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ANTIVIRAL THERAPY FOR HEPATITIS IN DIALYSIS PATIENTS: ALMATY CASE SERIES

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Abstract

Background: Patients with end-stage renal disease (ESRD) undergoing hemodialysis represent a high-risk group for chronic viral hepatitis and its complications. The development of pangenotypic direct-acting antivirals (DAAs) has significantly improved the prognosis of hepatitis C virus (HCV) infection in this population. However, local data from Central Asia, particularly Kazakhstan, remain limited.

Aim: To evaluate the efficacy and safety of antiviral therapy in a subgroup of 12 patients with chronic hepatitis B and/or C receiving maintenance hemodialysis at the Hepato Center in Almaty.

Methods: From a larger cohort of 164 hemodialysis patients with confirmed viral hepatitis, 12 patients received antiviral treatment between 2021 and 2023. Treatment regimens included pangenotypic DAAs for HCV (Sofosbuvir/Velpatasvir) and nucleos(t)ide analogs for HBV (entecavir or tenofovir). Sustained virological response (SVR12 and SVR24), liver function parameters, fibrosis regression (assessed via FibroScan), and adverse events were recorded.

Results: Of the 12 patients, 9 were HCV-positive (genotypes 1, 1b, or 3), 2 had HBV, and 1 had mixed HBV+HCV infection. All HCV patients were treated with SOF/VEL for 8–12 weeks. SVR12 and SVR24 were achieved in 100% of HCV-treated patients. The two HBV patients showed complete viral suppression after 24 weeks of treatment. One mixed-infection patient achieved full suppression of both viruses. FibroScan results showed fibrosis improvement in 7 of 10 patients re-evaluated post-treatment. Liver enzymes normalized in 11 patients. No severe adverse events occurred; two patients reported mild pruritus, and no anemia-related complications were observed.

Conclusion: Antiviral therapy with pangenotypic DAAs and nucleos(t)ide analogs was highly effective and well tolerated in hemodialysis patients with chronic hepatitis B and C. These findings demonstrate the feasibility and clinical benefit of integrating antiviral treatment into routine nephrology care for dialysis-dependent patients in Kazakhstan.

Keywords: *Hepatitis C, Hepatitis B, Hemodialysis, Direct-Acting Antivirals, Sofosbuvir/Daclatasvir, ESRD, Kazakhstan, SVR, Liver Fibrosis.*

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Резюме

ПРОТИВОВИРУСНАЯ ТЕРАПИЯ ГЕПАТИТА У ПАЦИЕНТОВ НА ДИАЛИЗЕ: СЕРИЯ СЛУЧАЕВ ИЗ АЛМАТЫ

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Актуальность: Пациенты с терминальной стадией хронической болезни почек (ХБП), получающие лечение программным гемодиализом, относятся к группе высокого риска по хроническим вирусным гепатитам и связанным с ними осложнениям. Разработка пангенотипных противовирусных препаратов прямого действия (ППДП) значительно улучшила прогноз у пациентов с инфекцией вируса гепатита С (ВГС) в данной популяции. Однако локальные данные по Центральной Азии, особенно по Казахстану, остаются ограниченными.

Цель: оценить эффективность и безопасность противовирусной терапии у подгруппы из 12 пациентов с хроническим гепатитом В и/или С, получающих программный гемодиализ в Гепатоцентре Алматы.

Методы: из общей когорты из 164 пациентов на гемодиализе с подтвержденным вирусным гепатитом 12 человек прошли противовирусное лечение в период с 2021 по 2023 год. Схемы терапии включали пангенотипные ППДП для ВГС (софосбувир + велпатасвир) и аналоговые нуклеозиды/нуклеотиды для ВГВ (энтековир или тенофовир). Оценивались устойчивый вирусологический ответ (УВО12 и УВО24), показатели функции печени, регресс фиброза (по данным ФиброСкана) и нежелательные явления.

Результаты: Из 12 пациентов у 9 был диагностирован ВГС (генотипы 1, 1b или 3), у 2 - ВГВ, и у 1 пациента – смешанная инфекция ВГВ+ВГС. Все пациенты с ВГС получали софосбувир /велпатасвир в течение 8–12 недель. УВО12 и УВО24 были достигнуты у 100% пациентов с ВГС. У двух пациентов с ВГВ через 24 недели терапии была достигнута полная супрессия вируса. Пациент со смешанной инфекцией достиг полной супрессии обоих вирусов. По данным ФиброСкана улучшение фиброза было зафиксировано у 7 из 10 пациентов, проходивших повторное обследование. Нормализация печеночных ферментов (АЛТ/АСТ) произошла у 11 пациентов. Серьезных нежелательных явлений не зарегистрировано; два пациента жаловались на умеренный кожный зуд, анемия или связанные с ней осложнения не наблюдались.

Вывод: Противовирусная терапия пангенотипными ППДП и аналогами нуклеозидов/нуклеотидов оказалась высокоэффективной и хорошо переносимой у пациентов на гемодиализе с хроническими гепатитами В и С. Полученные результаты подтверждают целесообразность и клиническую пользу интеграции противовирусного лечения в стандартную нефрологическую практику для пациентов на диализе в Казахстане.

Ключевые слова: *Гепатит С, Гепатит В, Гемодиализ, Противовирусные препараты прямого действия, Софосбувир Велпатасвир, ХБП, Казахстан, УВО, Фиброз печени.*

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Түйіндеме

ДИАЛИЗДЕГІ ПАЦИЕНТТЕРДЕГІ ГЕПАТИТКЕ ҚАРСЫ ТЕРАПИЯ: АЛМАТЫДАН ЖАҒДАЙЛАР СЕРИЯСЫ

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Өзектілігі: Созылмалы бүйрек ауруының терминалды сатысындағы (СБА) және гемодиализдегі пациенттер созылмалы вирусты гепатиттер мен олардың асқынуларына шалдыққан жоғары қауіп тобына жатады. Гепатит С вирусын (HCV) жұқтырған науқастарға арналған пангенотиптік тікелей әсер ететін вирусқа қарсы препараттардың (DAA) дамуы осы популяцияда болжамды едәуір жақсартты. Алайда, Орталық Азияда, әсіресе Қазақстанда, нақты клиникалық деректер аз.

Мақсаты: Алматы қаласындағы Гепатоорталықта гемодиализ қабылдап жатқан созылмалы гепатит В және/немесе С бар 12 пациентке жүргізілген вирусқа қарсы емнің тиімділігі мен қауіпсіздігін бағалау.

Әдістері: Вирусты гепатит расталған 164 гемодиализдегі пациенттің ішінен 12 пациент 2021–2023 жылдар аралығында вирусқа қарсы ем қабылдады. Емдеу сызбалары HCV үшін пангенотиптік DAA (софосбувир + велпатасвир), ал HBV үшін нуклеозидтік/нуклеотидтік аналогтар (энтековир немесе тенофовир) қолдануды қамтыды. Уақытша вирустық жауап (SVR12 және SVR24), бауыр ферменттері, фиброз деңгейінің өзгерісі (FibroScan арқылы) және жағымсыз құбылыстар тіркелді.

Нәтижелер: 12 пациенттің 9-ында HCV (1, 1b немесе 3 генотиптері), 2-інде HBV және 1-інде аралас (HBV+HCV) инфекция анықталды. Барлық HCV пациенттері софосбувир /велпатасвир препаратын 8–12 апта бойы қабылдады. SVR12 және SVR24 көрсеткіштері барлық HCV пациенттерінде 100% деңгейге жетті. HBV жұқтырған екі пациентте 24 апта емнен кейін вирус толық басылды. Аралас инфекциясы бар пациентте екі вирустың да толық басылуы байқалды. FibroScan нәтижелері бойынша 10 пациенттің 7-інде фиброздың төмендеуі тіркелді. Бауыр ферменттері 11 пациентте қалыпқа келді. Айтарлықтай жанама әсерлер болған жоқ; екі пациентте жеңіл тері қышуы байқалды, анемия мен соған байланысты асқынулар тіркелген жоқ.

Қорытынды: Пангенотиптік DAA және нуклеозид/нуклеотид аналогтарын қолдану арқылы жүргізілген вирусқа қарсы ем гемодиализдегі созылмалы вирусты гепатит В және С бар пациенттер үшін жоғары тиімді және жақсы көтерімді болды. Бұл нәтижелер Қазақстандағы диализге тәуелді науқастар арасында вирусқа қарсы терапияны нефрологиялық тәжірибеге енгізудің орындылығы мен клиникалық маңыздылығын көрсетеді.

Түйінді сөздер: *Гепатит С, Гепатит В, Гемодиализ, Тікелей әсер ететін вирусқа қарсы препараттар, Софосбувир, Велпатасвир, СБА, Қазақстан, Уақытша вирустық жауап, Бауыр фиброзы*

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Introduction

Chronic viral hepatitis, particularly hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, remains a significant global health concern, with an estimated 58 million people infected with HCV and over 296 million with HBV worldwide [9]. The burden is particularly notable among vulnerable populations, including patients with end-stage renal disease (ESRD) undergoing hemodialysis, who face an elevated risk of parenteral transmission due to the frequency of invasive vascular procedures and immunocompromised status.

Kazakhstan, a Central Asian nation with a rapidly developing healthcare infrastructure, has experienced a steady rise in chronic viral hepatitis cases. Between 2015 and 2020, the incidence of HBV and HCV in the country increased by 49.8% and 46.4%, respectively. National surveillance data show that the seroprevalence of anti-HCV antibodies reaches up to 5.1%, with regional variability driven by differences in healthcare access, historical transmission patterns, and socioeconomic disparities [5]. The Unified National Electronic Health System (UNEHS) identified 82,700 cases of chronic viral hepatitis between 2014 and 2019, of which 56.6% were HCV-related and 43.4% HBV-related [1]. Alarmingly, viral hepatitis coexists with a high burden of comorbidities such as diabetes mellitus, hypertension, and cardiovascular disease, further complicating clinical management.

Patients with chronic kidney disease (CKD), particularly those at stage 5 receiving maintenance hemodialysis, are disproportionately affected by chronic viral hepatitis. A nationwide registry in Kazakhstan revealed an increase in the prevalence of dialysis-treated ESRD from 135.2 to 350.2 per million population (PMP) between 2014 and 2018 [3]. Despite advances in renal replacement therapy, mortality remains substantial, especially among women and ethnic Russian populations.

The intersection of viral hepatitis and ESRD presents unique clinical challenges. HCV infection in dialysis patients has been associated with accelerated liver fibrosis progression, increased cardiovascular mortality, and a heightened risk of hepatocellular carcinoma [6,7]. Historically, interferon-based regimens were poorly tolerated and yielded suboptimal response rates in this population. However, direct-acting antivirals (DAAs), particularly pangenotypic agents such as sofosbuvir/velpatasvir, have revolutionized the therapeutic landscape [2]. Clinical trials and real-world studies have demonstrated SVR rates exceeding 95% in patients with advanced renal impairment, including those on dialysis [8].

Despite these global advancements, local real-world evidence from Central Asia remains scarce. Most existing studies are cross-sectional and lack outcome data on antiviral treatment in dialysis populations. Furthermore, limited access to molecular diagnostic tools and genotyping in some regions of Kazakhstan has hindered timely treatment initiation and monitoring.

In this context, the present study aims to address this knowledge gap by evaluating dialysis patients' demographic, virological, and clinical characteristics with chronic viral hepatitis in a tertiary hepatology center in Almaty. In particular, we focus on a subgroup of 12 patients who received antiviral therapy with DAAs or nucleotide analogs, assessing treatment outcomes, fibrosis regression, and safety in this high-risk population.

Materials and Methods

Study Design and Setting. This was a retrospective observational study conducted at the Hepato Center in Almaty, Kazakhstan, a tertiary-level referral center specializing in hepatology and nephrology. The study included patients undergoing maintenance hemodialysis who were diagnosed with chronic hepatitis B virus (HBV), hepatitis C virus (HCV), or HBV/HCV coinfection. Data were collected between January 2016 and December 2023 from electronic medical records and outpatient hepatology consultation logs.

Patient Selection. From an initial registry of 398 patients with documented chronic kidney disease (CKD) or ESRD, we screened for inclusion based on the following criteria:

- Age ≥18 years
- CKD stage 5 requiring maintenance hemodialysis
- Confirmed diagnosis of chronic HCV and/or HBV infection
- Absence of decompensated liver cirrhosis (Child-Pugh B or C)
- No concurrent HIV infection or hepatocellular carcinoma at baseline

The selection process involved several steps:

- Removal of duplicate entries (n=50)
- Exclusion of patients with earlier-stage CKD (n=149)
- Exclusion of patients with cirrhosis or other contraindicated conditions (n=35)

Following these criteria, a final cohort of 164 dialysis-dependent patients with confirmed viral hepatitis was established. Of these, 12 patients who initiated antiviral therapy were selected for treatment outcome analysis.

Treatment Protocols. Patients with chronic HCV infection were treated with sofosbuvir/velpatasvir (SOF/VEL) at a fixed oral dose of 400/100 mg once daily for 8 or 12 weeks, depending on the genotype and fibrosis status. Patients with HBV received entecavir (0.5 mg/day) or tenofovir (245 mg/day) as monotherapy. The decision regarding treatment regimen and duration was based on current EASL and KDIGO guidelines.

Data Collection and Variables. For all treated patients (n=12), the following data were extracted and analyzed:

- Demographic variables: age, sex, ethnicity
- Clinical data: genotype, fibrosis stage (via transient elastography), presence of cirrhosis, diabetes mellitus, arterial hypertension, and ascites
- Laboratory markers: ALT, AST, total bilirubin, HCV RNA or HBV DNA viral load
- Treatment outcomes: Sustained virological response at 12- and 24-weeks post-treatment (SVR12, SVR24)
- Safety: Reported adverse events, need for treatment interruption, hemoglobin trends during therapy

Liver fibrosis staging was assessed using FibroScan® (Echosens), with results reported in kilopascals (kPa) and categorized according to the METAVIR scoring system (F0 to F4). SVR was defined as undetectable viral RNA (for HCV) or DNA (for HBV) 12 and 24 weeks after treatment completion.

Statistical Analysis

Descriptive statistics were used to summarize the data. Categorical variables were expressed as counts and percentages. Continuous variables were presented as means ± standard deviation (SD) or medians with interquartile ranges, where appropriate. All data processing and analysis were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA).

Results

Patient Characteristics.

Among the final cohort of 164 dialysis patients with viral hepatitis, 12 individuals (7 males, 5 females; mean age 51.8 ± 11.2 years) underwent antiviral therapy and were included in the treatment analysis. Of these:

- 9 patients (75%) had chronic HCV monoinfection
- 2 patients (16.7%) had chronic HBV infection
- 1 patient (8.3%) had mixed HBV + HCV infection

The most frequently identified HCV genotypes were genotype 3 (4 patients) and genotype 1b (2 patients), with three cases remaining unclassified due to limited molecular diagnostic access. All HCV-infected patients received sofosbuvir/velpatasvir (SOF/VEL) for 8–12 weeks. HBV patients were treated with entecavir or tenofovir for 24 weeks or longer, based on clinical indications.

Virological Response

- All 10 patients with HCV (including one mixed infection) achieved **SVR12** and **SVR24**, confirming 100% virological cure.
- Both HBV patients achieved complete suppression of HBV DNA after 24 weeks of treatment.
- The patient with mixed infection showed undetectable HCV RNA and suppressed HBV DNA at both follow-up points.

Liver Fibrosis and Biochemistry

- Fibrosis staging (via FibroScan) at baseline showed:
  - F0–F1: 4 patients
  - F2–F3: 5 patients
  - F4 (cirrhosis): 3 patients
- Post-treatment elastography (available in 10 cases) demonstrated fibrosis regression in **7 patients**, including one cirrhotic patient who improved to F3.
- ALT and AST levels normalized in 11 of 12 patients, with one patient showing mild ALT elevation (<1.5× ULN).

Safety Profile.

Treatment was well tolerated. Two patients reported mild pruritus, but no severe adverse events or treatment discontinuations occurred. Hemoglobin levels remained stable throughout therapy; no dose adjustments for erythropoiesis-stimulating agents were required.

Structural Causes of CKD.

As shown in Table 1, chronic glomerulonephritis was the most common cause of ESRD in this subgroup (n = 4, 33.3%). Hypertensive nephropathy was reported in 3 patients (25%), and diabetic nephropathy in 2 patients (16.7%). One case each was attributed to mixed nephropathy (diabetic and hypertensive), polycystic kidney disease, and interstitial nephritis.

Table 1.

Structural Causes of CKD in 12 Treated Patients.

Cause of CKD	Number of Patients
Chronic glomerulonephritis	4
Hypertensive nephropathy	3
Diabetic nephropathy	2
Mixed nephropathy (diabetic, hypertensive)	1
Polycystic kidney disease	1
Interstitial nephritis	1

Table 2 summarizes the demographic and clinical characteristics of the 12 patients who received antiviral therapy at the Hepato Center in Almaty. The cohort consisted of 7 males (58.3%) and 5 females (41.7%), with a mean age of 51.8 ± 11.2 years. The average duration of end-stage renal disease (ESRD) was 119.4 ± 67.5 months, and patients had been on hemodialysis for an average of 96.5 ± 62.8 months. In 8 of the 9 HCV-infected patients, the infection was diagnosed before the initiation of dialysis, while in 1 case it occurred afterward. The mean duration of confirmed HCV infection was 111.2 ± 54.6 months.

Table 2.

Characteristics of the studied group of patients.

Parameter	Value
Number of patients, n	12
Sex, male/female (%)	7/5 (58.3 / 41.7)
Age, years	51.8 ± 11.2
Duration of end-stage renal disease (ESRD), months	119.4 ± 67.5
Duration on hemodialysis, months	96.5 ± 62.8
HCV infection (before/after start of dialysis), n	8 / 4
Duration of HCV infection (since diagnosis), months	111.2 ± 54.6

Dynamics of Laboratory and Fibrosis Parameters

Table 3 displays the dynamics of alanine aminotransferase (ALT) levels, liver stiffness by transient elastography, and METAVIR fibrosis stage before and after antiviral treatment.

Table 3.

Dynamics of Laboratory and Fibrosis Parameters.

№	ALT, U/L	ALT, U/L	Liver stiffness, kPa	Liver stiffness, kPa	Fibrosis stage	Fibrosis stage
	Before Tre/t	After Tre/t	Before Tre/t	After Tre/t	Before Tre/t	After Tre/t
1	62	21	11.8	6.3	F3	F0–F1
2	75	22	10.5	6.9	F3	F1
3	88	25	12.4	7.0	F3	F1–F2
4	54	18	9.8	6.2	F2–F3	F1
5	93	30	21.0	13.0	F4	F3
6	41	17	7.8	5.5	F1–F2	F0–F1
7	105	35	24.6	27.0	F4	F4
8	68	20	10.5	8.3	F3	F2–F3
9	58	23	6.5	4.3	F0–F1	F0–F1
10	72	21	5.7	5.4	F0–F1	F0–F1
11	65	22	5.1	4.4	F0–F1	F0–F1
12	80	28	12.0	10.2	F3	F3

All HCV-infected patients (n=9) were treated with sofosbuvir/velpatasvir (SOF/VEL) for 8–12 weeks. Sustained virological response was achieved in all HCV patients (SVR12 and SVR24 = 100%). Two HBV-infected patients treated with nucleos(t)ide analogues (entecavir or tenofovir) achieved complete suppression of HBV DNA after 24 weeks. One patient with mixed HCV/HBV infection achieved full suppression of both viruses. Among the 10 patients who underwent post-treatment elastography, 7 showed improvement in fibrosis stage. One cirrhotic patient (F4) improved to F3, while others regressed from F3 to F0–F1 or F2. ALT levels normalized in 11 out of 12 patients. No serious adverse events were recorded; two patients experienced mild pruritus, and no anemia-related complications were observed during treatment

Discussion

This study provides real-world evidence on the safety and efficacy of antiviral therapy in a high-risk population of patients with end-stage renal disease (ESRD) undergoing hemodialysis and chronically infected with hepatitis B virus (HBV), hepatitis C virus (HCV), or both. Despite a relatively small treatment group (n = 12), the outcomes observed reflect global trends and strongly support the integration of antiviral therapy into nephrology care pathways, especially in countries such as Kazakhstan, where the burden of viral hepatitis and renal failure continues to rise.

Consistent with international studies, all HCV-infected patients in our cohort achieved sustained virological response (SVR12 and SVR24) following an 8–12-week course of sofosbuvir/velpatasvir (SOF/VEL), a pangenotypic direct-acting antiviral (DAA) regimen [9]. These results mirror findings from the EXPEDITION-4 trial, which demonstrated SVR12 rates of 98% in dialysis-dependent patients receiving SOF/VEL, and other real-world studies showing excellent efficacy and tolerability in similar populations [5].

In our cohort, fibrosis regression was observed in 7 of 10 patients who underwent post-treatment transient elastography. This improvement was most pronounced among patients with elevated baseline ALT levels, suggesting that resolution of necroinflammatory activity may be an important early driver of liver stiffness reduction. One cirrhotic patient (F4) improved to F3, and several patients with bridging fibrosis (F3) or moderate fibrosis (F2) regressed to milder stages. These results highlight the potential reversibility of liver damage, even in patients on long-term dialysis, once viral eradication is achieved.

Importantly, no severe adverse events were reported. Two patients experienced mild pruritus, a common and usually self-limited side effect of DAAs. There were no anemia-related complications, and no dose adjustments to erythropoiesis-stimulating agents were necessary. This favorable safety profile is particularly relevant in the hemodialysis population, where polypharmacy and comorbidity burdens often limit treatment options.

The two HBV-infected patients in our study were treated with nucleos(t)ide analogues (entecavir or tenofovir), both of whom achieved complete viral suppression by 24 weeks. These findings are consistent with existing guidelines from the European Association for the Study of the Liver (EASL) and KDIGO, which recommend long-term antiviral therapy in HBV-positive dialysis patients to reduce the risk of liver decompensation and hepatocellular carcinoma.

One unique feature of this study is the inclusion of a patient with HBV/HCV coinfection, who achieved full suppression of both viruses with combined therapy. While coinfections pose complex therapeutic and monitoring challenges, our result supports the use of dual antiviral approaches in such patients, provided renal function and drug–drug interactions are closely monitored.

From an epidemiological standpoint, chronic glomerulonephritis and hypertensive nephropathy remained the leading causes of ESRD in this subgroup, aligning with national registry data from Kazakhstan. The integration of hepatology care into dialysis programs is therefore not only logical but necessary for improving long-term outcomes in this vulnerable population.

Limitations of our study include the small sample size and single-center nature of the analysis. However, the homogeneity of the cohort and the availability of pre- and post-treatment elastography and biochemical data strengthen the validity of the observed trends.

Conclusion

This case series adds to the growing evidence supporting the use of sofosbuvir/velpatasvir in patients on maintenance hemodialysis. High SVR rates, minimal adverse events, and potential fibrosis regression were achieved in all patients treated at the Hepato Center in Almaty. This experience validates the inclusion of DAA therapy in Kazakhstan's broader public health strategy for HCV elimination, particularly within renal care programs.

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