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Brief Communication

Rationality and designing immune therapy against chronic hepatitis B virus infection

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Hepatitis B virus (HBV)-induced chronic hepatitis B (CHB) and subsequent complications (liver cirrhosis and hepatocellular carcinoma) represent major threats to human health worldwide. About 370 million people are chronically infected with the HBV worldwide. Several antiviral drugs are now used in patients with CHB, however, a well-designed study for a National Institutes of Health (NIH, USA) consensus development conference that analyzed all randomized clinical trials with antiviral drugs in CHB patients from 1989 to 2008 have shown that no single drug treatment improved ultimate clinical outcomes or all intermediate outcomes of CHB, although improvements of some intermediate outcomes have been seen. However, adverse events during antiviral treatment occurred in about 50% patients. In addition, patients taking antiviral drugs should be periodically checked for viral, biochemical and immunological aspects of the HBV before, during and after cessation of therapy. However, the health care delivery system of developing country is unable to accomplish these. In this situation, mutant HBV may spread in community that may cause a devastating outcome.

The concept of immune therapy originated due to better understandings of pathogenesis of CHB and inefficacy of commercially-available antiviral drugs. Host immunity plays a pivotal role during induction, maintenance, and progression of liver damages in these patients. Again, the replication of the HBV can be minimized by host immune response. Thus, proper manipulation of host immunity may have therapeutic implications. Now, controversy remains about the design immune therapy in CHB patients. Studies have revealed that non antigen-specific immune modulators (gamma-interferon, interleukins, and growth factors) that upregulate or down regulate host immunity do not seem to be able stand the test of time as a better therapeutic endeavor in CHB patients (2).

A new mode of immune therapeutic strategy surfaced in early 1990s in which hepatitis B vaccine containing HBsAg were used as a therapeutic vaccine for containment of HBV and reduction of liver damages by inducing HBV-specific immune responses in CHB patients. To optimize the therapeutic regimen, vaccine therapy was applied in murine model of HBV carrier state, HBV transgenic mice (HBV

TM) (3) and in patients with CHB (4). Vaccine therapy with HBsAg was safe, but randomized-controlled trials failed to show its off-treatment efficacy (5). The safety and partial efficacy of this immune therapy has been assessed as pilot study in Bangladesh in adult (6) and pediatric patients with CHB (7). Cell-based vaccines have been applied in CHB patients (8), but, the inherent limitations of HBsAg-based vaccine therapy could not be overcome. In the mean time, it became evident that vaccine therapy containing only HBsAg may not be an appropriate approach to contain HBV replication and minimize liver damages in CHB patients because both HBsAg and HBcAg-specific immune responses are essential for these purposes. This has unfolded a new regimen of immune therapy for CHB patients. Safety and efficacy of a vaccine that contains both HBsAg and HBcAg has been assessed in HBV TM for moving forward to bring the information of the benches to bedsides of CHB patients. A phase-1 study has also been accomplished with HBsAg/HBcAg vaccine in CHB patients in Bangladesh. the first use of combined HBsAg/HBcAg vaccine in CHB patients worldwide (9). Also, application of vaccine has been made through mucosal route (nasal) in this trial. The scope and limitation of immune therapy as an evidence-based and innovative immune therapeutic approach in CHB patients would be discussed.

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Brief Communication

Fibroscan: Non-invasive liver diagnostic device for detection of liver fibrosis

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Transient elastography (Fibroscan®; Echosens, Paris, France) is a rapid, non-invasive and reproducible method of measuring liver stiffness[1]. A higher liver stiffness reflects more severe liver fibrosis. Recent meta-analyses have suggested liver stiffness measurement to be a reliable tool to detect advanced liver fibrosis and early liver cirrhosis[2, 3]. Most of the studies in the meta-analyses included patients with chronic hepatitis C from Western countries. More data from Asian populations were recently published. In a histologic series of 133 Chinese patients, among whom 50% have chronic hepatitis B, liver stiffness measurement correlated well with portal-portal bridging fibrosis on both