disorders occur due to high-density lipoproteins, which are counter-factors of atherogenicity and stone formation.

Noteworthy is the fact that diseases of the biliary system are poorly symptomatic in patients with diabetes mellitus, which is associated with the presence of diabetic autonomic neuropathy. In this category of patients quite often it is impossible to prevent the processes of lithogenesis, and it is necessary to treat already formed stones medicamentally and surgically. Surgery is a very powerful stress for patients with diabetes mellitus that can lead to decompensation of major body systems, so early diagnosis of gallstone formation and its prevention is necessary in this category of patients.

Considering the peculiarities in lipid metabolism changes in patients with combined pathology, it is necessary to carry out the multi-moment duodenal probe with the next evaluation of vesicular bile portion with further biochemical investigation in the following categories of patients. When evaluating the results of a biochemical investigation of bile, all changes should be taken into consideration, as separate data are not efficient in objective estimation. In this case, lithogenicity indices should be used: ratios such as bile acids / cholesterol and phospholipids / cholesterol. They are reliable for confirming the link should be influenced both for preventive and curative purposes. Isaxon index should be also used to determine the lithogenicity of bile. This index is a three-component system that more accurately indicates the increased lithogenic properties of bile. It should be obligatory for some bile samples carrying out laser polarimetry with next complying of polarization-correlation maps and selections and calculation of the crystallization coefficient.

Olenovych O.A.

PECULIARITIES OF ACID-REGULATING RENAL FUNCTION DISORDERS IN THE EARLY PERIOD OF ALLOXAN-INDUCED EXPERIMENTAL DIABETES

Department of Clinical Immunology, Allergology and Endocrinology
Higher State Educational Establishment of Ukraine
«Bukovinian State Medical University»

Diabetic kidney disease is one of the most severe complications of diabetes mellitus, which dramatically decreases the quality and duration of life of diabetic patients. This is a clinical diagnosis historically based, primarily, on the detection of proteinuria in diabetic patients, confirming a long existence of kidney damage with already practically irreversible changes at glomerular level. Meanwhile, acid-regulating renal function is known as one of the most sensitive indicators of the functional state of the nephron. Considering that, the objectives of this research was to study the condition of active acid-regulating renal activity in the early period of experimental diabetes mellitus (DM).

The experiments were carried out on 20 matured nonlinear male rats, weighted 0,1-0,2 kg, under the standard conditions of vivarium. For the experimental modeling of DM 10 animals were administered alloxan intraperitoneally in a diabetogenic dose of 160 mg/kg; 10 animals served as a control group. On 11^{th} day after the administration of diabetogenic substance all the experimental animals were withdrawn from the experiment. With the purpose to study the function kidney state, the animals were loaded with water in the volume of 5% of body weight, placed into individual cages for 2 hours to collect urine samples. Further analysis of urine samples, as well as blood plasma, collected at the moment of decapitation of animals, enabled the evaluation of acid-regulating renal function (urine pH, titrated acids, hydrogen ions and ammonia levels were detected).

As the results of investigation demonstrated, blood glucose concentration in rats with 11-day-long alloxan-induced diabetes significantly exceeded the value of the appropriate index in the control group rats by 2,2 times ($P<0,001$), expectedly followed by the development of glucosuria, that evidences the adequacy of the used experimental model.

On the 11^{th} day of the alloxan-induced hyperglycemia an active release of titrated acids and ammonia compounds in diabetic rats exceeded the control values 40,3% and 12,3% (respectively). At the same time, the excretion of ammonia, standardized in volume of glomerular filtrate, was reliably lowered (21,3%, $P<0,001$) as compared to the controls. Ammonia ratio demonstrated a

downward tendency as well, accompanied by non-reliable reduction of the integral indicator of kidney acid activity, such as urine pH. Moreover, an excretion of active hydrogen ions raised, and after standardization by volume of glomerular filtrate remained 22,2% ($P<0,05$) higher than in controls.

Hence, the obtained findings enable the suggestion that the mechanisms of urinary acidification associated with acido- and ammoniogenesis, with direct sodium-hydrogen antiport remain unchanged on 11th day of alloxan-induced diabetes, however acid-regulating renal function demonstrates the tendency to augmentation, probably due to an intensification of glomerular filtration, typical for the initial stages of diabetic kidney disease and leading to the elevation of filtration load of the nephron by acids and ammonia, and certifies the high efficacy of renal transport mechanisms for effective clearance of extracellular fluid from excessive acidic metabolites and ammonia against a background of diabetes mellitus.

Pankiv I.V.

VITAMIN B12 LEVELS IN METFORMIN-TREATED TYPE 2 DIABETES PATIENTS

Department of Clinical Immunology, Allergology and Endocrinology
Higher State Educational Establishement of Ukraine
«Bukovinian State Medical University»

Metformin is the most widely used oral antihyperglycaemic drug, but it may lower B_{12} status, which could have important clinical implications. There are limited data about the effect of metformin use on serum vitamin B12 levels in type 2 diabetes mellitus (DM) patients.

Aim of the research was to study serum Vitamin B12 levels in patients with type 2 diabetes mellitus who were receiving metformin and compared them to those never treated with metformin.

A total of 53 patients with type 2 DM (group 1, n=35, receiving metformin and group 2, n=25, never treated with metformin) from the endocrinology clinic in Chernivtsi were studied. Serum Vitamin B12 levels were measured in all patients. Diabetic neuropathy symptom score (DNS) was used to assess peripheral neuropathy.

The mean age of the study population was 51,9±9,3 years. Table 1 shows the baseline characteristics of the «metformin» and «no metformin» groups. The two groups were comparable except for duration of DM which was significantly greater in the metformin group. Duration of metformin use was 26,2±5,4 months (range 4–180 months). Daily dose of metformin was 839,2±53,1 mg (range 500–2500 mg). The cumulative dose of metformin was 970,8±517,2 g (range 85–10,590 g). The serum Vitamin B12 levels were 239,6±37,4 pg/ml in metformin group and 293,6±42,3 pg/ml in the no metformin group (p=0,37). When adjusted for duration of DM, metformin use was associated with a 57,2±7,3 pg/ml (p=0,03) lower serum Vitamin B12 levels. No significant increase in the prevalence of neuropathy (DNS score) was found in the Vitamin B12 deficient patients (levels <190 pg/ml) as compared to patients with normal Vitamin B12. Serum Vitamin B12 levels for the entire cohort were higher by 11,8±1,7 pg/ml (95% CI 6,3–17,0, p<0,01) for every 1 year increase in the DM duration. On univariate linear regression analysis with Vitamin B12 levels as the dependent variable and duration of metformin use as the predictor variable, duration of metformin use predicted a 0,8±0,4 pg/ml (95% CI 0,004–1,7 pg/ml, p=0,04) lower Vitamin B12 levels for every 1 month increase in the duration of metformin use. On stratifying duration of metformin use into no metformin use, 0–1 years, 1–5 years, and more than 5 years, it was found that a 20,1 pg/ml (p=0,64) and 37,3 pg/ml lower serum Vitamin B12 concentration was observed in individuals with a 0–1 years and 1–5 year duration of metformin use, respectively, compared with the group which had not received metformin.

Thus, metformin use was associated with a lower serum Vitamin B12 levels when adjusted for duration of diabetes mellitus. Increasing duration of diabetes mellitus was associated with higher serum Vitamin B12 levels.