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GLUCOSE-LOWERING THERAPIES IN TYPE 2 DIABETIC PATIENTS WITH COMORBID OVERWEIGHT/OBESITY AND ARTERIAL HYPERTENSION: RETROSPECTIVE ANALYSIS DATA

[1]Vivsiana Iryna, [1]*Marushchak Mariya, [1]Krynytska Inna, [2]Lepyavko Andriy, [3]Mazur Lyudmyla

[1]Department of Functional and Laboratory Diagnostics, I Horbachevsky Ternopil National Medical University, Maidan Voli 1, 46001 Ternopil, Ukraine.
[2]Department of Internal Medicine N2, I Horbachevsky Ternopil National Medical University, Maidan Voli 1, 46001 Ternopil, Ukraine.
[3]Department of Higher Nursing Education, Patient Care and Clinical Immunology, I Horbachevsky Ternopil National Medical University, Maidan Voli 1, 46001 Ternopil, Ukraine.

*marushchak@tdmu.edu.ua

Abstract

Type 2 diabetes mellitus (T2DM) patient outcomes, treatment options, and corresponding healthcare expenses are affected by the presence of different comorbidities. The aim of this work was to analyze the frequency of prescription of different types of glucose-lowering therapy in type 2 diabetic patients with comorbid overweight (OW)/obesity (OB) and arterial hypertension (AH); to evaluate the role of comorbidity in the choice of glucose-lowering therapy and its efficacy. We analyzed 579 medical records of type 2 diabetic patients, which were treated at inpatient Endocrinological department of the municipal non-profit enterprise "Ternopil University Hospital" of Ternopil Regional Council (Ternopil, Ukraine) in 2018-2019 years. It was found that the most of type 2 diabetic patients with normal body weight received oral hypoglycemic agents and insulin therapy, whilst OW/OB served as criterion for the choice of mono- or combined glucose-lowering therapy independently on presence/absence of AH. Therefore, body mass index was one of the main criteria for the choice of treating tactics at T2DM. At the same time prescription of the different schemes of glucose-lowering therapy to the type 2 diabetic patients with comorbid OW/OB and AH did not allow to reach the target levels of glycated hemoglobin, indicating insufficient effectiveness of therapy.

Keywords: *type 2 diabetes mellitus, comorbidities, therapy, effectiveness.*

Introduction

Diabetes mellitus (DM) is a global social and medical problem caused by the rapid spread of the disease and the development of serious complications such as micro- and macroangiopathies, which significantly reduce the quality and life expectancy of patients (1-4). It should be noted that DM is associated with a more severe course of coronavirus disease 2019 (5). A report from the International Diabetes Federation shows that in 2019 463 million people were diagnosed with DM worldwide, and of this figure, the majority (91%) suffered from type 2 diabetes (T2DM) (6).

The presence of other comorbidities or chronic diseases drastically affects DM patient outcomes, treatment and management options, and associated healthcare expenses (7). While the hallmark of T2DM is insulin resistance (IR), it is associated with other metabolic disorders such as dyslipidemia and obesity (8,9). At the same time up to 75% of adults with DM have concomitant arterial hypertension (AH) (10), which is the leading cardiovascular disease-attributable cause of morbidity and mortality among T2DM patients (11).

A wide range of glucose-lowering therapies is available for the treatment of T2DM patients, and each class has advantages and disadvantages based on their mechanisms of action and clinical experience (12). The complexity of interaction between T2DM, comorbidities, and emerging complications requires a clinical approach that manages risk while maintaining indicated therapeutic goals (13).

The current methods of T2DM treatment are oral insulin secretagogues, sulfonylureas, repaglinide, nateglinide, biguanides, thiazolidinediones, alpha-glucosidase inhibitors, pramlintide and exenatide (14). The first choice for the treatment of T2DM, based on its well-defined efficacy, safety profile, low-cost and potential to reduce the risk of cardiovascular events is metformin (15), which inhibits hepatic glucose production and improves insulin sensitivity (16). Decrease in IR is reached by intensification of kinase activity and processes of phosphorylation of insulin receptors. Such effects of insulin as transcription, translation and synthesis of key-enzymes responsible for translocation of the own glucose transporters on plasmatic membrane are intensified at the same time. These processes contribute to increase of glucose intake by hepatocytes, myocytes and adipocytes (17).

Insulin also can be used as hypoglycemic agent for T2DM patients. If an initial glycated hemoglobin (HbA1c) level exceeds 9%, insulin therapy is recommended for T2DM patients (18). Shestakova M.V. et al. suggest that insulin therapy is recommended for T2DM patients when changes of life style and therapy by oral hypoglycemic drugs do not allow to reach the effective control of glycaemia; timeous start of insulin therapy with selection of effective dose is important as well as timely intensifying of insulin therapy (19).

Therefore, the aim of our study was to analyze the frequency of prescription of different types of glucose-lowering therapies in type 2 diabetic patients with comorbid overweight (OW)/obesity (OB) and AH; to evaluate the role of comorbidity in the choice of glucose-lowering therapy and its efficacy.

Materials and methods

With an aim of retrospective analysis, we analyzed 579 medical records of type 2 diabetic patients, which were treated at in patient endocrinological department of the municipal non-profit enterprise "Ternopil University Hospital" of Ternopil Regional Council (Ternopil) in 2018-2019 years. All patients were divided into 6 study groups depending on the presence of OW/OB and AH. Distribution of the groups is shown in table 1. Age aspect did not have significant difference within the groups of the patients.

Verification of T2DM was performed according to recommendations of American diabetic association (2019) (14). Diagnostic criteria of T2DM were based on HbA1c level (≥6.5%), that was determined by automatic biochemical analyzer COBAS 6000 (Roche Hitachi, Germany) and on

glucose level that was determined by standard kit on automatic biochemical analyzer COBAS INTEGRA® 400 (Roche Diagnostics). Level of insulin in blood was determined by immunoenzyme analyzer of company "Thermo Scientific Multiskan FC". IR was evaluated by HOMA-IR index (Homeostasis Model Assessment for Insulin Resistance), that was calculated according to the formula: HOMA-IR = (fasting glucose of plasma, mmol/L × fasting insulin of plasma, mIU/mL) / 22.5.

Diagnosis of AH of the 1 stage was concluded according to recommendations of ESC/ESH on AH (2018), represented at the congress of European society of cardiologists (ESC) (20). Left ventricle hypertrophy was proved by electrocardiography.

Body mass index (BMI) was calculated according to the formula: BMI = body weight (kg) / height (m^2). The data were interpreted according to the recommendations of WHO: normal weight within 20.0 – 24.9 kg/m^2; excessive weight (preobesity) – 25.0-29.9 kg / m^2; obesity of the 1st degree – 30.0-34.9 kg/m^2; obesity of the 2nd degree – 35.0-39.9 kg/m^2 and obesity of the 3rd degree > 40.0 kg/m^2 (21).

We analyzed the frequency of prescription of mono- and combined glucose-lowering therapy at T2DM combined with OW/OB and AH and evaluated the role of comorbidity in the choice of corrective therapy and its effectiveness.

Nowadays, the 1st line drug in the treatment of T2DM in Ukraine, which is used most often according to recommendations of American Diabetes Association (ADA) and European Association for the Study of Diabetes is metformin (22-24). According to analysis of medical cards the patients took metformin in the dosage that provides effectiveness and maximal tolerance to the medicine, which was 1500-2000 mg/day.

Combined therapy used by the part of the patients, included metformin and derivatives of sulfonylurea in effective therapeutical dosages. Representative of the group of sulfonylurea drugs that was used most often in the treatment of T2DM because of its price policy, was gliclazide (25). At evaluation of the therapeutical effectiveness the target value of HbA_1c less than 7.0 % was estimated according to recommendations of ADA concerning control of glycaemia (14).

Patients with severe form of T2DM with significant chronic complications of the disease and patients who could not reach the glycaemia compensation by oral hypoglycemic agents, received combined treatment by adding basal insulin to metformin or intensive scheme of insulin therapy.

Study results were analyzed using STATISTICA 7.0 and MedCalc software. The Kolmogorov-Smimov test was used to compare probability distributions. Quantitative values, due to their non-parametric distribution, are presented in the form of median, lower, and upper quartiles, and compared using the Mann-Whitney test. For frequency values, the percentage ratio and its 95% confidence interval were calculated, and their comparative analysis was performed using Pearson's chi-square test and Fisher's bilateral test.

Results

Analysis of characteristics of carbohydrate metabolism has shown that levels of glucose, insulin and HOMA-IR index in the blood of patients of different study groups were statistically different by analysis of rank variations of Craskell-Wallace. Thus, level of glycaemia was the highest in patients with T2DM with normal body weight combined with AH. It was statistically higher for 25.1 % comparing to such value in patients with excessive body weight, T2DM and AH. Insulin level was statistically higher in the 5th group of patients with T2DM with excessive body weight combined with AH comparing to the 1st group (for 42.8 %) and to the 4th group (for 19.7 %). HOMA-index in patients with comorbid course of T2DM, OW/OB and AH was statistically higher comparing to the results of patients with T2DM and normal body weight, particularly for 22.7 % the 5th group and for 22.1 % - in the 6th group (table 2). At comparison of characteristics of carbohydrate metabolism in the 5th and 6th groups of patients, the statistical difference in the values was not present.

Evaluation of the severity of T2DM course has shown that inpatient treatment included the patients with moderate severity (316 patients) and with severe course (263 patients). Amount of patients with comorbid course of T2DM, OW and AH was statistically higher comparing to the patients of the 2nd group with moderate and severe course of T2DM. The same tendency was noted among the patients with comorbid course of T2DM, OB and AH, their amount was statistically higher comparing to the 3rd research group with moderate and severe course of T2DM (table 3). It should be noted that within the patients from the 1st, 2nd and 3rd groups the moderate severity of the course of DM prevailed, when among the patients from the other study groups moderate and severe courses were revealed nearly equally. Possibly it was connected with concomitant AH.

Analysis of compensation degree of DM showed that among the study patients 89 persons were subcompensated, 490 – decompensated. It should be noted, that uncompensated patients prevailed at all study groups. Herewith the number of both subcompensated and uncompensated patients with comorbid course of T2DM, OB and AH was statistically higher comparing to the same amount of the patients with T2DM and OB (table 4).

Analysis of the performed therapy revealed that the patients included into study received different types of glucose-lowering therapy. Patients of the 1st and 4th groups with normal body weight, T2DM and present/absent AH included predominantly decompensated persons with condition of moderate severity; most often they received oral hypoglycemic agents and insulin therapy. Patients from the 2nd and 3rd groups received mono- and combined per oral therapy almost equally. Patients from the 5th and 6th research groups received predominantly combined therapy. Analysis of dependence of hypoglycemic therapy prescribed to patients with T2DM on their BMI revealed statistically higher frequency of prescribing of oral hypoglycemic agents and insulin therapy to the patients with normal body weight (66.67 %), comparing to the overweighed and obese patients ($p<0.05$). Metformin was prescribed predominantly to the patients with overweight (45.45 %). Obese patients received equally mono- and combined oral therapy (40.91 %). Analysis of dependence of prescription of hypoglycemic therapy to the patients with T2DM and AH depending on BMI revealed statistically higher frequency of prescribing of oral hypoglycemic agents and insulin therapy to the patients with normal body weight (50.85 %) comparing to overweighed and obese patients ($p<0.05$). Combined therapy was prescribed predominantly to the patients with OW (39.69 %) and OB (52.88 %) (table 5). The results we obtained reflect the influence of comorbidity on the choice of glucose-lowering therapy at T2DM.

Different approaches to glucose-lowering therapy in patients with T2DM combined with OW/OB and AH does not enable to reach the target levels of HbA1c (table 6). According to results of our research the maximal effectiveness of prescribed therapy was observed in patients with T2DM and comorbid OB, which received mono- and combined oral therapy.

Table 6. HbA1c levels in type 2 diabetic patients with comorbid OW/OB and AH

Groups	Level of HbA1c			
	Target (<7.0 %)		High (>7.0 %)	
	N	%	n	%
T2DM+normal weight (n=39)	6	15.38	33	84.62
T2DM+OW (n=33)	5	15.15	28	84.85
T2DM+OB (n=22)	7	31.82	15	68.18
T2DM+ normal weight +AH (n=59)	8	13.56	51	86.44
T2DM+OW+AH (n=131)	13	9.92	118	90.08
T2DM+OB+AH (n=295)	53	17.97	242	82.03
χ^2 Pearson's, p	χ^2=8.88; p=0.114			

Discussion

AH is a common concomitant disease, associated with DM. High correlation between DM

and AH may be connected with general mechanisms of IR (26,27). But prescription of such antidiabetic drugs as insulin and sulfonylurea derivatives (28), according to the literature data, leads to elevation of arterial pressure within the several years after confirming the diagnosis of T2DM.

We found that type 2 diabetic patients with normal body weight and present/absent AH received combined glucose-lowering therapy – metformin and basal insulin or intensive scheme of insulin therapy. Type 2 diabetic patients with comorbid OW/OB and present/absent AH received both monotherapy (metformin) and combined therapy, including metformin and sulfonylurea derivatives in effective therapeutical dosages.

It is known that metformin increases sensitivity to insulin (29) and, therefore, may potentially decrease hyperinsulinemia and risk of AH in patients taking this drug. Hypoglycemic mechanism of metformin includes improving sensitivity of the tissues to insulin, decreasing IR and increasing sensitivity of peripheral tissues to insulin. Herewith suppression of the glucose synthesis occurs in liver, utilization of glucose increases, oxygenation of the fatty acids diminishes. Metformin slows down the absorption of carbohydrates in intestines, stimulates glucose utilizing by the cells of intestinal mucosa and smoothest the peaks of glycaemia after eating. Metformin is an antidiabetic oral drug, which action is characterized by suppression of gluconeogenesis through weakening of metabolism of lactate in the liver and slowing down the signaling pathway of glucagon (30). Results of Diabetes Prevention Program (DPP) research show the long-term effectiveness of life style modification and metformin intake for decrease the risk and postponing of development of T2DM in overweighed or obese people. Stable decrease of body weight at metformin intake is also confirmed in DPP Outcomes Study. Metformin's pleiotropic effects have a positive influence on a lipid profile, significantly decreasing the level of lipoproteins of the low density and increasing the level of lipoproteins of high density comparing to placebo (31).

Thus, metformin is well tolerated, it is not associated with hypoglycemia, promotes decrease of body weight, is safe in short and long perspective; moreover, it has cardioprotective effects. There is a need to proceed the further research to reveal the mechanisms of decrease of blood pressure at metformin intake, though some biological effects of metformin may explain such beneficial influence. Metformin protects cardiovascular system from oxidative stress and inflammation by means of 5'-adenosine monophosphate activated protein kinase-dependent and independent pathways (32). Clinical trials confirmed anti-atherogenic effects of metformin (33). Metformin suppresses the synthesis of glycation end products (34), glucose induced endothelial dysfunction (35), increases the synthesis of nitric oxide and improves angiogenic functions (36).

Therefore, metformin is recommended to the type 2 diabetic patients with comorbid OW/OB and AH. At the same time results of our retrospective study revealed the low efficacy of the present approaches of glucose-lowering therapy in patients with T2DM combined with comorbid OW/OB and AH concerning achievement of the target levels of HbA1c.

Conclusions

The most of type 2 diabetic patients with normal body weight received oral hypoglycemic agents and insulin therapy, whilst overweight/obesity served as criterion for the choice of mono- or combined glucose-lowering therapy independently on presence/absence of arterial hypertension. Therefore, body mass index was one of the main criteria for the choice of treating tactics at type 2 diabetes mellitus. At the same time prescription of the different schemes of glucose-lowering therapy to the type 2 diabetic patients with comorbid overweight/obesity and arterial hypertension did not allow to reach the target levels of glycated hemoglobin, indicating insufficient effectiveness of treatment.

References

1. Savych A, Marchyshyn S, Basaraba R, Lukanyuk M. Antihyperglycemic, hypolipidemic and antioxidant properties of the herbal mixtures in dexamethasone-induced insulin resistant rats. Pharmacologyonline. 2020; 2: 73-82.
2. Kritsak M, Konovalenko S, Stechyshyn I, Pavliuk B. Biotechnological methods of local treatment of infected wounds in diabetes mellitus in an experiment. Pharmacologyonline. 2021; 2:97-104.
3. Posokhova K, Stechyshyn I, Krynytska I, Marushchak M, Birchenko I, Klishch I. Comparative study of the effect of various forms of quercetin on experimental diabetes. Rom J Diabetes Nutr Metab Dis. 2018;25(4):383-8.
4. Degen A, Krynytska I, Kamyshnyi A. Changes in the transcriptional activity of the entero-insular axis genes in streptozotocin-induced diabetes and after the administration of TNF-α non-selective blockers. Endocrine regulations. 2020;54(3):160-71.
5. Kamyshnyi A, Krynytska I, Matskevych V, Marushchak M, Lushchak O. Arterial Hypertension as a Risk Comorbidity Associated with COVID-19 Pathology. Int J Hypertens. 2020;2020:8019360.
6. International Diabetes Federation. IDF Diabetes Atlas edition 2019. International Diabetes Federation [Internet]. [cited 2020 Aug 21]. Available from: https://www.idf.org/aboutdiabetes/what-is-diabetes/facts-figures.html.
7. Nowakowska M, Zghebi S, Ashcroft D, et al. The comorbidity burden of type 2 diabetes mellitus: patterns, clusters and predictions from a large English primary care cohort. BMC Med. 2019;17(1):145.
8. Hevko U, Kozak K, Krynytska I, Marushchak M. Diagnostic value of a complete blood count in type 2 diabetes mellitus and comorbidities. *Arch Balk Med Union.* 2020;55(4):601-7.
9. Marushchak M, Krynytska I, Mazur L, Klishch I, Gabor G, Antonyshyn I. The Relationship between Experimental Alimentary Obesity and Hard Tooth Tissues Mineralization. Jordan Medical Journal. 2017;51(1):25-33.
10. Long AN, Dagogo-Jack S. Comorbidities of diabetes and hypertension: mechanisms and approach to target organ protection. J Clin Hypertens (Greenwich). 2011;13(4):244-51. doi:10.1111/j.1751-7176.2011.00434.x
11. Akalu Y, Belsti Y. Hypertension and Its Associated Factors Among Type 2 Diabetes Mellitus Patients at Debre Tabor General Hospital, Northwest Ethiopia. Diabetes Metab Syndr Obes. 2020;13:1621-31.
12. Marushchak M, Hevko U, Krynytska I, Danylevych Y, Danchak S, Mazur L. Does comorbid obesity or chronic pancreatitis influence the choice and effectiveness of glucose-lowering therapy in type 2 diabetic patients? Archives of the Balkan Medical Union. 2021;56(1):24-32.
13. Thrasher J. Pharmacologic management of type 2 diabetes mellitus: available therapies. The American Journal of Cardiology. 2017;130(6S):S4-S17.
14. American Diabetes Association. Standards of medical care in diabetes – 2019 abridged for primary care providers. Clin Diabetes. 2019;37(1):11-34.
15. Akram M. Diabetes mellitus type II: treatment strategies and options: a review. J Diabetes Metab. 2013;4:9.
16. Zhuravleva L, Shekhovtsova Y. Comorbidity of chronic pancreatitis and diabetes type 2: possible options of pharmacoteraphy. Practical Doctor. 2016;5(3):21-5.
17. Demidova I, Gorohova T. Mechanism Of Action And Clinical Use Of Metformin (siofor®): Review Of Literature. Farmateka. 2009;17:10-5.
18. Petznick A. Insulin management of type 2 diabetes mellitus. Am Fam Physician. 2011;84(2):183-90.
19. Shestakova M, Elizarova S, Jabbar A. A review of insulin lispro for the treatment of patients with type 2 diabetes mellitus. Diabetes mellitus. 2016;19(3):242-50. [in Russian]. doi: 10.14341/DM2003429-34
20. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of

arterial hypertension. Eur Heart J. 2018;39(33):3021-104.
21. Department of Health and Human Service Centers for Disease Control and Prevention. Body Mass Index: Considerations for Practitioners. 1st ed. [ebook]; 2015 [cited 2021 Nov 22]; Available from: http://www.cdc.gov/obesity/downloads/bmiforpactitioners.pdf
22. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycaemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetologia. 2018;61(12):2461-98.
23. Derzhavnyy ekspertnyy tsentr MOZ Ukrayiny [Internet]. Nakaz Ministerstva okhorony zdorov'ya № 1118; 2012. Unifikovanyy klinichnyy protokol pervynnoyi ta vtorynnoyi (spetsializovanoyi) medychnoyi dopomohy tsukrovoho diabetu 2 typu. 2012 [cited 2021 Nov 22]; [in Ukraine]. Available from: https://www.dec.gov.ua/wp-content/uploads/2019/11/2012_1118ykpmd.pdf
24. Cosentino F, Grant PJ, Aboyans V, et al. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020;41(2):255-323.
25. Tron'ko N, Yefimov A, Tkach S. Peroral'naya sakharosnizhayushchaya terapiya bol'nykh sakharnym diabetom 2 tipa: taktika i blizhayshiye perspektivy [Internet]. health-ua.com spetsíalízovaniy medichniy zhurnal. 2015 [cited 2021 Nov 22]. [in Russian]. Available from: http://health-ua.com/article/17694-peroralnaya-saharosnizhayushaya-terapiya-bolnyh-sahamym-diabetom-2-tipa-ta
26. Tseng C-H. Metformin and Risk of Hypertension in Taiwanese Patients With Type 2 Diabetes Mellitus. Journal of the American Heart Association. 2018;7:e00886.
27. Tseng CH. Exogenous insulin use and hypertension in adult patients with type 2 diabetes mellitus. Arch Intern Med. 2006; 166:1184–9.
28. Sehra D, Sehra S. Hypertension in type 2 diabetes mellitus: do we need to redefine the role of sulfonylureas? Recent Adv Cardiovasc Drug Discov. 2015;10:4–9.
29. Yang X, Xu Z, Zhang C, Cai Z, Zhang J. Metformin, beyond an insulin sensitizer, targeting heart and pancreatic β cells. Biochim Biophys Acta. 2017;1863:1984–90.
30. Miller RA, Chu Q, Xie J, Foretz M, Viollet B, Birnbaum MJ. Biguanides suppress hepatic glucagon signalling by decreasing production of cyclic AMP. Nature. 2013;494(7436):256-60.
31. DeFronzo RA, Goodman AM. Efficacy of metformin in patients with non-insulin-dependent diabetes mellitus. The Multicenter Metformin Study Group. N Engl J Med. 1995;333(9):541-9.
32. Scheen AJ, Esser N, Paquot N. Antidiabetic agents: potential anti-inflammatory activity beyond glucose control. Diabetes Metab. 2015; 41:183–194
33. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet. 1998;352(9131):854-65.
34. Ishibashi Y, Matsui T, Takeuchi M, Yamagishi S. activity beyond of metformin and irbesartan on advanced glycation end products (AGEs)-RAGE-induced proximal tubular cell injury. Pharmacol Res. 2012;65:297–302.
35. An H, Wei R, Ke J, et al. Metformin attenuates fluctuating glucose-induced endothelial dysfunction through enhancing GTPCH1-mediated eNOS recoupling and inhibiting NADPH oxidase. J Diabetes Complications. 2016 30:1017–24.
36. Yu JW, Deng YP, Han X, Ren GF, Cai J, Jiang GJ. Metformin improves the angiogenic functions of endothelial progenitor cells via activating AMPK/eNOS pathway in diabetic mice. Cardiovasc Diabetol. 2016;15:88.

Table 1. Groups of patients with T2DM

№	Groups	n	%
1	T2DM+normal weight	39	6.74
2	T2DM+OW	33	5.70
3	T2DM+OB	22	3.80
4	T2DM+ normal weight + AH	59	10.19
5	T2DM+ OW+AH	131	22.63
6	T2DM+OB+AH	295	50.95

Table 2. Values of carbohydrate metabolism in patients of different age groups

Groups	Glucose, mmol/L	HbA1c, %	Insulin, mIU/mL	HOMA-IR, U
T2DM+normal weight (n=39)	9.94 (7.32; 12.40)	9.10 (7.70; 11.82)	10.35 (6.74; 15.47)	4.75 (3.15; 6.07)
T2DM+OW (n=33)	10.50 (8.20; 13.57)	8.60 (7.30; 9.40)	14.35 (9.11; 16.61)	5.79 (4.79; 7.77)
T2DM+OB (n=22)	9.49 (6.98; 11.60)	8.35 (6.80; 9.20)	13.45 (7.79; 18.31)	4.89 (4.01; 6.16)
T2DM+ normal weight +AH (n=59)	10.45 (8.20; 13.70)	8.70 (7.55; 10.03)	12.35 (8.10; 15.87)	5.18 (4.31; 6.94)
T2DM+OW+AH (n=131)	8.35 (7.10; 11.36)	8.60 (7.50; 10.10)	14.78 (11.37; 18.52)	5.83 (4.86; 6.89)
T2DM+OB+AH (n=295)	9.37 (7.74; 11.80)	8.40 (7.30; 9.50)	13.94 (10.25; 17.10)	5.80 (4.62; 6.95)
Craskell-Wallace criterion	H=14.35; p=0.014*	H=10.47; p=0.063	H=21.17; p<0.001*	H=18.98; p=0.002*
P	p_{4-5}<0.05*	-	p_{1-5}<0.05*; p_{4-5}<0.05*	p_{1-5}<0.05*; p_{1-6}<0.05*
Note. * – statistically significant results.				

Table 3 – Severity of course of T2DM combined with OW/OB and AH

Groups		Severity						χ^2, p
		Mild course		Moderate severity		Severe course		
		n	%	N	%	n	%	
1	T2DM+normal weight (n=39)	0	0	29	78.38	10	21.62	χ^2=15.16; p<0.05*; p_{2-5}<0.05* p_{3-6}<0.05*
2	T2DM+OW (n=33)	0	0	23	71.88	10	28.13	
3	T2DM+OB (n=22)	0	0	13	59.09	9	40.91	
4	T2DM+ normal weight +AH (n=59)	0	0	35	59.32	24	40.68	
5	T2DM+OW+AH (n=131)	0	0	67	51.94	64	48.06	
6	T2DM+OB+AH (n=295)	0	0	149	50.68	146	49.32	
Note. * – statistically significant results.								

Table 4 – Degree of compensation of T2DM combined with comorbid OW/OB and AH

Groups		Degree of compensation						χ^2, p
		Compensation		Subcompensation		Decompensation		
		N	%	n	%	n	%	
1	T2DM+normal weight (n=39)	0	0	3	7.69	36	92.31	χ^2=12.84; p<0.05*; p_{3-6} <0.05*
2	T2DM+OW (n=33)	0	0	5	15.15	28	84.85	
3	T2DM+OB (n=22)	0	0	8	36.36	14	63.64	
4	T2DM+ normal weight +AH (n=59)	0	0	4	6.78	55	93.22	
5	T2DM+OW+ AH (n=131)	0	0	22	16.79	109	83.21	
6	T2DM+OB+ AH (n=295)	0	0	47	15.93	248	84.07	
Note. * – statistically significant results.								

Table 5 – Characteristics of glucose-lowering therapies in type 2 diabetic patients with comorbid OW/OB and AH

Groups		Therapy of T2DM						χ^2, p
		Oral hypoglycemic agents+ insulin therapy		Monotherapy (metformin)		Combined therapy (metformin+ gliclazide)		
		N	%	n	%	n	%	
1	T2DM+normal weight (n=39)	26	66.67	9	23.08	4	10.26	χ^2=83.66; p<0.001*; p_{1-2}<0.05* p_{1-3}<0.05* p_{4-5}<0.05* p_{4-6}<0.001*
2	T2DM+OW (n=33)	7	21.22	15	45.45	11	33.33	
3	T2DM+OB (n=22)	4	18.18	9	40.91	9	40.91	
4	T2DM+ normal weight +AH (n=59)	30	50.85	13	22.03	16	27.12	
5	T2DM+OW+AH (n=131)	41	31.30	38	29.01	52	39.69	
6	T2DM+OB+AH (n=295)	42	14.24	97	32.88	156	52.88	
Note. * – statistically significant results.								