2016

Should the Pharmacologic Management for Chronic Hepatitis C Encompass a Response Guided Therapy Treatment Plan?

Sarah Viscarra
University of North Dakota

Should the Pharmacologic Management for Chronic Hepatitis C Encompass a Response Guided Therapy Treatment Plan?

Sarah Viscarra RT (R), PA-S
Department of Physician Assistant Studies, University of North Dakota School of Medicine & Health Sciences
Grand Forks, ND 58202-9037

UND School of Medicine & Health Sciences
University of North Dakota

Abstract

Pharmacologic advances have been made with the development of new drug therapies that essentially cure the hepatitis C virus, such as sofosbuvir. The purpose of this study is to determine whether sofosbuvir should encompass a response guided therapy treatment plan versus a standard treatment protocol, in efforts to limit the risk of adverse effects and to minimize the cost of treatment. The systematic review of literature retrieved from Pub Med and Cochrane, explored studies that compared a standard treatment protocol of 12 weeks, in male and female adults ages 18-90 years, to response guided therapy treatment plans based on each individual's sustained virologic response. Reducing the duration of treatment will decrease the risk of adverse side effects, and lower the cost of therapy. This information will help practitioners guide appropriate length of HCV treatment based on each individual patient, to ensure a sustained viral load.

Introduction

It is now estimated in the United States alone, there are nearly 3.9 million people suffering from chronic HCV, with nearly 22,000 new infections yearly. There are 350,000 HCV related deaths yearly worldwide, with approximately15,000 in the United States alone. In 2007, the deaths associated with HCV exceeded the mortality rates linked to AIDS. As the disease progresses there is an increased risk of cirrhosis (Fig. 1), ascites, portal hypertension, encephalopathy, and liver cancer (Franciscus, 2015).

Statement of the Problem

Pharmacologic advances have been made in recent years with the development of new drug therapies, such as, sofosbuvir, which essential "cures" HCV by eradicating the RNA viral load from the system. Nonetheless, these pharmacologic remedies are costly, averaging roughly a $1000 per pill daily, for a minimum of 12-24 weeks. In addition, there are many side effects that affect drug adherence such as hemolytic anemia, depression, nausea, vomiting, or diarrhea.

Research Question

The purpose of this study was to determine whether the pharmacologic regimen, sofosbuvir, for the management of chronic HCV should encompass a response guided therapy treatment plan versus a standard treatment protocol, in efforts to limit the risk of adverse side effects and to greatly minimize the cost of treatment.

Literature Review

- An et al. (2014) reported a SVR of 95% at 12 weeks with sofosbuvir and ledipasvir. The SVR was 94% with sofosbuvir and ledispavir at 8 weeks (Table 1).
- Akoth et al. (2015) stated 76% of patients on a regimen of sofosbuvir, ledipasvir, and NS3/4A for 6 weeks. Overall 76% of patients retained a SVR while 22% of patients experienced a viral relapse.
- Abbott et al. (2015) reported a 4 week treatment using a small open-label nonrandomized, clinical trial that examined 25 African American genotype 1 patients using sofosbuvir. The study showed 48% retained a SVR.
- Harris, Schwab, and Ward (2015) performed a small retrospective observational cohort study to measure whether the previous response guided therapy protocol was applied properly using boceprevir and telaprevir. Of 134 patients 15% met the qualifications for ending therapy.

Table 1. Responding During and After Treatment

Response	LDV-SOF for 8 Wk (N=215)	LDV-SOF+RBV for 8 Wk (N=216)	LDV-SOF for 12 Wk (N=216)
HCV RNA <25 IU/ml			
During treatment period- no./total no. %			
At wk 2	190/215 (88)	195/214 (91)	197/216 (91)
At wk 4	215/215 (100)	211/213 (99)	216/216 (100)
After end of treatment-no. (%)			
At wk 4	207 (96)	**205 (95)**	**208 (96)**
At wk 12	202 (94)	**201 (93)**	**206 (95)**
Virologic failure during treatment	0	0	0
Relapse in pts with HCV RNA < 25 IU/ml at end of treatment- no. (%)	11(5)	9(4)	3(1)
Lost to follow up	1	5	7
Withdrew consent	1	1	0

N= number of patients LDV= ledipasvir SOF= sofosbuvir RBV= ribavirin

An, D., Bernstein, D., Chojkier, M., Di Bisceglie, A., Ghalib, R., Gordon, S., . . . Svarovskaia, E. (2014). Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic hcv without cirrhosis. New England Journal of Medicine, 370(20), 1883.

Figure 1. Liver Cirrhosis

Magnifico, L. (2013) The facts about hepatitis c: prognosis and life expectancy. Healthline. Retrieved from http://www.healthline.com/health-slideshow/hepatitis-prognosis-and-life-expectancy

Discussion

An et al. (2014) demonstrated a high percentage of patients were able to achieve a SVR with 8 weeks of treatment using sofosbuvir. The authors did not include race or ethnicity as an inclusion criteria. Race is definitely an area that needs to be explored more. The study was also done on genotype 1 patients. Other genotypes need to be evaluated.

Akoth et al. (2015) data suggests that 6 weeks of treatment is effective in achieving a SVR in certain individuals. Factors such as low viral load and early fibrosis could indicate whether the patient should endure a shorter treatment protocol, such as 4 weeks, versus the standard 12 weeks. However, more research should be conducted with larger sample studies, and should include individuals with a decompensated liver (Figure 1).

Abbott et al. (2015) acknowledged a correlation with achieving a SVR in just 4 weeks of treatment in individuals with an HCV RNA baseline level of less than 6 million IU/ml. The data suggests response guided therapy may be feasible in individuals with a low viral load, and are without cirrhosis. However they state that more research is needed with a larger population size and race.

Harris, Schwab, and Ward (2015) suggest providers do not follow the response guided therapy protocol properly, due to the provider's lack of knowledge and proper training with the treatment, and the fear of discontinuing the drug too early. The authors state that managed care pharmacists need to implement strategies that will aim for better physician training and compliance with the response guided therapy guidelines, if it were ever implemented for sofosbuvir.

The data suggests response guided therapy may be feasible in individuals with a low viral load, and are without cirrhosis. Research limitations include small population size, race, and viral load. Provider knowledge is essential in response guided therapy plans, as many providers did not follow the protocol properly and discontinued treatment later than needed.

Applicability to Clinical Practice

- A standard 12 weeks of therapy could potentially be lowered to 6 weeks in select individuals thus lowering the treatment costs and side effects.
- It was noted there is a dire need for clinical pharmacists to implement a better strategy to effectively train physicians how to incorporate a response guided therapy method based on proper guidelines. Proper training is essential to avoid longer durations of treatment due to lack of knowledge and training given to providers.

References

Abbott, S., Akoth, E., Chavez, J., Emmanuel, B., Gross, C., Kattakuzhy, S., . . . Wilson E. (2015). Four-week direct- acting antiviral regimens in noncirrhotic patients with hepatitis c virus genotype 1 infection. *Annals of Internal Medicine. 163*(12). 899-907. doi: 10.7326/M15-0642

An, D., Bernstein, D., Chojkier, M., Di Bisceglie, A., Ghalib, R., Gordon, S., . . . Svarovskaia, E. (2014). Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic hcv without cirrhosis. *New England Journal of Medicine*, *370*(20), 1879-1888. doi:10.1056/NEJMoa1402355

Beavers, K., Brainard, D., Chaung, S., Ding, X., Gane, E., Herring, R., . . .Yoshida, E. (2014). Concordance of sustained virologic response 4, 12, and 24 weeks post-treatment with sofosbuvir-containing regimens for hepatitis c virus. *Hepatology, 61*(1), 41-45.

Franciscus, A. Hcv training workshop. (2015). *HCV Advocate*, *18*. Retrieved 22-28. from http://hcvadvocate.org/hepatitis/training _resources.asp

Harris, J., Ward, M., & Schwab, B. (2015). Is response-guided therapy being applied in the clinical setting? The hepatitis c example. *American Health and Drug Benefits, 8*(1),

Magnifico, L. (2013) The facts about hepatitis c: prognosis and life expectancy. *Healthline.* Retrieved from http://www.healthline.com/health-slideshow/hepatitis-prognosis-and-life-expectancy

Acknowledgements

I would like to make a statement of appreciation to the faculty members of the Physician Assistant master's program at the University of North Dakota. I also want to give a special thanks to Dr. McCleary for her gracious guidance as my advisor.