517. Characterization of Novel Hepatitis B Virus B/C Intergenotypic Recombinants in Terminal Reverse Transcriptase Sequences among Chronic Hepatitis B Patients

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Session: 59. Hepatitis B and C in Varied Settings
Thursday, October 5, 2017: 12:30 PM

Background. Chronic hepatitis B (CHB) remains a severe global public health concern. Hepatitis B virus (HBV) can be divided into 8 genotypes with different geographical distribution and virological features. We demonstrated genotypes B and C prevalent in southern and northern China, respectively, had divergent genotype-dependent amino acid polymorphisms and variations in reverse transcriptase (RT) gene, a target of anti-HBV therapy. Recently B/C intergenotypic recombination was reported in RT but its prevalence and clinical implications are elusive. This study aimed to characterize novel intergenotypic recombinants in HBV RT and to dissect their association with HBV-related clinical indexes.

Methods. A total of 220 CHB cases were enrolled in China. Sera were tested for ALT, AST, or HBV serologic markers or DNA. HBV RT sequences were amplified, sequenced and genotyped. Recombination analysis was done with Simplot program.

Results. 29.1% (64/220) of the cases had genotype B while 70.9% genotype C. Though no intergenotypic recombination was detected for genotype C, 37.5% (26/64) of genotype B HBV had recombination with genotype C at 3’ end of RT. No significant difference was found in ALT or AST, or HBsAg positive rate among the cases with the recombinant 3’ end, or genotype B or C. Remarkably, HBV DNA of the untreated recombinant cases was significantly higher than that of pure genotype B group, though not significantly different from that of genotype C group. The untreated recombinants also had higher mutation rates at 3 residues throughout RT (m53, 134, 213, 222, 271, 319 and 340) compared with parental genotypes, among which 3–4 substitutions were co-detected for one recombinant. Moreover, a majority of the recombinant HBV carriers were born on the South/North interface of China.

Conclusion. Novel HBV B/C intergenotypic recombination at the 3’ end of RT is associated with higher HBV DNA, interlinked RT point mutations and birthplace among Chinese patients. Our findings shed new light on the clinical, virological and epidemiological characteristics of novel intergenotypic recombinants. The emergence of new HBV recombinants may contribute to a dramatically enhanced heterogeneity in disease manifestations, treatment response and prognosis among CHB cases.

Disclosures. All authors: No reported disclosures.

518. APRI Score as a Predictor of Significant Liver Fibrosis in Chronic Hepatitis B
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Session: 59. Hepatitis B and C in Varied Settings
Thursday, October 5, 2017: 12:30 PM

Background. Chronic hepatitis B (CHB) is a global public health problem. Histologic staging of liver fibrosis is crucial to identify patients who need antiviral treatment. As an alternative to percutaneous liver biopsy (PLB), Aminotransferase Platelet Ratio index (APRI) score was recently validated by the WHO. We aimed to evaluate the performance of APRI score in predicting significant fibrosis (SF) in patients with CHB.

Methods. We conducted a retrospective study including 179 patients aged ≥ 15 years with documented CHB and who underwent a PLB during the period 2008-2016. A SF was defined according to METAVIR score (≥ 2). ROC curves assessed the performance of APRI score in predicting SF. We estimated PLB cost of 60 Dollars in our institution.

Results. Mean age of patients was 37.6 ± 10 years and sex ratio was 1.48. There were 93 patients with SF (52%) who had a high level of aspartate aminotransferase (ASAT) (71.4 ± 38 vs. 34 ± 16 IU/L; P < 0.001) but a low level of platelet count (195 ± 53 vs. 208 ± 52 G/L; P = 0.04). APRI score was significantly higher in patients with SF (1.1 ± 0.7 vs. 0.48 ± 0.26; P < 0.001). Multivariate analysis using logistic regression showed that only APRI score was independently predictive of a SF (HR = 3.78, 95% CI 1.23–11.66; P = 0.02). APRI predicted accurately SF with an Area Under the Receiving Operating Curve (AUC) of 0.7 (CI 95% 0.62–0.77; P < 0.001). At a threshold of 0.5, APRI had a sensitivity of 62%, a specificity of 68%, a positive predictive value of 64.4% and a negative predictive value of 60.7%. The number of avoided PLB with APRI score was 112 PLB with a diagnostic accuracy of 62.5%. Subsequently, the saved cost was estimated to be around 6720 Dollars.

Conclusion. APRI score was well performing in predicting SF in patients with CHB. This could be of paramount importance particularly in developing countries given that this non-invasive score may help to assess liver fibrosis in CHB. Larger scale and analytic prospective studies are required in order to strengthen the accuracy of this score.

Disclosures. All authors: No reported disclosures.

519. Effectiveness and Safety of Sofosbuvir/Ledipasvir and Paritaprevir/ritonavir/ Ombratuvir + Dasabuvir in Patients with Chronic Kidney Disease: Results from ERCHIVES
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Session: 59. Hepatitis B and C in Varied Settings
Thursday, October 5, 2017: 12:30 PM

Background. Chronic kidney disease (CKD) was a relative contraindication to HCV treatment in the interferon/ribavirin era due to poor tolerability and lower efficacy. Our aim was to determine the effectiveness treatment completion, and safety of sofosbuvir/ledipasvir (SOF/LDV) and paritaprevir/ritonavir/ombratuvir/dasabuvir (PrOD) regimens in persons with CKD.

Methods. We identified all persons started on a SOF/LDV or PrOD regimen in ERCHIVES before 30 April 2016. We excluded those with missing HCV genotype, or eGFR values. We determined treatment completion, sustained virologic response (SVR) rates and proportion of persons with worsening renal function or developing grade 3/4 anemia.

Results. We identified 9,837 persons on SOF/LDV, 3,826 on SOF/LDV+RBV, 1,017 on PrOD and 2,944 on PrOD+RBV. Genotype 1a was the predominant genotype for SOF/LDV+RBV (77.3% no RBV, 70.0% with RBV) and PrOD+RBV (79.5%) groups, while only 4.3% of PrOD with no RBV group were genotype 1a. Among treated patients, the prevalence of patients with stage 4–5 CKD was 0.8% (SOF/LDV + RBV), 1.1% (SOF/LD/No RBV), 2.2% (PrOD + RBV) and 5.4% (PrOD no RBV). Among 13,663 total persons on SOF/LDV, 67.8% completed treatment while the treatment completion rate of those on PrOD was 74.0% (N = 2,932/3,961) (79.5%) groups, while only 4.3% of PrOD with no RBV group were genotype 1a. Among treated patients, the prevalence of patients with stage 4–5 CKD was 0.8% (SOF/LDV + RBV), 1.1% (SOF/LD/No RBV), 2.2% (PrOD + RBV) and 5.4% (PrOD no RBV). Among 13,663 total persons on SOF/LDV, 67.8% completed treatment while the treatment completion rate of those on PrOD was 74.0% (N = 2,932/3,961) (Table 1). The overall SVR rates of persons on SOF/LDV or PrOD regimens were 96.3%. A drop in treatment completion rates was seen in CKD stage 4–5 and those on PrOD+RBV; but the impact of RBV on SVR was unclear. While about one-third of the persons with a CKD stage 1–2 experienced a >10 mL/minute/1.73m2, about 15% decline among those with CKD stage 3. The incidence of grade 3/4 anemia by CKD stages increased significantly across the treatment groups. Grade 3/4 anemia ranged from 9.7% (SOF/LDV) to 21.8% (PrOD) among patients with CKD stage 1–2 (Table 2).

Conclusion. SVR rates among persons treated with SOF/LDV or PrOD were high in the CKD population despite 22% not completing the treatment regimen. Incidence of grade3/4 anemia increased significantly in CKD stage 4–5 across the treatment groups.

Table 1. Treatment Completion and sustained virologic response rates by regimen and stage of chronic kidney disease.

| CKD stages | SOF/LDV only | SOF/LDV + RBV | PrOD only | PrOD + RBV |
|------------|--------------|---------------|-----------|------------|
| Initiated, N | 3630 | 3631 | 848 | 2624 |
| Completed, N | 3653 | 3652 | 728 | 1664 |
| % completed | 64.5 | 74.1 | 88.5 | 70.8 |

Disclosures. All authors: No reported disclosures.
are also at risk for HIV and syphilis as well as neonatal abstinence syndrome (NAS). A substantial portion of HCV-exposed children are insured by Medicaid. The patterns of testing in this population are unknown. We sought to assess HCV-exposed children pattern of testing for HCV and other perinatal infections in children insured by KY Medicaid.

Methods. We identified HCV-exposed infants (ICD-10-CM code Z20.5) insured by KY Medicaid from 10/1/15 to 9/30/16. The primary outcome was HCV testing by PCR (CPT 87520 [HCV, direct probe]), 87521 (HCV, amplified probe), 87522 (HCV RNA, Quantitative) or antibody (CPTs 86603-4). Testing for HIV (CPTs 86870, 86872, 87397, 87398) and syphilis (CPT 86592) were also recorded. NAS was defined as presence of ICD-10-CM code P96.1 in any diagnosis field. Descriptive statistics were used.

Results. During the study period, 625 children with 4005 [median 3, Interquartile range (IQR) 1–8] claims were HCV-exposed. The majority of children were white (393, 69%), non-Hispanic (409, 67%) and male (318, 51%). Patterns of testing are shown in the Table.

Table: Medicaid claims for tests performed in children perinatally exposed to HCV

| Test          | Number of Children | Median Age (months) |
|---------------|--------------------|---------------------|
| HCV PCR       | 69 (11)            | 3 (2, 6)            |
| HCV antibody  | 11 (2)             | 6 (2, 8)            |
| HIV PCR       | 30 (5)             | 2 (2, 3)            |
| HIV antibody  | 8 (1)              | 2 (2, 3)            |
| Syphilis      | 26 (4)             | 2 (2, 3)            |

*A child may have been tested for more than one infection during the study period. Among HCV-exposed, 197 (32%) were diagnosed with NAS; but only 3 (1.5%) of these children were tested for perinatal infections whereas 84 (19.6%) of children with no documented NAS were tested (P < 0.001).

Conclusion. The proportion of HCV-exposed infants with a claim for HCV testing is low in the KY Medicaid population; testing for other perinatally-acquired infections is even less common. Children with NAS were less likely to be tested. Statewide guidelines for appropriate testing in children with perinatal HCV exposure and NAS are urgently needed.

Disclosures. C. Espinosa, Empra: Investigator, Research grant. The Medicines company: Investigator, Research grant. Astrazeneca: Investigator, Research grant. Merck: Employee, Salary. GlaxoSmithKline, Inc.: Investigator, Research grant. Multiple Industry Sponsors (Merck, sanofi pasteur, Novartis, GlaxoSmithKline, Pfizer, Gllead: Sub inves

522. Fibrosis Progression and Incidence of Cirrhosis and Hepatic Decompensation in Persons Treated With Paritaprevir/Ritonavir/Ombitasvir/ Dakusbavir: Results from ERCHEVES

Data are limited regarding the effect of paritaprevir/ritonavir, ombitasvir, dakusbavir regimen (PrOD) upon the rate of liver fibrosis progression and incidence of cirrhosis and hepatic decompensation after treatment for HCV.

**Methods.** Within ERCHEVES (Electronically Retrieved Cohort of HCV Infected Veterans), we identified HCV infected persons treated with PrOD and treatment-naive controls to determine the effect of PrOD treatment upon subsequent progression of fibrosis and incident cirrhosis and hepatic decompensation. Controls were propensity-score matched based on demographic and clinical characteristics. We excluded those with HIV coinfection, positive HBsAg, hepatocellular carcinoma at baseline and those with missing HCV RNA or FIB-4 scores. Fibrosis progression and liver cirrhosis were assessed using the FIB-4 score.

**Results.** The final propensity score matched sample included 1,473 PrOD-treated individuals, and an equal number of matched, untreated controls. PrOD-treated patients had significantly reduced median FIB-4 scores over time, compared with controls (median absolute change in FIB-4 = -0.7 [IQR -1.51, -0.3] vs. -0.06 [IQR -0.38, 0.49]; P = 0.0001). Compared with matched controls, PrOD-treated patients had an 86% relative reduction in the risk of incident cirrhosis over 2,241 patient-years of follow-up (adjusted HR 0.14 [95% CI 0.08-0.23]). Treatment with PrOD was also associated with delayed time to first hepatic decompensation event (P < 0.001). In sensitivity analysis, the exclusion of patients with baseline cirrhosis did not materially alter the estimates of effect.

**Conclusion.** Treatment with PrOD is associated with a significant reduction in fibrosis progression, a longer time to the development of cirrhosis, and reduced risk of