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The Ethics, Cost, and Evidence Surrounding Current Pharmacological Treatment of Hepatitis C Virus Infection

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Three million people in the United States have hepatitis C virus (HCV) infection.[1] Worldwide, an estimated 130 to 150 million people are infected with HCV.[2,3] The release of effective and expensive agents for HCV in 2014 has resulted in Medicaid rationing and restrictive coverage by insurers with a large population needing therapy.[1]

Hepatitis C virus is a quiet, slowly progressing disease hat increases risk of liver failure, cirrhosis, and liver cancer and is the most common pathway to liver transplantation. Standard treatments nearly 20 years ago included weekly injections of pegylated interferon with daily ribavirin and protease inhibitors boceprevir and telaprevir with much lower cure rates and significant adverse effects that reduced adherence to therapy and poor treatment outcomes.[4]

Twenty-five years after HCV was discovered, the direct-acting antiviral (DAA) sofosbuvir (Sovaldi) (Gilead Sciences, Foster City, California) emerged as the breakthrough cure in 2014. In a short time, the Food and Drug Administration approved additional DAA agents: a ledipasvir/sofosbuvir combination (Harvoni; Gilead Sciences) and the combination of ombitasvir/paritaprevir/ritonavir/dasabuvir (Viekira Pak; AbbVie, North Chicago, Illinois). These lifesaving drugs had a steep cost ranging from $83 000 to $95 000 for a 12-week course of treatment. Reported reasons for the high drug cost include the drug's "value," high probability of cure, and low probability of relapse.[4] The cost of these agents resulted in a 13.1% increase in prescription drug spending in 2014, with some states experiencing significant problems funding the therapy. As a result, some states began to restrict access or refused to pay for DAA therapy.[5] Lack of transparency surrounding pricing, access barriers, rationing, and care disparities have resulted in congressional inquiry, advocacy group mobilization, and legal challenges.[1]

Hepatitis C virus has high prevalence among the homeless, severely mentally ill, prisoners, and intravenous drug users. Others at risk include those receiving blood transfusions before 1992, those with sexual contact with an infected person, those with exposure in a healthcare setting, or those born to an infected mother. The emerging at-risk group now is composed of aging infected baby boomers with the risks of liver cirrhosis, failure, and cancer, which is expected to increase.[1]

RATIONING BY COST AND EVIDENCE?

Nearly 350 000 persons die worldwide of chronic HCV infection. Emerging DAAs are highly effective with tolerability allowing even the most ill to be treated. Cost and access issues have resulted in many persons being unable to receive treatment, not only in the United States but also across the world.[6] Nearly three-fifths of state Medicaid programs have placed restrictions on treatment. In 2015, 33 states spent more than $1 billion a year treating HCV with Sovaldi. Furthermore, this amount was enough to treat only 2.4% of all Medicaid patients with HCV. If DAA therapy was provided for all eligible persons with HCV infection, there would be nothing left in current state budgets for other lifesaving drug therapies.[7]

As a result, many states restrict use of Sovaldi and Harvoni (ledipasvir/sofosbuvir) to patients with the most advanced cases of liver disease or for patients who can provide certification from a liver transplant specialist or gastroenterologist that DAA treatment is needed immediately. In some cases, therapy can be denied to persons

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who continue to abuse alcohol or drugs or if in whom it was judged that the therapy would provide little benefit.[7] In the United Kingdom, an estimated 215 000 persons have HCV infection. In 2016, the National Health Service, while recommending treatment using DAAs, also capped the number treated per year to 10 000 persons, with much protest with continuing negotiations to reduce drug prices to expand treatment.[8] While the new DAA agents are not the most expensive on the market, cost is a concern because of the numbers of persons infected with HCV.[9]

ETHICAL IMPLICATIONS

It is unusual to have an effective treatment available on the market and ask patients to wait and see how their disease progresses.[9] Perhaps the dilemma here can be best described in this question posed by Dr Leonard Fleck[10] (paraphrased): "Do all persons infected with HCV have a just claim to treatment that averages $100 000.00 with an average cure rate of 95% and costs less than $1000.00 to produce?"

Before you answer, consider further Dr Fleck's observations. Hepatitis C virus infection is a public health threat. Approximately 70% of persons with HCV will not develop liver cancer or advanced cirrhosis. If the 3.2 million persons with HCV receive treatment, this would result in $300 billion in sales. Costs of therapy for those Medicaid eligible and for those in the prison system are truly impossible for states to pay both ethically and economically. Consider also the argument that it is more cost effective to treat the consequences of HCV infection compared with curing HCV infection. The 20-year cost of treating expected liver disease and cancer is estimated at $130 billion, which is far below the expense of therapy.[10] And what about quality of life for both these options?

Consider also that in 2013 the United States spent $17 billion on statins with the purpose of preventing heart attack and stroke. Dr Fleck writes that no one proposed for this class of drugs that the United States should wait and see who suffered a myocardial infarction or stroke and survived before offering statin treatment.[10] So what about now?

Finally, consider those cases of DAA treatment that fail. While this is not an element in the advertising night after night on television, the presence of resistance-associated variants has been implicated in reducing viral sensitivity to DAAs. This reduces the efficacy of DAAs and is correlated with poor responses to treatment and therapeutic failure. In addition, response to DAA treatment is also a function of individual factors such as the extent of liver fibrosis, response to previous therapy, the patient's viral load and virus genotype, and the presence of viral variants. Despite the evidence that DAAs are very effective against HCV, considering the number of patients infected and risks of resistance to therapy, there will be considerable numbers of patients who will experience virological failure to treatment.[11] More research is needed to discover why DAAs fail and best practices for prescribing to reduce failure.

THE FUTURE

These questions are difficult for everyone. How to provide access and sustainability? What is the best course when HCV is a disease with an unpredictable course and not everyone with HCV dies of liver disease? How will therapy be paid for? Who should receive therapy? In response to these questions, countries outside the United States have also adopted restricted access treatment protocols directing how and when to treat with DAAs using patient stratification, with interferon-free DAA therapy only for patients with advanced cirrhosis or fibrosis.[6]

With cost appearing to be the most significant barrier to significant HCV eradication, these ethical debates will continue. Is there an appropriate profit margin for drug manufacturers? How can access to new therapies be equitable across all of society and the world? Do we treat HCV now to avoid liver damage and failure and associated costs of care or ration and provide care for those with significant liver disease? These questions can be answered only in shared discussions between healthcare, government, drug companies, and the tax payers who fund everyone in some way sitting at the table.[6]

Further research is needed as well for stratification of treatment. The patient with cirrhosis, decompensated cirrhosis, and other comorbidities appears to benefit the most from DAA therapy. Next are asymptomatic patients with advanced fibrosis or cirrhosis. Again, because disease progression is not predictable, risks related to delay of treatment are not fully known.[6]

CLINICAL NURSE SPECIALIST ADVOCACY

Allocation of DAA therapies in the future require decision making based on emerging evidence regarding the outcomes of deferring or denying a cure for HCV.[6] Insurance coverage is tenuous at best with approval processes requiring endless hours that would be better used for the provision of patient care. While industry payment assistance programs do help some patients, access remains an issue.[4] Hopefully, prices will fall once generic alternatives come to market.[9]

Patients and their caregivers are wedged between big "pharma" and government with regard to drug pricing and access. When will the taxpayer contributions that helped fund research for lifesaving therapies be quantified and acknowledged and used as a basis for decision making regarding drug access? How much profit is enough? How much of rationing is an excuse to distribute therapy based on merit of life? The value and impact of clinical nurse specialist advocacy are incredibly important to answer these questions. Let your voice be heard in all the discussions. Be present at the table.

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