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Abstract Book

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Material and methods: We retrospectively collected data on heavily treated patients receiving regimens containing dolutegravir 50 mg once daily. The patients were followed up in National Institute of Infectious Disease "Matei Bals". We focused on efficacy (viral load levels and CD4 count) and tolerability (clinical data and laboratory tests) of cART containing dolutegravir.

Results: We identified 35 patients, 20 women with median age of 27 years old, diagnosed in their childhood. Median number of antiretroviral regimens was six before started dolutegravir containing cART.
The reason for switching to dolutegravir containing regimen was in almost half of the cases (17/35 cases) intolerance to therapy, in 14/35 cases the lack of viral suppression and in 4/35 cases replacing an old drug (didanosine or fosamprenavir). All patients switched for intolerance or for replacing an old drug (Group A) had undetectable viral load at initiation and mean CD4 level was 598.1 cells/mm3. In patients with virologic failure (Group B), the mean CD4 was 244.3 cells/mm3. In patients with virologic failure the most used drugs associated with dolutegravir was boosted darunavir and tenofovir (10/14 cases) and in five cases we used at least five drugs (two reverse transcriptase inhibitors, etravirine, dolutegravir and boosted darunavir). At 12 weeks, CD4 levels increased in average with 75.3 cells/ mm3 in group A and with 34.4 cells/ mm3 in Group B. In group A, three patients experienced viral load blips and the rest remained undetectable. In group B, five patients reached viral suppression in 12 weeks and another four after 24 weeks, two were lost to follow up after first month and the rest encountered two logs decrease in viral load at 24 weeks. From 35 patients, two experienced neurologic adverse events (one headache and one nightmare) and replaced dolutegravir in group A. Two patients from group A and one in Group B had grade 1 increase in hepatic enzymes, with no clinical effect and they continued the dolutegravir-containing regimen with subsequent normalization of the hepatic lab test.

Discussions: In our multidrug experienced patients introduction in therapeutic use of a new integrase inhibitor had good outcome, due to a carefully selection of patients and antiretroviral combinations, avoiding low active drugs or using four or five partially active molecules.

Abstract 84

Hepatotoxicity induced by antituberculous treatment in patients coinfected with HIV, tuberculosis and chronic hepatitis C

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Background: Hepatotoxicity due to antituberculous drugs limits treatment in patients coinfected with HIV, tuberculosis and viral hepatitis. Its risk increases in case of advance stage of liver disease. Objective of our study was to determine risk factors for hepatotoxic reactions during treatment of TB in patients coinfected with HIV and HCV.

Materials and methods: The study included 86 patients coinfected with HIV, tuberculosis and chronic hepatitis C: 25 women (29.1%) and 61 men (70.9%), mean age was 36,3±3,8 years. All patients underwent diagnostic tests such as complete blood count, urinalysis, blood chemistry, ultrasound of the abdomen. HIV infection was diagnosed with the detection of HIV antibodies (ELISA and Western blot) and HIV viral load (PCR). CHC was confirmed by detection of HCV RNA in the blood (PCR) and antibody to HCV (ELISA). Diagnosis of pulmonary and extra-pulmonary TB was confirmed according to medical history, clinical data, results of X-ray or CT scan, bacteriological tests (sputum smear microscopy, sputum culture for M. tuberculosis), cerebrospinal fluid tests, histological examination of biopsy samples of lymph nodes. Statistical analysis was performed using the software package Statistica 6.0 and Microsoft Excel 2010. Descriptive statistics of frequency distributions, summary measurements and variability measurements were used. The association of each variable with the presence of hepatotoxicity was evaluated by means of the Mann-Whitney test.

Results: Clinical and laboratory signs of hepatotoxicity during antimycobacterial therapy

were observed in 47 patients (57.0%) coinfected with HIV/TB/CHC. In majority of cases (69.4%) it developed during the first two weeks of therapy. There was a significant ($p<0.05$) increase in liver enzymes: ALT (up to 154.9±11.9 IU/l), AST (up to 145.4±13.0 IU/l), GGT (up to 87.8±9.9 IU/l), alkaline phosphatase (up to 144.5±29.1 IU/l) and total bilirubin levels (up to 53.7±8.7 μmol/l). Conducting ultrasound examination of the abdomen in dynamics showed significantly higher ($p<0.05$) rate of hepatomegaly (75.6%), changes in acoustic density of the liver (79.1%), heterogeneity of hepatic parenchyma (74.4%) and expansion of intrahepatic bile ducts (40.7%). Factors that significantly increase the risk of hepatotoxic reactions in patients with coinfection of HIV/TB/CHC are the number of CD4+-cells<200/ml (OR=3.922, 95% CI 1,586-9,698, $p<0.01$), advanced stages of liver fibrosis (OR=8.533, 95% CI 2,842-25,618, $p<0.01$), baseline increased ALT and AST (OR=4.362, 95% CI 1,478-12,873, $p<0.01$) and hyperbilirubinemia (OR=3.214, 95% CI 1,184-8,724, $p<0.05$), the administration of HAART during the intensive phase of antituberculous treatment (OR=4.800, 95% CI 1,647-13,991, $p<0.01$), pulmonary tuberculosis (OR=2.923, 95% CI 1,183-7,221, $p<0.05$), bacterioexcretion (OR=3.214, 95% CI 1,184-8,724, $p<0.05$) and chronic viral hepatitis B coinfection ($p<0.05$).

Conclusions: Hepatotoxic events occur during the treatment of TB in majority of patients coinfected with HIV/TB/HCV. Multivariate logistic regression showed that the following factors increased the risk of hepatoxicity: CD4+ count of < 200cells/mm3, advanced stages of liver fibrosis, baseline increased ALT and AST and hyperbilirubinemia, the administration of HAART during the intensive phase of antituberculous treatment, pulmonary tuberculosis, bacterioexcretionand chronic viral hepatitis B coinfection.

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Results of pegylated interferon alfa-2b treatment in children with chronic hepatitis C

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Background: Assessment of effectiveness, safety and tolerance of pegylated interferon (PEG-IFN) alfa-2b in children with chronic hepatitis C (CHC).

Methods: The study included the observation of 79 pediatric patients with CHC (aged 3 to 18 years). All children were treated in 11 different regional pediatric infectious disease hospitals of Ukraine for the time period of year 2012 to 2014. The treatment plan included PEG-IFN alfa-2b 60 μg/m2 subcutaneous once a week and ribavirin 15 mg/kg daily. CHC-patients with genotype 1 (G1) were treated for 48 weeks, genotype 2-3 (G2-3) for 24 weeks.

Results: Among children 59.6% were boys. By age: 14 to18 years (50.6%), 3 to 10 years (34.2%). 36.7% patients with CHC had concomitant pathology (hematological diseases (40%), hemophilia (16.6%) and asthma (15.3%)). Most children were infected with horizontal route of transmission (70.8%), but 18.9% were infected vertically. By genotype: G1b (72.2%), G3a (24%), G2 (2.5%) and G1a subtypes (1.3%) respectively. At the beginning of treatment in 60.7% patients viral load was > 600000 IU / ml., 45.6% patients had 1.5 times elevated levels of liver enzymes (ALT, AST), in 25.3% - twice elevated levels, but 29.1% patients had normal levels. During treatment the side effects of antiviral therapy such as hyperthermia syndrome, anemia and leukopenia were observed in 25.5% children.

Conclusions: In completely treated children with CHC a sustained virologic response (SVR) was attained in 63.2% cases. By genotype, the SVR was achieved in 57.8% of G1 and 81.8% of G2-3 HCV patients respectively.