

OPTIONS OF CORRECTING INSULIN RESISTANCE AND PROINFLAMMATORY CYTOKINE LEVELS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS*

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Introduction. Mortality due to cardiovascular events remains a problem of modern medicine [1]. It should be noted that cardiovascular morbidity increases significantly among the patients with type 2 diabetes mellitus and metabolic syndrome [2]. Insulin resistance (IR) triggers a vicious circle of symptoms that eventually lead to severe cardiovascular complications. At the same time, IR does not occur spontaneously, as, according to modern ideas, the initiating factor of both IR and the entire metabolic cascade is usually obesity, which in its turn leads to the development of hypertension and can reduce peripheral tissue sensitivity to insulin and subsequent accumulation of body weight. Adipocytokines synthesized by the adipose tissue are involved in systemic low-intensity inflammation, which contributes to the development and progression of cardiovascular diseases. In particular, there is a positive correlation between blood leptin levels and insulin

sensitivity, body mass index, waist circumference, hyperglycemia, atherogenic dyslipidemia, endothelial dysfunction, and the progression of leptin and insulin resistance is associated with higher risks of cardiovascular diseases. Nowadays, cardioprotective properties are the requirement for new generations of hypoglycemic drugs [3]. According to the EMPA-REG OUTCOME study, empagliflozin significantly reduced cardiovascular (by 38%) and total (by 32%) mortality [4]. However, the effect of empagliflozin on leptin levels, IR levels, and major cardiovascular risk factors in obese type 2 diabetic patients remains poorly understood. All of the above has served the basis for studying the effect of empagliflozin on insulin and leptin resistance and proinflammatory cytokine levels.

Objective. To study the effect of empagliflozin on insulin and leptin resistance in obese patients with type 2 diabetes mellitus, pro-inflammatory cytokine levels.

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MATERIALS AND METHODS

On the basis of Therapeutic department 1 in Ivano-Frankivsk Central City Clinical Hospital, 100 patients with type 2 diabetes mellitus who had been receiving metformin for at least 6 months but had not reached the target HbA1c level ($> 7,5\%$, but $< 9\%$ at the time of enrolment in the study) and had not been taking SGLT2 inhibitors, as well as 10 practically healthy individuals were examined (WHO criteria since 1999). The average age of patients was 47.9 ± 3.4 years. Except for arterial hypertension and cardiovascular complications, cardiovascular diseases were revealed neither in medical history nor during examination. The study did not include individuals with GFR lower than $60 \text{ ml/min per } 1.73 \text{ m}^2$, rare inherited disorders (lactose deficiency, lactose intolerance, glucose-galactose malabsorption), as well as other contraindications to empagliflozin, listed in the instructions for its use. All patients underwent a conventional clinical examination, which included measurements of height (H), body weight (BW), waist circumference (WC) and blood pressure (BP). Body mass index (BMI) was calculated by Quetelet index ($\text{BMI} = \text{BW}/\text{H}^2, \text{ kg/m}^2$). To determine the type of obesity, the ratio of the waist circumference to the thigh volume was calculated. The condition of carbohydrate metabolism was assessed by the level of blood glucose and glycosylated haemoglobin. Leptin content (norm $3.7\text{--}11.1 \text{ ng/ml}$) was determined by «Diagnostics Biochem Canada Inc» kit. The level of endogenous insulin was determined by enzyme immunoassay using «DRG Diagnostics» reagents

(Germany). To verify IR, HOMA-IR index was calculated — the value above 2.5 was regarded as an objective criterion for IR. The measurement of IL-6 levels in blood serum was performed with a kit of test systems manufactured by Bender MedSystem (Austria), serum CRP levels were identified by turbidimetric method using «BioSystems» reagents. Statistical analysis was performed according to variation-statistical method. When analysing the material, the average values (M), their standard errors (m) and the confidence interval were calculated. Statistical significance was assessed by Student's t-test for dependent and independent samples, with irregularity in the distribution Mann-Whitney U-test was used. Differences were considered significant at $p < 0.05$. The dependence of the indices was estimated according to Spearman method calculating the correlation coefficient. Statistical processing of the material was performed with the help of variation and descriptive statistics using a standard package of statistical calculations Statistica 6.0, Foxbase, Exel 6.0. The clinical trial followed the safety measures provided for the patient's health in such cases, the protection of their rights, human dignity and moral and ethical standards, in accordance with the principles of the Declaration of Helsinki on Human Rights (1964) and the Convention on Human Rights and Biomedicine, respective laws of Ukraine, permission of the Commission on Medical Ethics at Ivano-Frankivsk National Medical University. All patients signed an informed consent to participate in the study.

RESULTS AND THEIR DISCUSSION

Depending on BMI, patients were randomized into 4 groups. Group I included 45 patients with $\text{BMI} < 24.9 \text{ kg/m}^2$ (22.7 ± 0.22), Group II — 46 patients with BMI from 25.0 kg/m^2 to $29.9 \text{ kg/m}^2 \pm 0.41$, Group III — 47 patients with BMI from 30.0 kg/m^2 to 34.9 kg/m^2 , Group IV — 50 patients with BMI from 35.0 kg/m^2 to 39.9 kg/m^2 , patients with third-degree obesity were not included in the study. It is known that adipocytes in case of obesity express not only adipokines such as adiponectin, leptin, but also elevated levels of TNF- α , which, in its turn, stimulates the production

of IL-6 [5]. High sensitivity-CRP is a sensitive general marker of low-grade tissue inflammation that is not only associated with features of insulin resistance, but also has independently predicted development of hypertension, Metabolic syndrome, T2DM and CVD [6]. IL-6 has been suggested to promote CRP production by the liver as a component of sub-clinical inflammation related to obesity [7]. Data on cytokine levels obtained in the study are presented in Table 1.

The analysis of our studies has showed that patients of all surveyed groups have signifi-

Table 1

**IL-6 and CRP levels in patients with type 2 diabetes mellitus
with different BMI (M ± m)**

Parameter	Control group, n = 10	Group I, n = 45	Group II, n = 46	Group III, n = 47	Group IV, n = 50
IL-6, pg/ml	13,88 ± 2,11	28,41 ± 0,53*	41,87 ± 2,51*#	48,68 ± 0,76*#	56,99 ± 2,64*#
CRP, mg/l	2,21 ± 0,33	3,02 ± 0,26*	5,12 ± 0,2*#	5,96 ± 0,2*#	6,54 ± 0,12*#

Note.

* the difference is probable in relation to the indices of the control group ($p < 0,05$);

the difference is probable in relation to the indices of Group I ($p < 0,05$).

Table 2

**Leptin, insulin resistance indices in patients
with type 2 diabetes mellitus depending on BMI, (M ± m)**

Parameter	Practically healthy (n = 10)	Group I, n = 29	Group II, n = 31	Group III, n = 20	Group IV, n = 20
Hb Alc, %	4,14 ± 0,07	7,92 ± 0,41*	8,01 ± 0,49*	8,15 ± 0,37*	8,18 ± 0,49*
BMI, kg/m ²	22,7 ± 1,12	23,7 ± 0,22	27,83 ± 0,32*#	33,03 ± 0,41*#	37,1 ± 0,67*#
WC, cm, f	76,64 ± 0,34	86,73 ± 0,89*	102,8 ± 1,49*#	108,70 ± 2,48*#	116,70 ± 3,96*#
WC, cm, m	90,08 ± 0,52	97,43 ± 0,48*	118,43 ± 2,2*#	120,07 ± 2,30*#	126,70 ± 2,96*#
HOMA IR	2,32 ± 0,06	4,45 ± 0,41*	6,05 ± 0,99*#	8,80 ± 0,63*#	9,83 ± 0,51*#
Leptin, ng/ml	5,4 ± 1,56	11,05 ± 1,3*	27,37 ± 3,2*#	35,2 ± 3,41*#	39,2 ± 4,11*#

Note:

* the difference is probable in relation to the indices of practically healthy people ($p < 0,05$);

the difference is probable in relation to the indices of Group I ($p < 0,05$).

cantly increased IL-6 levels, compared with the control group ($p < 0,05$) (Table 1). Thus, IL-6 levels have doubled in patients from Group I (patients with T2DM without obesity); Group II, III and IV patients have IL-6 levels that are significantly higher than those from Group I ($p < 0,05$), and in the control group ($p < 0,05$), IL-6 levels have increased with the weight gain. Accordingly, similar highest levels of CRP have been found in patients from Group IV, which indicate high pro-inflammatory activity in the group of patients with T2DM and obesity. The type of obesity is important; in our study, patients had an abdominal type of obesity, which is not only one of the criteria of the metabolic syndrome, but also a cardiovascular risk factor. Indices of leptin levels and IR in patients of these groups are presented in Table 2.

We have made a correlation analysis between IR and leptin indices. In patients from Group I, a direct correlation of medium

strength between leptin and HOMA-IR ($r = 0,505$, $p < 0,05$) has been found. In patients from Group II, a strong direct correlation has been revealed between such indices as HOMA-IR and leptin ($r = 0,846$, $p < 0,05$), a direct correlation of medium strength — between leptin and BMI ($r = 0,537$, $p < 0,05$), WC in men ($r = 0,397$, $p < 0,05$). The same tendency has been observed in patients from Group III and IV. In Group III, a direct correlation of medium strength between leptin and HOMA-IR ($r = 0,886$, $p < 0,05$) has been found, in patients of Group IV ($r = 0,736$, $p < 0,05$). Thus, the development of leptin resistance syndrome is inextricably linked with the development of insulin resistance.

Depending on the prescribed treatment, all patients were randomized into 4 groups. Patients from Group I A and IV A received basic treatment, i.e., metformin in an individual dose. Patients from Group I B and IV B were

prescribed empagliflozin 10 mg/day in addition to metformin. Patients continued to receive previously prescribed antihypertensive, hypolipidemic therapy throughout the study without correction.

After a 6-month course of treatment with SGLT2 inhibitors, a positive significant dynamics of the main metabolic parameters was observed. Data on the dynamics of metabolic parameters of patients with normal BMI (Group I) and overweight patients (Group II) have already been published by us [8], so we present data on the patients from Group III and IV (Table 3). Thus, the dynamics of carbohydrate metabolism in the examined patients has shown to be more pronounced ($p < 0.05$) in patients of all groups who received complex treatment with empagliflozin as compared with baseline therapy. Besides, as it can be seen in the table, the use of empagliflozin had made a significant effect ($p < 0.05$) on anthropometric parameters and markers of IR (HOMA-IR, leptin).

Table 4 shows the dynamics of cytokines (IL-6, CRP) under the influence of treatment. As proved by our data, patients receiving SGLT2 inhibitor have revealed significantly decreased levels of IL-6 ($p < 0.05$), regardless of BMI. CRP levels also have decreased signifi-

cantly ($p < 0.05$) in all patients receiving empagliflozin, regardless of BMI; patients undergoing basic therapy, haven't shown any decrease of the levels mentioned above.

The analysis of the literature and the data obtained by us during the study show that IL-6 and CRP levels in patients with type 2 diabetes mellitus increase with the growth of BMI [9] and IR. Tangvarasittichai S. et al. point out that increased TNF- α , IL-6, CRP and insulin resistance are associated with T2DM in abdominally obese subjects. Systemic inflammatory cytokines are used as the screening tool in adults of intermediate risk for CVD and T2DM to trigger more immediate intervention [10]. Other authors have proved the inverse correlation of the new adipokine vaspin and omentin with waist circumference, fat mass and BMI [11]. Resulting from our study, correlations between leptin and HOMA-IR in patients with type 2 diabetes and different body weight confirm the idea of the interdependent nature of insulin and leptin resistance development [12].

An important factor in cardiovascular complications is not so much weight as abdominal obesity. In our study, regardless of gender WC has significantly decreased under the influence of empagliflozin. BMI and HOMA-IR index have been significantly reduced only in over-

Table 3

Metabolic parameters of examined patients with type 2 diabetes mellitus (M \pm m)

Parameter	Therapy duration	Group III, n = 20		Group IV, n = 20	
		III A, n = 10	III B, n = 10	IV A, n = 10	IV B, n = 10
BMI, kg/m ²	before tr.	33,03 \pm 0,41	33,08 \pm 0,39	37,1 \pm 0,67	37,12 \pm 0,35
	6 months	32,98 \pm 0,39	31,16 \pm 0,34*	37,01 \pm 0,55	35,01 \pm 0,50*
WC, cm, f	before tr.	108,85 \pm 2,38	109,16 \pm 2,29	116,36 \pm 3,68	116,88 \pm 3,91
	6 months	108,13 \pm 2,56	106,81 \pm 2,54*	115,75 \pm 2,18	112,86 \pm 3,21*
WC, cm, m	before tr.	120,07 \pm 2,30	120,07 \pm 2,30	126,69 \pm 2,96	126,70 \pm 2,90
	6 months	120,02 \pm 2,33	115,6 \pm 1,88*	126,68 \pm 2,17	121,5 \pm 1,31*
HbA1c, %	before tr.	8,13 \pm 0,36	8,17 \pm 0,38	8,16 \pm 0,49	8,2 \pm 0,47
	6 months	8,11 \pm 0,40	7,21 \pm 0,39*	8,11 \pm 0,54	7,2 \pm 0,41*
HOMA-IR	before tr.	8,78 \pm 0,62	8,82 \pm 0,64	9,80 \pm 0,50	9,86 \pm 0,52
	6 months	8,71 \pm 0,63	7,21 \pm 0,58*	9,78 \pm 0,51	7,82 \pm 0,51*
Leptin, ng/ml	before tr.	35,1 \pm 3,42	35,3 \pm 3,40	39,3 \pm 4,09	39,1 \pm 4,13
	6 months	35,15 \pm 3,35	29,81 \pm 2,61*	38,6 \pm 2,22	21,6 \pm 1,29*

Note:

* the difference is significant in relation to the index before treatment.

**Dynamics of cytokine levels (IL-6, CRP)
under the influence of treatment, M±m**

Group	Parameter	Before treatment	After treatment	Δ, %
Group IA (n = 14)	IL-6	28,54 ± 0,49	28,12 ± 0,58	1,47
	CRP	3,01 ± 0,24	3,00 ± 0,27	0,33
Group IB (n = 15)	IL-6	28,28 ± 0,51	19,98 ± 0,64*#	29,35
	CRP	3,03 ± 0,28	2,45 ± 0,21*#	19,14
Group IIA (n = 15)	IL-6	41,37 ± 2,28	41,07 ± 2,19	0,73
	CRP	5,10 ± 0,21	5,06 ± 0,24	0,78
Group IIB (n = 16)	IL-6	41,97 ± 2,51	34,11 ± 1,613*#	18,73
	CRP	5,14 ± 0,19	4,01 ± 0,22*#	21,99
Group IIIA (n = 10)	IL-6	49,01 ± 0,74	48,01 ± 0,74	2,04
	CRP	5,95 ± 0,22	5,88 ± 0,29	1,18
Group IIIB (n = 10)	IL-6	48,16 ± 0,81	37,28 ± 0,92*#	22,59
	CRP	5,96 ± 0,18	4,21 ± 0,32*#	29,36
Group IVA (n = 10)	IL-6	57,02 ± 2,84	56,89 ± 2,91	0,23
	CRP	6,55 ± 0,11	6,50 ± 0,1	0,76
Group IVB (n = 10)	IL-6	56,97 ± 2,55	41,38 ± 2,51*#	27,37
	CRP	6,53 ± 0,13	4,69 ± 0,15*#	28,18

Note:

Δ, % — the ratio of the final value to the initial value of the index in percentage;

Probability between indices before and after treatment * — $p < 0,05$; # — $p < 0,05$ in comparison between Group A and B.

weight patients receiving empagliflozin, patients with normal BMI have shown insignificant weight loss, while other studies performed in animals indicate a significant weight loss with empagliflozin [13]. These changes may be related to a significant decrease in leptin levels, as well as the effect of empagliflozin on visceral fat. Our study has proved a significant effect of empagliflozin on CRP and IL-6 levels in all patients with type 2 diabetes mellitus, regardless of BMI, which is probably due to a reduction of WC, a decrease in leptin levels in our patients undergoing the treatment. Other authors have shown that empagliflozin im-

proves insulin resistance and has anti-inflammatory effects: it decreases the level of CRP and residual lipoproteins, reduces renal expression of inflammatory cytokines and chemokines [14]. Thus, cardiovascular protection by means of empagliflozin, which has been confirmed by many researchers [15], may be partially due to lower levels of leptin, IR and proinflammatory cytokines. Therefore, in our opinion, there is a need for further research aimed at studying the effect of empagliflozin on the level of adipokines in patients with type 2 diabetes mellitus.

CONCLUSIONS

1. An increase of IL-6 and CRP levels along with weight gain in patients with type 2 diabetes mellitus has been revealed.
2. A significant effect of empagliflozin on anthropometric parameters and markers of insulin resistance (HOMA-IR, leptin) in patients with type 2 diabetes mellitus and obesity has been proved.
3. Patients taking empagliflozin have shown significantly ($p < 0,05$) lower levels of IL-6 and CRP, regardless of BMI.

REFERENCES

1. Townsend N, Wilson L, Bhatnagar P, et al. *Eur Heart J* 2016;37(42): 3232-3245.
2. Katsiki N, Mikhailidis DP, Banach M. *Acta Pharmacologica Sinica* 2018;39(7): 1176-1188. <https://doi.org/10.1038/aps.2018.40>.
3. Pérez-Pérez A, et al. *Cytokine Growth Factor Rev* 2017; 35: 71-84.
4. Scherthaner G, Scherthaner-Reiter MH, Scherthaner GH. *Clin Ther* 2016;38(6): 1288-1298. <https://doi.org/10.1016/j.clinthera.2016.04.037>.
5. Choi KM, Lee J, et al. *Diabetes Res Clin Pract* 2004;64: 99-106.
6. Niskanen L, Laaksonen DE, Nyssönen K, et al. *Hypertension* 2004;44: 859-865. <https://doi.org/10.1161/01.HYP.0000146691.51307.84>.
7. Mechanick JI, Zhao S, Garvey WT. *Glob Heart* 2018; 13(2): 113-127. <https://doi.org/10.1016/j.gheart.2017.10.003>.
8. Didushko OM, Kobrynska OY, et al. *Prensa Med Argent* 2020;2: 003.
9. Rodrigues KF, Pietrani NT, Bosco AA, et al. *Arch Endocrinol Metab* 2017;61(5): 438-446. <https://doi.org/10.1590/2359-3997000000254>.
10. Tangvarasittichai S, Pongthaisong S, Tangvarasittichai O. *Indian J Clin Biochem* 2016;31(1): 68-74. <https://doi.org/10.1007/s12291-015-0514-0>.
11. Kravchun NO, Alkhamid MKh, Misiura KV, et al. *Probl Endocrine Pathol* 2021;75(1): 34-42. <https://doi.org/10.21856/j-PEP.2021.1.05>.
12. Katsiki N, Mikhailidis DP, Banach M. *Acta Pharmacol Sin* 2018;39(7): 1176-1188. <https://doi.org/10.1038/aps.2018.40>.
13. Park SH, et al. *Cardiovasc Diabetol* 2020;19: 19. <https://doi.org/10.1186/s12933-020-00997-7>.
14. Hattori S. *Diabetol Metab Syndr* 2018;10: 93. <https://doi.org/10.1186/s13098-018-0395-5>.
15. Vallon V, Verma S. *Ann Rev Physiol* 2021;83(1): 503-528. <https://doi.org/10.1146/annurev-physiol-031620-095920>.

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The objective of this study was to investigate the effect of empagliflozin on insulin resistance, leptin and proinflammatory cytokine levels in patients with type 2 diabetes.

Materials and methods. 100 patients with type 2 diabetes with normal weight, overweight and obesity of various degrees were examined. Anthropometric indicators were taken. Levels of leptin, IL-6, CRP in blood serum were determined, HOMA index was calculated.

Results. Insulin resistance in all groups of patients was associated with abdominal obesity, hyperleptinemia ($r = 0.505$, $p < 0.05$), ($r = 0.846$, $p < 0.05$), ($r = 0.886$, $p < 0.05$), ($r = 0.736$, $p < 0.05$) in patients from Group I-IV. Patients of all examined groups have shown a significant increase in IL-6 levels, compared with the control group ($p < 0.05$), but the level of IL-6 in patients from Group II, III and IV have been significantly higher than those from Group I ($p < 0.05$) and the control group ($p < 0.05$) and has increased along with the weight gain. Similarly, the highest indices of CRP levels have been found in patients from Group IV which proves a high pro-inflammatory activity in these patients with type 2 diabetes and obesity. After a 6-month course of treatment patients taking empagliflozin, regardless of BMI, have shown significantly decreased levels of both IL-6 ($p < 0.05$), and CRP ($p < 0.05$). Levels of leptin ($p < 0.05$) and HOMA index ($p < 0.05$) were significantly reduced in obese patients, too.

Conclusions. As a result of the study, it has been established that the use of empagliflozin in the dose of 10 mg per day for 6 months has had a significant effect on anthropometric parameters and markers of insulin resistance (HOMA index, leptin) in patients with type 2 diabetes and obesity. A significant decrease in the levels of IL-6 and CRP under the influence of empagliflozin, regardless of the patient's weight has been revealed.

Key words: type 2 diabetes mellitus, interleukin-6, C-reactive protein, empagliflozin.

МОЖЛИВОСТІ КОРЕКЦІЇ ІНСУЛІНОРЕЗИСТЕНТНОСТІ
ТА РІВНІВ ПРОЗАПАЛЬНИХ ЦИТОКІНІВ
У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ 2 ТИПУ

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Метою проведеної роботи було вивчення впливу емплагліфлозину на показники інсулінорезистентності, лептину та рівні прозапальних цитокінів у хворих на цукровий діабет 2-го типу.

Матеріали та методи. Проведено обстеження 100 пацієнтів із ЦД2 типу з нормальною, надлишковою масою тіла та ожирінням різного ступеня. Знято антропометричні показники. Визначено рівні лептину, ІЛ-6, СРБ в сироватці крові розраховано індекс НОМА-ІР.

Результати. Інсулінорезистентність у всіх групах хворих асоціювалась із абдомінальним типом ожиріння, гіперлептемією ($r = 0,505$, $p < 0,05$), ($r = 0,846$, $p < 0,05$), ($r = 0,886$, $p < 0,05$), ($r = 0,736$, $p < 0,05$) у пацієнтів I-IV групи. У хворих всіх обстежених груп встановлено істотне підвищення рівня ІЛ-6, в порівнянні з групою контролю ($p < 0,05$), проте рівень ІЛ-6 у пацієнтів II, III та IV груп був достовірно вищим, ніж в I групі ($p < 0,05$), та групі контролю ($p < 0,05$) та зростав по мірі збільшення ваги. Аналогічно найвищі показники рівня СРБ були у пацієнтів IV групи, що вказує на високу прозапальну активність у групі хворих із ЦД 2 типу та ожирінням. Після проведеного 6-ти місячного курсу лікування у пацієнтів, які приймали емплагліфлозин, незалежно від ІМТ, достовірно знизились рівні як ІЛ-6 ($p < 0,05$), так і СРБ ($p < 0,05$). Також достовірно знизились рівні лептину ($p < 0,05$) та індексу НОМА-ІР ($p < 0,05$) у пацієнтів із ожирінням.

Висновки. В результаті дослідження встановлено, що застосування емплагліфлозину 10 мг/д протягом 6 місяців мало достовірний вплив на антропометричні показники та маркери інсулінорезистентності (індекс Хома, лептин) у хворих на ЦД 2 типу та ожиріння. Виявлено достовірне зниження рівнів ІЛ-6 та СРБ під впливом емплагліфлозину, незалежно від ваги пацієнта.

Ключові слова: цукровий діабет 2 типу, інтерлейкін-6, С-реактивний білок, емплагліфлозин.