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SAFETY AND EFFICACY OF LONG-TERM TREATMENT WITH NUCLEOS(T)IDE ANALOGUES IN CHRONIC HEPATITIS B

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Abstract. Chronic hepatitis B (CHB) remains a major global public health problem, leading to progressive liver disease, cirrhosis, and hepatocellular carcinoma. Long-term antiviral therapy with nucleos(t)ide analogues (NAs) is the cornerstone of CHB management, aiming to suppress hepatitis B virus (HBV) replication, prevent disease progression, and reduce liver-related complications. Despite proven antiviral efficacy, prolonged NA therapy raises concerns regarding drug resistance, safety, renal and bone toxicity, and long-term patient adherence.

This study was conducted at the Khorezm Regional Multidisciplinary Medical Center and aimed to evaluate the safety and efficacy of long-term treatment with nucleos(t)ide analogues in patients with chronic hepatitis B. Patients were assessed based on virological, biochemical, and clinical parameters during extended antiviral therapy. The results demonstrate that long-term NA treatment effectively suppresses HBV replication, improves liver function, and is generally well tolerated, confirming the importance of continuous antiviral therapy in the management of chronic hepatitis B.

Key words: chronic hepatitis B, nucleos(t)ide analogues, antiviral therapy, safety, efficacy, HBV DNA

Introduction. Chronic hepatitis B is a viral liver disease caused by persistent infection with the hepatitis B virus and affects more than 250 million people worldwide. It is a leading cause of liver cirrhosis, hepatic decompensation, and hepatocellular carcinoma, accounting for significant morbidity and mortality, particularly in endemic regions [1,2].

The natural course of CHB is dynamic and influenced by viral replication activity, host immune response, and environmental factors. Persistent viral replication plays a central role in liver inflammation and fibrosis progression, making long-term suppression of HBV DNA a key therapeutic goal [3].

Nucleos(t)ide analogues, including entecavir and tenofovir, are first-line agents recommended by international clinical guidelines due to their potent antiviral activity and high genetic barrier to resistance [4,5]. These agents inhibit HBV reverse transcriptase, effectively suppressing viral replication and reducing necroinflammatory activity in the liver. Long-term NA therapy has been shown to decrease the risk of cirrhosis, liver failure, and hepatocellular carcinoma [6].

However, chronic hepatitis B often requires prolonged or lifelong antiviral treatment, especially in HBeAg-negative patients. Therefore, assessment of long-term safety and efficacy is of critical importance. Potential adverse effects, particularly renal dysfunction and bone mineral density loss associated with certain NAs, as well as issues of treatment adherence, remain important clinical considerations [7,8].

This study aims to evaluate the long-term outcomes of NA therapy in a regional clinical setting, focusing on both therapeutic efficacy and safety.

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Aim of the study. The aim of this study was to assess the safety and efficacy of long-term treatment with nucleos(t)ide analogues in patients with chronic hepatitis B.

Materials and methods. A prospective observational study was conducted between 2024 and 2025 at the Khorezm Regional Multidisciplinary Medical Center. A total of 78 patients aged 20–60 years with confirmed chronic hepatitis B were enrolled.

The diagnosis of CHB was established based on the persistence of hepatitis B surface antigen (HBsAg) for more than 6 months, elevated or fluctuating alanine aminotransferase (ALT) levels, and detectable serum HBV DNA. Patients were divided into two groups.

The first group consisted of 50 patients receiving long-term antiviral therapy with nucleos(t)ide analogues (entecavir or tenofovir) for at least 24 months. The second group included 28 patients with CHB under regular observation who had not yet initiated antiviral therapy and served as a comparison group.

Inclusion criteria were confirmed CHB diagnosis, age over 18 years, and informed consent. Exclusion criteria included co-infection with hepatitis C, hepatitis D, or HIV, decompensated liver cirrhosis, hepatocellular carcinoma, severe renal disease, pregnancy, and previous liver transplantation.

All patients underwent clinical examination, biochemical blood tests (ALT, AST, bilirubin), virological assessment (HBV DNA levels by PCR), and evaluation of renal function. Treatment efficacy was assessed by virological suppression (undetectable HBV DNA), normalization of ALT levels, and clinical improvement. Safety was evaluated based on adverse events, renal function parameters, and patient tolerance during long-term therapy.

Results. At baseline, patients with chronic hepatitis B demonstrated elevated ALT levels and detectable HBV DNA, indicating active viral replication. After long-term treatment with nucleos(t)ide analogues, a significant reduction in HBV DNA levels was observed in the treated group, with the majority of patients achieving undetectable viral load after 24 months of therapy ($p < 0.01$).

Biochemical response was characterized by normalization of ALT levels in most patients receiving NA therapy, reflecting reduced hepatic inflammation. In contrast, patients in the untreated group showed persistent viral replication and fluctuating liver enzyme levels.

Long-term NA therapy was generally well tolerated. No severe adverse events leading to treatment discontinuation were observed. Mild renal function changes were noted in a small proportion of patients receiving tenofovir, but these changes were clinically insignificant and reversible with monitoring and dose adjustment. Overall, patient adherence to therapy was high, and treatment continuity was maintained throughout the observation period.

Discussion. The results of this study confirm the high efficacy of nucleos(t)ide analogues in suppressing HBV replication and improving biochemical markers in patients with chronic hepatitis B. Sustained viral suppression is essential for preventing disease progression and reducing the risk of cirrhosis and hepatocellular carcinoma.

Long-term safety analysis demonstrated that NA therapy is well tolerated when patients are appropriately monitored. The low incidence of adverse effects supports the use of entecavir and tenofovir as first-line agents in long-term CHB management. Regular assessment of renal function and individualized treatment strategies are important to ensure optimal safety outcomes.

Early initiation of antiviral therapy and long-term follow-up in regional multidisciplinary medical centers allow effective disease control and improve long-term prognosis in patients with chronic hepatitis B.

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Conclusions. Long-term treatment with nucleos(t)ide analogues in chronic hepatitis B is highly effective in achieving sustained viral suppression and biochemical remission. Antiviral therapy is generally safe and well tolerated, with minimal adverse effects under regular monitoring. Continuous NA therapy remains a cornerstone of chronic hepatitis B management and plays a crucial role in preventing disease progression and improving patient outcomes.

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