Case Report

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Efficacy of Entecavir Treatment in a 8-Year-Old Child with Chronic Hepatitis B

Kronik Hepatit B'li Sekiz Yaşında Çocuk Hastada Entekavir Tedavisinin Etkinliği

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ABSTRACT

Although the incidence of hepatitis B virus (HBV) infection has decreased significantly in Turkey since the introduction of universal immunization programs and blood donor screening, few children are still infected vertically with HBV. In Turkey, entecavir is approved for use for treating chronic hepatitis B (CHB) in children aged 16 years and older. The American Association for the Study of Liver Diseases 2018 Hepatitis B Guidance reported that entecavir can be used for treating CHB in a weight-based dosing in children aged 2 years and older. Eight-year-old children with CHB unresponsive to lamivudine (LAM) treated successfully with entecavir without significant adverse effect. In children younger than 16 years, use of entecavir may be considered for treating CHB if there is no adequate response to LAM.

Keywords: Chronic hepatitis B, hepatitis B virus, entecavir, child

ÖZ

Evrensel bağışıklama programları ve kan bağışçısı taramasının başlamasından bu yana Türkiye'de hepatit B virüsü (HBV) enfeksiyonu insidansı önemli ölçüde azalmasına rağmen, az sayıda çocuk hala vertikal olarak HBV ile enfekte olmaktadır. Türkiye'de entekavir, 16 yaş ve üzeri çocuklarda kronik hepatit B (KHB) tedavisinde kullanım için onaylıdır. Amerikan Karaciğer Hastalıkları Araştırmaları Derneği 2018 Hepatit B Rehberi, entekavirin 2 yaş ve üzeri çocuklarda vücut ağırlığına göre KHB tedavisinde kullanılabileceğini bildirmiştir. Lamivudine (LAM) yeterli yanıt alınamayan, sekiz yaşında KHB'li bir çocuk hastada entekavir ile tedavi başarılı sonuçlandı ve belirgin bir yan etki gözlenmedi. On altı yaşından küçük çocuklarda da, LAM yeterli yanıt yoksa, KHB tedavisinde entekavir kullanımı düşünülebilir.

Anahtar Kelimeler: Kronik hepatit B, hepatit B virüsü, entekavir, çocuk

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Introduction

It is known that more than 360 million people (6% of the world's population) are chronically infected with hepatitis B virus (HBV) worldwide. The incidence of HBV infection has decreased dramatically since the introduction of universal immunization programs and blood donor screening in various countries. However, a significant number of children are still infected with HBV each year, chronic HBV infection often develops and appropriate follow-up is required (1). Although chronic HBV infection mostly follows a benign course during childhood and adolescence, complications such as cirrhosis and hepatocellular carcinoma (HCC) can sometimes develop before adulthood. In the literature, the rates of development of cirrhosis and HCC before adulthood in children with chronic HBV infection have been reported as 3-5% and 0.01-0.03% (2,3).

There are five drugs approved by the US Food and Drug Administration for the treatment of children with chronic hepatitis B (CHB): Interferon-alfa, lamivudine (LAM), adefovir, entecavir (ETV), and tenofovir (4).

In this case report, we aimed to present a 8-year-old pediatric patient whose treatment was successful after starting ETV for his CHB treatment.

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Case Report

A 4.5-year-old boy was admitted to the pediatric gastroenterology outpatient clinic with hepatitis B surface antigen (HBsAg) positive (quantitative HBsAg 468.9 IU/mL), very high hepatitis B virus (HBV)-DNA level (>10^7 IU/mL), and persistently normal alanine aminotransferase (ALT) levels [upper limit of normal (ULN) approximately 40 IU/L]. According to the The European Association for the Study of the Liver 2017 guideline, the patient was diagnosed with hepatitis B e antigen (HBeAg)-positive chronic HBV infection (previously termed "immune tolerant" phase) (5). From his previous history, we learned that her mother had HBeAg positive chronic HBV infection and was given both the vaccine and hepatitis B immunoglobulin (HBIG) within 12-24 hours after birth.

At the age of 6.5-year-old, serum ALT levels began to exceed 2 times the ULN. All other possible causes of elevated serum ALT levels were investigated and excluded. We decided that he passed into HBeAg-positive CHB phase because of the presence of serum HBeAg positive, high HBV-DNA levels and high ALT. Since most patients may enter the HBeAg-negative infection phase by representing spontaneous HBeAg seroconversion and HBV-DNA suppression, we followed his for 6 months without liver biopsy, with monitoring serum HBeAg, ALT, and HBV-DNA levels for every months. However serum HBeAg positivity, high HBV-DNA levels and high ALT persisted for 6 months, then liver biopsy performed. In the histology activity index examination performed according to the Ishak grading and staging system, moderate liver necroinflammation (grade: 8) and fibrosis (stage: 2) were detected. When he was 8-year-old, LAM (3 mg/kg/day) was started for the treatment of CHB. Although serum ALT levels returned to normal limits (biochemical response), it was considered appropriate to switch to another oral antiviral agent from LAM, since the HBV-DNA level was measured as 154,000 IU/mL at the 24th week of antiviral treatment. Because of there was no other approved antiviral drug in this age group, switching to another drug was not considered at that time. At the 13th month of LAM treatment, serum HBV-DNA level was found to be 3120 IU/mL. However, at that time, the American Association for the study of liver diseases (AASLD) 2018 Hepatitis B Guidance was published. Since it was reported that ETV can be used in children aged 2 years and older in the AASLD 2018 Hepatitis B Guidance, it was planned to switch from LAM to ETV for the treatment of CHB. Written consent from his parent and approval from the Republic of Turkey Ministry of Health Turkish Medicines and Medical Devices Institution (REİYS-2019-02-171344) were obtained before ETV was started for the treatment of CHB. When he was 8-year-old, ETV was started at 0.5 mg/day on a weight basis as recommended in the AASLD 2018 Hepatitis B Guidance. The serum HBV-DNA level was still detectable despite a decrease of >1 $\log_{10}$ IU/mL 12 months after the start of ETV therapy (partial virological response). Approximately 2 years after initiation of ETV therapy, loss of HBeAg and anti-HBe seroconversion (serological response) occurred with undetectable serum HBV-DNA. No adverse reaction related to ETV was observed in our patient since the beginning of the treatment. If the patient's HBeAg seroconversion and serum undetectable HBV-DNA remain stable, we will plan to discontinue ETV therapy after at least 12 months of consolidation therapy is completed.

Discussion

When both vaccine and HBIG are administered to newborns of HBeAg positive mothers within 12-24 hours after birth, 90% protection can be achieved. In newborns of HBeAg negative mothers, the protection rate rises up to 98% (6,7,8). In her previous history, our patient's mother had HBeAg positive chronic HBV infection and there was transmission despite properly vaccination and HBIG administration.

In Turkey, treatment with 3 oral antiviral drugs has been approved when starting treatment for children aged 2-18 years with CHB: LAM, ETV and tenofovir. LAM is used from 2 years of age as recommended in the guideline published by the AASLD in 2018. Tenofovir can be used in children aged 12 years and older, as recommended in the 2013 guideline published by The European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) (4) and the AASLD 2018 Hepatitis B Guidance (9). ETV is used for the treatment of CHB in children aged 16 years and older, as recommended in the ESPGHAN guideline published in 2013 (4). According to the Turkish Health Practice Communiqué, if the HBV-DNA level is above 50 IU/mL at week 24, it is possible to switch to another oral antiviral agent. In the AASLD 2018 Hepatitis B Guidance, it was reported that ETV can be used from the age of 2 years (9). While our patient was at the 24th week of LAM treatment, his HBV-DNA level was found to be 154.000 IU/mL, therefore it was deemed appropriate to switch to ETV.

To the best of our knowledge, this is the first report in Turkey on the use of ETV in a 8-year-old child.

We think that ETV can be used as an alternative antiviral agent to LAM in children with CHB in Turkey, even if they are younger than 16 years of age.

Ethics

Informed Consent: It was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.H.E., M.E., Design: H.H.E., M.E., Data Collection or Processing: H.H.E., M.E., Analysis or Interpretation: H.H.E., M.E., Literature Search: H.H.E., Writing: H.H.E.

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