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EXPEDIENCY OF ORAL ANTIVIRAL MEDICINE FOR MANAGEMENT OF HEPATITIS C VIRUS (HCV) INFECTION IN CHILDREN

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Abstract:

Desired Objective: *Aspire of this study is to uncover the evidences of the usefulness of antiviral medicine typically Sofosbuvir/Ledipasvir for the treatment of Hepatitis C Virus (HCV) infection in children.*

Study Design: *Descriptive and Cross Sectional*

Duration and Setting: *Duration for this study was nine months starting from April, 2018 to March, 2019 and study was conducted in Pediatrics department of the Mayo Hospital Lahore.*

Methodology: *We enrolled patients, who were with diagnostics of positive Hepatitis C Virus (HCV) PCR and were the age of six to fifteen years after conducting and considering the histopathology and some examinations. The strength of the patients was 44 children having mean age of 10.52 years. Male patients were dominating with total of 28 boys and female were 16 girls. Made the Hepatitis C Virus (HCV) genotyping according to the affordability of the patients. Kept all the patients on the one dose of Sofosbuvir/Ledipasvir on daily bases. For the cases of cirrhosis established or INF-experienced, ribavirin added additionally. After four weeks of treatment, LFT and RFT of every patient were taken and after twelve weeks PCR was performed. Treatment was comprised on total 12 weeks and with the extension of 24 weeks for cirrhosis established. For analyzing the collected data, the software used was SPSS v-20.*

Results: *Among all genotypes, genotype-1 was the leading type having 75 percent. 44 patients attained sustained virological response SVR-12 having 90.9 percent and rest four patients got partial virological response having 9.1 percent. Associated Hepatitis B Virus (HBV) was detected in ten patients and these patients were treated Entecavir for the whole period of treatment. All the patients attained sustained virological response SVR-12 with decrease in little of HBV while cases of INF-experienced were responsive with sustained virological response SVR-12 that were 14 patients with 31.8 percent.*

Conclusion: *Oral antiviral (90 Sofosbuvir 400 mg or Ledipasvir 90mg) is effectively useful for the management of Hepatitis C Virus (HCV) infection in children.*

Keyword: *Hepatitis C virus (HCV), Sofosbuvir or Ledipasvir, Pediatrics, Genotype, Antiviral.*

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INTRODUCTION:

In all over the world, Hepatitis C virus (HCV) is prevailing with considerable occurrence rate and is responsible for the majority of the health issues. With respect to the statistics of one report of the World Health Organization (WHO) 170 million population is victim of Hepatitis C virus (HCV). In this report there was no typical information about the pediatrics given however current review by World Health Organization (WHO) contains this data. About 13.2 million children are with positive Hepatitis C virus (HCV) [1]. Treatment for Hepatitis C virus (HCV) enhanced significantly when direct acting antiviral drug was approved first time for treatment of HCV in year 2011. For the treatment of HCV, there are more than ten régimes got license for adult patients. Every régime in this treatment can get more than 90 percent sustain virological response (SVR) after the management of twelve weeks. In these days even chronic Hepatitis C virus (HCV) in adults can easily be treated [2]. When we consider the pediatric patients of Hepatitis C virus (HCV), up to now there was single régime present i.e. interferon combined with ribavirin therapy sustain virological response (SVR) was not as per the required response. Genotype-1 and genotype-4 had the sustain virological response (SVR) up to 64 percent and was less than this where the chronic infection persisted and noted up to 50 percent. On the other hand, the genotype-2 and genotype-4 sustain had virological response (SVR) of 89 percent. Along with this, interferon combined with ribavirin therapy had the requirement of long treatment period containing 24 to 48 weeks and very restricted follow-up. Interferon combined with ribavirin therapy had disadvantage of a number of side-effects which can be cause of perthitic amenability or dictate the change in dose of the patients [3, 4]. For the treatment of Hepatitis C virus (HCV) in younger patients > 12 years, FDA made the approval of usage of Sofosbuvir or Ledipasvir in 2017. More researches appraised the usage of Sofosbuvir or Ledipasvir for the age of 6 to 11 years and got the efficient and safe results [5, 6]. Keeping these considerations in mind we opted to adopt this therapy and to analyze it usefulness for the management of Hepatitis C virus (HCV) in patients of six to fifteen years. Aim of this study is to uncover the evidences of for the usefulness of antiviral medicine typically Sofosbuvir/Ledipasvir for the treatment of Hepatitis C Virus (HCV) infection in children [7, 8].

METHODOLOGY:

We enrolled patients, who were with diagnostics of positive Hepatitis C Virus (HCV) PCR and were the age of six to fifteen years after conducting and considering the histopathology and some examinations. The strength of the patients was 44 children having mean age of 10.52 years. Male patients were dominating with total of 28 boys and female were 16 girls. All the patients with positive reports of PCR were referred for interviews to the departments of Gastroenterology and Hepatology of Mayo Hospital Lahore. Before the start of treatment, LFT, ALT, AST, abdominal ultrasound and alkaline phosphatase tests of every patient were taken. Made the Hepatitis C Virus (HCV) genotyping according to the affordability of the patients. Kept all the patients on the one dose of Sofosbuvir400 mg or Ledipasvir 90 mg on daily bases. Dose was adjusted to half for the patients less. For the cases of cirrhosis established or INF-experienced, ribavirin 10-15 mg/kg/day additionally added. After four weeks of treatment, LFT and RFT of every patient were taken and after twelve weeks PCR was performed. Treatment was comprised on total 12 weeks and with the extension of 24 weeks for cirrhosis established. For analyzing the collected data, the software used was SPSS v-20.

RESULTS:

The number of the patients for this study was 44 children having mean age of 10.52 years. Male patients were dominating with total of 28 boys and female were 16 girls. Made the Hepatitis C Virus (HCV) genotyping according to the affordability of the patients. Only 24 having percentage of 54.50 percent among total was in position to undergo genotyping. Among all genotypes, genotype-1 was the leading type containing the 18 patients having 75.00 percent, and from them 16 were of genotype-1A and 2 were of genotype-1B. Rest six patients were of genotype-4.

Table-1 Genre of Patients

Patients Gender	Number	Percentage
Boys	28	63.63%
Girls	16	36.37%
Total	**44**	**100%**

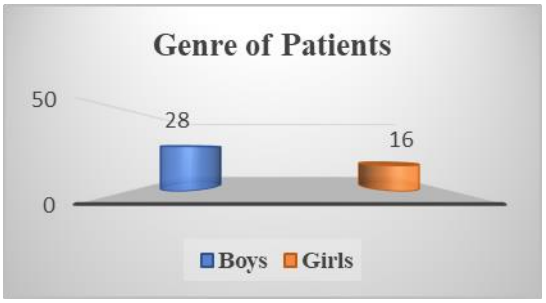


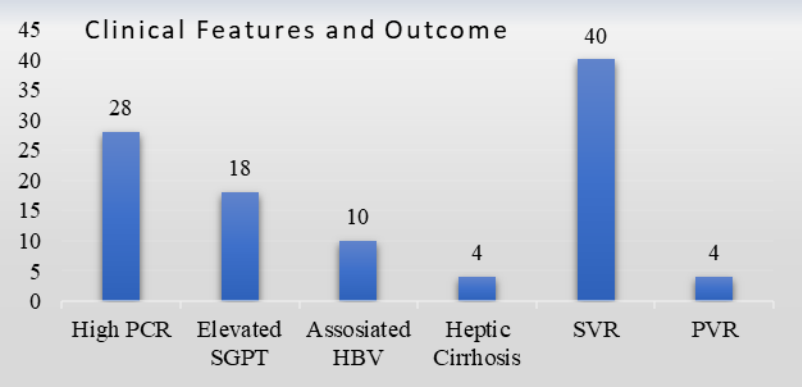
Table-2 Genotyping of HCV

Genotype	Patients	Percentage
Genotype-1	18	75.00 %
Genotype-2	0	-
Genotype-3	0	-
Genotype-4	06	25.00%
Total	**24**	**100%**

The 28 patients were with high level of PCR of > one 800,000 IU/ ml while the mean, minimum and maximum levels were 9,016,862 IU/ml, 4,871 IU/ml and 35,175,925 IU/ml. In 18 patients having percentage 40.90 percent, SGPT levels were raised up. The 14 patients having percentage of 31.80% were with the history of previous treatment of HCV with interferon among these cases 8 cases were with non-responding behavioral response, 2 cases were such that were not able to endure the side effects of interferon and 4 patients had to discontinue their treatment because they had got autoimmune hepatitis in the period of treatment. In these patients, 86.00% patients were of genotype-1 and 14.00% were of genotype-4. Associated Hepatitis B Virus (HBV) was detected in 10 patients and these patients were treated Entecavir or Tenofovir for the whole period of treatment.

Table-3 Clinical Features and Outcome After Use Sofosbuvir/Ledipasvir

Presentations	Patients	Percentage
High Level of PCR	28	63.63%
Elevated SGPT Levels	18	31.80%
Associated HBV	10	22.72%
Established Hepatic Cirrhosis	04	09.90%
Sustained Virological Response after Treatment	40	90.90%
Partial Virological Response after Treatment	04	9.10%



Four patients were with established hepatic cirrhosis and these patients were with history of acute lymphoblastic leukemia and had associated Hepatitis B Virus (HBV). After the period of treatment 40 patients attained sustained virological response SVR-12 having 90.9 percent and rest four patients got partial virological response having 9.1 percent. All the patients attained sustained virological response SVR-12 with decrease in little of HBV while cases of INF-experienced were responsive with sustained virological response SVR-12 that were 14 patients with 31.8 percent. In our study the management there was good tolerating trend with only single case of headache.

DISCUSSION:

Even there is great advancement is occurred in the treatment of Hepatitis C virus HCV for the patients of elder ages, very inadequate is for the younger age patients [9]. In all over the world, for the treatment of Hepatitis C virus HCV there is a revolutionary change occurred in the shape of innovative oral antiviral medicines. Since for the treatment of Hepatitis C virus (HCV) in younger patients > 12 years, FDA made the approval of usage of Sofosbuvir or Ledipasvir in 2017. More researches appraised the usage of Sofosbuvir or Ledipasvir for the age of 6 to 11 years and got the efficient and safe results. In other two studies the participants were also five and six year was starting age while other were fifteen and sixteen year. The mean age for these studies was 12.50 years and here also male patients were dominating with the ratio male vs female was near two ratio one. The diagnosis of Hepatitis C virus HCV for this study was made by blood or transfusion of blood product. Modern-day presentations show that major cause of HCV infection is vertical transmission. But in advance regions of the world for the reason of the functioning screening of blood this infection has reduced, for example in United State of America. And that is the reason behind very little amount of cases of HCV were found in children from the year of 1994 [10]. Outcomes of studies of these regions are very changed from the outcomes of studies in those regions which contains evolving countries. Studies here in these regions showed that the major reason of Hepatitis C Virus (HCV) infection was the infection which is blood based [11, 12].

Another reason of Hepatitis C Virus (HCV) infection is transfusion of blood which is observed remarkably in the cases of repeated transfusion of blood. Result of different studies are 67.32% patients were infected with HCV in Iraq, 40.72% in Jordan, 40.00% in Saudi Arabia and 42.41% in Morocco [13]. Almost all patients of our concern were infected due to these two reasons; blood based or transfusion of blood. For the reason of affordability of the almost half patients were undergone by genotyping. Only 24 having percentage of 54.50 percent among total was in position to undergo genotyping. Among all genotypes, genotype-1 was the leading type containing the 18 patients having 75.00 percent, and from them 16 were of genotype-1A and 2 were of genotype-1B. Rest six patients were of genotype-4. On the other hand, in the study of Hussein NR et al the percentage of genotyping was 23.00% patients were of genotype-1, 2.30% patients were of genotype-2, 20.92% patients were of genotype-3 and 53.00% patients were of genotype-4 [14]. The results of a methodical assessment for the prevalence of Hepatitis B Virus reflects that most leading type was the genotype-4 after this genotype-1 and thirdly genotype-3. From this study we can conclude that in the gulf the most dominating type is the genotype-4 and on the other hand it also can be considered that in subcontinent the dominating type is genotype-1 and genotype-3 rather than genotype-4. But in our study the dominating type was genotype-4 [15]. One study shows that the genotype-1 is the more complicated to manage and it has sustained virological response SVR-12 up to 64 % whereas genotype -2 and genotype -3 has sustained virological response SVR-12 up to 85 % [16]. When the treatment of anti-viral added with the treatment

that was of associated Hepatitis B Virus, this may be the reason of flaring up the Hepatitis B Virus [17,18]. In our case upon completing the treatment there was no record of any flaring up and these outcomes of our study are similar with the study of Liu CJ et al, there was a 100% SVR-12 [19]. According to the Aziz H et al the level of Viremia linked with response to anti-viral oral medicines but in our case, the patients who were with the high level of Viremia i.e. > 800,000 IU/ml, got the full SVR with about the total of patients [20]. On the other hand, a handsome amount of the studies concluded that lower viral load expects a good response with management which contained the INF-treatment, insufficient were interrelated with the oral antiviral [21,22]. In our study the management there was good tolerating trend with only single case of headache neglecting the results of some other studies which have a series of small side-effects just like these side-effects were common in these studies vomiting, nausea, abdominal pain, headache, oropharyngeal pain, diarrhea, fatigue, pyrexia and cough. The older treatments gained the maximum SVR only reaching up to 64 % and having the lower limit of 50% response but the most noticeable aspect of our study is its SVR of 90.90% and result of our study is similar to results of studies which have SVR of 97.14% and 99% [23]. Some similar outcomes were got in adult patients who have got treatment for 24 months were with cirrhosis [24]. The results of our study are appealing results that can be supportable for the elimination of HCV in children by using the Sofosbuvir or Ledipasvir like these oral ani-viral are used for the adults.

CONCLUSION:

Oral antiviral (90 Sofosbuvir 400 mg or Ledipasvir 90mg) is effectively useful for the management of Hepatitis C Virus (HCV) infection in children for the years of above six years and less than seventeen years. Also, more studies can be conducted on the use of Sofosbuvir or Ledipasvir for the children of the age between three to six years.

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