EFFICACY AND SAFETY OF DIRECT-ACTING ANTIVIRAL AGENTS IN CHILDREN WITH CHRONIC HEPATITIS C AND ONCOHEMATOLOGICAL DISEASES

Matyakubova Feruza Egamovna

Assistant, Department of Infectious Diseases, Faculty of Postgraduate Education, Samarkand State Medical University, Samarkand, Uzbekistan.

Abstract. Background. Chronic hepatitis C virus (HCV) infection in children with oncohematological diseases represents a significant clinical challenge. Immunosuppressive therapy and prolonged chemotherapy may contribute to increased viral replication, hepatic complications, and interruptions in antineoplastic treatment. The introduction of direct-acting antiviral agents (DAAs) has substantially improved the possibilities of HCV eradication in this vulnerable population. Current evidence demonstrates that DAAs provide high rates of sustained virological response (SVR12) and a favorable safety profile in children aged three years and older. Particularly relevant evidence comes from a prospective pharmacokinetic study involving children with acute lymphoblastic leukemia (ALL), in which all participants achieved SVR12 following ledipasvir/sofosbuvir treatment.

Keywords: chronic hepatitis C, children, oncohematological diseases, direct-acting antivirals, sofosbuvir, ledipasvir, acute lymphoblastic leukemia, sustained virological response, chemotherapy.

Introduction. Chronic hepatitis C virus (HCV) infection remains an important public health problem, particularly among children with underlying diseases requiring prolonged immunosuppressive treatment. The coexistence of HCV infection and oncohematological disorders, including acute lymphoblastic

leukemia, acute myeloid leukemia, and lymphomas, creates a complex clinical situation requiring coordinated management by infectious disease specialists, hepatologists, and pediatric oncologists. In this population, HCV infection may be associated with persistent hepatic inflammation, increased aminotransferase activity, and progressive liver injury. Immunosuppressive treatment and intensive chemotherapy may further complicate the clinical course of viral hepatitis. HCV-associated hepatitis flares can necessitate modification or temporary interruption of chemotherapy, potentially affecting the effectiveness of cancer treatment [1,2].

The development of direct-acting antiviral agents has fundamentally changed the management of chronic HCV infection. Unlike interferon-based regimens, DAAs directly inhibit specific stages of viral replication, allowing shorter treatment courses, higher cure rates, and substantially improved tolerability [3].

Current approaches to antiviral treatment in children. According to current AASLD/IDSA recommendations, antiviral treatment is indicated for all children and adolescents with chronic HCV infection aged three years and older, irrespective of disease severity [1].

The principal pangenotypic DAA regimens include:

- Sofosbuvir/velpatasvir (SOF/VEL): a combination targeting the HCV NS5B polymerase and NS5A protein, generally administered for 12 weeks.

- Glecaprevir/pibrentasvir (GLE/PIB): a combination of NS3/4A protease and NS5A inhibitors, generally administered for 8 weeks in eligible treatment-naive patients without cirrhosis or with compensated cirrhosis.

- Ledipasvir/sofosbuvir (LDV/SOF): an effective combination for genotypes 1, 4, 5, and 6, generally administered for 12 weeks [1].

Dosing in pediatric patients is determined by age, body weight, treatment history, genotype where relevant, and liver disease stage. The selection of an appropriate

regimen in children receiving chemotherapy requires additional consideration of concomitant medications and potential pharmacokinetic interactions.

Efficacy of DAAs in children with oncohematological diseases

Evidence from pediatric clinical trials and systematic reviews demonstrates consistently high antiviral efficacy. Indolfi et al. Reported that DAAs were associated with excellent virological outcomes and a favorable safety profile in children and adolescents with chronic HCV infection [3].

Particularly important findings were reported by AbdelMagid et al. In a prospective pharmacokinetic study published in 2024. The investigation included 22 children aged 6 to under 12 years with genotype 4 chronic HCV infection. Ten patients had acute lymphoblastic leukemia and were receiving maintenance chemotherapy, while 12 children without malignancies constituted the comparison group.

All participants received weight-based ledipasvir/sofosbuvir treatment for 12 weeks. Remarkably, all 22 children achieved sustained virological response, with no adverse events requiring treatment interruption or permanent discontinuation. Pharmacokinetic analysis demonstrated comparable drug exposure in children with ALL and those without malignancies [4].

Safety and potential drug–drug interactions

The safety of DAA therapy in children with oncohematological diseases requires particular attention because chemotherapy and antiviral treatment may produce overlapping adverse effects.

The principal clinical considerations include:

1. Hepatotoxicity. Changes in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and bilirubin levels may occur during cancer

treatment. Distinguishing chemotherapy-related hepatic toxicity from HCV-associated inflammation is essential.

2. Hematological toxicity. Anemia, neutropenia, and thrombocytopenia are common complications of chemotherapy. Although modern DAAs generally have a favorable hematological safety profile, complete blood count monitoring remains important.
3. Drug–drug interactions. Some antiviral agents influence drug transporters and metabolic pathways involved in the elimination of antineoplastic medications. Protease inhibitor-containing regimens may require particular caution when combined with drugs metabolized through CYP3A4 pathways, including certain vinca alkaloids and tyrosine kinase inhibitors [2,5].
4. Renal function. Renal function should be assessed before and during treatment when clinically indicated, particularly in children receiving nephrotoxic chemotherapy or supportive medications.

Economides et al. Investigated concomitant administration of DAAs and chemotherapy in 21 adult cancer patients with HCV infection. SVR was achieved in 20 patients (95%). The study demonstrated that concurrent antiviral and antineoplastic treatment may be feasible when potential drug interactions are carefully evaluated [5]. Although these findings are derived from an adult population, they provide useful supporting evidence for multidisciplinary treatment strategies.

Before initiating antiviral therapy, the following investigations are recommended:

- Quantitative HCV RNA determination and HCV genotype assessment when required for regimen selection.

- Evaluation of ALT, AST, total bilirubin, albumin, and coagulation parameters.

- Assessment of renal function and complete blood count.

- Evaluation of hepatic fibrosis and exclusion of decompensated liver disease.

- Comprehensive review of chemotherapy and supportive medications for potential drug interactions.

During treatment, clinical condition, liver biochemical parameters, and relevant hematological and renal indicators should be monitored according to the patient's oncological status. Quantitative HCV RNA testing 12 weeks after completion of therapy is recommended to confirm SVR12.

The timing of antiviral treatment should be discussed individually. Treatment may be initiated before, during, or after chemotherapy, depending on oncological urgency, expected drug interactions, and the patient's clinical condition. Antiviral therapy should not unnecessarily delay essential cancer treatment [1,2,6].

The updated recommendations of the 9th European Conference on Infections in Leukaemia (ECIL-9) also emphasize the importance of systematic viral hepatitis screening and individualized management in patients with hematological malignancies and hematopoietic cell transplantation [6,7].

Conclusion. Direct-acting antiviral agents have significantly improved the treatment prospects for children with chronic hepatitis C and concomitant oncohematological diseases. A multidisciplinary approach involving pediatric infectious disease specialists, hematologists, oncologists, and clinical pharmacologists is essential to optimize antiviral treatment while maintaining the continuity and effectiveness of cancer therapy.

hattacharya D, Aronsohn A, Price J, Lo Re V. Hepatitis C Guidance 2023 Update: AASLD-IDSA Recommendations for Testing, Managing, and T

pera AM. Safety of direct acting antiviral treatment for hepatitis C in

o

a

t

o

ndolfi G, Giometto S, Serranti D, Bettiol A, Bigagli E, De Masi S, et al. Systematic review with meta-analysis: the efficacy and safety of direct-a

bdelMagid AM, Abbassi MM, Ebeid FS, Farid SF, El-Sayed MH. Ledipasvir/sofosbuvir in hepatitis C virus-infected children with h

nonomides MP, Mahale P, Kyvernitakis A, Turturro F, Kantarjian H, Naing A, et al. Concomitant use of direct-acting antivirals and chemotherapy in h

ikulska M, van Bömmel F, Mouliade C, Indolfi G, Kefalakes H, von Lilienfeld-Toal M, et al. Updated recommendations for the management of hepatitis B, C, and E virus infections in patients with haematological malignancies and those undergoing haematopoietic cell transplantation: recommendations from the 9th European Conference on Infections in L

atyakubova F. E. CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF HEPATITIS C IN CHILDREN WITH HEMATOLOGICAL MALIGNANCIES: A REVIEW // Экономика и социум. 2026. №6-3 (дата обращения: 09.11.2026).