中文題目：慢性Ｂ型肝炎病患服用核苷(酸)類抗病毒藥物對骨質及腎功能之影響

英文題目：Effects on bone mineral density and renal toxicity in chronic hepatitis B patients with nucleot(s)ide antiviral agents

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Background:

Entecavir (ETV) and Tenofovir disoproxil fumarate (TDF) are preferred initial therapy for adults with treatment-naive chronic hepatitis B (CHB) and immune-active disease with excellent response and less resistant. Renal dysfunction and decrease in bone mineral density (BMD) have been reported in patients with HIV or CHB treated with long-term TDF. This study is to evaluate the renal and bone effects of TDF compared with ETV in chronic hepatitis B patients.

Methods:

This is a retrospective study at Kaohsiung Chung-Gung memorial hospital, Taiwan, from June 2013 to June 2017. Patients with CHB, persistence of hepatitis B surface antigen (HBsAg) seropositivity more than 6 months, were prescribed of TDF or ETV for 3 years or above. Patient demographics and clinical characteristics, including height, weight, underlying disease, status of liver fibrosis and hepatocellular carcinoma were obtained from the reviewed medical records. Baseline asparate aminotransaminase, alanine aminotransaminase, total bilirubin, albumin, parathyroid hormone, serum calcium, serum creatinine, serum phosphate, spot urine protein and creatinine were checked before the use of TDF or ETV. Renal function was assessed by serum creatinine, estimated glomerular filtration rate, renal threshold phosphate concentration (TmPO4/GFR), and urine protein to creatinine ratio (UPCR) at 12-week intervals. Dual energy x-ray absorptiometry (DEXA) scans of the spine and both femurs were performed by using a Hologic system at baseline, week 48, week 96, and week 144.

Descriptive analysis of all variables was performed. Change in bone density and renal function were compared between the two groups by using an independent sample t-test. Categorical variables were compared using the Chi-Square test. Predictive factors of bone density change were assessed by logistic regression in both univariate and multivariate mode.

Results:

A total of 317 patients diagnosed with chronic hepatitis B were included in this study as follows: TDF (n=157) and ETV (n=160) with baseline characteristics similar among groups. The prevalence of osteopenia or osteoporosis (T score <-1) was much higher in TDF group at 48 weeks at the hip neck (61.5% TDF vs 46.5% ETV, P = .026), the total hip (24.6% TDF vs 13.2% ETV, P = .031), and the lumbar spine (45.1% TDF vs 28.9% ETV, P = .011), and at 96 weeks at the total hip (32.1% TDF vs 17.7% ETV, P = .014), and the lumbar spine (47.3% TDF vs 32.7% ETV, P = .03). The TDF group showed significant mean percentage decrease from baseline in BMD at 48 weeks at the hip neck (−3.56% TDF vs −0.99% ETV, P < .001) and the lumbar spine (−2.32% TDF vs 0.17% ETV, P < .001), at 96 weeks at the hip neck (−4.47% TDF vs −1.02% ETV, P < .001), the total hip (−3.79% TDF vs 0.62% ETV, P < .001), and the lumbar spine (−1.96% TDF vs 0.05% ETV, P = .003), and at 144 weeks at the hip neck (−3.63% TDF vs −0.84% ETV, P = .003), the total hip (−3.05% TDF vs 1.36% ETV, P = .005), and the lumbar spine (−2.1% TDF vs 0.75% ETV, P = .004). In multivariate analysis, predictive factor of bone density loss at 144 weeks was the use of TDF. The mean percentage decline of eGFR was significant in TDF group at every follow-up time point. TmPO4/GFR, and UPCR were similar among both treatment groups.

Conclusions: This study suggested CHB patients treated with TDF may experience decreased bone density loss and increased risks of renal deficits compared to those treated with ETV.