A prospective cohort study of 95 critically ill full-term neonates was performed. Fifty

| Group I / AKI - (n=50) | Group II / AKI + (n=45) |
|------------------------|-------------------------|
| SCr, µmol/L, M±m       | 54.1±1.67               | 68.7±2.31*                |
| SCysC, mg/L, M±m       | 1.56±0.02               | 1.75±0.02*                |
| Ua1-MG, mg/L, M±m      | 32.8±1.19               | 42.8±2.89*                |
| Uβ2-MG, mg/L, M±m      | 2.66±0.13               | 2.55±0.18                 |

Table 1. Neonatal renal data.

ROC analysis was conducted with calculation of appropriate operational characteristics to determine prognostic and diagnostic value of the presented serum and urinary protein biomarkers concerning neonatal AKI (Tab. 2).
Table 2. Results of ROC analysis of urinary protein biomarkers for neonatal AKI

| Cut-off level | SCr 81.0 µmol/L | SCysC 1.59 mg/L | Uα1-MG 42.0 mg/L | Uβ2-MG 2.95 mg/L |
|---------------|-----------------|-----------------|------------------|------------------|
| AUROC         | M 0.74          | 0.83            | 0.73             | 0.56             |
| 95% CI        | 0.61-0.86       | 0.74-0.91       | 0.64-0.84        | 0.5-0.68         |
| p (AUC)       | 0.006           | <0.001          | 0.001            | 0.23             |
| Se, %         | M 48.4          | 88.9            | 62.2             | 71.1             |
| 95% CI        | 30.2-66.9       | 75.9-96.3       | 46.5-76.2        | 55.7-83.6        |
| Sp, %         | M 97.2          | 64.0            | 86.0             | 41.8             |
| 95% CI        | 85.5-99.9       | 49.2-77.1       | 73.3-94.2        | 28.7-55.9        |
| PPV, %        | M 93.8          | 68.9            | 80.0             | 50.0             |
| 95% CI        | 67.7-99.1       | 60.2-76.5       | 65.9-89.2        | 42.8-57.2        |
| NPV, %        | M 68.6          | 86.5            | 71.7             | 63.9             |
| 95% CI        | 60.8-75.6       | 73.2-93.8       | 65.9-89.2        | 50.4-75.5        |
| PLR           | M 17.4          | 2.47            | 4.44             | 1.22             |
| 95% CI        | 2.4-124.5       | 1.68-3.62       | 2.16-9.17        | 0.91-1.64        |
| NLR           | M 0.53          | 0.17            | 0.44             | 0.69             |
| 95% CI        | 0.38-0.75       | 0.07-0.41       | 0.30-0.65        | 0.40-1.20        |

SCr is a late and non-specific marker of reduced glomerular filtration rate. It is insensitive to acute changes in kidney function. Neither the cause, location of renal disease (e.g. pre-renal versus intrinsic; affected renal tubule segment; nephrotoxic versus ischemic AKI) nor the extent of renal damage are adequately reflected by SCr concentration. Also, SCr is influenced by several non-renal factors such as muscle mass, medications taken, diet and tubular secretion, thus causing inaccuracies in making the diagnosis of AKI [5]. The diagnostic model with determination of SCr level did not demonstrated high discriminating ability with cut-off level ≥ 81.0 µmol/L (AUROC 0.74, p<0.05). Low Se (48.4%) with high Sp (97.2%) was determined for this laboratory test. CysC is a non-glycosylated, low molecular weight, cation protein that is regularly synthesized by most nucleated cells. CysC is also a more accurate marker for estimation of glomerular filtration rate in paediatric patients with AKI. Elevation of CysC occurs before elevation of SCr; therefore, CysC can be used as a preferable marker for early detection of AKI, as well as in future AKI outcome studies and clinical trials [6]. When making the diagnosis of AKI in term newborns the diagnostic model with determination of SCysC level demonstrated high discriminating ability with cut-off level ≥ 1.59 mg/L (AUROC 0.83, p<0.001), better than SCr. High Se (88.9%) with insufficiently high Sp (64.0%) was determined for SCysC level. α1-MG is a glycosylated protein of molecular weight estimated to be between 26 kDa and 33 kDa according to the type of measurement containing 167 amino acids. α1-MG is synthesized in the liver, that is half of protein glycosylated protein of molecular weight (11,8 kDA) polypeptide and has similar structure to the CH3 domain of the immunoglobulin molecule. α1-MG is a single-chain, low molecular weight (11,8 kDA) polypeptide and has similar structure to the CH3 domain of the immunoglobulin molecule [7]. Therefore, considering AUROC values, the results of the conducted statistical analysis demonstrated that the biggest diagnostic value concerning AKI determination in critically ill newborns was peculiar for the model with determination of SCysC level (AUROC 0.83, p<0.001 with cut-off level ≥ 1.59 mg/L). Similar diagnostic value was found in the models with determination of Scr (AUROC 0.74, p<0.05 with cut-off level ≥ 81.0 µmol/L) and Uα1-MG (AUROC 0.73, p<0.05 with cut-off level ≥ 42.0 mg/L). The model with determination of Uβ2-MG (AUROC 0.56, p>0.05 with cut-off level 2.95 mg/L) demonstrated the absence of diagnostic value concerning AKI determination in term newborns.

Prospects for further research are directed to the development of a comprehensive prognostic-diagnostic mathematic model concerning determination of AKI in term and preterm newborns including the most important risk factors, clinical signs, laboratory and instrumental methods of examination, investigation of their value and introducing into the practical work of medical establishments.

References:

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Interleukin-18 takes a special place among the immunoregulatory mediators. It is one of the key cytokines in the congenital and acquired immune response formation. Interleukin-18 takes part in the activation of cytotoxic T-lymphocytes, NK cells, macrophages, dendritic cells, thereby «providing» an autoimmune response of the organism. Currently, a cartilage oligomeric matrix protein (COMP) is considered as a marker of cartilage damage. It is a non-collagen matrix protein. Its entry into the blood is correlated with the exchange in the tissue of the cartilage. The process in thyroiditis is accompanied not only by quantitative, but also qualitative changes in the immune system. Interleukin-18 takes a special place among the immunoregulatory mediators. It is one of the key cytokines in the congenital and acquired immune response formation. Interleukin-18 takes part in the activation of cytotoxic T-lymphocytes, NK cells, macrophages, dendritic cells, thereby «providing» an autoimmune response of the organism. Currently, a cartilage oligomeric matrix protein (COMP) is considered as a marker of cartilage damage. It is a non-collagen matrix protein. Its entry into the blood is correlated with the exchange in the tissue of the cartilage. The process in thyroiditis is accompanied not only by quantitative, but also qualitative changes in the immune system.

Materials and Methods. The study involved 35 patients with autoimmune thyroiditis and osteoarthritis (main group) and 18 patients isolated from autoimmune thyroiditis (comparison group) aged 23 to 65 years; women predominated (85.7% and 83.3%, respectively).

Results. The duration of the anamnesis with autoimmune thyroiditis varied within 3-18 years, with joint damage 2-19 years. Estimation of hormonal status of the thyroid gland showed that individuals with euthyroid status accounted for 22.9% of the main group and 27.8% of the comparison group. Decrease in thyroid function of easy or moderate severity was determined in 77.1% and 72.2% of patients, respectively. The diagnosis of osteoarthritis was established on the basis of patient complaints, objective and radiological examination data. The pain syndrome and the expressiveness of morning stiffness in osteoarthritis were determined with the Huskison scale and the Likert scale. Interleukin-18 in serum was tested by ELISA - a set of reagents «Protein contour»; COMR is a set of COMP ELISA. Norms were obtained by examining 20 practically healthy people of the same sex and age. Statistical processing was carried out with help of variational statistics methods using the Statsoft Statistica 8.0 software packages and Microsoft Excel 2010 software. Results and its discussion. Study of the interleukin-18 level in the blood serum showed its increase both in the main group (2.4 times) and in the comparison group (1.6 times) in relation to healthy individuals (241.4 ± 13.7) pg/ml. That is, the content of interleukin-18 in the main group of patients was 571.4 ± 17.9 pg/ml in the comparison group - 397.1 ± 12.9 pg/ml. This increase in patients with isolated autoimmune thyroiditis was probably more associated with the autoimmune component of the disease, and its significant increase in comorbid conditions was a result of the development of joint synovial tissue inflammation. That is, the development of autoimmune processes in thyroiditis is accompanied not only by quantitative, but also qualitative changes in the immune system parameters and their mutual relations. This «ensures» the activation of autoimmune mechanisms of the disease. At the same time, the content of interleukin-18 did not depend on the localization of the processes in the joints, the duration of the diseases and the osteoarthritis x-ray stage and the thyroid gland functional state. Study of the COMP level in patients with autoimmune thyroiditis and osteoarthritis has shown an increase of this index was found (21.9 ± 1.2 U/l) at the control - 9.2 ± 0.7 U/l. In patients with a third X-ray stage of joint damage (9 people), this parameter was higher than in the whole group (26.7 ± 1.1 U/l). That is, the direct dependence of the COMP content from the severity of morphological changes in the joint was determined. It should be noted that the severity of inflammatory changes in the joint and its derivatives did not correlate with the size of the COMP. Also, there was no correlation between the value of COMP, the content of interleukin-18 and the stage of functional activity of the thyroid gland.

Conclusions. An active inflammatory process that occurs in osteoarthritis and autoimmune thyroiditis in the joints is accompanied by interleukin-18 cytokine activation. It probably shows not only the immune system’s stress due to an inflammatory reaction with osteoarthritis but also autoimmune processes with thyroiditis. An increase in the content of COMP, one of the components of the cartilage matrix, in patients with combine pathology makes it possible to use this indicator with dynamic observation and evaluation of the therapy effectiveness.

References:

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