Perspective

Hepatitis C Drugs Made in Pakistan

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Abstract:
Hepatitis C is among the most prevalent liver diseases in the world caused by hepatitis C virus and it further predisposes the patient to liver cancers. This virus is transmitted through the use of infected syringes, infected blood transfusions and sexual contact with affected individuals. This disease is asymptomatic initially but may follow an acute or chronic progressive course. Pakistan has a significant ratio of hepatitis affected patients with every one out of 20 individuals being seropositive. The treatment of hepatitis and its success is dependent upon the early diagnosis of the disease through the identification of anti HCV antibodies and further disease confirmation by detection of HCV RNA through nucleic acid amplification tests. Ferozsons pharmaceutical company is credited with the introduction of effective Hepatitis C treatments in Pakistan which were initially were expensive. However, with the development of new and better medicines the cost reduced effectively and the treatment is now affordable by people with low income. Many actions have been taken at the government level which have made mass screening of the individuals along with appropriate and timely supply of medications possible. Another important step in eradicating Hepatitis C is the education of the public by advertisements, seminars and HCV courses conducted by specialists. Project ECHO deserves mention, as it shows that people treated according to ECHO methodology have better prognosis than the others.

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Introduction:

Hepatitis C is a disease caused by the Hepatitis C virus (HCV). The virus can cause both acute and chronic hepatitis[1]. In many patients of chronic hepatitis symptoms do not appear initially. The virus is transmitted via blood borne route i.e. via infected syringes[2], through blood transfusion and unsafe sexual practices[3]. A number of patients with chronic Hepatitis C can develop hepatocellular carcinoma[4].

Hepatitis C is found throughout the world. The greatest prevalence is found in the WHO Eastern Mediterranean region and the WHO European region (2.3% and 1.0% respectively). Prevalence of HCV in other WHO regions varies from 0.5 to 1.0%. In countries which were lacking in infection control, HCV infection is seen widespread in the general population. India exhibits a seroprevalence of 0.9% whereas Egypt exhibits a seroprevalence of 22%[4]. Pakistan has been facing an HCV epidemic of historical proportions, one person in every 20 Pakistanis is infected[5]. In Pakistan HCV contributes a major share to the liver disease burden. Unfortunately, in most of the cases, the virus is acquired through the health care procedure[6]. No decrease in HCV disease burden has been observed during the last 3 decades.

The determination of virus genotype has significant consequences on the therapy response and disease management. Therefore, it is essential for the prevalent genotype of HCV in a region to be documented. The prevalent HCV genotype in Pakistan is 3a (58.16%), followed by 3b (9.05%), 2a(6.70%), 1a(6.22%) and 1b(2.39%)[7].

Both Interferon and Sofosbuvir have seen to be effective against genotype 1a but treatment with Sofosbuvir has fewer adverse effects and more tolerability. Direct-acting antivirals (DAAs) have revolutionized the treatment of hepatitis C. This newer class of drugs targets

specific steps in viral replication. DAAs have shorter treatment times, fewer side effects and higher SVR rates than other drugs[8].

WHO aims to eliminate the virus by the end of 2030[9]. This can be achieved only be mass screening and administration of timely treatment as no vaccine for HCV has been developed yet. The mainstay of screening for HCV is to screen for anti-HCV antibodies in the high-risk group. The serum cut-off ratio value indicates if there is need of supplemental assay to confirm initially reactive test. The confirmed diagnosis is based upon the detection of HCV RNA in the serum of affected patient i.e. upon the nucleic acid amplification test (NAAT)[10].

Project ECHO stands for "Extension for Community Healthcare Outcomes". It is a collaborative model of medical education and care management that empowers clinicians everywhere to provide better care to more people, right where they live. Project ECHO aims at reforming and enhancing the way education and knowledge are delivered to reach more people in villages and underprivileged communities. Project ECHO with international affiliation has trained a number of physicians across Pakistan in liver diseases management. Health Net Pakistan is implementing Project ECHO in Pakistan for Hepatitis and Liver care.

Ferozsons in collaboration with HealthNet has organized various activities and events under the project ECHO to raise awareness among the general public about liver disease emphasizing in particular on Hepatitis B and C with respect to their immunization, symptomatology and treatment. Students and children (particularly those belonging to rural areas) were engaged via various activities and story-telling to deliver to them the information in an effectively manner.

In addition to this, Ferozsons has now also collaborated with HealthNet Pakistan to provide an innovative Diabetes management and training Continuous Medical Education (CME) programme for the primary care healthcare professionals. The pharmaceutical company has played a significant role in checking the Hepatitis C disease burden in Pakistan with the timely introduction of cost-effective drugs.

This article aims at discussing the timeline of anti-HCV drug introduction and development in Pakistan's pharmaceutical scenario and elaborates the strategies for elimination of the virus from among the masses.

Objectives:

The purpose of this study is to achieve high cure rates through standardized medicines and to overcome traditional limitations in documentation and performance / outcome measures through the use of an integrated EMR platform. The documentation of the diagnosis, treatment, compliance and cure and to use standardised treatment protocol for curing patients. All these efforts will play major role to achieve the main aim i.e. the elimination of this disease from our country.

Discussion:

HCV Treatment Program:

New infection with HCV gets cured by person's own immune reaction, therefore it doesn't need any treatment. Notwithstanding, when HCV disease gets persistent, treatment is important. The aim of Hepatitis C treatment is to cure the disease.

In July 2018, WHO updated its "Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C infection." WHO's updated 2018 guidelines suggest treatment with Pan-genotypic direct-acting antivirals (DAAs). DAAs can treat most people with HCV infection, and treatment span is short (generally 12 to 24 weeks), depending upon the presence of cirrhosis of Liver.

WHO suggests treating all people with chronic HCV disease beyond 12 years old with Pan-genotypic DAAs. These DAAs are expensive in high income countries. Nonetheless, they have become less expensive in many nations with low income, because of different generic versions of these drugs.

Treatment Journey in Pakistan:

In 2006 Ferozsons and Bago enter into a Joint-venture. In this way, in Pakistan through this joint-venture with Bago group established production of generic Interferon. In 2010, Pegylated Interferon started to process here locally. Later in 2014, there was a landmark achievement to introduce Sofosbuvir in Pakistan under a special program at 1% of the USA cost. The production of first locally and officially licensed Sofosbuvir generic

by Ferozsons started in 2016. In the next year Sofosbuvir–Ledipasvir and Sofosbuvir–Velpatasivir were introduced on named patient basis and Daclatasvir was also launched.

Generics Expanded Access to Treatment:

As different generics was introduced, the treatment became more affordable and a larger patient population started to benefit. Sofosbuvir was available at a rate of almost $300 in year 2015 and in the next year, further generic forms started to reduce the expense, ranging from $30-$58. Later, the owning company, Gilead, licensed generic forms. The treatment then cost $40-55. The single pill treatment became affordable to the extent of $140 and China sourced Sof / Dac were available at the rate of $30-45. The availability of different affordable generic forms increased the number of patients getting treatment from 65000 to almost 250k-400k. In this way, the disease became cheaper to treat with time.

Work with Government:

The big goal is now to work with government, to increase the number of people getting screened in early stages and getting treatment by threefold. Mass screening is a big factor in this pathway and requires capacity building. An End to End Test-Treat-Cure Program needs to be developed where the centre should be equipped with HCV-EMR (HCV-electronic medical records) systems and proper screening should be done and as the patient is diagnosed with HCV infection at chronic stage, the patient should get documented and provided with medicine at the same centre. To ensure follow up, the patient will be advised to come back to take new medicine after submitting the empty bottles in subsequent month's visit.

Educate to Eliminate:

Different programs about awareness and as well as management are important to involve the public, health care providers and medical professionals and to expand the treatment scale. KOLs (Key Opinion Leaders) can spread the word and influence a larger audience. Advertisements on the screen can also be very effective.

Seminars with emerging physicians will catch their attention and their interest in this field will be of great benefit to the community. HCV courses for PCPs in partnership with GI societies can be started in highest prevalence districts first.

Project ECHO through Government:

Project ECHO (Extension for Community HealthCare Outcomes) is a collaborative model of medical education and care management that empowers clinicians everywhere to provide better care to more people, right where they live. Through this program, awareness is provided in School and students from different medical institutes volunteer for the awareness campaigns. Doctors as well as medical students educate school going children about the spread as well as prevention from Hepatitis C. Healthcare providers also get training to better treat the disease under this project. Project ECHO has been accepted by the whole world as an effective tool to improve patient care. Published data shows that patients who got care from the health care providers trained under ECHO training programs had better outcomes than those treated at specialized referral hospitals, with no such training. Government can help a great deal in managing it for HCV.

Conclusion:

Hepatitis C is one of the most serious liver infections leading to hepatocellular carcinoma. However, the hepatitis can be effectively treated through the use of various medications that have been developed and are improving with time. The treatment of hepatitis C by the using appropriate medications require timely and accurate diagnosis through screening of anti HCV antibodies as well as the knowledge of the specific virus genotype causing the disease. Ferozsons has introduced new anti-viral hepatitis medications and is developing them at local level. In order to achieve the WHO aim of worldwide eradication of Hepatitis C by 2030, association with the government is essential in order to mass screen, treat and further prevent the recurrence in patients as well as to educate the public about this disease.

References:

1. Indolfi G, Easterbrook P, Dusheiko G, El-Sayed MH, Jonas MM, Thorne C, et al. Hepatitis C virus infection in children and adolescents. Lancet Gastroenterol Hepatol. 2019;4(6):477-487.
2. Sweeney S, Ward Z, Platt L, Guinness L, Hickman M, Hope V, et al. Evaluating the cost-effectiveness of existing needle and syringe programmes in

preventing hepatitis C transmission in people who inject drugs. Addiction. 2019;114(3):560-570.

3. Ramière C, Charre C, Miailhes P, Bailly F, Radenne S, Uhres AC, et al. Patterns of Hepatitis C Virus Transmission in Human Immunodeficiency Virus (HIV)-infected and HIV-negative Men Who Have Sex With Men. Clin Infect Dis. 2019;69(12):2127-2135.
4. Gupta E, Bajpai M, Choudhary A. Hepatitis C virus: Screening, diagnosis, and interpretation of laboratory assays. Asian J Transfus Sci. 2014;8(1):19-25.
5. Al Kanaani Z, Mahmud S, Kouyoumjian SP, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Pakistan: systematic review and meta-analyses. R Soc Open Sci. 2018;5(4):180257.
6. Arshad A, Ashfaq UA. Epidemiology of Hepatitis C Infection in Pakistan: Current Estimate and Major Risk Factors. Crit Rev Eukaryot Gene Expr. 2017;27(1):63-77.
7. Haqqi A, Munir R, Khalid M, Khurram M, Zaid M, Ali M, et al. Prevalence of Hepatitis C Virus Genotypes in Pakistan: Current Scenario and Review of Literature. Viral Immunol. 2019;32(9):402-413.
8. Gupta V, Kumar A, Sharma P, Arora A. Newer direct-acting antivirals for hepatitis C virus infection: Perspectives for India. Indian J Med Res. 2017;146(1):23-33.
9. Schillie S, Wester C, Osborne M, Wesolowski L, Ryerson AB. CDC Recommendations for Hepatitis C Screening Among Adults - United States, 2020. MMWR Recomm Rep. 2020;69(2):1-17.
10. Khudur Al-Nassary MS, Mahdi BM. Study of Hepatitis C Virus Detection Assays. Ann Med Surg (Lond). 2018;36(4):47-50.