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RESEARCH ARTICLE

Arterial Hypertension and Diabetes Mellitus: Therapy with Telmisartan, Interrelation Modeling, Approaches to Diagnosis and Complex Therapy

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Abstract

Diabetes mellitus (DM) is an illness for an increasing number of people. Among the consequences that DM leads in the first place can be called degradation changes in the body, ultimately leading to limited physical capabilities. In DM, one of the related phenomena is a high risk of cardiovascular diseases (CVDs). This is due to the following factors: a) already the presence of risk factors before the DM development; b) the presence of obesity; c) arterial hypertension (AH). AH is present in 75-80% of patients with DM type 2, with half of them die. Due to the fact that AH and DM have a pathogenetic relationship, this fact naturally increases the risk of death. On the basis of data from Polyclinic No. 3 in St. Petersburg (Russia), a group of 200 patients with DM (female, age range 45-65) with concomitant AH were selected. The control group consisted of 100 females of the same age. Therapy was carried out with Telmisartan, with a dosage of 85 mg for a period of 8 weeks. As a result of the therapy, telmisartan has shown a positive effect on such parameters as carbohydrate metabolism and insulin resistance, as well as lipid metabolism. For patients with metabolic syndrome, during the period of therapy, telmisartan was noted to significantly ($p \leq 0.05$) reduce the rates associated with lipid metabolism. First of all it affected the cholesterine rate in the blood .Also obtained reliable data on the triglycerides reduction (TG), from 1.67 mmol/l 2.0 times more than half of the patients (41% of 75% who had elevated TG levels) undergoing telmisartan therapy. In addition, a decrease in the load on the AH time index, as well as a decrease in microalbuminuria rate was noted in patients. This indicates the organ-protective effect of telmisartan therapy. Permanent control of blood pressure is of primary importance for CVD prevention in patients with DM. When prescribing an antihypertensive agent, it is necessary to take into account RAAS-blocking drugs (renin-angiotensin-aldosterone system). Telmisartan has shown a positive effect on carbohydrate metabolism, reduced the elevated lipids levels (in particular, TG), and also affected insulin resistance.

Keywords: *DM (diabetes mellitus), AH (arterial hypertension), CVD (cardiovascular disease), telmisartan.*

Introduction

Diabetes mellitus (DM) is an illness affecting an increasing number of people. Among the DM-caused consequences in the first place include degradation changes, ultimately leading to limited physical capabilities. High risk of cardiovascular diseases (CVD) is one of the common DM comorbidities. All of the comorbidities stated can result as fatal. A steady increase in the number of DM-connected cases all over the planet has been recorded. By 2018, patients with DM numbered over more than 200 million people, then a quarter of a century later their number will increase by a third [1, 2]. Almost all (at least 90%) are patients with DM type 2. The main organs that are exposed to the negative effects of DM and AH associated with DM are the heart, kidneys, as well as the blood vessels of the brain and retina. As a rule, the lethal outcome of the joint action of these two diseases is associated with a third, coronary heart disease (hereinafter-CHD). Less significant, but fatal factors may be myocardial infarction, renal failure, irreversible changes that occur when the blood circulation in the brain is impaired.

According to some reports, an increase in diastolic AD (blood pressure) on each 6 mm of mercury contributes to the development of coronary artery disease with a probability of 25%, and stroke - 0.5 times higher than coronary heart disease (40%). The maximum among these diseases with an increase in blood pressure increases the risk of renal failure, by 3-4 times [3, 4].

For DM type 2, almost in 80% of cases the development of DM is preceded by AH [5]. All these diseases, as mentioned above, are interconnected also at the physiological level. So, insulin resistance (hereinafter -IR) contributes to the emergence and development of hyperinsulinemia. The latter is a major factor in the AH development. If an increased insulin concentration is detected in the blood plasma, then AH progression is highly likely to happen (Arnlöv et al., 2005).

As you know, hyperinsulinemia contributes to an increase in blood pressure due to several factors [6, 7]:

- Insulin increases the level of activity of the sympathetic adrenal system (SAS).
- Insulin increases the absorption of sodium ions in the kidney tubules. The consequences of this are an increase in the concentration of Na^+ and Ca^{2+} ions in the vessel walls, which ultimately leads to their lumen narrowing, an increase in their peripheral resistance, and, ultimately, a vasospasm.
- Is followed by insulin blockade of enzyme activity involved in ion exchange (Na-K-ATPase and Ca-Mg-ATPase). That's the cause for their concentration increases.

Among modern methods of treating DM with concomitant AH, insufficient attention has been paid to Telmisartan therapy. In fact, this chemical compound has not been tested in patients with DM with AH. This was the main aim of this study. In addition, we have conducted a comparative analysis of DM therapies with concomitant AH, and developed recommendations based on the analysis.

The main goal of this work is to analyze the results of Telmisartan therapy for patients with DM with concomitant AH. In the telmisartan therapy analysis, a comprehensive approach was used (physiological parameters monitoring, carbohydrate and lipid metabolism rates). An integrated approach should facilitate the diagnosis, as well as the treatment tactics.

Materials and Methods

Based on the data from the case histories, a group of 200 patients with DM (female, age range 45-65) with concomitant AH was selected in polyclinic No. 3 in St. Petersburg (Russia). The average age was 58.4±3.5. Telmisartan was administered with a dosage of 85 mg over a period of 8 weeks. A control group of 100 patients of the same age range did not receive telmisartan, but underwent standard DM treatment (insulin). At the beginning of therapy, blood samples were taken from all patients. The same was repeated after 8 weeks of therapy.

The following indicators were taken into account: TG level (hereinafter, the unit of measurement is mmol/l), the total cholesterine concentration in the blood (or TC), as well as various groups of lipoproteins that differ in terms of density - low (LDL), high (HDL) and very low (VLDL). The obtained parameters were compared with the control group, as well as with patients with DM with AH before starting telmisartan therapy. Reliability was evaluated using a two-sample t-test, with a significance level of $p \leq 0.05$. For statistical processing the program Past was used, v. 3.0

Results

As a result of the therapy, Telmisartan has shown a positive effect on such parameters as carbohydrate metabolism and insulin resistance, as well as lipid metabolism (Fig. 1). Telmisartan during the treatment period first of all significantly ($p \leq 0.05$) significantly decreased the indicators associated with lipid metabolism in the group of patients with metabolic syndrome. First of all, these changes affected the level of cholesterine in the blood .Also obtained reliable data on the reduction of triglycerides (TG), from 1.67 mmol/l 2.0 times more than half of the patients (41% of 75% who had elevated TG levels) undergoing Telmisartan therapy.

In addition, other reliable results were recorded: a decrease in the load on the AH time index, as well as a decrease of microalbuminuria in patients. This indicates the organ-protective effect of telmisartan therapy.

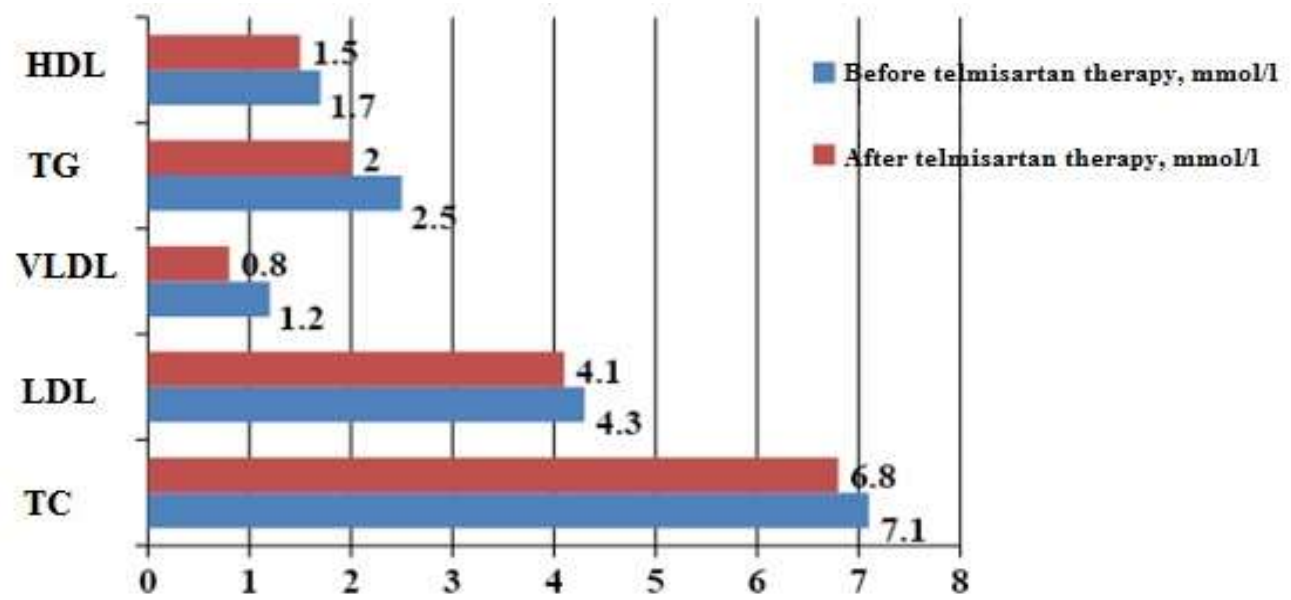

Fig. 1: The level of lipid metabolism in the group of patients treated with telmisartan, before and after treatment

Command term: TC-total cholesterine in the blood, LDL-Low Density Lipoproteins, VLDL-Very Low Density Lipoproteins, TG triglycerides, HDL-High Density Lipoproteins.

As can be seen from Fig. 1, telmisartan had the maximum effect on TC, VLDL, TG and HDL. For these indicators, the differences are significant ($p \leq 0.05$, Table 1).

Table 1: Lipid metabolism in patients with AH in the control group and in the group with telmisartan therapy

Indicators, mmol/l	Control	Before telmisartan therapy	After telmisartan therapy
TC	6.9±0.1	7.0±0.12	6.7±0.11
LDLD	4.1±0.1	4.2±0.1	4.0±0.1
VLDL	0.9±0.09	1.1±0.1	0.75±0.09
TG	2.2±0.3	2.4±0.3	1.9±0.25
HDL	1.65±0.05	1.68±0.05	1.59±0.09

Indicators of lipid metabolism in the control group stay between the group of patients before telmisartan therapy and after therapy. At the same time, in all cases, telmisartan therapy reduced the main indicators of lipid metabolism. In addition to the above effects, chosen treatment with telmisartan was noted to have a pronounced antihypertensive effect.

These data correspond for a dosage of 80 mg every day, for patients with different AH forms (mild to moderate), as well as with concomitant metabolic syndrome. Data were obtained confirming a significant decrease in pressure level, both systolic and diastolic.

These data are reliable for the entire period of the day. The results can be used as confirmation of a decrease in pressure load, AH on the condition of affected organs. In addition to drug therapy, there are a number of other strategies aimed at preventing, preventing and reducing existing DM and AH.

Therapeutic Strategies

The main focus of such strategies is to reduce blood pressure to a normal level. This, in turn, further reduces the risk of diseases such as stroke, heart attack and AH. Preventive measures include a change in the life of the patient. This is a complex set of conditions and requirements, including a diet that excludes the intake of a high amount of carbohydrates in the bloodstream (the norm is 800-1500 kcal/day), various kinds and regular physical activities, as well as giving up smoking (if present).

For all these requirements, the patient's weight is monitored. In the case of its reduction, we can talk about a positive effect on the AH therapy, and also, as a consequence, the abolition of pressure-reducing drugs follows. Apart from the diet, such physical activities as walking are relevant, this has become widespread in recent years. The duration of walks should be

at least half an hour a day, with 2-4 days free from those. Inclusion of loads into prophylactic methods also contributes to the normalization of blood pressure, blood lipids and a decrease in insulin resistance. In addition to preventive therapies, pharmacological ones are no less important. Therapy begins with the appointment of drugs, but taking into account existing diseases and physiological disorders, such as high blood pressure and insulin resistance.

When prescribing an antihypertensive agent, it is necessary to take into account drugs whose action blocks RAAS (renin-angiotensin-aldosterone system). Taking such drugs significantly reduces the risk of DM itself, as shown by numerous clinical studies (e.g., CAPP, HOPE, LIFE, etc.). Blockers include primarily drugs, APF inhibitors, and angiotensin receptor antagonists (ARA).

The action of these inhibitors and blockers is manifested in an increase in the sensitivity of tissues and cell membranes to insulin, in a general regression of the development of DM type 2, an improvement in blood carbohydrate content, and normalization of lipid metabolism. Thus, a combination of prophylactic methods as a prevention of the development and progression of DM and AH, as well as pharmacological, normalizing carbohydrate and lipid metabolism, can effectively fight DM and AH, at least in the early stages of development.

Discussion

DM type 2 is a very serious disease, the result of which, as a rule, is disability and death. This statement has found numerous confirmations: among elderly patients (from 65 years old) more than half (60%) have various kinds of complications, such as cardiovascular diseases (40%) [8].Probability of developing diseases associated with the cardiovascular system is 4 times higher in patients with DM type 2 compared with the control [9, 11].

The risk of premature (sudden) death also increases; at about the same level as in people who have had myocardial infarction, but do not have DM type 2. Even in developed countries with a modern medical system, in terms of the number of deaths, DM holds a stable 3-4 place among other diseases.

In addition to sudden death and the development of CVD diseases, DM leads to the development of blindness, or, at best, to a general decrease in vision. The development of CVS diseases contribute to the effects associated with hyperglycemia. There is a direct correlation between the development of angiopathy and the level of glycemia in DM type 2. There is evidence directly indicating that even with an increase of only 1% in the level of glycemia, there is a comprehensive increase in the risk of various diseases: mortality due to DM increases by 20%, due to a heart attack - by 15%, due to vascular diseases - by 40%.

The likelihood of developing cataracts increases by 20% [12]. At the same time, death rates between groups of patients with DM type 1 and type 2 differ by more than 2 times - 30 and 70%. Considering the age factor, patients with DM type 2 have a shorter life and a 2-fold greater likelihood of premature death compared with the control of the same age. One of the methods for preventing DM is the constant monitoring of the patient's blood pressure [13].

In the case of a combination of high blood pressure and DM type 2, monitoring and preventing the increase in glycemia reduces the likelihood of a number of diseases, in particular complications at the level of micro vessels. Blood pressure control is more indicative (decrease if it exceeds 140/80 mm Hg), which yields significant results for sudden death (a 25% probability decrease), stroke death (40%), and visual acuity deficiency (a 50% decrease) [14].

Thus, control over the level of blood pressure is more effective than control over the level of glycemia. Moreover, with lower blood pressure (up to 80 mm Hg diastolic blood pressure), the risk of developing CVS diseases is more than half reduced.

Therapy associated with the prevention of AH also reduces the likelihood of death (by 15%), and, to a greater extent, the likelihood of death due to CVS diseases [15, 16]. In modern therapy, general recommendations related to AH and DM have been developed [17, 23]. These include the measures we have already mentioned to reduce body weight, control body mass indicators, and limit the use of salt along with food. The norm of blood pressure (less than 130/80 mm Hg).

Monotherapy with one medicine was rejected; preference was given to complex treatment. The exceptions with monotherapy are only drugs related to blockers and RAAS inhibitors.

In connection with the presence of orthostatic hypotension, all actions associated with the measurement of blood pressure should be carried out in the vertical body position. The general focus of therapy should be comprehensive and related to the prevention of all factors leading to the development of CVS diseases. Telmisartan considered in our work also belongs to those of the complex effects mentioned in the recommendations. The positive effects of telmisartan therapy include an improvement in lipid metabolism, a decrease in pressure indicators, both systolic and diastolic blood pressure, as well as stabilization of carbohydrate metabolism.

Conclusions

Telmisartan has shown a positive effect on the parameters of carbohydrate metabolism, reduces the increased content of lipids (in particular, TG), and also affects insulin resistance.

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