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Comparison of All Oral With Sub-Cutaneous Drugs Response in Chronic Hepatitis C Patients Using Non -Invasive Markers

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Abstract:
Background: *World-wide, hepatitis C infection is the chief cause of acute and chronic hepatitis. Chronic hepatitis C is treated by many agents encompasses diminution of inflammation, preclusion of fibrosis, cirrhosis and hepato-cellular carcinoma and virus annihilation. In addition, diverse anti-viral therapies i.e.* ***all oral*** *and* ***sub-cutaneous*** *drugs have been administered with variable side effects. In recent times, different Non-Invasive markers (NIM's) have been introduced for the assessment of liver fibrosis which includes APRI Index, fibro test, forns test, fibrosis 4 (FIB-4) score etc.*
Objective: *The main aim and objective of the study is to compare the responses of* ***all oral*** *and* ***sub-cutaneous*** *drug treatment in chronic hepatitis C by using NIM's (FIB-4 Score and APRI Index).*
Method*: Eighty two patients with chronic hepatitis C participated in this research study. Patients were separated in to two distinctive groups i.e.* ***all-oral*** *and* ***sub-cutaneous*** *group of forty one pts each.* ***Non-probability sampling technique*** *was applied.* ***Non-invasive markers*** *i.e. APRI and Fibrosis 4 index were used to analyze the responses.* ***'Wilcoxon signed rank test'*** *and means were used to compare the responses.* ***Consent*** *was signed by the willing contributors. Privacy of the data was guaranteed to the respondents. For the analysis of the acquired data* ***SPSS 23.00 version*** *was used.*
Results: *In sub-cutaneous group, 21 males and 20 females took part having mean age bracket of 41-50 years. While in all-oral group, 14 males and 27 females participated with mean age of 41-50 years. According to the results evaluated, all-oral drugs were more effective in treating liver fibrosis.*
Conclusion: A*ll-oral drugs are highly effective in improving non-invasive markers representing liver histology.*
Keywords: *Non-invasive markers, chronic hepatitis C, all-oral drugs, Sub-cutaneous drugs, FIB-04 Score, APRI Index*

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I. Introduction

Globally, the chronic liver disease of differing etiologies is thought to be the most protuberant causes of morbidity and mortality [1-5]. Following distinctive pathological stages, chronic liver disease progresses from trifling hepatic inflammation devoid of fibrosis to advance hepatic cirrhosis and fibrosis [6-8]. Among chronic liver disease, chronic hepatitis C is the core streamline, which forms the foundation for fibrosis and cirrhosis [9]. In addition, diverse anti-viral therapies (i.e. all oral and sub-cutaneous drugs) have been administered posing variable side effects [10]. The gold- standard technique to access hepatic progression and histology is considered to be liver biopsy, which is one of the primogenital and precise technique. Besides, altered scoring system has also been established and reformed [11-14]. In recent times, different Non-Invasive markers (NIM's) have been introduced for the assessment of liver fibrosis. These NIM's are often used in clinical practice [15-18]. AST to platelet ration, FIB-4 score, APRI Index fibro test, forn's test are few NIMS's used currently [19-25].

The main aim and objective of the study is to compare the responses of all-oral and sub-cutaneous drug treatment in chronic hepatitis C infection by using NIM's (FIB-4 Score, APRI Index).

II. Literature Review

World-wide, hepatitis C infection is the chief cause of acute and chronic hepatitis. According to the assessment of World Health Organization (WHO), approximately 3% of the entire world's population is suffering from hepatitis C virus (HCV) globally, its predominantly chronic hepatitis C, affecting more than 180 million who are at the risk of advancing fibrosis or cirrhosis [26-28].

Chronic hepatitis C is treated by numerous components which encompass diminution of inflammation, preclusion of fibrosis, cirrhosis and hepato-cellular carcinoma and virus annihilation. Nowadays, the paramount

effective treatment is sustained virologic response (SVR) which functions as superlative [29, 30]. Even though treatment choices are predisposed by the genotype, combination therapy in contrast to monotherapy achieved advanced response rate [31-33].

Sofosbuvir (SOF) by category is a HCV NS5B polymerase inhibitor which causes inhibition of HCV replication and its life cycle. In addition, Sofosbuvir is an innovative direct-acting antiviral agent (DAA) which was permitted for management of chronic hepatitis C virus carrying infections for genotypes 1 to 4. In trail study, patients infected with HCV ought to receive PegIFN, RBV and SOF for approx 12 weeks and the data obtained from the study depicted results in SVR12 rates of 50%–90% [34-35].

III. Methodology

Eighty two patients with chronic hepatitis C participated in this research study, which took place at a **Baqai Medical University Hospital, Nazimabad Karachi from 2015-2018**. Non-probability sampling technique was applied. The patients were separated in to **two distinctive group's** i.e. **sub-cutaneous** and **all-oral group** of forty one pts. The patients in **all-oral group** received **SOF 400mg+daclatasvir 60mg once daily for 12-24 weeks, SOF 400mg+velpatasvir 100mg daily for 12 weeks and SOF 400mg+ RBV for 24 weeks** while **sub-cutanoeous group** received **PegIFN 180mg weekly+ SOF 400mg once daily+ RBV daily for 12 weeks**. The **dose of RBV depends on the weight of the patien**t. The patients with **weight <75kg received 1000mg** while on the other hand the pt with weight **>75kg received 1200mg of RBV**. **Non-invasive markers** i.e. **APRI and Fibrosis 4 index** were used to analyze the responses. **'Wilcoxon signed rank test' and means** were used to compare the responses. Consent was signed by the willing contributors. Privacy of the data was guaranteed to the respondents. For the **analysis of the acquired data SPSS 23.00 version was used**.

IV. Results

TABLE 1: DEMOGRAPHIC VARIABLE

		Subcutaneous Group		**All-oral Group**	
Characteristic		**N**	**%**	**N**	**%**
GENDER	Male	21	51.2 %	14	34.1%
	Female	20	48.78%	27	65.8%
AGE	12-20 years	2	4.8%	2	4.8%
	21- 30 years	2	4.8%	7	17.07%
	31-40 years	11	26.8%	8	19.5%
	41-50 years	13	31.7%	11	26.8%
	51-60 years	11	26.8%	5	12.1%
	61-70 years	1	2.4%	4	9.7%
	71-80 years	1	2.4%	4	9.7%
GENOTYPE	G1	6	14.6%	2	4.8%
	G2	Not recorded in this group	Not recorded in this group	1	2.4%
	G3	29	70.7%	26	63.4%
	G5	1	2.4%	Not recorded in this group	Not recorded in this group
	Unknown	5	12.1%	12	29.2%
MEDICATION	EXP	29	70.7%	10	24.3%
	NAÏVE	12	29.2%	31	75.6%

Table 1 shows the demographic variable for this research investigation. In this study, total 82 patients, diagnosed with chronic hepatitis C took part. These 82 patients were divided in to **sub-cutanoeus** and **all-oral groups**. In **sub-cutaneous group**, **21 males and 20 females** took part having **mean age bracket of 41-50 years**. Out of **41 patients**, type 1 genotype was seen in 6 patients, type 3 in 29 patients and type 5 in 1 patients while on the other hand genotype of 5 patients was not recorded. Furthermore, **12 patients** were administered with medicine for the very first time (**treatment Naive**) whereas **29** were medicated previously (treatment experienced) but the virus endured. While, in **all-oral g**roup, **14 males** and **27 females** participated with **mean age of 41-50 years**. As far as the genotype was concerned, type 1 was seen in 2 patient's type 2 in 1 patient and

type 3in 26 patients. Genotype of 12 patients was not recorded. Moreover, **31** patients were **treatment Naive** while **10** were **treatment Experienced**.

TABLE: 2 TEST STATISTICS

	After_FIB - Before_FIB	After_APRI - Before_APRI	After_FIB - Before_FIB	After_APRI - Before_APRI
Z	-5.086[b]	-3.091[b]	-4.228[b]	-5.132[b]
Asymp. Sig. (2-tailed)	.000	.002	.000	.000

a. Wilcoxon Signed Ranks Test
b. Based on positive ranks.

Hepatic fibrosis assessment at the end of the treatment by means of non-invasive markers in both the groups was analyzed by means of Wilcoxon signed rank test. Since, the probability value (p) for FIB-04 index in sub-cutaneous group as indicated in above table 2 is less than the alpha value (p=0.00, alpha <0.05, N=41), it suggests that data is statically significant. Correspondingly, the probability value for APRI index (p) in sub-cutaneous group is less than the alpha value (p=0.02, alpha <0.05, N=41) indicating the statically significant data. Likewise, in all-oral group, probability value (p) for FIB-04 and APRI index is less than the alpha value (p=0.00, alpha <0.05, N=41) which concludes that data is statically significant i.e. rejecting null hypothesis.

TABLE 3: DESCRIPTIVE STATISTICS

	Sub-cutaneous group (mean ± SD)	All-oral group(mean ± SD)
Fib-04 score	1.765±1.550	1.616±1.483
APRI score	1.389±2.149	0.574±0.476

According to results evaluated from the above table 3, all-oral antiviral drugs are more effective in treating liver fibrosis in contrast to sub-cutanoeous group in chronic hepatitis C patients.

V. Discussion

This research investigation illustrated that **all-oral drugs** are more efficient in treating fibrosis than the **sub-cutanoeous drugs** in CHC. The **customary therapy** of chronic HCV infection until 2011 was combination regimen of PegIFN and RBV for 24–72 weeks with 40–60% success rate with very high rates of adverse effects [36-38]. Introduction of first DAAs in 2011 was a game changer in eradication of hepatitis C as a major cause of liver disease [39]. In addition, by 2013, SOF was introduced as a HCV NS5B inhibitor and permitted for treatment of HCV infection as a combination therapy with PegIFN and RBV [35]. It has been investigated in different studies that **all-oral drug**s are more effective & tolerable in treating HCV RNA than the subcutaneous one [35,40, 41]. With knowing that the definitive HCV treatment will be available, there is an enormous distress to clear HCV infection until 2030 globally. On the other hand, there are key steps en route for obliteration of HCV which should be addressed in the program of HCV eradication including ; national screening programs for finding the patients with HCV infection, preventive strategies, accessibility and affordability of high effective regimens in developing countries, development of HCV vaccine and paying extraordinary consideration to special patient groups like that of thalassemia, HCV/HIV Co-infection kidney- disease and liver-transplant patients [39, 42].

VI. Conclusion

In conclusion, **all-oral drugs regimens are highly effective in improving NIMs representing liver histology.**

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