ORIGINAL RESEARCH PAPER

Healthcare

LONG-TERM HEALTH OUTCOME AMONG HCV PATIENTS WITH ADVANCED LIVER FIBROSIS TREATED THROUGH HCV ELIMINATION PROGRAM IN GEORGIA

KEY WORDS: Hepatitis C, Antiviral therapy, Sustainable viral response, Liver fibrosis

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ABSTRACT

Goal: The main objective of our study was to evaluate the effect of long-term treatment in patients with high liver fibrosis who have achieved a sustainable viral response (SVR) after receiving direct antiviral medication (DAA). Assess socio-demographic characteristics and clinical /laboratory data role in changing the level of liver fibrosis.**Methods:** The study cohort included patients from the Hepatitis C Elimination Program treated with direct antiviral drugs (DAA), with high-grade elastography-determined liver fibrosis (> = F3), and patients with a FIB4 score above 3.25 and sustainable viral response is achieved within 12-24 weeks after completion of treatment. The study group was selected retrospectively from Clinic Neolab's medical database and records. A total of 150 patients were studied. Data were processed in the statistical program SPSS24. The Wilcoxon Signed Ranks test was used from the statistical tests.**Results:** The study was conducted in 2020. These data were determined both before and after treatment. After treatment on the metavir scale, liver damage levels improved in 51.7% of patients.Statistical analysis showed that the change in fibrosis level after treatment was statistically significant (P <0.001). The study normalized data from laboratory studies such as Alt (85,3%) and Ast (80 5%).

INTRODUCTION:

Approximately 71 million people worldwide live with chronic hepatitis C, and most of them are at risk of developing cirrhosis and liver cancer. WHO estimates that in 2016, approximately 399,000 people died of hepatitis C, mainly from cirrhosis and HCC (primary liver cancer). (WHO, Hepatitis C. Key Facts, 9 July 2019)

According to the CDC, out of 100 people infected with the hepatitis C virus, 60-70 will develop chronic liver disease, 5 to 20 people will develop cirrhosis within 20-30 years, and 1 to 5 people will die of cirrhosis complications or HCC. (Prevention, 2020) (ML., Hepatitis C virus therapy in the direct acting antiviral era, 2014) (Sebastiani G, 2014).

Unfortunately, the problem with hepatitis C is also due to the fact that no prophylactic measures have been developed to date, such as vaccinations or specific immunoglobulins that have protected people from hepatitis C. Therefore, the only effective way to fight the disease is timely detection of the disease and antiviral treatment.

In June 2016, WHO developed a global strategy to combat viral hepatitis. The global strategy aims to reduce new HCV cases by 90% and reduce viral hepatitis mortality by 65% by 2030.

In 2015, Georgian National Center for Disease Control and Public Health with USA Centers for Disease Control and Prevention (CDC), conducted seroprevalence survey and fount that the prevalence in the country is high at 7.7% and active hepatitis C is present in 5.4% of the population. In April 2015, based on existing studies and the global burden of the disease, the Government of Georgia launched the Hepatitis C Elimination Program.

This program made it possible to study a large number of people with a high stage of hepatic fibrosis, infected with hepatitis C, and to observe after achieving a sustainable viral response.

Various studies have shown that the use of direct antiviral medications (DAAs) can cure a large proportion of those infected, which will ultimately reduce the transmission and spread of hepatitis C. Several studies have confirmed the positive effects of hepatitis C treatment on disease progression. (Yu-Chi Lee, Tsung-Hui Hu, Chao-Hung Hung, Sheng-Nan Lu, Chien-Hung Chen, Jing-Houng Wang, 2019 Apr 2) (Giannini EG, Crespi M, Demarzo M, Bodini G, Furnari M, Marabotto E, Torre F, Zentilin P, Savarino V, 2019 Mar) (van der Meer AJ, 2016 Oct;) (Hirsh D. Trivedi, MD, Steven C. Lin, MD, and Daryl T.Y. Lau, MD, MSc, MPH, , October 2017)

Statistical analysis

Quantitative data entry, processing and statistical analysis were performed using SPSS v.23.0 of the statistical package. Descriptive statistical methods were used to estimate the study variables in the target populations. Bivariate analysis was performed using t-test for quantitative data for comparison before and after treatment. The Pearson Chi-Square test (Pearson Chi-Square) and its modification, namely the Fisher's Exact Test, were used to determine the correlation between the dichotomous variables. Odds Ratio [OR] with 95% Confidence Interval [CI] was used to estimate the association strength between dichotomous variables. If necessary, the so-called. Mantel-Haenszel stratification analysis was used to exclude "confouding factors".

The mean age of the patients enrolled in the study was 48.8 years, the minimum age was 25 years, and the maximum was 66 years. The most numerous were in the 46-50 age group, 29.3% representative.

Alcohol users were 60 (40%) at the start of treatment and their share dropped to 11.3% after completion. Injection drug were used before treatment by 10.7% (16), only 3.3% (5) of patients after treatment. There were 72% (108) smokers at the start of treatment, after treatment the proportion of smoking patients reduced to 52%.

Analysis of quantitative indicators of liver elastography (Fibroscan KPA) showed that the mean fibrosis rate for the whole group was 22.64 units before treatment and 15.43 units after treatment. The change obtained with this is statistically significant (P <0.001).

Fibrosis levels also decreased after treatment according to the FIB4 rate. The mean before treatment was 5,26, after treatment it became 3,23.

Bivariate analysis revealed no statistically significant difference between sex, alcohol, tobacco, injecting drug use, and fibrosis levels before or after treatment. Also, a link

between fibrosis levels and BMI levels was not confirmed either before or after treatment.

We studied whether factors such as tobacco, alcohol, injecting drug use, or obesity were risk factors for fibrosis. None of them were found to be overweight (OR = 1,816 (95% CI 0,751-4,390; Mantel-Haensze Chi2-test = 1,233; p = 0,267), alcohol (OR = 0,628 (95% CI 0,267-1,477; Mantel-Haensze Chi2) -test = 0,725; p = 0,395), injectable drugs (OR = 1,160 (95% CI 0,562 - 2,396; Mantel-Haensze Chi2-test = 0,046; p = 0,830), high ALT level (OR = 1,135 (95%) CI 0,326 - 3,944; Mantel-Haensze Chi2-test = .014; p = 0,906), high level of AST (OR = 0,204 (95% CI 0,023 - 1,800; Mantel-Haensze Chi2-test = 1,313; p = 0,252) There is no risk factor for reducing fibrosis levels as a result of treatment.

Conclusion and Recommendations

1. Achieving SVR after direct antiviral treatment among HCV patients with advanced liver fibrosis results in a significant improvement in liver fibrosis levels after 2 years of treatment.
2. Modification of liver hardness was assessed within the study;
3. Patients who have achieved SVR are at a lower risk of developing decompensated liver, HCC, and other liver-related diseases;
4. Direct antiviral treatment has a very positive effect in terms of fibrosis regression;
5. 2. The more patients who achieve SVR, the more positive the distant outcome of fibrosis in these patients.
6. 3. Monitoring of liver fibrosis should be performed both at the beginning of treatment and after treatment.
7. 5. Using direct antiviral medications, fibrosis regression will be of great practical value for planning the subsequent treatment period.

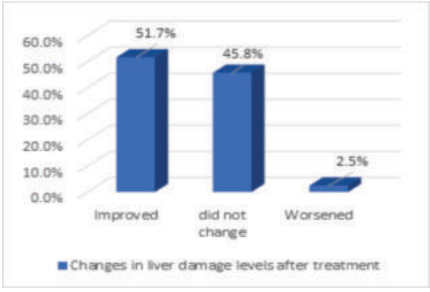

Diagram 1. Changes before and after treatment of liver damage, Wilcoxon test for two related selections

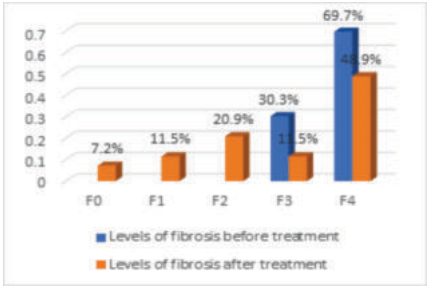

Diagram 2. Comparison of fibroscan results before and after treatment

Changes in laboratory study rates within the study look as follows. (Table 1)

Characteristic	Unit	Baseline (mean)	Follow-up (mean)	Mean difference	95% CI	p-value
ALT	U/mL	110	29.2	80.8	63,57-87.14	< .0001
AST	U/mL	98.62	33.53	65.09	53.34-71,31	< .0001
PLTS	109/L	166.40	195.60	29.2	17,13-41,13	< .005
Hb	g/dL	15.06	14.94	0.12	0,90-2,10	0.31
Spleen length	mm	125,08	123,85	1,22	1,50-3,96	0.36
Spleen width	mm	49,46	49,38	0,08	1,34-1,68	0 992

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