



EFFICACY OF THE SOFOSBUVIR AND LEDIPASVIR IN TREATMENT OF CHILDREN SUFFERING FROM INFECTION OF HEPATITIS C VIRUS

¹Dr Muhammad Mubeen Qayyum, ²Dr Siddique Abbas, ³Dr Danish Nawaz
¹Medical Officer, RD Basti Nawaz Khan Rind Zahir Peer Tehsil Khanpur, District Rahim Yar Khan
²Medical Office, RHC Habibabad Tehsil Pattoki, District Kasur
³Medical Officer, DHQ Lodhran

Abstract:

Objectives: The aim of this research work is to find out the effectiveness of the oral antiviral (Sofosbuvir/Ledipasvir) in the treatment of the children suffering from hepatitis C virus infection.

Methodology: This research work carried out in the Pediatrics department of Shaikh Zayed Medical College and Hospital Rahim Yar Khan from June 2018 to March 2019. All the patients with positive Polymerase Chain Reaction (PCR) of HCV having age from 7 to 18 years were the part of this research work. Background history, clinical assessment and examination of the patients carried out. The genotyping of HCV was also carried out. We gave Sofosbuvir or Ledipasvir to all the patients of this research work on daily basis. We also added the Ribavirin for the patients who were INF-experienced or present with the established liver cirrhosis. We carried out the follow up with the function of liver, function of kidney and Polymerase Chain Reaction (PCR) at twelve week of treatment and then after the 12 week. The Total duration of this treatment was twelve weeks which increased to twenty-four weeks in some patients who were present with established liver cirrhosis. SPSS V.20 was in use for the statistical analysis of the collected information.

Results: There were total twenty-two patients with an average age of 12.50 years, 63.60% (n: 14) patients were male and 36.40% (n: 8) patients were females. The most dominant genotype was genotype-1 (75.0%). We achieved the sustain virological response-12 in 90.90% (n: 20) patients, remaining 9.10% (n: 2) patients were present with partial response of HCV. We found the co-infection of HBV in 5 patients, in the duration of treatment all these patients kept on the Entecavir. All the patients obtained sustain virological response-12 for hepatitis C virus with the reduction in the power of HBV infection. Even the patients with INF-experienced (seven patients, 31.80%) were available as responsive with the sustain virological response-12. There was well toleration to the treatment.

Conclusion: Sofosbuvir or ledipasvir has much effectiveness in the treatment of the HCV infection among children and this treatment is well-tolerable.

KEYWORD: Liver Cirrhosis, Sofosbuvir, Entecavir, Co-Infection, Genotyping, Kidney, Ribavirin.

Corresponding author:

Dr. Muhammad Mubeen Qayyum,
Medical Officer, RD Basti Nawaz Khan Rind Zahir Peer Tehsil Khanpur,
District Rahim Yar Khan

QR code



Please cite this article in press Muhammad Mubeen Qayyum et al., *Efficacy Of The Sofosbuvir And Ledipasvir In Treatment Of Children Suffering From Infection Of Hepatitis C Virus.*, Indo Am. J. P. Sci, 2019; 06(12).

INTRODUCTION:

HCV infection is very serious issue in the whole world. According to the information of WHO, there was occurrence of infections due to HCV in more than seventy-one million people of the world in 2015. There was no data about the children in that report. In another report, WHO stated that there is an estimation of incidence of antibody of HCV in pediatrics as 13.20 (with a range from 11.50 to 21.20) million children. The treatment of the HCV stated from the direct antiviral medicine in 2011. There is license of greater than ten regimens for the treatment of the HCV infection in adult patients. Every regime can obtain sustain virological response greater than 90.0% with only a treatment of twelve weeks. Now, it is much easy to treat the HCV in adult patients. For the pediatric patients, a single regimen available was interferon and/or ribavirin regimen. Sustain virological response of this regimen was much lower than the requirement as for genotype-1 and genotype-4 the value of sustain virological response touched to 64.0% but it may be even lower reaching to only fifty percent when there was much high viral load. Whereas genotype-2 and genotype-3, sustain virological response value was 89.0%.

There are many side effects with the use of the Interferon and/or ribavirin that results adverse compliance or necessitate the modification of the dose. Five different research works assessed the use of these medicines for the children from six to eleven year of age and found effectiveness and safety. This research work also used this treatment method among children of greater than six year of age to check the effectiveness of this treatment.

METHODOLOGY:

All the patients who got admission in the Pediatrics department of Shaikh Zayed Medical College and Hospital Rahim Yar Khan with positive polymerase chain reaction (PCR) of HCV from June 2018 to March 2019 were the part of this research work. Medical assessment, physical examination and history about the patients gathered. We also gathered the information about the complete count of blood, total level of serum bilirubin, AST, alkaline

phosphates, ALT, ultrasound of the abdomen cavity and genotyping of HCV. We gave the Sofosbuvir 400.0 milligram/Ledipasvir 90.0 milligram once in a day. If the age of the patient was lower than twelve years then we gave the half dose. We also added Ribavirin 10-15 mg/kg per day if the patient was present with the established liver cirrhosis.

We performed the follow up of all the patients for the function of liver and kidneys in fourth week of the treatment. We carried out the Polymerase Chain Reaction (PCR) at twelve weeks and then after the 12th week (Sustain Virological Response-12). The complete duration of the treatment was twelve weeks. This duration was prolonged to twenty-four weeks in the patients who were present with the established liver cirrhosis. SPSS V. 20 was in use for the statistical analysis of the collected information.

RESULTS:

There were total twenty-two patients of this research work. The average age of the patients was 12.50 years. There were total 63.60% (n: 14) male and 36.40% (n: 8) were the female patients. HCV genotype was carried out by 54.50% (n: 12) patients only because of the financial issues. Nine patients among them were present with genotype-1 (75.0%); all these patients were genotype-1a except one patient who was present with the genotype-1b. Remaining 3 patients were genotype-4. The level of Polymerase Chain Reaction (PCR) was much high (greater than one 800000 IU/ml) in 63.60% (n: 14), average level was 9016862 IU/ml, lowest level was 4871 IU/ml and highest was 35175925 IU/ml. There was elevated SGPT in 40.90% (n: 9) patients. Twenty patients were present with history of transfusion of blood. Total seven patients were present with previous treatment with the usage of Interferon. The co-infection of HBV was present in five patients; they also got treatment with the Entecavir and/or Tenofovir in the duration of this treatment period. Two patients were present with the established liver cirrhosis. Among them, one patient got the treatment of Interferon but stopped the treatment after few months due to no response.

Table I: Gender Distribution of Sample (n=22)

Gender Distribution		No	Percent
Gender	Male	14	63.6
	Female	8	36.4

At the end of the treatment, we found the negative Polymerase Chain Reaction (PCR) in 90.90% (n: 20) patients, remaining 2 patients were present with the low virological response. The patients with established cirrhosis got the treatment for twenty-four weeks. All the patients tolerated this treatment, only one patient reported the complication of headache. This was because of the sinusitis that got treatment but there was no interruption in the treatment.

DISCUSSION:

HCV infection is the serious issue of the health in the whole world. There is revolution in the treatment of HCV with the invention of many antiviral drugs. In this current research work, the youngest patient was of six year of age but in another research work conducted in Pakistan used these regimens on the patients of five year of age and above and got the favorable results. The male is dominant in quantity similar to the reports from UK, Canada and USA. In USA, there is no pediatric patient obtained HCV infection from blood born after the 1994. This finding is much opposite with the findings of the research works conducted in countries which are under development. There was high occurrence of the HCV infection among the patients who got repeated transfusion of blood; approximately 67.30% in Iraq, 40.0% in Saudi Arabia, 40.70% in Jordan and 42.40% in Morocco. Only half of the patients were able to perform the genotyping (54.50%) because of the financial issues. The most dominant genotype was Genotype-1 followed by the Genotype-4; there was no case of genotype- 2 or genotype-3.

Research work conducted in the past in our country showed that in the south areas of the country, 50.0% samples were present with the Genotype-1 whereas 35.0% were present with genotype-4. While one other research work from the north areas discovered that 53.0% patients were present genotype-4, whereas genotype-1 was present in 23.0% and 20.90% for genotype-3 and finally genotype-2 in 2.30%.

The genotype-4 is much common in Egypt but in India and Nepal, genotype-1 and genotype-3 are much dominant as compared to the other genotypes. According to some research works of the past, the treatment of the genotype-1 is much difficult with the Ribavirin. The therapy with the oral medication can flare up the infection of HBV; hence all the patients suffering from HBV infection got the treatment for anti-HBV. Most of the patients got favorable outcome at the end of the research work. This finding is much consistent with the outcome of the research work conducted in Taiwan. The factor of extent of Viremia has relation with the response to oral antiviral. There are some limitations of this research

work as the sample size of this research work was much short. We were unable to perform genotyping for all the patients due to high financial costs.

CONCLUSION:

Ledipasvir or sofosbuvir are very effectual in the treatment of the hepatitis C virus infection among the small aged children. This treatment is also much tolerable among them. There is a requirement of more research works to check its usage of younger age children having age from 3 to 6 years.

REFERENCES:

1. Quintero, J., Juampérez, J., Julio, E., Cabello, V., Mercadal-Hally, M., Soler-Palacín, P., ... & Rodrigo, C. (2019). Ledipasvir/sofosbuvir combination for chronic hepatitis C infection in children and adolescents. *Anales de Pediatría (English Edition)*, 90(3), 141-147.
2. Nwaohiri, A., Schillie, S., Bulterys, M., & Kourtis, A. P. (2018). Towards elimination of hepatitis C virus infection in children. *The Lancet Child & Adolescent Health*, 2(4), 235-237.
3. Padhi, S., Maharshi, S., Gupta, G. K., Garg, K., & Nijhawan, S. (2018). Efficacy and safety of direct acting antiviral therapy for chronic hepatitis c in thalassemic children. *Journal of pediatric hematology/oncology*, 40(7), 511-514.
4. Marascio, N., Mazzitelli, M., Pavia, G., Giancotti, A., Barreca, G. S., Costa, C., ... & Casalnuovo, F. (2019). Clinical, Virological Characteristics, and Outcomes of Treatment with Sofosbuvir/Ledipasvir in Two Pediatric Patients Infected by HCV Genotype 4. *Cells*, 8(5), 416.
5. El-Araby, H. A., Behairy, B. E., El-Guindi, M. A., Adawy, N. M., Allam, A. A., Sira, A. M., ... & Salem, M. E. (2019). Generic sofosbuvir/ledipasvir for the treatment of genotype 4 chronic hepatitis C in Egyptian children (9–12 years) and adolescents. *Hepatology international*, 1-9.
6. Squires JE, Balistreri WF. Hepatitis C Virus Infection in Children and Adolescents. *Hepatol Commun*. 2017;1(2):87–98. doi: 10.1002/hep4.1028
7. El-shabrawi MH, Kamal NM. Burden of pediatric hepatitis C. *World J Gastroenterol*. 2013;19(44):7880–8. doi:10.3748/wjg.v19.i44.7880
8. El-Guindi MA. Hepatitis C Viral Infection in Children: Updated Review. *Pediatr Gastroenterol Hepatol Nutr*. 2016;19(2):83–95. doi: 10.5223/pghn.2016.19.2.83

9. Daw MA, Dau AA. Hepatitis C virus in Arab world: a state of concern. *Sci World J.* 2012; 2012:719494. doi:10.1100/2012/719494
10. Hussein NR, Tunjel I, Basharat Z, Taha A, Irving W. The treatment of HCV in patients with haemoglobinopathy in Kurdistan Region, Iraq: A single centre experience. *Epidemiol Infect.* 2016;144(8):1634–1640. doi: 10.1017/S0950268815003064
11. Mohamoud YA, Riome S, Abu-raddad LJ. International Journal of Infectious Diseases Epidemiology of hepatitis C virus in the Arabian Gulf countries: Systematic review and meta-analysis of prevalence. *Int J Infect Dis.* 2016; 46:116-125. doi: 10.1016/j.ijid.2016.03.012
12. Manns MP, Wedemeyer H, Cornberg M. Treating viral hepatitis C: Efficacy, side effects, and complications. *Gut.* 2006; 55:1350- 1359. doi: 10.1136/gut.2005.076646
13. Aggeletopoulou I, Konstantakis C, Triantos C, Manolakopoulos S. Risk of hepatitis B reactivation in patients treated with direct-acting antivirals for hepatitis C. *World J Gastroenterol.* 2017; 23:4317–4323. doi: 10.3748/wjg.v23.i24.4317
14. Wang C, Ji D, Chen J, Shao Q, Li B, Liu J, et al. Hepatitis due to Reactivation of Hepatitis B Virus in Endemic Areas Among Patients with Hepatitis C Treated with Direct-acting Antiviral Agents. *Clin Gastroenterol Hepatol.* 2017;15(1):132–136. doi: 10.1016/j.cgh.2016.06.023
15. Liu CJ, Chuang WL, Sheen IS, Wang HY, Chen CY, Tseng KC, et al. Efficacy of Ledipasvir and Sofosbuvir Treatment of HCV Infection in Patients Coinfected with HBV. *Gastroenterology.* 2018;154(4):989–997. doi: 10.1053/j.gastro.2017.11.011
16. Aziz H, Aziz M, Gill ML. Analysis of Host and Viral-Related Factors Associated to Direct Acting Antiviral Response in Hepatitis C Virus Patients. *Viral Immunol.* 2018;31(3):256-263. doi: 10.1089/vim.2017.0124.
17. Indolfi, G., Hierro, L., Dezsofi, A., Jahnel, J., Debray, D., Hadzic, N., ... & Smets, F. (2018). Treatment of chronic hepatitis C virus infection in children: a position paper by the Hepatology Committee of European Society of Paediatric Gastroenterology, Hepatology and Nutrition. *Journal of pediatric gastroenterology and nutrition*, 66(3), 505-515.
18. German, P., Mathias, A., Brainard, D., & Kearney, B. P. (2016). Clinical pharmacokinetics and pharmacodynamics of ledipasvir/sofosbuvir, a fixed-dose combination tablet for the treatment of hepatitis C. *Clinical pharmacokinetics*, 55(11), 1337-1351.
19. Murray, K. F. (2017). Hepatitis C Virus Infection in Children. *Gastroenterology & hepatology*, 13(3), 184.