and n (%). [1]: Results of the comparison among groups. [2]: Results of the comparison among pre-treatment, post-treatment 3rd month and post-treatment 6th month measures. [3]: Results of the comparison among three groups according to alterations of hematologic parameters. [a]: There was statistically significant difference between pre-treatment and post-treatment 3rd month.. [b]: There was statistically significant difference between pre-treatment and post-treatment 6th month.. [c]: There was statistically significant difference between post-treatment 3rd month and post-treatment 6th month.[e]: There was statistically significant difference between group 1 and group 3. [f]: There was statistically significant difference between group 2 and group 3. [i]: There was statistically significant difference between group 2 and group 3.

Monocyte counts were 0.47 ± 0.12 10^9/L before the treatment and 0.57 ± 0.12 10^9/L in mix insulin therapy subgroup at six months, p = 0.004; monocyte percentage was % 6.11 ± 1.74 before the treatment and %7.51 ± 2.57 in mix insulin therapy subgroup at six months p = 0.039; Basophils counts were 0.1 ± 0.02 10^9/L before treatment and 0.09 ± 0.04 10^9/L in intensive insulin therapy subgroup at six months, p: 0.005; Eosinophil percentage was %2.27 ± 1.6 before treatment and %1.99 ± 1.18 in intensive insulin using subgroup at six months, p: 0.042. Lymphocyte and basophils counts were significantly decreased at six months insulin treatment as compared to the pretreatment values. There was no statistically significant difference found in other parameters (Table 3 and 4).

Table 5: Distributions of the demographic and hematological parameters according to the OAD subgroups.

		Metformin (n=13)	Metformin + sulfonylurea (n=23)	Metformin + DPP4 analogues (n=15)	[1]p
Age (year)		50.23 ± 9.19	53.3 ± 9.87	56.67 ± 10.88	0.245
Gender (male)		4 (30.8)	13 (56.5)	9 (60)	0.235
DM duration (month)		17.92 ± 20.62	54.17 ± 54.13	47.54 ± 40.26	0.077
Hba1c	Pre-Treatment	8.17 ± 2.59	7.88 ± 1.86	7.85 ± 2.15	0.910
	Post-Treat. 3rd Month	5.93 ± 0.8	7.42 ± 1.35	6.54 ± 0.85	**0.001** [e,f]
	Post-Treat. 6th Month	6.72 ± 0.92	7.32 ± 1.16	7.2 ± 1.12	0.286
	[2]p	**0.025** [a]	0.227	0.071	
	[3]p		0.243		
WBC	Pre-Treatment	8130.77 ± 2756.32	8386.96 ± 1704.35	7973.33 ± 2022.89	0.832
	Post-Treat. 3rd Month	7923.08 ± 3016.39	8321.74 ± 1856.43	7746.67 ± 1154.41	0.681
	Post-Treat. 6th Month	7430.77 ± 2144.13	8052.17 ± 1621.13	7753.33 ± 1539.88	0.588
	[2]p	0.460	0.654	0.869	
	[3]p		0.654		
Hb	Pre-Treatment	13.59 ± 1.76	13.36 ± 1.5	13.17 ± 1.8	0.795
	Post-Treat. 3rd Month	13.21 ± 1.16	13.39 ± 1.57	13.24 ± 1.94	0.933
	Post-Treat. 6th Month	13.13 ± 1.18	12.95 ± 1.09	13.66 ± 1.88	0.309
	[2]p	0.075	0.075	0.493	
	[3]p		0.963		
Plt	Pre-Treatment	280923.1 ± 79898.3	278739.1 ± 76384.9	276600 ± 83117.7	0.990
	Post-Treat. 3rd Month	274615.4 ± 68476.9	283695.7 ± 86306.2	266600 ± 67921.0	0.797
	Post-Treat. 6th Month	265230.8 ± 63989.8	262260.9 ± 72357.8	248400 ± 71596.9	0.782
	[2]p	0.333	0.193	0.164	
	[3]p		0.883		
MCV	Pre-Treatment	84.56 ± 8.41	84.84 ± 6.01	86.03 ± 4.99	0.803
	Post-Treat. 3rd Month	84.5 ± 7.63	84.42 ± 5.02	85.31 ± 5.84	0.895
	Post-Treat. 6th Month	84.92 ± 6.71	85.03 ± 5.2	86.28 ± 5.78	0.768
	[2]p	0.766	0.448	0.322	
	[3]p		0.819		
MPV	Pre-Treatment	8.19 ± 1.12	8.21 ± 1.53	7.69 ± 0.89	0.421
	Post-Treat. 3rd Month	7.99 ± 0.97	7.91 ± 1.32	7.59 ± 0.93	0.604
	Post-Treat. 6th Month	8.39 ± 1.55	7.87 ± 0.94	8.06 ± 1.12	0.439
	[2]p	0.443	0.184	0.153	
	[3]p		0.579		

Data were shown as mean ±standard deviation and n (%). [1]: Results of the comparison among groups. [2]: Results of the comparison among pre-treatment, post-treatment 3rd month and post-treatment 6th month measures. [3]: Results of the comparison among three groups according to alterations of hematologic parameters. [a]: There was statistically significant difference between pre-treatment and post-treatment 3rd month. [e]: There was statistically significant difference between group 1 and group 3. [f]: There was statistically significant difference between group 2 and group 3.

The group receiving oral antidiabetic therapy was divided into 3 subgroups. These subgroups consisted of patients using only metformin, patients using metformin + sulfonylurea and patients using metformin + DPP4 analogues Hematological parameters, white blood cell formulas and HbA1c levels were examined in both subgroups. There was no statistically significant difference in both parameters before treatment and at six months (Table 5 and 6).

Discussion

The results of this study showed that glucose control significantly lowers HbA1c levels together with blood sugar regulation. On the other hand causes a significant decrease in the number of basophils, eosinophils, platelets, lymphocytes. These findings are very important. Significant numerical and proportional decrease in the number of basophils, eosinophils, platelets, lymphocytes suggest that regulation of blood sugar has an anti-inflammatory activity. Diabetic patients are more prone to certain infections than those without DM. Regulation of blood glucose increases the anti-inflammatory activity and reduces predisposition to infections. However, in vitro and in vivo more studies are needed for further investigation.

Diabetes Mellitus is a chronic metabolic disorder due to insulin deficiency or defects on the effect of insulin and requiring a continuous medical care. There is disturbance in body metabolism and energy utilization from carbohydrates, fats and proteins insufficiently [5].

Table 6: Distributions of the hematological parameters according to the OAD subgroups.

		Metformin (n=13)	Metformin + sulfonylurea (n=23)	Metformin+ DPP4 analogues (n=15)	[1]p
Neu %	Pre-Treatment	57.06 ± 7.06	57.35 8 .26	60.6 ± 10.44	0.458
	Post-Treat. 3rd Month	59.19 ± 10.06	58.62 ± 7.71	58.32 ± 5.28	0.957
	Post-Treat. 6th Month	56.81 ± 6.93	57.39 ± 8.39	58.41 ± 5.64	0.840
	[2]p	0.495	0.583	0.499	
	[3]p		0.803		
Neu	Pre-Treatment	4.61 ± 1.6	4.82 ± 1.2	4.87 ± 1.77	0.886
	Post-Treat. 3rd Month	4.75 ± 2.29	4.91 ± 1.39	4.52 ± 0.66	0.740
	Post-Treat. 6th Month	4.24 ± 1.4	4.65 ± 1.3	4.57 ± 1	0.626
	[2]p	0.576	0.638	0.668	
	[3]p		0.787		
Lym %	Pre-Treatment	32.92 ± 6.28	31.97 ± 8.16	31.34 ± 6.95	0.857
	Post-Treat. 3rd Month	31.32 ± 9.25	31.98 ± 7.6	31.39 ± 4.82	0.955
	Post-Treat. 6th Month	33.29 ± 6.91	33.43 ± 8.43	31.48 ± 5.36	0.698
	[2]p	0.600	0.450	0.976	
	[3]p		0.892		
Lym	Pre-Treatment	2.94 ± 1.52	2.67 ± 0.86	2.5 ± 0.62	0.536
	Post-Treat. 3rd Month	2.74 ± 1.53	2.65 ± 0.78	2.45 ± 0.62	0.720
	Post-Treat. 6th Month	2.79 ± 1.42	2.65 ± 0.67	2.41 ± 0.52	0.531
	[2]p	0.546	0.986	0.874	
	[3]p		0.597		
Mono %	Pre-Treatment	6.95 ± 1.94	7.35 ± 2.75	6.56 ± 1.95	0.600
	Post-Treat. 3rd Month	6.74 ± 2.18	6.51 ± 3.17	6.96 ± 2.11	0.879
	Post-Treat. 6th Month	7.18 ± 1.92	6.53 ± 1.97	6.7 ± 1.74	0.615
	[2]p	0.541	0.171	0.697	
	[3]p		0.959		
Mono	Pre-Treatment	0.61 ± 0.3	0.6 ± 0.26	0.51 ± 0.15	0.437
	Post-Treat. 3rd Month	0.49 ± 0.16	0.53 ± 0.25	0.52 ± 0.16	0.866
	Post-Treat. 6th Month	0.52 ± 0.17	0.53 ± 0.21	0.52 ± 0.18	0.985
	[2]p	0.300	0.296	0.938	
	[3]p		0.790		
Eos %	Pre-Treatment	2.16 ± 1.41	2 ± 1.37	2.49 ± 1.94	0.641
	Post-Treat. 3rd Month	1.83 ± 1.44	1.64 ± 0.82	2.44 ± 1.58	0.165
	Post-Treat. 6th Month	1.8 ± 1.09	1.63 ± 0.74	2.84 ± 1.89	**0.018** [f]
	[2]p	0.257	0.226	0.449	
	[3]p		0.118		
Eos	Pre-Treatment	0.17 ± 0.11	0.16 ± 0.13	0.2 ± 0.18	0.731
	Post-Treat. 3rd Month	0.14 ± 0.1	0.14 ± 0.08	0.2 ± 0.16	0.219
	Post-Treat. 6th Month	0.14 ± 0.09	0.13 ± 0.08	0.23 ± 0.16	**0.032** [f]
	[2]p	0.241	0.290	0.529	
	[3]p		0.184		
Baso%	Pre-Treatment	0.93 ± 0.31	0.91 ± 0.45	0.77 ± 0.34	0.747
	Post-Treat. 3rd Month	0.94 ± 0.37	0.87 ± 0.47	0.91 ± 0.38	0.904
	Post-Treat. 6th Month	0.93 ± 0.31	0.88 ± 0.39	0.83 ± 0.3	0.729
	[2]p	0.995	0.837	0.278	
	[3]p		0.740		
Baso	Pre-Treatment	0.09 ± 0.06	0.07 ± 0.07	0.07 ± 0.05	0.850
	Post-Treat. 3rd Month	0.06 ± 0.07	0.09 ± 0.05	0.07 ± 0.06	0.310
	Post-Treat. 6th Month	0.07 ± 0.05	0.07 ± 0.04	0.07 ± 0.05	0.955
	[2]p	0.255	0.269	1.000	
	[3]p		0.849		

Data were shown as mean ±standard deviation and n (%). [1]: Results of the comparison among groups. [2]: Results of the comparison among pre-treatment, post-treatment 3rd month and post-treatment 6th month measures. [3]: Results of the comparison among three groups according to alterations of hematologic parameters. [f]: There was statistically significant difference between group 2 and group 3.

The incidence of anemia is increased in patients with diabetes. The reason is multifactorial. Chronic hyperglycemia causes abnormal red blood cells and renal sympathetic denervation is associated with oxidative stress and autonomic neuropathy [6]. Hypoxic environment occurs in the renal tubulo interstitial. The amount of erythropoietin produced by the peritubular fibroblasts reduces and becomes inappropriate production. The earliest and the most important reason of anemia in diabetic patients is inappropriately and low erythropoietin levels [1]. Systemic inflammation, functional hematinic deficiencies, erythropoietin resistance and reduced red cell survival also drive anemia in the setting of impaired renal compensation [7].

Mean platelet volume (MPV Mean Platelet Volume), measured by the hematology analyzers, is a marker showing platelet function and activation. Altered platelet morphology and function can be considered as a factor for risk of micro-and macrovascular diseases [2, 8]. Large platelets are younger and more reactive. Therefore, these platelets secrete more serotonin and β-thromboglobulin, contain more intense granules and produce more thromboxane A2 [9-12]. All of these give rise to a procoagulant effect and may cause thrombotic vascular complications. It may talk about the relationship between changes in platelet function especially MPV and diabetic vascular complications [2].

There are many studies showing the relationship between MPV and diabetes mellitus. There are studies showing the relationship between MPV and level of fasting blood glucose, postprandial blood glucose, and impaired fasting glucose and HbA1c levels in diabetic peripheral arterial disease. MPV values was found increased in all of these studies [2, 13-18]. We did not found significant change in MPV values but a significant decrease found in platelet counts in OAD group at six month. Avoid an increase in MPV, falling in platelet counts showed that OAD therapy may be effective in preventing vascular complications of diabetes mellitus.

Diabetes mellitus is a chronic inflammatory disease. In studies, peripheral blood leukocyte count [19], acute phase reactants such as C-reactive protein (CRP) [20], interleukin 6 (IL-6) [21], tumor necrosing factor α (TNF-α) [22], serum-amyloid A (S-AA) [23, 24], was found increased in patients with impaired fasting glucose or insulin resistance. An inverse relationship was shown between HbA1c levels and inflammatory cytokine levels in the blood. This chronic inflammatory process is is supressed by regulation of blood glucose [3]. A prospective study including twenty-study meta-analysis showed that number of peripheral blood leukocytes, basophils, eosinophils and neutrophils increased, no change in the number of monocytes in patients with Type 2 DM [4]. We found significant difference in the number of lymphocytes ($p = 0.029$) and basophils ($p = 0.029$) in insulin using group in 6th month. This result shows that insulin therapy may be effective in suppressing chronic inflammatory process. A statistically significant relationship was showed between blood leukocyte count and glucose intolerance in the study made by Gokulakrishnan K. and et al [25].

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