Pediatr Pol 2024; 99 (3): 266-269
DOI: https://doi.org/10.5114/polp.2024.143135
Submitted: 28.03.2024, Accepted: 14.05.2024, Published: 20.09.2024

PEDIATRIA Polska
Polish Journal of PAEDIATRICS

CASE REPORT

Eight-week treatment with sofosbuvir/velpatasvir may be effective in curing hepatitis C in children

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ABSTRACT

Sofosbuvir/velpatasvir (SOF/VEL) is a safe and effective regimen used for the treatment of chronic hepatitis C. The standard treatment duration is 12 weeks. There are no data available to support the shortened treatment. We aimed to present a case of an 11-year-old boy treated with a generic SOF/VEL for 8 weeks. The patient was admitted to our department 12 weeks after the end of treatment to establish the efficacy of the therapy (sustained virological response, SVR12). Laboratory testing revealed aminotransferases and bilirubin levels within the normal ranges, there were no abnormalities in the abdomen ultrasound, and transient elastography did not reveal any liver fibrosis. Hepatitis C virus (HCV) RNA tested with reverse-transcription polymerase chain reaction method was undetectable. The patient achieved SVR12. We conclude that shortening treatment with SOF/VEL to 8 weeks may be effective for HCV elimination in children. The possibility of treatment shortening should be confirmed in further studies on larger groups of paediatric patients.

KEY WORDS:

children, hepatitis C, sofosbuvir/velpatasvir.

INTRODUCTION

Hepatitis C virus (HCV) infection is considered as a major public health threat. Approximately 3.25 million children (aged 0–18 years) live with active hepatitis C worldwide [1]. It is estimated that 25-40% of children with vertical HCV infection spontaneously clear the virus during the first 4-7 years of life, whereas others develop chronic infection, which usually has a milder course compared to that seen in adults [2]. According to recent data, cirrhosis may occur in a third of patients infected during childhood, after a median of 33 years, irrespective of the route of the infection [3]. A study in adolescents (12–17 years old) with chronic hepatitis C showed that more than 10% of them presented with significant liver fibrosis [4].

The World Health Organisation (WHO) has an ambitious plan to eliminate hepatitis C by 2030. Novel therapies based on direct-acting antivirals (DAAs) have revolutionised the treatment of HCV infection in both adults and children. They are now recommended by the WHO and European Society for Paediatric Gastroenterology, Hepatology, and Nutrition for the treatment of chronic hepatitis C in adolescents and children aged 3 years and older [5, 6]. According to the recent systematic review and meta-analysis on the DAAs in children and adolescents, their efficacy, defined as sustained virological response 12 weeks after the end of treatment (SVR12), was 100% (95% CI: 96–100), and the therapy was well tolerated and safe [7]. There are currently 3 pangenotypic regimens (glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, and sofosbuvir/velpatasvir/voxilaprevir) and 3 regimens with genotype-specific activity (sofosbuvir/ledipasvir, grazoprevir/elbasvir, and sofosbuvir plus ribavirin, which is no longer recommended) approved by the European Medi-

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TABLE 1. Direct-acting antivirals approved by the European Medicines Agency and the United States Food and Drug Administration for treatment of chronic hepatitis C in children

Drug	Available formulations	HCV genotype	Approval (age)
Glecaprevir/pibrentasvir	Tablets 100/40 mg Oral pellets 50/20 mg (in sachet)	Pangenotypic	≥ 3 years (EMA and FDA)
Sofosbuvir/velpatasvir	Tablets 400/100 mg Tablets 200/50 mg Oral pellets 200/50 mg (in sachet) Oral pellets 150/37.5 mg (in sachet)	Pangenotypic	≥ 3 years (EMA and FDA)
Sofosbuvir/velpatasvir/voxilaprevir	Tablets 400/100/100 mg	Pangenotypic	≥ 12 years (EMA)
Sofosbuvir/ledipasvir	Tablets 400/90 mg Tablets 200/45 mg Oral pellets 200/45 mg Oral pellets 150/33.75 mg	1, 4–6	≥ 3 years (EMA and FDA)
Elbasvir/grazoprevir	Tablets 50/100 mg	1, 4	≥ 12 years (EMA and FDA)

EMA – European Medicines Agency, FDA – Food and Drug Administration

cines Agency and the United States Food and Drug Administration with age-specific limitations [6, 7] (Table 1).

Due to the lower burden of infection, the high cost of DAA therapy, and only recently approved DAAs for children, national policies on hepatitis C management (systematic testing and treatment) are lacking in many countries [2, 8]. Thus, only a small proportion of children with HCV infection were diagnosed and treated, in particular in low- and middle-income countries [2]. As a result, several gaps in our knowledge concerning the effects of DAA treatment in children still exist.

Recently we reported excellent efficacy and a good safety profile of standard 12-week, fixed-dose sofosbuvir/velpatasvir (SOF/VEL) treatment used in children aged 6–18 years with chronic hepatitis C [9]. We suggested that shortening the treatment duration from 12 to 8 weeks might be also effective, as most treated children presented with undetectable HCV RNA even at 4 weeks of therapy. This would be advantageous, mainly due to the economic reasons. However, there are no data available to support the shortening of the treatment with SOF/VEL in children. Thus, the aim of this report was to present a case report of a child successfully treated with a generic SOF/VEL for 8 weeks.

CASE REPORT

An 11-year-old boy, Ukrainian war refugee, was treated with a generic SOF/VEL for 8 weeks (fixed dose of 400/100 mg, Velpanat, Natco Pharma Limited, India, under license from Gilead Sciences Ireland). The patient started treatment against hepatitis C in Ukraine in February 2022, shortly before the Russian invasion. He was evacuated to Poland together with the orphanage where he had lived, without any medical documentation, with one package of SOF/VEL tablets for the second month of his therapy. The third medicine pack was left in Ukraine and timely shipment was impossible. Children in Poland are not included in the national therapeutic program for hepatitis C, so we were not able to organise the supply of the remaining 28 tablets. Thus, the treatment was ended after 8 weeks. The patient was admitted to our department 12 weeks after the end of treatment to establish the efficacy of the therapy (defined as SVR12). At admission, he was in a general good condition, weighting 33 kg, without any significant abnormalities in physical examination. Laboratory testing revealed normal levels of aminotransferases (alanine aminotransferase was 16 IU/l, and aspartate aminotransferase 31 IU/l) and bilirubin 6.5 μmol/l. The abdomen ultrasound was normal, and transient elastography (FibroScan 530, Echosense, France) did not reveal any liver fibrosis (median of the liver stiffness measurement was 4.1 kPa corresponding to F0/1 in Metavir scale) or steatosis (CAP 196 dB/m). Hepatitis C virus RNA tested with reverse-transcription polymerase chain reaction method was undetectable, which confirmed that the boy had achieved SVR12 and eliminated the HCV despite the shortened 8-week duration of the therapy.

DISCUSSION

Treatment with SOF/VEL is safe and effective for HCV eradication [9, 10]. The duration of DAA therapy depends on the chosen drug, HCV genotype, cirrhosis status, and previous treatment experience (Table 2). Shortening the treatment with SOF/VEL from 12 to 8 weeks would be beneficial mainly for economic reasons. An alternative pangenotypic therapy (glecaprevir/pibrentasvir) lasts 8 weeks in most cases, and it is of similarly high efficacy [11]. Our case report shows that in children with chronic HCV infection, this shortened SOF/VEL treatment duration may be enough to achieve SVR12 and viral eradication.

So far, 12 weeks is the recommended treatment duration for SOF/VEL in both treatment-naïve and treatment-experienced patients without cirrhosis and with compensated cirrhosis (Child-Pugh A). Treatment for

TABLE 2. Duration of treatment with direct-acting antivirals in children according to the chosen drug, hepatitis C virus genotype, status of cirrhosis, and previous antiviral treatment

Drug	HCV genotype	Cirrhosis	Previous antiviral treatment	Treatment duration (weeks)
Glecaprevir/pibrentasvir	All	No/compensated	No	8
	1, 2, 4–6	No	Yes	8
		Compensated		12
	3	No/compensated		16
Sofosbuvir/velpatasvir	All	No/yes	No/yes	12
Sofosbuvir/velpatasvir/voxilaprevir	All	No	No	8
		No	Yes	12
		Compensated	Yes/no	12
Sofosbuvir/ledipasvir	1, 4–6	No	Yes/no	12
	1, 4–6	Compensated	Yes	24 or 12 with RBV
	1	No	No	8*
Elbasvir/grazoprevir	1, 4	No/compensated	Yes/no	12**

HCV – hepatitis C virus, RBV – ribavirin
** May be considered*
*** Consider 16 weeks (with RBV) in patients with baseline HCV RNA viral load > 800 000 IU/ml, with NS5A polymorphism*

8 weeks is not indicated [12]. However, there is some evidence available from clinical studies and real-world data regarding shortening therapy with SOF/VEL in adults [13–16]. Two phase 2 studies evaluated the efficacy and safety of SOF/VEL ± ribavirin (RBV) for 8 weeks in treatment-naïve, non-cirrhotic participants, and their results revealed SVR12 rates ranging from 81 to 100% in participants infected with HCV genotype 1 and 2 [13–14]. Another phase 2 study (HepNet Acute HCV-V Study) analysed the efficacy and safety of SOF/VEL for 8 weeks in 20 adult participants with acute HCV monoinfection and showed that 90% of participants in the intention-to-treat (ITT) population achieved SVR12 (95% CI: 69.9–97.2) [15]. Real-world data from the Scottish Hepatitis C Database evaluated a cohort of 90 treatment-naive, non-cirrhotic patients infected with genotype 3 HCV with F2/3 fibrosis who were treated with SOF/VEL for 8 weeks [16]. SVR12 rates were high: for the ITT population 95.6% (95% CI: 89–98.8), and for per-protocol 100% (95% CI: 95.7–100) [16]. However, a multicentre randomised REACT study, which was designed to analyse the outcomes of shortening treatment with SOF/VEL to 6 weeks, was halted early because this shortened course appeared to be less effective than a standard 12-week course in adult patients with recently acquired HCV infection [17].

Similar studies are lacking in children. One paediatric study with another SOF-based combination, SOF/ledipasvir, on a small number of children revealed that shortening of the treatment to 8 weeks was effective [18]. Results of the PANDAA-PED study on 50 children aged 6–18 years treated with a standard 12-week SOF/VEL regimen revealed that 35 of 50 patients presented with undetectable HCV RNA at 4 weeks of treatment and in another 13 it was below the lower limit of detection (LLOD, < 15 IU/ml). After 8 weeks of the therapy, in 2 patients HCV RNA was below the LLOD and undetectable in the remaining 48 children. These observations support the idea of shortening the therapy also with SOF/VEL [9]. In addition, there were patients who omitted tablets for as much as 5 days during therapy, without any impact on the treatment efficacy. Children with chronic hepatitis C usually present with no or mild liver disease, and thus they should be considered as easy-to-treat. In addition, some problems with swallowing tablets/pellets may occur in paediatric patients, which also supports the idea of treatment shortening.

Our report is limited by the lack of any essential patient's medical reports regarding his pretreatment history (viral load, genotype, aminotransferase activity, elastography) for obvious reasons (the boy was a Ukrainian refugee). However, his guardian claimed that the patient had been qualified for the antiviral treatment of chronic hepatitis C according to the current Ukrainian recommendations, which are comparable with the WHO and European guidelines [5, 6, 19].

CONCLUSIONS

Based on our experience, shortening treatment with SOF/VEL to 8 weeks may be effective for HCV elimination in children. The possibility of treatment shortening should be confirmed in further studies on larger groups of paediatric patients, which we hope will be encouraged by our report.

DISCLOSURES

1. Institutional review board statement: Not applicable.
2. Assistance with the article: None.

3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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