Effect of Semaglutide on the Psoriatic Lesion in Patients With Type 2 Diabetes Mellitus

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1. Study design

Observational, prospective study, interventional cohort study was conducted at the University Clinical Centre of the Republic of Srpska, the Skin and Venereal Diseases Clinic.

Cohort 1. Patients with DMT2 and psoriasis, who are already on metformin therapy in the maximally tolerated dose and to whom semaglutide will be introduced into the therapy, according to the Instructions for the drug, approved by the Agency for medicinal products and medical devices of Bosnia and Herzegovina (ALIMS BIH), as well as the indications approved by the Health Insurance Fund of the Republic of Srpska, namely: DMT2, BMI >30 kg/m2, HbA1c >7% in the maximum tolerated dose of semaglutide (0.25mg, 0.5mg per week or 1.0mg per week).

Cohort 2. Patients with DMT2 and psoriasis, who are already on metformin therapy in the maximally tolerated dose and other oral antidiabetics, except on therapy with GLP-1 RA and SGLT-2 inhibitors.

The patients were treated with semaglutide, they received the drug free of charge, and at the suggestion of a specialist endocrinologist in doses and according to the method of administration (subcutaneous) as described in the Instructions for the drug use. The drug is registered for use by ALIMS BIH.

Subjects: A total of 30 patients divided into two cohorts, one is patients with DMT2 and psoriasis who received the drug semaglutide along with previous antidiabetic therapy, the other is patients with psoriasis and DMT2, but who remained on the current antidiabetic therapy and did not receive

the drug semaglutide. In all patients, the diagnosis of psoriasis was made on the basis of a typical clinical picture, the existence of clearly limited erythematous plaques with non-adherent whitish squamous, determined by clinical examination and scoring by means of the PASI score (2). 30 subjects were included in the research itself, namely two groups of 15 subjects. One group consisted of 15 subjects with psoriasis and DMT2 on metformin therapy who were prescribed semaglutide according to the existing indication for the drug, and the other control group consisted of 15 subjects with psoriasis and DMT2 who were on metformin or any other antidiabetic therapy, except for GLP-1 agonists. Subjects corresponded comparatively by age and gender.

The age of the subjects in both groups was from 18-70 years, and the sample included subjects of both sexes. The aforementioned selection of subjects and the size of the sample itself ensured representativeness of the sample and objective research results for the examined population.

Criteria for inclusion in the study: Patients who signed a personal consent to participate in the study, patients with a typical clinical picture of moderately-severe to severe plaque psoriasis (PASI SCORE ≥10) and DMT2 diagnosed at least 6 months before inclusion in the study, patients who receive therapy prescribed by endocrinologist, patients who were not treated with immunosuppressive therapy.

Criteria for non-inclusion in/exclusion from the study: Other forms of psoriasis, other chronic, inflammatory diseases (data obtained by reviewing the medical history), drugs that can cause the appearance of psoriasis (lithium, systemic antimalarials, systemic corticosteroids) - for the past 3 months, systemic therapy of vulgaris psoriasis 3 months before inclusion in the study, patients on therapy with other GLP-1 RAs except semaglutide (liraglutide, dulaglutide, lixisenatide), SGLT-2 inhibitors (empagliflozin and dapagliflozin) and NSAIDs, photo UVB therapy, patients who did not personally sign consent to participate in the study.

Criteria for exclusion from the study: Subject's request for exclusion from the study, patients diagnosed with another pathological condition, adverse reactions to semaglutide described in the available Instructions for the drug: nausea, vomiting, allergic reaction at the localization of drug administration.

Clinical and demographic characteristics of patients

The severity and activity of the disease was determined by the PASI score and the DLQI Index twice in total during the research, during the first and second visit. Determination of the presence of MS in subjects was performed according to the IDF (*International Diabetes Federation*) definition.

To assess disease activity, i.e. skin surface affected by changes (erythema, infiltration and extent of squamous matter), the PASI score was used. Assessment of the clinical picture of psoriasis using the PASI score, by using the above-mentioned method, was performed a total of two times, during the 3 months that the research lasted.

All demographic characteristics of the patients, as well as anthropometric parameters, were also collected. Medical history was used for general demographic and social epidemiological data (name and surname, date of birth, age, gender), as well as anthropometric measurements (body height and weight, body mass index-BMI).

Biochemical analyses

Biochemical analyses were performed on the blood sample of the subjects, 12-14 hours after the last meal, a total of two times during the research, during the first and second visit, and the patients were informed about this beforehand. Part of the serum was used to determine the concentration of fasting glucose, fasting insulin, HgbA1C, urate, total cholesterol, triglycerides, and LDL and HDL cholesterol, which was performed at the Institute for Laboratory Diagnostics of the

University Clinical Centre of the Republic of Srpska. The second part of the serum was used to determine the concentration of serum TNF-α, IL-1β, IL-6, IL-17, CRP and IL23. The final analysis of these biochemical parameters was carried out at the Center for Biomedical Research of the Faculty of Medicine of the University of Banja Luka. The safety of the use of semaglutide, i.e. its side effects (the most common side effects: nausea, vomiting, allergic reaction at the localization of drug application) was also monitored by telephone in patients diagnosed with DMT2 and psoriasis.

Measurement techniques

Serum concentration of TNF-α, IL-1β, IL-6, IL-17, CRP and IL23, fasting glycemia values and HbA1c were determined from venous blood, as well as determination of insulin, urate, total cholesterol, triglycerides, LDL and HDL-cholesterol in the serum. The patients were monitored clinically and laboratory (PASI SCORE and DLQI, HbA1c, fasting GUC, fasting insulin, urate, lipid status) during two study visits in the period of 0 and 3 months, and the mentioned parameters were measured twice in total.

Baseline visit: Before the start of the clinical examination and serum sampling, the patients were required to sign the Patient Informed Consent, in which all procedures were explained, as well as patients' rights and obligations during the study trial in which they will voluntarily participate. After signing the Informed Consent, a clinical examination by a dermatovenerologist (PASI and DLQI) and an endocrinologist was performed, as well as blood sampling for biochemical and hormonal analyzes of blood sugar (GUC), cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, insulin, HbA1c, urate. Blood samples were taken (a total of two test tubes) at the Institute for Laboratory Diagnostics of the University Clinical Center of the Republic of Srpska, at no cost to the patients.

During the next 12 weeks of the study, the patient was called by phone, every month - a total of 3 times - in order to confirm the administration of the drug or the possible existence of adverse reactions to the drug, described in the available Instructions for the drug.

Visit after 12 weeks: the patient underwent a clinical examination by a dermatovenerologist (PASI and DLQI) and an endocrinologist, as well as blood sampling for biochemical and hormonal analyzes (blood sugar (GUC), cholesterol, HDL cholesterol, LDL cholesterol, triglycerides, insulin, HbA1c, urate). Blood samples were taken (a total of two tubes) at the Institute for Laboratory Diagnostics of the University Clinical Center of the Republic of Srpska, at no cost to the patient.