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# Effect of empagliflosin on renal filtration in patients with coronary heart disease undergoing percutaneous coronary intervention

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| *Aim* | To evaluate the effect of empagliflozin on glycemia and renal filtration function in patients with stable ischemic heart disease (IHD) and type 2 diabetes mellitus (DM2) who underwent a percutaneous coronary intervention (PCI). |
| *Materials and methods* | This study included 40 patients with stable IHD and DM2 (age, 63 (58; 65) years; DM2 duration, 7 (4; 15) years) who had indications for an elective PCI. At baseline in the total sample, the level of glycated hemoglobin was 7.2 (6.5; 8.3) %; 48.7% failed to achieve glycemic goals. A decrease in glomerular filtration rate (GFR) to below 60 ml/min/1.73 $m^2$ was observed in 10.3% of patients. All patients were divided into two group by simple randomization with successively assigned numbers. The main group consisted of 20 patients who received empagliflozin 10 mg/day in addition to their previous hypoglycemic therapy irrespective of their baseline glycemic control. Patients of the comparison group (n=20) continued on their previous hypoglycemic therapy as prescribed by their endocrinologist. The follow-up duration was 6 months. Statistical analysis was performed with the Statistica 10.0 software. |
| *Results* | The empagliflozin treatment improved the glycemic control; in the comparison group, no significant changes in glycemic control were observed. In both groups, GFR significantly decreased during the follow-up period; median decreases in GFR were –6.0 ( –16.0; 4.0) and –8.4 ( –26.5; 2.5) ml/min/1.73 $m^2$ in the main and comparison groups, respectively (p=0.646). No significant changes in 24-h proteinuria were observed for patients taking empagliflozin. In the control group, the 24-h urinary protein excretion significantly progressed (p=0.011) during the follow-up period. |
| *Conclusion* | In patients with DM2 and stable IHD who underwent a PCI, addition of empagliflozin 10 mg/day to their current hypoglycemic therapy was associated with a significant improvement of glycemic control. The decrease in GFR during the empagliflozin treatment did not significantly differ from the value for patient receiving the other hypoglycemic therapy. |

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## Introduction

Despite some decrease in cardiovascular mortality, cardiovascular diseases (CVD) remain the leading cause of death in patients with diabetes mellitus (DM) [1]. At the same time, diabetic kidney disease, an equally dangerous complication of DM, comprises an independent predictor of cardiovascular complications and death [2].

Selecting the best possible antidiabetic drug for achieving target glycemic control and slowing down the progression of DM complications continues to present challenges to researchers and practitioners. In the EMPA-REG OUTCOME study, empagliflozin, a sodium-glucose co-transporter 2 (SGLT2) inhibitor, had a beneficial effect on cardiovascular risk factors, such as hyperlipidemia, obesity and hypertension, reducing the risk of cardiovascular complications in patients having type 2 DM and a documented history of CVD [3]. Although a subanalysis of this study revealed a beneficial effect of the drug on renal outcomes, the underlying mechanisms are still not fully understood [4]. In patients subjected to X-ray-guided interventions, particularly percutaneous coronary intervention (PCI), which is the most commonly used myocardial revascula-

rization technique in coronary artery disease (CAD), the use of empagliflozin is insufficiently studied. Thus, the effect of empagliflozin on kidney filtration in this category of patients is of interest. The objective of the present study was therefore to assess the effects of empagliflozin on the levels of blood sugar and kidney filtration in patients with stable CAD and type 2 DM who underwent PCI.

## Materials and methods

The study was approved by the local ethics committee. All patients signed the informed consent form prior to being included in the study. The cohort included 40 patients with stable CAD and type 2 DM, who had indications that prompted them to undergo routine PCI. Exclusion criteria were as follows: previous myocardial revascularization, acute coronary syndrome, decompensated chronic heart failure, active comorbidity, decreased glomerular filtration rate (GFR)<45 mL/min/1.73m2, age over 85 years old at inclusion.

All subjects were divided into two groups by simple randomization using sequential numbers. Group 1 consisted of 20 (10 male and 10 female) patients who agreed to take empagliflozin in addition to the previous antidiabetic therapy regardless of a baseline degree of glycemic control. The drug was administered at a dose of 10 mg/day for 1 month before and 5 months after a scheduled PCI (the total duration of treatment was six months). Group 2 consisted of 20 (10 male and 10 female) patients who continued using their usual antidiabetic treatment throughout the study. The characteristics of the groups are provided in Table 1.

The following clinical measurements were recorded in all subjects at baseline and 6 months after randomization: fasting venous blood glucose, glycated hemoglobin (HbA1c), urinalysis, and 24-hour urine protein. Serum creatinine and GFR were determined at baseline, 48 hours after PCI and 6 months following randomization.

Serum glucose was determined by the hexokinase method; HbA1c – by the enzymatic endpoint method on a Konelab 30i automated biochemical analyzer. Serum creatinine levels were measured using the Jaffe method using Thermo Fisher Scientific (Germany) standard test systems on the Konelab 30i automated biochemical analyzer. Renal filtration was determined by calculating GFR using the CKD-EPI formula (Chronic Kidney Disease Epidemiology Collaboration [2009, 2011 Revision]). Urinalysis was performed using UrineRS H10 (HTI, USA) test strips on a CL-500 automatic

**Table 1.** Clinical characteristics of patients at the time of inclusion, by groups

| Parameter | Group 1 (empagliflozin), n=19 | Group 2 (control), n=20 | p |
|---|---|---|---|
| Male, n (%) | 10 (52.6) | 10 (50) | 1.000 |
| Age, years | 62 (59; 66) | 63 (59; 65) | 0.967 |
| Body mass index, kg/m2 | 35.2 ± 6.4 | 32.4 ± 4.1 | 0.246 |
| History of hypertension, n (%) | 19 (100.0) | 20 (100.0) | 1.000 |
| Duration of history of type 2 DM, years | 8.0 (6.0; 16.0) | 6.5 (5.0; 9.5) | 0.382 |
| CKD according to GFR<br>1, n (%)<br>2, n (%)<br>3a, n (%) | <br>9 (47.4)<br>8 (42.1)<br>2 (10.5) | <br>8 (40.0)<br>10 (50.0)<br>2 (10.0) | <br>0.751<br>0.751<br>1.000 |
| CKD according to 24-hour proteinuria, A1, n (%) | 19 (100) | 20 (100) | 1.000 |
| Duration of CAD history, years | 2.0 (2.0; 5.0) | 3.5 (3.0; 6.0) | 0.069 |
| History of MI, n (%) | 7 (36.8) | 10 (50.0) | 0.523 |
| Multi-vessel coronary disease, n (%) | 12 (63.2) | 14 (70.0) | 0.741 |
| Injected volume of contrast agent, mL | 200 (100; 200) | 200 (160; 240) | 0.424 |
| ACE inhibitors/ARBs, n (%) | 17 (89.5) | 19 (95.0) | 0.605 |
| Statins, n (%) | 17 (89.5) | 17 (85.0) | 1.000 |
| Antidiabetic therapy<br>Diet, n (%)<br>OADs, n (%) | <br>2 (10.5)<br>8 (42.2) | <br>3 (15.0)<br>14 (70.0) | <br>1.000<br>0.111 |
| Insulin therapy, n (%) | 2 (10.5) | 1 (5.0) | 1.000 |
| Combination therapy (insulin + OADs), n (%) | 7 (36.8) | 2 (10.0) | 0.065 |

The data are expressed as M±SD; n (%); Me (Q25; Q75).
ARBs, angiotensin II receptor blockers, ACE, angiotensin-converting enzyme; CAD, coronary artery disease; MI, myocardial infarction; OADs, oral antidiabetic drugs; DM, diabetes mellitus; CKD, chronic kidney disease.


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urine analyzer (HTI, USA). The 24-hour urine protein assay was performed using the colorimetric method based on a reaction with pyrogallol red on a Belur 600 analyzer (Russia). The urine sediment was examined under a microscope to assess bacteriuria.

The onset of adverse events and reactions during the administration of empagliflozin was evaluated throughout the study. Patients recorded hypoglycemic conditions if typical symptoms appeared or if blood glucose levels were<3.9 mmol/L. Empagliflozin and metformin treatments, if administered, were discontinued 48 hours before the introduction of an X-ray agent to prevent acute kidney injury. When antidiabetic drugs were not used, hyperglycemia was corrected through the introduction of rapid-acting insulin with fasting and postprandial glycemic control. The discontinued drugs were restarted subject to serum creatinine control 48 hours after the X-ray procedure. The diagnosis of acute kidney injury associated with the introduction of the X-ray agent was assessed under the KDIGO guidelines [5].

The statistical analysis of the findings was performed using Statistica 12.0. Statistical hypotheses on the distribution were tested using the Kolmogorov-Smirnov/Lilliefors test and the Shapiro-Wilk test. Quantitative variables with normal distribution were described in terms of mean and standard deviation. Quantitative variables with non-normal distribution were presented as median and interquartile ranges (first and third quartiles). The differences between two independent groups in quantitative measures were estimated by the Mann-Whitney U-test (pu). An analysis of differences in rates between two independent groups was performed using the 2×2 contingency tables and Fisher's exact test with a two-sided confidence interval (pF). The two dependent variables were compared using the Wilcoxon test (pW). Cohen's Q-test (pQ) was used to compare fractions in the dependent samples. The analysis of repeat measurements was estimated using the Friedman test, followed by post-hoc comparisons of variables using the Wilcoxon test. The statistical significance was p=0.05.

## Results

At the time of inclusion, all patients were comparable in terms of their clinical condition and medical history. A total of 39 patients completed the study (19 patients in the empagliflozin group –one patient discontinued the drug due to an adverse event – and 20 patients in the control group). All patients included in the study had hypertension. Most patients in both groups used renin-angiotensin-aldosterone system blockers as a part of anti-hypertensive therapy. Hypolipidemic therapy with statins was administered equally often in both patient groups.

The proportion of patients with multi-vessel coronary disease according to coronary angiography; previous myocardial infarction (MI) was comparable in both groups. The revascularization technique was decided individually for each patient through a multidisciplinary consultation, which included a cardiologist, an endovascular interventional radiologist, and a cardiac surgeon, during which the indications prompting PCI were determined. The same volume of contrast agent was used during the procedure in both groups.

The duration of type-2 DM history did not differ between the groups. The rate of use of different oral antidiabetic drugs did not differ between the groups (Table 2). About 60% of patients in the empagliflozin group and 40% in the control group had poor baseline control of carbohydrate metabolism (HbA1c). Empagliflozin improved glycemic control – as an example, only 31.6% of patients taking empagliflozin failed to achieve their individual target levels of HbA1c by the end of the study. In the subgroup of patients with non-target baseline glycemic control, the median decrease in HbA1c over the study period was –1.8 (–2.3; –0.5) % vs. –0.5 (–1.8; 0.25) % in the subgroup of patients with target glycemia levels. No episodes of hypoglycemia were reported in patients taking empagliflozin. There were no statistically significant changes in the glycemic control parameters in the control group. Changes in markers of glycemia observed in both groups are shown in Table 3.

The baseline measures of renal function as assessed by GFR did not differ statistically significantly between the groups. Within the first 48 hours following PCI, no statistically significant reduction in GFR was observed in both groups. Six months later, by contrast, GFR decreased significantly in both the treatment and control groups (p<0.05 for all). There were no differences in the rates of GFR reduction between the groups during those six months.

No significant changes in 24-hour proteinuria levels were reported in patients taking empagliflozin. There was a statistically significant progression in 24-hour urinary protein excretion in the control group during the six months of follow-up. Changes in the 24-hour proteinuria did not differ statistically significantly between the groups. Changes in renal function indicators are shown for both study groups in Table 4.

One case of acute kidney injury identified according to the KDIGO criteria during an X-ray-guided intervention was reported in the treatment group [5]. Since GFR

did not reach the target level necessary to clear the drug, treatment was restarted following stabilization of serum creatinine. GFR had not recovered to the baseline levels by the end of the study.

Although bacteriuria was detected through urinalysis in 36.8% (n=7) of patients taking empagliflozin during the first month following the start of therapy, asymptomatic bacteriuria could be considered as an explanation for this since there were no clinical signs of urinary tract infection. Moreover, two patients taking empagliflozin reported symptoms of genital infection: vaginal itching and burning. One patient discontinued use of the drug due to this complication, while the other resolved the problem through increased personal hygiene measures.

## Discussion

There were reportedly no previous studies using empagliflozin for patients before scheduled PCI. Our study investigates the use of patients with type 2 DM and CAD who had indications prompting PCI procedures as a model of high risk for renal injury. Our findings show that the administration of empagliflozin, in addition to previous antidiabetic therapy, allowed a statistically significant decrease in HbA1c levels to be achieved. By the end of the study, 73.7% of patients taking empagliflozin achieved their individual HbA1c target levels with the highest reduction of glycemia in the subgroup of patients with non-target baseline levels of HbA1c. Thus, the administration of empagliflozin over the course of the month prior to PCI is likely to become a useful tool in achieving DM compensation before a revascularization procedure [6].

In this study, a decrease in GFR over six months of follow-up was observed in both groups, and the median decrease in GFR was significantly different. In the control group, a significant progression in 24-hour protein excretion levels was observed over the 6-month follow-up. Here, proteinuria levels were the same as at inclusion, i.e., normal or slightly elevated.

A subanalysis conducted in the EMPA-REG OUTCOME study [4] showed that empagliflozin was

**Table 2.** Groups of oral antidiabetic drugs used in study groups before the study

| Group of drugs | Group 1 (empagliflozin), n=15 | Group 2 (control), n=16 | p |
|---|---|---|---|
| Biguanides, n (%) | 7 (46.6) | 10 (62.4) | 0.523 |
| Sulfonylurea derivatives, n (%) | 4 (26.7) | 1 (6.3) | 0.182 |
| DPP4i*, n (%) | – | 1 (6.3) | 1.000 |
| Biguanides + sulfonylurea derivatives, n (%) | 4 (26.7) | 4 (25.0) | 1.000 |

* DPP4i, dipeptidyl peptidase 4 inhibitors.

**Table 3.** Changes in glycemic control in the study groups

| Parameters | Group 1 (empagliflozin), n=19 | Group 2 (control), n=20 | $p_{1-2}$ |
|---|---|---|---|
| **Fasting glycemia, mmol/L** | | | |
| Baseline | 10.1 (7.8; 11.7) | 7.45 (6.5; 9.8) | 0.074 |
| 6 months | 7.4 (6.1; 10.3) | 8.0 (6.5; 9.5) | 0.771 |
| $\Delta_{\text{baseline-6 months}}$, mmol/L | -1.2 (3.0; 0.7) | 0.05 (-1.2; 0.75) | **0.046** |
| p baseline – 6 months | p=0.013 | p=0.586 | |
| **HbA1c, %** | | | |
| Baseline | 8.0 (6.7; 9.1) | 7.0 (6.3; 7.7) | 0.061 |
| 6 months | 6.7 (5.8; 7.9) | 7.6 (6.3; 9.1) | **0.026** |
| Changes from baseline to 6 months, % | -1.1 (-2.3; -0.2) | 0.6 (-0.4; 1.6) | **0.003** |
| p baseline – 6 months | **0.005** | 0.198 | |
| **Failure to achieve target HbA1c, n, %** | | | |
| Baseline | 11 (57.9) | 8 (40.0) | 0.343 |
| 6 months | 6 (31.6) | 10 (50.0) | 0.191 |
| p baseline – 6 months | **0.025; (Q=5.0, df=1)** | 0.480; (Q=0.5, df=1) | |

The data is expressed as Me (Q25; Q75). The statistically significant differences are in bold type.


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**Table 4.** Changes in renal function measures in the study groups

| Parameters | Group 1 (empagliflozin), n=19 | Group 2 (control), n=20 | $p_{1-2}$ |
|---|---|---|---|
| **GFR, mL/min/1.73m²** | | | |
| Baseline | 87 (71; 97) | 89 (76; 98) | 0.771 |
| 48 hours after PCI | 84 (65; 98) | 94 (76; 99) | 0.478 |
| $Changes_{baseline\text{-}48\ hour}$, mL/min/1.73 m² | -2.0 (-7.0; 2.0) | -5.0 (-7.0; 4.5) | 0.945 |
| 6 months | 77 (63; 94) | 76 (58; 91) | 0.569 |
| $Changes_{baseline\text{-}6\ months}$, mL/min/1.73 m2 | -6.0 (-16; 4) | -8.4 (-26.5; 2.5) | 0.646 |
| p (baseline-48 hours-6 months) | **0.021** ($\chi$2=7.68, df=2) $p_{1-2}$= 0.268; $p_{1-3}$=0.046; $p_{2-3}$=0.457 | **0.020** ($\chi^2$ =7,77, df=2) $p_{1-2}$=0.489; $p_{1-3}$=0.033; $p_{2-3}$=0.035 | |
| **24-hour proteinuria, mg/day** | | | |
| Baseline | 40 (0; 60) | 51 (0; 72) | 0.646 |
| 6 months | 46 (35; 90) | 71 (66; 83) | 0.061 |
| $Changes_{baseline\text{-}6\ months}$, mg/day | 0 (-20; 58) | 48 (14; 75) | 0.074 |
| p | 0.268 | **0.011** | |

The data is expressed as Me (Q25; Q75). The statistically significant differences are in bold type.

associated with a slowed renal dysfunction progression. The progression of microalbuminuria, doubling levels of serum creatinine and initiation of renal replacement therapy or death associated with kidney disease were reported significantly less often in patients taking empagliflozin than in the placebo group (odds ratio [OR] 0.61; 95% confidence interval [CI] 0.53–0.70; p<0.001). However, there were no differences in the incidence of new cases of albuminuria between the groups.

Literature analysis showed that the use of SGLT2 inhibitors was associated with a decrease in GFR by approximately 4–6 mL/min/1.73m2 during the initiation of therapy with subsequent stabilization [7], which is associated with increased tone in the afferent glomerular arteriole and reduced hyperfiltration in patients taking these medications [8]. A study using an experimental model of diabetes in mice showed that the use of empagliflozin did not cause a decrease in the number of functioning nephrons, i.e., the drug had no direct effect on the morphology of the kidneys [9].

The positive effects of SGLT2 inhibitors on urinary protein excretion in diabetic nephropathy were confirmed by several clinical and experimental studies. For example, the administration of empagliflozin in a model of diabetic nephropathy in mice was associated with a significant decrease in albuminuria regardless of the presence of hypertension, in addition to an antihyperglycemic effect [10]. Several clinical studies have recently been conducted that assess the effect of SGLT2 inhibitors on renal outcomes in patients with non-diabetic nephropathy. However, their findings have not yet been published [11]. At the same time, an experimental study investigating the use of empagliflozin in non-diabetic nephropathy showed contradictory results for 24-hour proteinuria [12]. Thus, the nephroprotective effect of SGLT2 inhibitors may be mediated by hypoglycemic, anti-inflammatory and possibly other pleiotropic effects. In this study, one patient developed an acute kidney injury following an X-ray-guided intervention during the use of empagliflozin. In the EMPA-REG OUTCOME study, the incidence of acute renal failure in the empagliflozin group was 11.2% in patients with a GFR of less than 60 mL/min/1.73m2 and 3.2% in patients with a GFR of 60 mL/min/1.73m2 or more; in the control group, the incidence rates were14.3% and 3.9%, respectively. However, the study did not include patients scheduled for PCI [4].

In this study, 36.8% of patients taking empagliflozin had asymptomatic bacteriuria. According to the literature, the prevalence of asymptomatic bacteriuria in patients with DM varies from 9 to 27% in female and from 0.7 to 11% in male patients [13]. At the same time, a lower incidence of bacteriuria was observed in studies investigating SGLT2 inhibitors [14]. The discrepancy between our findings and the previously published data can probably be attributed to the heterogeneity of samples, including differences in sample sizes and screening methods.

## Conclusions

Concomitant 10 mg/day use of empagliflozin alongside the previous antidiabetic treatment during the month

prior to PCI and for five months after the intervention allows significant improvements in glycemic control. The decrease in GFR during empagliflozin use was not significantly different from that observed in the group of patients receiving other antidiabetic therapy both in the 48 hours following the introduction of the contrast agent and after a six-month follow-up.

A further prospective study investigating the effects of empagliflozin on the rate of acute renal injury associated with the use of contrast agents as well as the long-term course of CAD and chronic kidney disease, including in patients without disorders of carbohydrate metabolism, is recommended.

## Study limitations

The limitations of the study are a small size of sample and non-evaluating earlier markers for kidney dysfunction.

*No conflict of interest is reported.*

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REFERENCES


1. Wright AK, Kontopantelis E, Emsley R, Buchan I, Sattar N, Rutter MK et al. Life Expectancy and Cause-Specific Mortality in Type 2 Diabetes: A Population-Based Cohort Study Quantifying Relationships in Ethnic Subgroups. Diabetes Care. 2017;40(3):338–45. DOI: 10.2337/dc16-1616
2. Svensson MK, Cederholm J, Eliasson B, Zethelius B, Gudbjörnsdottir S. Albuminuria and renal function as predictors of cardiovascular events and mortality in a general population of patients with type 2 diabetes: A nationwide observational study from the Swedish National Diabetes Register. Diabetes and Vascular Disease Research. 2013;10(6):520–9. DOI: 10.1177/1479164113500798
3. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. New England Journal of Medicine. 2015;373(22):2117–28. DOI: 10.1056/NEJMoa1504720
4. Wanner C, Inzucchi SE, Lachin JM, Fitchett D, von Eynatten M, Mattheus M et al. Empagliflozin and Progression of Kidney Disease in Type 2 Diabetes. New England Journal of Medicine. 2016;375(4):323–34. DOI: 10.1056/NEJMoa1515920
5. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney International Supplements. 2012;2(1):1–138. [Av. at: http://www.nephro.ru/content/files/standards/KDIGO_GN_AKI_anemia.pdf]
6. Michurova M.S., Kononenko I.V., Smirnova O.M., Kalashnikov V.Yu. Effects of diabetes compensation by various classes of antihyperglycemic agents on endovascular intervention outcomes in patients with type 2 diabetes mellitus. Diabetes mellitus. 2014;17(1):34–40. [Russian: Мичурова М.С., Кононенко И.В., Смирнова О.М., Калашников В.Ю. Влияние компенсации углеводного обмена и вида гипогликемизирующей терапии на исходы эндоваскулярных вмешательств у больных сахарным диабетом 2 типа. Сахарный диабет. 2014;17(1):34-40]. DOI: 10.14341/DM2014134-40
7. Dekkers CCJ, Gansevoort RT, Heerspink HJL. New Diabetes Therapies and Diabetic Kidney Disease Progression: the Role of SGLT-2 Inhibitors. Current Diabetes Reports. 2018;18(5):27. DOI: 10.1007/s11892-018-0992-6
8. Zou H, Zhou B, Xu G. SGLT2 inhibitors: a novel choice for the combination therapy in diabetic kidney disease. Cardiovascular Diabetology. 2017;16(1):65. DOI: 10.1186/s12933-017-0547-1
9. Kidokoro K, Cherney DZI, Bozovic A, Nagasu H, Satoh M, Kanda E et al. Evaluation of Glomerular Hemodynamic Function by Empagliflozin in Diabetic Mice Using In Vivo Imaging. Circulation. 2019;140(4):303–15. DOI: 10.1161/CIRCULATIONAHA.118.037418
10. Gembardt F, Bartaun C, Jarzebska N, Mayoux E, Todorov VT, Hohenstein B et al. The SGLT2 inhibitor empagliflozin ameliorates early features of diabetic nephropathy in BTBR ob/ob type 2 diabetic mice with and without hypertension. American Journal of Physiology-Renal Physiology. 2014;307(3):F317–25. DOI: 10.1152/ajprenal.00145.2014
11. Gonzalez DE, Foresto RD, Ribeiro AB. SGLT-2 inhibitors in diabetes: a focus on renoprotection. Revista da Associação Médica Brasileira. 2020;66(Suppl 1):s17–24. DOI: 10.1590/1806-9282.66.s1.17
12. Kulikov A.N., Beresneva O.N., Parastaeva M.M., Okovityi S.V., Ivanova G.T., Ivkin D.Yu. et al. Influence of empagliflozin on the kidneys in normoglycemic rats with heart failure. Nefrología. 2017;21(2):83–92. [Russian: Куликов А.Н., Береснева О.Н., Парастаева М.М., Оковитый С.В., Иванова Г.Т., Ивкин Д.Ю. и др. Влияние эмпаглифлозина на состояние почек у нормогликемических крыс с сердечной недостаточностью. Нефрология. 2017;21(2):83-92]
13. Volgina G.V. Asymptomatic bacteriuria: modern management and treatment Lecture. Nephrology and Dialysis. 2012;14(1):6–14. [Russian: Волгина Г.В. Бессимптомная бактериурия – современная тактика диагностики и лечения (лекция). Нефрология и диализ. 2012;14(1):6-14]
14. Nicolle LE, Capuano G, Ways K, Usiskin K. Effect of canagliflozin, a sodium glucose co-transporter 2 (SGLT2) inhibitor, on bacteriuria and urinary tract infection in subjects with type 2 diabetes enrolled in a 12-week, phase 2 study. Current Medical Research and Opinion. 2012;28(7):1167–71. DOI: 10.1185/03007995.2012.689956




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