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Clinical significance of hypophosphatemia during antiviral therapy for chronic hepatitis B

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Background/Aims: Antiviral therapy is essential for patients with chronic hepatitis B (CHB) for preventing progression of hepatitis and related complications. Although antiviral agents have been reported to cause hypophosphatemia, the actual incidence and clinical significance remain unclear. We investigated the incidence and clinical impact of hypophosphatemia in a large cohort of CHB patients. **Methods:** This retrospective cohort study included CHB patients who started antiviral therapy between 2005 and 2015, and were followed up for at least 1 year. Antiviral agents included lamivudine (16.3%), entecavir (44.5%), adefovir (8.7%), tenofovir (15.6%), lamivudine + adefovir (13.5%), and others (1.4%). A total of 4,335 patients were analyzed after excluding patients with liver cirrhosis, diabetes mellitus, or hypertension. Hypophosphatemia was defined as a serum phosphorus level ≤ 2.5 mg/dL. The primary outcome was changes in renal function. Secondary outcomes were the incidences of infection and changes in serum potassium. **Results:** Hypophosphatemia occurred in 1.7% of patients. (75/4,335). Although significant deterioration of renal function was observed in all patients (control group: -3.91 mL/min/1.73m² at 12 months & -6.89 mL/min/1.73m² at 24 months vs. hypophosphatemia group: -2.96 mL/min/1.73m² at 12 months, & -7.60 mL/min/1.73m² at 24 months), there were no differences between groups. (12 month; $p=0.526$, 24 months; $p=0.968$). The incidence of infection were also comparable between groups: 64.7% (2756/4260) in the control group vs. 62.7% (47/75) in the hypophosphatemia group ($p=0.716$). There were no significant differences in serial changes of serum potassium. **Conclusions:** The incidence of hypophosphatemia during antiviral therapy was low in our large cohort of CHB patients. Our results suggest that hypophosphatemia itself was not a surrogate marker of adverse renal or overall outcomes.

