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Hematological Effects of Antiviral Drugs for Hepatitis C Virus

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ABSTRACT

Background: Direct-acting antivirals (DAAs) have replaced interferon-based therapies in the treatment of HCV infection. Despite general success, treating some patient populations with antiviral medication is still difficult. Even though serious adverse effects are uncommon, they can nonetheless occur, particularly in individuals with advanced liver disease.

Objective: Our goal was to assess the haematological effects of antiviral medications in chronic HCV patients.

Patients and methods: The total number of patients included, were 50. Males represented 27 (54.0%) of total patients and females represented 23 (46.0%). The mean age of the studied patients was 46.24 ± 9.67 years**.** All patients were thoroughly examined, and full labs were obtained before start and 3 & 6 months after treatment.

Results: SVR was 100% in our research (P-value 0.001). Three- and six-months following therapy, there was a statistically significant increase in mean corpuscular volume (MCV) and hematocrit (HCT) (P-values = 0.035 and 0.048, respectively). Three months after starting therapy, haemoglobin levels rose, although the increases weren't statistically significant (P-value = 0.719). Six months after starting therapy, haemoglobin showed a statistically significant improvement (P-value = 0.019). Six months following the start of therapy, the platelet count increased statistically significantly (P-value = 0.038). Six months following therapy, our study found statistically significant reductions in total bilirubin (P-value = 0.001), ALT (P-value = 0.012), AST (P-value = 0.001), and AFP (P-value = 0.002).

Conclusions: Results indicated that the sofosbuvir-daclatasvir medication combination is safe for Egyptians and that it plays a key role in the treatment of HCV with fewest side effects.

Keywords: Hematological, Antiviral drugs, DAAs, HCV.

INTRODUCTION

The treatment choices for people with chronic HCV infection have changed as a result of the emergence of very effective all-oral, interferon-free medicines, and the majority of patients may now achieve viral clearance. With more than 95% efficacy, little side effects, and a brief 8–12 week treatment period, DAAs such Asunaprevir/daclatasvir, Elbasvir/Grazoprevir, and Ledipasvir/Sofosbuvir have recently gained popularity. This has improved cure rates and treatment safety [(1-3)].

Despite general success, treating some patient populations with antiviral medication is still difficult. Even while serious adverse effects are uncommon, they are not entirely unheard of, particularly in individuals with advanced liver disease, in whom ribavirin (RBV) use is nevertheless advised [(4-5)].

In controlled research, low rates of DAA-related side effects have been documented; nonetheless, investigations conducted in the real world have revealed new toxicities and drug-drug interactions in specific groups [(6-7)]. Our goal was to assess the haematological effects of antiviral medications in chronic HCV patients.

PATIENTS AND METHODS

This was a cross-sectional study that was conducted at HCV-treatment Unit of Ain Shams University Hospital. The study was done through the period from February to August 2018.

The total number of patients included, were 50. Males represented 27 (54.0%) of total patients and females represented 23 (46.0%). The mean age of the studied patients was 46.24 ± 9.67 years **(P-value = 0.443).** All patients were thoroughly examined and full labs were obtained before start and 3 & 6 months after treatment.

Exclusion criteria: Hepatitis B patients. Patients with impaired kidney function (estimated GFR< 60%). Patients on Ribavirin. The patients do not have any hematological disease either acute or chronic, hereditary or acquired.

All studied patients were subjected to:

1. Complete history taking.
2. Comprehensive clinical assessment (general and local).
3. Abdominal U/S.
4. Routine laboratory investigations: (was done at the start of the study and after 3 and 6 months):
   - ✓ Complete blood picture.
   - ✓ Peripheral blood film, Reticulocytic count (corrected).
   - ✓ LDH, and serum ferritin (when indicated).
   - ✓ Liver function tests (AST, ALT, alkaline phosphatase, total bilirubin, direct bilirubin, prothrombin time, and S. albumin).
   - ✓ Kidney function test (blood urea and serum creatinine).

Ethical approval: Ain Shams Medical Ethics Committee, Faculty of Medicine, Ain Shams University gave its approval to this study. All participants gave written consents after receiving all information. The Helsinki Declaration was followed throughout the study's conduct.

Statistical Analysis

SPSS version 20.0 was used to tabulate and statistically analyse the collected data. The mean ± SD

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(standard deviation) and the lowest and maximum of the range were computed for numerical parametric data. The median and first and third interquartile ranges were computed for numerical nonparametric data. The number and% were computed for categorical data. The independent t-test should be used for inferential analysis when there are two independent groups with parametric data, and the Mann Whitney U should be used when there are two independent groups with non-parametric data. For inferential analysis on qualitative data, the Chi-square test for independent groups was utilised. $P \leq 0.05$ was considered significant.

RESULTS

Table (1) showed that there was no statistically significant change between before and after three months regarding demographic data. Females were 46% and males were 54%

Table (1): Comparison between pre and after 3 months as regards age and sex

		Pre (No,=50)		After 3 months (No,=50)		Chi Square Test/ Paired t test	
		No	%	No	%	x^2/t**	p value
Sex	Female	23	46.0%	23	46.0%	0.000	1.000
	Male	27	54.0%	27	54.0%		
Age	Mean ± SD	46.24 ± 9.67		44.88 ± 7.88		0.771**	0.443

Concerning MCV, MCH, and HCT, there was a statistically significant decrease in pre compared to after 3 months (Table 2).

Table (2): Comparison of the CBC before and after three months

	Pre (No,=50)		After 3 months (No,=50)		Paired T test	
	Mean	SD	Mean	SD	r	p value
RBC (10^6/ml)	4.74	0.47	4.89	0.47	-1.613	0.110
HB (g/dl)	11.42	1.86	11.57	2.28	-.361	0.719
MCV (fl)	80.82	7.02	83.66	6.24	-2.139	0.035
HCT (%)	32.98	7.00	35.58	5.97	-1.998	0.048
MCH (pg/cell)	27.64	2.00	29.64	1.24	-6.013	<0.001
MCHC (g/dl)	31.60	2.29	31.94	1.99	-0.793	0.430
RDW (μm)	11.93	1.07	12.00	0.88	-0.388	0.699

Table (3) showed after three months that there was no statistically significant difference concerning PLT.

Table (3): Comparison of PLT before and after three months

	Pre (No,=50)		After 3 months (No,=50)		Paired T test	
	Mean	SD	Mean	SD	r	p value
MPV (10^5/μl)	8.18	0.91	8.48	0.92	-1.668	0.098
PLT (10^4/μl)	227.08	55.74	248.76	62.00	-1.650	0.102

T. bill showed a statistically significant rise before and after three months (Table 4).

Table (4): Comparison of T. Bill and D. Bill before and after three months

	Pre (No,=50)		After 3 months (No,=50)		Paired T test	
	Mean	SD	Mean	SD	r	p value
T. Bill	0.94	0.07	0.88	0.10	3.296	0.001
D. Bill	0.43	0.09	0.39	0.08	1.763	0.081

Regarding liver enzymes there was a statistically significant decrease after three months compared to before (Table 5).

Table (5): Comparison of liver enzymes before and after three months

	Pre (No,=50)		After 3 months (No,=50)		Paired T test	
	Mean	SD	Mean	SD	r	p value
AST (U/L)	18.98	4.62	16.76	3.62	2.573	0.012
ALT (U/L)	27.90	6.44	19.58	4.82	7.316	0.000

Concerning PCR, there was a statistically significant rise before compared to after three months (Table 6).

Table (6): Comparison of PCR before and after three months

	Pre (No,=50)		After 3 months (No,=50)		Chi square test	
	No	**%**	**No**	**%**	**X^2**	**p value**
Positive	50	100%	0	0%	100.00	<0.001
Negative	0	0%	50	100%		

Table (7) showed with the exception of RBC that there was a statistically significant reduction in pre- compared to after 6 months.

Table (7): Comparison of the CBC before and after six months

	Pre (No,=50)		After 6 months (No,=50)		Paired T test	
	Mean	**SD**	**Mean**	**SD**	**r**	**p value**
RBC (10^6/ml)	4.74	0.47	6.02	1.40	-1.302	0.196
MCV (fl)	80.82	7.02	85.10	5.40	-3.418	0.001
HB (g/dl)	11.42	1.86	12.28	1.75	-2.390	0.019
HCT (%)	32.98	7.00	36.60	4.09	-3.158	0.002
MCH (pg/cell)	27.64	2.00	30.42	0.81	-9.119	<0.001
MCHC (g/dl)	31.60	2.29	33.14	1.59	-3.910	<0.001
RDW (μm)	11.93	1.07	12.46	0.83	-2.751	0.007

Regarding MPV and PLT, there was a statistically significant decrease in pre- compared to after six months (Table 8).

Table (8): Comparison of PLT before and after six months

	Pre (No,=50)		After 6 months (No,=50)		Paired T test	
	Mean	**SD**	**Mean**	**SD**	**r**	**p value**
MPV (10^5/μl)	8.18	0.91	9.50	0.90	-7.320	<0.001
PLT (10^4/μl)	227.08	55.61	316.86	77.91	-2.106	0.038

DISCUSSION

The total number of patients included, were 50. Males represented 27 (54.0%) of total patients and females represented 23 (46.0%). The mean age of the studied patients was 46.24 ± 9.67 years **(P-value = 0.443).** All patients were thoroughly examined and full labs were obtained before start and 3 & 6 months after treatment.

In our study, mean corpuscular volume (MCV) and hematocrit (HCT) increased statistically significantly 3 and 6 months after therapy (P-values = 0.035 and 0.048, respectively). Three months after starting therapy, haemoglobin levels rose, although the increases weren't statistically significant (P-value = 0.719). Six months after starting therapy, haemoglobin showed a statistically significant improvement (P-value = 0.019).

Six months following the start of therapy, the platelet count increased statistically significantly (P-value = 0.038).

In our analysis, we showed that Sofosbuvir/daclatasvir was often used. The most frequent negative side effects in the patient group were tiredness, headaches, and gastrointestinal issues, but not haematological problems. These results were consistent with those mentioned in earlier investigations [7-8].

Six months following therapy, our study found statistically significant reductions in total bilirubin (P-value = 0.001), ALT (P-value = 0.012), AST (P-value = 0.001), and AFP (P-value = 0.002). Our study's 100% SVR (P-value 0.001) result is consistent with those of comparable cohorts [8].

The current investigation demonstrated that following therapy, test biomarkers improved. This outcome is in line with other research, which showed that DAAs not only completely eradicate HCV but also considerably enhance liver function [9].

Several trials conducted in Egypt have shown that the combination of sofosbuvir, daclatasvir, and ribavirin is both secure and efficient. 946 Egyptians with chronic HCV were included in a cohort to receive sofosbuvir and daclatasvir therapy, both with and without ribavirin. The SVR12 rate was 94% overall, 95% in the group that was easiest to treat and received

sofosbuvir and daclatasvir, and 92% in the group that was hardest to treat and received sofosbuvir, daclatasvir, and ribavirin [7, 8, 9].

El-Khayat *et al.* [10] reported 92% SVR rates in cirrhotic patients who had never received treatment and 87% in those who had. Anaemia, weariness, headaches, and pruritus were the most frequently reported side effects. HCC and hepatic encephalopathy were serious adverse events that occurred in individuals with Child-Turcotte-Pugh score class B. In their trial, **Mohamed *et al.*** [11] showed that DAA combinations improved biochemical markers and clinical outcomes.

The majority of discontinuations were brought about by patient withdrawal and pregnancy in a sizable cohort of patients (18378) [12] who got generic sofosbuvir/daclatasvir with or without ribavirin. The overall SVR rate was 95.1% in this group and five patients died [12].

In a different recent study, the adverse events experienced by 149,816 chronic hepatitis C patients receiving various regimens under Egypt's national HCV treatment programme were assessed. In this trial, 1.7% of patients experienced adverse events, and 68% of them experienced serious adverse events, mostly those on sofosbuvir and ribavirin. The two adverse effects that were most often reported were anaemia and hyperbilirubinemia. In 0.02% and 0.06% of treated individuals, respectively, HCC and death were noted. Male patients with cirrhosis, high bilirubin levels and low haemoglobin, platelet, and albumin levels, as well as those with these conditions were more likely to experience adverse events [13].

Our study has some limitations. Besides the small cohort, we could not identify adverse events associated with medications.

CONCLUSION

- Our findings confirmed the safety of the sofosbuvir-daclatasvir regimen among Egyptians and point to a crucial role for those medication combinations in the most effective treatment of HCV.
- The sofosbuvir-daclatasvir regimen was effective in the treatment of HCV infection, leading to prolonged improvement in liver function.

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Competing interests: Nil.

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