



EFFECT OF DAPAGLIFLOZIN IN NON-ALCOHOLIC FATTY LIVER DISEASE

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ANNOTATION The development of non-alcoholic fatty liver disease (NAFLD), and hence insulin resistance, then type 2 diabetes mellitus in obese patients is of great importance in the choice of treatment tactics, duration, and possible ambiguous outcomes in the progression of NAFLD. Recent evidence suggests that sodium glucose cotransporter-2 (SGLT2) inhibitors inhibit the development of non-alcoholic steatohepatitis in humans, as well as improve liver steatosis in obese patients with type 2 diabetes.

Keywords: Non-alcoholic fatty liver disease, steatosis, Dapagliflozin, SGLT2 inhibitors

Purpose: To evaluate the effectiveness of dapagliflozin in patients with NAFLD on the background of insulin resistance

Research materials and methods: we used 10 mg of dapagliflozin for 3 months in 36 patients with non-alcoholic fatty liver disease aged 20-65 years. The diagnosis of NAFLD was established by abdominal ultrasound. All patients underwent biochemical and anthropometric studies, bio impedance measurement, abdominal ultrasound before and after treatment, as well as a comparative analysis.

Research results: The average age of patients was 44,33±8,2 years. Of the 36 patients, 20 were men and 16 were women. In a comparative analysis, we observed a significant decrease in the biochemical markers of liver damage (ALT, GGT), insulin, and the index of insulin resistance. Bioimpedance measurement indicators (total fat, visceral fat). The average body mass index decreased

significantly: at admission, the average was $31,05 \pm 3,44$, after treatment it decreased to $28,9 \pm 2,34$ ($p < 0,05$).

Conclusion. Our study showed the potential efficacy of an SGLT-2 inhibitor in NAFLD in patients without diabetes mellitus. The results showed a significant improvement in biochemical parameters, insulin sensitivity, lipid profile, body component composition, and weight loss during dapagliflozin therapy for NAFLD.

Relevance. Due to the recent high prevalence of obesity and metabolic syndrome (MS), NAFLD is considered to be the chronic liver disease with the highest growth rate worldwide, with the overall prevalence of NAFLD currently estimated at 25% in the general adult population [1,2].

To date, the treatment of NAFLD is mainly based on lifestyle interventions and early treatment of associated cardiometabolic risk factors [3,4].

Several groups of drugs have entered clinical trials for use as specific therapy for NAFLD; most of them are drugs used to treat type 2 diabetes mellitus (T2DM), which is one of the main risk factors for the development of NAFLD [5]

Sodium-glucose cotransporter 2 (SGLT2) inhibitors lower blood glucose levels by promoting urinary glucose excretion and have been shown to improve cardiovascular and renal outcomes in patients with type 2 diabetes. Recent prospective studies have demonstrated histological improvement in glucose metabolism-related steatosis and fibrosis with SGLT2 inhibitor [9,10]. SGLT2 inhibitors also improve adiposity, liver enzyme levels, and liver steatosis and fibrosis in patients with type 2 diabetes and NAFLD.

Purpose of the study: To evaluate the efficacy of dapagliflozin in patients with non-alcoholic fatty liver disease associated with insulin resistance

Materials and methods of research: We examined 36 patients with NAFLD and insulin resistance aged 20-65 years, the average age of which was $45,3 \pm 6,2$. Of these, 20 were men and 16 were women. All patients were diagnosed with liver

steatosis based on ultrasound examination. To assess insulin resistance (IR), we used the calculated index HOMA IR. The HOMA IR index was calculated using the online calculator HOMA IR on the website <https://mdcalc.ru/homair/calc.php>. To determine the cocomponent composition of the body in percentage (total fat, visceral fat, water) in seven The patients underwent bioimpedance measurements using the PICOOC device (China), and anthropometry was also performed (weight, waist circumference were measured, and BMI was calculated).

Exclusion criteria: patients with established diabetes mellitus and other chronic liver diseases, taking medications that could potentially improve the course of steatohepatitis.

The examination of patients was carried out in the department of arterial hypertension and rehabilitation of the Samarkand branch of the Republican specialized cardiology scientific practical medical center, in a private clinic in the city of Samarkand, in outpatient settings in city polyclinics. All patients were recommended lifestyle modification (daily physical activity of moderate intensity and adherence to a low-calorie diet) and were additionally prescribed a drug from the group inhibitors SGLT2 - dapagliflozin at a dose of 10 mg per day.

Comparisons were made using paired Student's t-tests of biochemical parameters (ALT, AST, GGT, glucose, insulin levels, HOMA-IR index), bioimpedance parameters (weight, BMI, % total fat, visceral fat, water) before and after 3 months of dapagliflozin administration.

Research results: Results of biochemical parameters such as ALT, AST, GGT, blood glucose, insulin and HOMA-IR, triglycerides and HDL before and after taking dapagliflozin (10 mg) for 3 months are shown in Table 1.

Table 1.

Comparative analysis of biochemical parameters before and after treatment (n=36)

Biochemical indicators	Initially	After 3 months of therapy	r
AST (U/L)	34,9 ± 17,42	24.5 ± 16.6	0.005
ALT (U/L)	68,68± 24,7	36,42± 18,86	0.001
GGT (U/L)	68,7 ± 18,82	43,21 ± 14,41	0.001
glucose (mmol/l)	5,6 ± 0,58	5.3 ± 0,54	0.005
Insulin	26,4±6,85	13,8±4,3	0,005
HDL (mmol/L)	1,13 ± 0.31	1,44 ± 0,32	0.001
Serum TG (mmol/L)	1,9 ± 0,8	1.56 ± 0,56	0.001
HOMA-IR	5,76±1,76	3,15±1,13	0,005

Levels all biochemical parameters except blood glucose significantly decreased after treatment compared to baseline. The average ALT level in patients before treatment was 68,68± 24,7 U/L, and after treatment it was 36,42± 18,86 U/L. The average AST level in patients before treatment was 34,9 ± 17,42 U/L, and after treatment the average decrease was 24,5 ± 16,6 U/L. The decrease was from 6.4 to 16.31 U/L (95% CI). The average GGT level decreased from 68,7 ± 18,82 U/L to 43,21 ± 14,41 U/L. The insulin level decreased from 26,2 mU/L to 13,8±4,3 mU/L. The average HOMA-IR index in patients before treatment was 5,76±1,76, and after treatment there was a decrease to 3,15±1,13.

Blood glucose was the only parameter that did not change significantly after dapagliflozin treatment, with the mean blood glucose level in patients before treatment being 5,6 mmol/L and after treatment being 5,3 mmol/L.

Bioimpedancemetry parameters also significantly decreased after 3 months of dapagliflozin therapy.

The patients' total fat upon admission was 38,9±6,14%, after treatment it was 31,76±5,24, of which the proportion of visceral fat decreased from 15,41±3,29% to 11,24±3,36%, the proportion of body fluid in the subjects upon admission was 41,08±5,21%, after treatment the indicators were 46,67±5,7%, the waist circumference of the patients upon admission was 99,05±12,39 cm, after treatment it was 93.31±1.96 cm, the average BMI upon admission was 31.05±3.44, after

treatment it decreased to $28,9 \pm 2,34$. The average weight of patients before treatment was $90,4 \pm 5,82$ kg, and then an average decrease was observed to $83.5 \pm 2,43$ kg.

In all patients we noted good tolerability of the drug; only one patient experienced a side effect in the form of genital fungal infection.

Discussion. In our study, we found significant improvement in various biochemical parameters of liver enzymes after three months of dapagliflozin therapy. The anthropometric status of patients (WC, weight, BMI) and body component composition (% total fat, visceral fat, water) also improved after dapagliflozin therapy, which was also reported Ribeiro Dos Santos and etc. and Tobita H. et al. [7,8]. Most of our patients had mild to moderate hepatic steatosis as reported by abdominal ultrasound, which showed significant improvement after dapagliflozin therapy.

Jan W Eriksson et al. in their placebo-controlled studies in obese patients without diabetes mellitus, after 24 weeks of therapy with dapagliflozin compared with placebo, found significant differences between groups in weight and systolic blood pressure, with dapagliflozin being well tolerated by patients [9,10].

All these data confirm the efficacy of sodium-glucose cotransporter-2 inhibitors in improving biochemical parameters, in reducing weight, BMI in NAFLD and the safety of this group of drugs in patients without diabetes.

Conclusions

In summary, our results showed a significant reduction in the levels of biochemical markers of liver damage, insulin and insulin resistance index, improvement in lipid profile, body composition, and weight loss with dapagliflozin therapy in NAFLD. Our results were similar to those of previous studies in patients with and without diabetes.

Based on this, potential mechanisms by which SGLT2 inhibitors improve hepatic steatosis include reductions in body weight and visceral fat, inflammation, and improvement in insulin resistance.

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