Spectrum Journal of Innovation, Reforms and Development
Volume 15, May, 2023 | ISSN (E): 2751-1731
Website: www.sjird.journalspark.org

FENOFIBRATE IN THE COMPLEX TREATMENT OF COMPLICATIONS OF TYPE 2 DIABETIC RETINOPATHY

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ABSTRACT:
Today, diabetes mellitus is considered a "pandemic", and the number of patients with this disease and its complications is increasing day by day. Diabetes mellitus is a severe complication of diabetic retinopathy that leads to blindness and disability in people. Timely detection, prevention and effective treatment of this complication are among the urgent tasks facing endocrinologists. Today, taking into account such risk factors as hyperglycemia, dyslipidemia and uncontrolled arterial hypertension, which play a leading role in the pathogenesis of complications of diabetic retinopathy, many studies are being carried out in the world on the effective complex treatment of this complication. This article talks about the next study conducted at the multidisciplinary clinic of the Tashkent Medical Academy.

Keywords: DM - Diabetes mellitus, Diabetic retinopathy, Dyslipidemia, Fenofibrate (Tricor).

Introduction

In 2017, according to the IDF, there were 425 million people with diabetes worldwide, and that number is expected to reach 629 million by 2045. According to a 2003 report by U.S. cardiologists, 80% of patients with CHD die from cardiovascular disease (CVD), and 75% of patients with CHD end up in the hospital with recurrent CVD. Especially in these patients, the

accession of vascular atherosclerosis exacerbated the negative consequences of the process and even accelerated the process. The role of dyslipidemia in the pathogenesis of atherosclerosis is particularly important, and it usually occurs in the form of "cholesterol triad" (hypertriglyceridemia, increased VLDL and decreased HDL).

Diabetic retinopathy is one of the serious causes of decreased visual acuity, and this complication is especially common in diabetic patients of working age. Though laser therapy is considered the main method of diabetic retinopathy treatment, it is practically carried out at the last stages of retinopathy and does not always give the expected results, as a result of which the patient may lose the ability to see for the rest of his life. In fact, the ideal situation for doctors is to prevent this complication from progressing to the next stages and reduce the need for laser therapy. This has caused increased attention to fenofibrate worldwide in recent years.

Material and Methods

Fifty-two patients with type 2 diabetes mellitus and diabetic retinopathy with a duration of diabetes not exceeding 8-15 years (10.10 ± 0.26) were examined. Of these patients, 37 (71.1%) were women and 15 (28.8%) were men. The patients' age ranged from 45 to 65 years, the mean age in the group was 54.6±2.52 years. Body mass index (BMI) of the patients was 26.15 ± 0.47 (kg/m2). All patients had systolic and diastolic BP 140 and 90 mm higher, respectively (see table).

All patients were divided into 3 such groups depending on what drug they received or did not receive, and the type of study parameter: main, comparative and control group. The number of patients in the main group was 27 who received fenofibrate, tricor 145 mg (Abbot Laboratories) once a day in the morning. There were 25 patients in the control group, in this group fenofibrate was not received and were under observation.

№	Groups	Number of patients (%)
1	**Main group**	27 (51.9)
3	**Control group**	25 (48.1)

№	General characteristics	Indicators (number of patients = 91)
1	Age (years)	54.6 ± 2.52
2	Gender (Male)	28.8%
3	BMI (kg/m2)	26.15 ± 0.47
4	Duration of type 2 diabetes mellitus (years)	10.10 ± 0.26
5	Arterial blood pressure (mm Hg)	140 ± 2.67 90 ± 1.38

Research results and discussion.

In the blood tests of the patients glycated hemoglobin (HbA1c (%)) was 7.2% ± 0.38 in the main group, 7.3% ± 0.53 in the comparison group, 7.1% ± 0.38 in the control group, plasma glucose content in venous blood after breakfast in the main group was 7, 1 ± 0.52 mmol/l, in

the control group 7.3 ± 0.63 mmol/l, in the control group 7.32 ± 0.55 mmol/l, in the main group 11.5 ± 0.82 mmol/l, in the control group 11.3 ± 0.67 mmol/l. L in the control group 2 h after a meal and reached 11.2 ± 0.64 mmol/l (see table).

№	Glycemic profile	Indications at the first visit	
		Main	Control
1	Glycated hemoglobin, HbA1c (%)	7.2% ± 0.38	7.1% ± 0.38
2	Glucose (fasting), mmol/l	7.1 ± 0.52	7.32 ± 0.55
3	Glucose (2 hours after meal), mmol/l	11.5 ± 0.82	11.2 ± 0.64

№	Glycemic profile	Indications after 6 months		p-value
		Main	Control	
1	Glycated hemoglobin, HbA1c (%)	7.2%±0.37	7.1% ± 0.37	p1<0.05 p2<0.05
2	Glucose (fasting), mmol/l	7.35 ± 0.69	7.1 ± 0.67	p1<0.05 p2<0.05
3	Glucose (2 hours after meal), mmol/l	10.8 ± 0.52	10.9 ± 0.59	p1<0.05 p2<0.05

In the main group it was noted that changes on the ocular fundus of the patients were stable, visual acuity improved. At primary examination 27 patients of the main group were diagnosed with microangiopathic complications of DR, 17 of them had nonproliferative stage of DR, 10 - preproliferative stage of diabetic retinopathy. Although there were no changes in patients of the main group after 6 months of investigation, there were positive changes in the dynamics of ocular fundus changes. It was noticed that it manifested itself differently in different patients. Decrease in the number of hemorrhages on the ocular fundus, decrease in the number of microaneurysms, decrease in the number of small intraretinal hemorrhages were noted.

After 3 months of study, all patients were re-examined for carbohydrate metabolism and the parameters in the main group were compared with the results in the other groups. Glycosylated hemoglobin, HbA1c (%) was 7.2%±0.37 in the control group, 7.3%±0.39 ($p<0.05$) in the control group, 7.1%±0.37 ($p<0.05$) in the control group. The amount of glucose (mmol/L) in the blood of patients examined on an empty stomach at lunchtime was 7.4±0.72 in the main group and 7.1±0.67 ($p<0.05$) in the control group. The amount of glucose determined 2 hours after a meal (mmol/L) was 10.8±0.52 ($p<0.05$) in the main group and 10.9±0.59 ($p<0.05$) in the control group.

Lipid spectrum (mmol/L):	Indications at the first visit			p-value
	Main	Control	Healthy control group (HCG)	
Triglycerides	2.3 ± 0.12	2.4 ± 0.17	1.05 ± 0.03	p1<0.05 p2<0.05 p3<0.05
LDL	3.2 ± 0.34	3.7 ± 0.35	2.1 ± 0.06	p1<0.05 p2<0.05 p3<0.05
HDL	0.89 ± 0.06	0.83 ± 0.04	1.5 ± 0.03	p1<0.05 p2<0.05 p3<0.05
Total cholesterol	5.3 ± 0.75	6.0 ± 0.72	3.6 ± 0.12	p1<0.05 p2<0.05 p3<0.05

p1 = p-value relative to HCG and main group values
p2 = p-value relative to hCG and comparison group values
p3 = p-value relative to hCG and control group

Lipid spectrum (mmol/L):	Indications after 6 months		p-value
	Main	Control	
Triglycerides	1.6 ± 0.1	2.32 ± 0.16	p1<0.01 p2=0.72
LDL	2.4 ± 0.28	3.73 ± 0.36	p1<0.01 p2=0.8
HDL	1.43 ± 0.09	0.85 ± 0.05	p1<0.01 p2=0.9
Total cholesterol	4.1 ± 0.70	5.9 ± 0.74	p1<0.05 p2=0.73

p1 = asosiy guruh va qiyosiy guruh ko'rsatkichlariga nisbatan p-miqdor
p2 = asosiy guruh va nazorat guruh ko'rsatkichlariga nisbatan p-miqdor

As can be seen from the above tables, the lipid profile in the blood of patients was determined in the 3 groups before the study and after 6 months, while in the control group of healthy people these parameters were studied only before the study and compared with the results of the other groups. Significant changes in lipid profile were observed in the main and comparison groups (patients receiving fenofibrate). In particular, according to the results, triglycerides in the main group decreased from 2.3 ± 0.12 mmol/l to 1.6 ± 0.1 mmol/l at the end of the study. This index was lower by 0.3 mmol/l compared to the main group (p<0.01). But in patients in the control

group the change in this index was a decrease of 0.08 mmol/l, and compared to the main group it was 0.62 mmol/l lower (p=0.72). Low-density lipoproteins (LDL) decreased from 3.2 ± 0.34 mmol/l to 2.4 ± 0.28 mmol/l in the main group (p<0.01). In the control group, patients had a 0.03 mmol/L increase in LDL, and the overall difference compared with the main group was 1.33 mmol/L after 6 months (p<0.8). There was also a distinct improvement in high-density lipoproteins in the main group, and HDL increased from 0.89±0.06 mmol/L to 1.43±0.09 mmol/L. In the control group, HDL increased by 0.02 mmol/L, which was 0.58 mmol/L worse than in the main group (p=0.9). The main and comparison groups had similar results for total cholesterol, and after 6 months, the difference for this index was 0.1 mmol/L (p<0.05). However, despite the 0.1 mmol/L decrease in total cholesterol in the control group, total cholesterol was 5.9 ± 0.74 mmol/L, and this value remained significantly higher than the target values, and the difference with the baseline group was also high (p<0.73). In conclusion, although fenofibrate and rosuvastatin led to improvements in patients with respect to the effect on the lipid profile in the body, the benefits for some parameters were distributed differently. For example, improvements in TG and HDL counts were noted in the main group, whereas the comparison group prevailed in terms of LDL and total cholesterol counts.

Dynamics of visual acuity at the beginning and at the end of the study in patients of the compared groups (M±m)

Visiting time	Groups		P-value
	Main	Control	
1st visit (before treatment)	0,68±0,03	0,65±0,05	P>0,05
2nd visit (after treatment)	0,69±0,02	0,59±0,04	P<0,01

In the main group it was noted that changes on the ocular fundus of the patients were stable and visual acuity improved. Diabetic retinopathy was diagnosed in 27 patients of the main group at primary examination, 17 of them had nonproliferative stage of diabetic retinopathy and 10 of them had preproliferative stage of diabetic retinopathy. Although there were no changes in the patients of the main group after 6 months of study, there were positive changes in the dynamics of ocular fundus changes. It was noticed that it manifested itself differently in different types of patients. Decrease in the number of hemorrhages on the ocular fundus, decrease in the number of microaneurysms, decrease in the number of small intraretinal hemorrhages were noted.

Changes in the stages of diabetic retinopathy in the compared groups before and after the study

№	**Stages of diabetic retinopathy**	**Initially**		**After 6 months**	
		Control	**Main**	**Control**	**Main**
1	Nonproliferative	12	17	11	17
2	Preproliferative	13	10	14	10

In one of the patients in the control group, it was noted that non-proliferative diabetic retinopathy progressed to the preproliferative stage. This was caused by the increased number of retinal hemorrhages in the fundus of the eye. In 5 patients (41.66%) of this group, changes in the fundus of the non-proliferative stage were observed.

Conclusion

1. During the treatment, indicators of carbohydrate metabolism decreased in the main group against the background of hypoglycemic treatment, glycated hemoglobin decreased by 0.1%, fasting by 0.2 mmol/l, and postprandial glycemia by 0.5 mmol/l.
2. According to the analysis of fundus examinations, the development of diabetic retinopathy slowed down and improved, and visual acuity improved in the main group.

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