A Retrospective analysis of costs and trends in the treatment of HCV in the setting of specialty pharmacy

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ABSTRACT

Specific Aims: The goal is to determine the incidence of therapy failures in Hepatitis C Virus (HCV) by viral genotype (GT), the costs of therapy, and to investigate trends or specific viral genotypes causing a higher incidence of failure in therapy.

Subjects: Patients had to be over 18 and had to have started therapy for HCV at any point during 2018. Patients were excluded from analysis if they did not have a definitive follow-up SVR result reported back to the treating pharmacy.

Methods: Data was collected through retrospective chart review and de-identified by pharmacy staff. Demographic data, clinical comorbidities and the length and choice of drug therapy was collected. Data was then analyzed through application of Chi-square and one-way ANOVA.

Main Results: Subjects (n=604) on average were 59.2 (±11.6) years of age, with a majority (56%) being of the GT1a. Gender was significantly different between GTs ($P<0.05$), 1A being primarily male (60% vs 40%) and 3 being higher in female patients (56% vs 44%). GT3 had a significantly lower rate of therapy success (91%, $P<0.05$). The cost of HCV therapy was not significantly different between GT groups despite a significant difference in choice of therapy ($P<0.001$). Stratified by GT, the only significant patient factors include average age ($P<0.001$) and the presence of hypertension ($P<0.05$), GT1b being the highest in these categories.

Conclusions: GT3 had the lowest incidence of therapy success. Analysis of patient factors does not clearly explain this phenomenon, and may be due solely to the viral genotype. The cost of therapy is found to be even amongst GT groups. Additional research may be done to investigate GT groups 4, 5 and 6, or focus on patients who have failed previous HCV therapy.

INTRODUCTION:

Hepatitis C (HCV) is a virus that infects up to 100 million people globally every year and is associated with significant costs and morbidity[1]. Hepatitis C infections target the liver, leading to cirrhosis and potentially progressing to hepatocellular carcinoma. Transmission of this disease is possible through several means, primarily blood to blood, through intravenous drug use, needlestick incidents, or through sexual contact with an infected individual. Many older adults were at increased risk due to blood products not being properly screened for HCV until the 70s-90s[3]. Currently, HCV is among the leading causes of hepatocellular carcinoma, liver related death and transplants[6]. Infection with this virus can lead to either acute or chronic infections, both of which can be potentially life-altering and dangerous diagnoses. Depending on the genetics of the virus, of which there are 6 primary genotypes (GT) with various subtypes, the treatment of choice will differ, and the baseline efficacy of these therapeutic options will vary mildly. Guidelines for treating HCV will depend not only their viral GT, but also the progression of the disease regarding the presence of cirrhosis and whether the patient is treatment naïve or has been through a prior treatment. New therapies and guidelines have been introduced in recent years, but the virus remains a significant source of health care costs and patient risks.

Patients currently being treated for chronic HCV face an expensive course of therapy, ranging from $63,000 to more than $190,000[4] based on the genotype of their virus and any associated conditions that may influence therapy. Based on demographic and viral information, the course of therapy may not prove effective, unable to overcome any comorbidities or the spread of the disease within the patient. However, current Direct Acting Antiviral therapy for HCV has been shown to be very effective, even in adherence rates around 80%[7]. Previous research has shown that taking into account quality of life and potential future comorbidities associated with liver disease, hepatitis, and any potential down-range issues such as liver failure and transplants, these therapies are generally very cost effective at prices below a range

of $144,400 to $225,000[1], a figure which is getting more and more achievable as therapies progress.

For this study, the purpose is to determine if there are any clinical or demographic factors, such as viral genotype, demographics or clinical comorbidities that may influence the chance of success in treating HCV, and to be able to then use this information to aid in the treatment of patients being served in a pharmacy setting. Another goal with this study is to determine the total cost of medication therapy for patients being treated for HCV. Therapy success will be determined if a patient achieved a sustained viral response (SVR) by showing undetectable viral load within the blood 12 weeks after the completion of therapy.

METHODS:

Design This study was completed as a retrospective cohort medical chart review of patients with HCV who received their therapy at a specialty pharmacy.

Subjects Patients were eligible for this study if they were above the age of 18 and if they started and completed a course of therapy for the treatment of HCV from January 1- December 31, 2018, as determined by fill start date at Avella Specialty Pharmacy.

Measures Data was collected through a chart data search as performed by an independent group of employees within Avella Specialty Pharmacy. This data was de-identified and then provided to the researchers for analysis. Patient demographic data included age, gender and reported ethnicity. Clinical data collected included GT and subtypes (separated by the 7 major groups; 1A, 1B, 2, 3, 4, 5, 6), liver fibrosis stage, the presence of comorbidities, SVR as reported by the patient and/or patients' physician, as well as prior HCV therapy/response, current HCV therapy and length of therapy. All reported data was categorical, such as indicating the presence of a comorbidity or the specific type of GT. Medication cost

information was determined through research of Average Wholesale Prices (AWP) per week, and extrapolating this to length of therapy as reported through the collected data[5].

Data Collection Data was collected through the analysis of already present information within patient profiles of patients receiving HCV medication at Avella Specialty Pharmacy. Data was collated and de-identified for further analysis prior to the release to the researchers.

Data analysis As analyzed through the data report, we had adequate populations for the first four genotype groups (1a, 1b, 2 and 3). Data was stratified per these four groups, and then further stratified depending on if the 12-week post therapy viral load test was shown to determine therapy success (SVR). Categorical data was analyzed through the application of chi-squared testing, while nominal data was analyzed to find the mean and standard deviation. The nominal data was then further analyzed through a one-way ANOVA and post-hoc Tukey's test to determine significance. The apriori p-value was 0.05.

RESULTS

The demographic characteristics of the patients are listed in Table 1. Examining the average age of each GT group, there was a significant difference ($P<0.001$), with GT3 being the youngest average age at 54 years (±12.9). Gender, stratified by GT was significantly different when examining all four GTs ($P<0.05$), but on further analysis it appears that GTs 1A and 3 are the only outliers against each other ($P<0.05$). The majority of patients were GT1a (n= 336, 56%), then 1b (n=93, 15%), 2 (n=94, 16%) and 3 (n=81, 13%). Genotypes 4 (n=8), 5 (n=1) and 6 (n=2) didn't have enough subjects to be notable and were not included in further analysis.

The percentage of patients in each GT group who had achieved an SVR is also shown in Table 1, with GT group 3 appearing significantly different after comparing Undetected

(achieve SVR) against Detected (not achieving SVR) (P<0.05). SVR was also reported in the data set as 'unsure' and 'lost to follow-up', as these are not definitive results they were excluded from analysis.

Table 2 shows the drug cost information average and standard deviations for each group, examining the total population for each GT. The cost ranges from $71,754.50-$77,727.55, with GT3 being the cheapest and GT1b the most expensive. Analyzing the total cost information through a one-way ANOVA, there was no significant cost of therapy differences between GT groups (P=0.69).

Table 3 lists the fibrosis score assigned to each GT group, however only GT1b and 2 were found to be different (P<0.05) from one another. Table 4 lists the collected comorbidities and coinfections listed for each GT, with only the presence of comorbid hypertension differing between the GT groups (P<0.05).

Table 5 lists the various frequencies of each GT group completing a course of therapy with a specific drug. As expected based on current IDSA guidelines, there are significant differences between which drugs are selected most often for each viral GT, with Epclusa, Harvoni and Mavyret being used most often (p<0.001).

DISCUSSION

From the completed analysis, we have determined that there is a significant difference in therapy success or failure due to HCV GT based on SVR results reported by a patient or provider to a specialty pharmacy. Patients had a higher chance of achieving SVR if infected with GT1B (99%), and a significantly worse chance of achieving SVR if infected with a GT 3 virus (91%), (P<0.05). Our own analysis does not clearly point to why this difference may exist, but

possibilities include initial viral load, or the extent of the liver or comorbid disease states within this patient group. There is a significant age difference between the groups, with GT3 at the youngest average group at 54 years (P<0.001). The only comorbidity to reach significance, the presence of hypertension (P<0.05) also has GT3 with the lowest percentage of individuals with this comorbidity (22%) compared to the other GT groups. Current alcohol usage approached significance (p-value = 0.055), however the highest incidence took place in group 1A, who had an incidence of therapy success that is in line with the other groups despite this social behavior. Examining the cost of therapy stratified into the four largest GT groups, there was no significant difference when looking at the average cost of therapy (P = 0.69). The fibrosis scores for each GT group were found to be non-significant when examined as a whole (P=0.15).

When attempting to stratify the analysis to determine what characteristics may explain the difference in therapy effectiveness, no direct comparisons were found to be significant save for the distribution of fibrosis scores between GT groups 1B and 2 (P<0.05). As these two GT groups had the same percentage of therapy success however, this comorbidity by itself may not play a large role towards determining the chance for success. Gender was also found to be different between GT groups 1A and 3 (p=0.012), 1A favoring male patients (60% vs 40%) while GT3 favors female patients (56% vs 44%). As GT1A had SVR attainment in line with the other groups, this may be a unique consideration for the medications used to treat GT3 that could potentially influence therapy.

Within this study, the distribution of therapy choices in table 5 is likely the largest factor to play a role in determining the average cost of therapy, but it is difficult to determine how it may affect overall therapy efficacy. It appears that the trends seen in this study generally agree with IDSA recommendations for treatment of each GT[2] based on the observed difference in therapy choices for each group (P<0.001). Based on medication data received from the

pharmacy, the patients in the GT 3 group are being treated following IDSA guidelines but are still experiencing a lower incidence of therapy success, a fact which seems to be in agreement with current literature[8][9].

The limitations of this study include a small patient sample size for viral GT groups 4, 5 and 6, and a small population of patients who have experienced a documented failure in medication therapy. Admittedly, with the sharp rise in efficacy of direct acting antiviral medications as compared to prior options to treat HCV, therapy failures may be more difficult to assess. We were also limited in relying on patient and physician responses to the specialty pharmacy's SVR inquiries, such that some results were not definitive, reported only as 'unsure' by patient or "lost to follow up" by physician. If the pharmacy or researchers had access to the full lab data, a deeper analysis could potentially be completed. Additional study with an even larger population base may be able to assess any significant patterns in patients with a documented failure in previous HCV therapy, still having a detectable viral load following medication therapy.

CONCLUSIONS

Other than the distribution of HCV medication utilized - likely due to guideline recommendations, almost all other demographic and clinical aspects of patients receiving HCV therapy at a specialty pharmacy were found to be equally distributed, or in the case of average age and the presence of hypertension, tended to skew favorably towards the group that actually had worse outcomes. Patients with GT 3 were found to have the lowest incidence of achieving SVR. GT1A, 1B and 2 had similar incidences of therapy success, with the only significant differences in the presence of comorbidities and demographics being GT1b being the oldest on

average and most likely to have comorbid hypertension. Additionally, the reported fibrosis score spread showed that GT1B was significantly higher than GT2.

The main outcomes from this study seem to be simply that medications for the treatment of HCV are very effective for a majority of patients, with a shown success rate above 90% for all analyzed groups. Even in the presence of comorbidities and social factors that impede the medication or act to further organ damage, none of these factors seemed to significantly impact the ability of the medication to succeed in therapy. Though there is some difference in efficacy based on certain characteristics, the clinical outcomes for patients infected with HCV are generally positive. This is in line with other recent research done on HCV patients, with a focus on our analyzed GT groups. Achievement of SVR while taking direct acting antivirals is very likely, and not easily influenced by comorbidities or clinical factors[8]. On average, the cost of therapy will be the same regardless of the HCV GT that infects a patient, but it is the variance in patient GT that appears to have the largest impact on clinical outcomes when examining patients stratified by viral GT. Per our research, and current literature sources, it appears that those patients in GT group 3 will have a harder road to therapy success[9].

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TABLES AND FIGURES

Table 1. Patient Demographic by GT

GT n (%)	1A n= 336 (56)	1B n= 93 (15)	2 n= 94 (16)	3 n= 81 (13)	P-value
Mean Age, years (±SD)	59.1 (10.9)	63.8 (9.5)	59.7 (13.2)	54.0 (12.9)	**<0.001[a]**
Gender: n (%)	Male - 201 (60) Female - 135 (40)	Male - 46 (49) Female - 47 (51)	Male - 49 (52) Female - 45 (48)	Male - 36 (44) Female - 45 (56)	**0.041[a]**
Treatment Naive Undetectable: n (%)	268 (80)	78 (84)	73 (67)	61 (63)	0.68[b]
Treatment Experienced Undetectable: n (%)	48 (14)	11 (12)	10 (9)	10 (10)	0.81[b]
Therapy Undetectable SVR: n (%)	329 (98)	92 (99)	92 (98)	74 (91)	**0.008[b]**
Detectable SVR: n (%)	7 (2)	1 (1)	2 (2)	7 (9)	

[a] one-way ANOVA, [b] Chi-Square

Table 2: Total cost of treatment by GT

GT	1A	1B	2	3	P-value[a]
Average Total Cost of therapy, $ (± SD):	$73,759.22 ($34,744.52)	$77,727.55 ($36,192.62)	$74,578.64 ($32,058.08)	$71,754.50 ($31,034.53)	0.69

[a] one-way ANOVA

Table 3: Liver Fibrosis score by GT

GT[a]	1A	1B	2	3
F0: n (%)	47 (15)	7 (10)	16 (20)	14 (19)
F1: n (%)	69 (22)	13 (18)	17 (21)	11 (14)
F2: n (%)	58 (19)	10 (14)	21 (26)	9 (12)
F3: n (%)	45 (14)	15 (20)	8 (10)	14 (19)
F4: n (%)	93 (30)	28 (38)	19 (23)	26 (35)

[a]Chi-square, 4x5, P=0.15

Table 4: Comorbidities by GT

GT	1A n=336	1B n=93	2 n=94	3 n=81	P-value[a]
HIV Coinfection n (%)	7 (2)	1 (1)	0 (0)	0 (0)	0.48[b]
HBV Coinfection n (%)	14 (4)	1 (1)	2 (2)	4 (5)	0.51
PPI Use n (%)	63 (19)	21 (23)	13 (14)	17 (21)	0.51
History of Illicit Drug use n (%)	94 (28)	17 (18)	17 (18)	20 (25)	0.12
Current Illicit Drug use n (%)	16 (5)	3 (3)	3 (3)	5 (6)	0.48
History of Alcohol use n (%)	48 (14)	7 (8)	12 (13)	15 (19)	0.19
Current Alcohol use n (%)	53 (16)	7 (8)	10 (11)	6 (7)	0.055
Comorbid Anxiety n (%)	23 (7)	7 (8)	6 (6)	6 (7)	0.96
Comorbid Chronic Kidney Disease n (%)	12 (4)	6 (6)	6 (6)	2 (2)	0.37
Comorbid Depression n (%)	74 (22)	23 (25)	17 (18)	22 (27)	0.50
Comorbid Diabetes n (%)	50 (15)	20 (22)	11 (12)	9 (11)	0.18
Comorbid Hepatocellular carcinoma n (%)	4 (1)	0 (0)	0 (0)	1 (1)	0.63[b]
Comorbid Hyperlipidemia n (%)	51 (15)	16 (17)	13 (14)	4 (5)	0.08
Comorbid Hypertension n (%)	126 (38)	37 (40)	29 (31)	18 (22)	**0.038**

[a]Chi-square [b] Fisher's Exact test

Table 5. Medication therapy utilized

GT[a]	1a	1b	2	3	AWP $ per week[5]
Epclusa 400mg-100mg n (%)	65 (16)	16 (15)	71 (65)	50 (54)	$7,476.00
Harvoni 90mg-400mg n (%)	136 (34)	43 (39)	1 (1)	0 (0)	$9,450.00
Mavyret 100mg-40mg n (%)	168 (42)	40 (37)	36 (33)	38 (41)	$3,959.97
Viekira XR n (%)	0 (0)	1 (1)	0 (0)	0 (0)	$8,331.96
Vosevi 400mg-100mg-100mg n (%)	21 (5.2)	4 (4)	1 (1)	5 (5)	$7,476.00
Zepatier 50mg-100mg n (%)	5 (1.3)	5 (4)	0 (0)	0 (0)	$5,460.00

[a]Chi-square, P-value <0.001

APPENDICES

Patient ID	Age	Gender	Medication Name	Therapy Start Date (1/1/18 - 12/31/18)	SVR (Undetected, Detected, Lost to Follow up, Unsure)	Current Regimen Duration, weeks	Genotype (1-6)	Metavir/ Fibrosis Score (F0-F4)	Patient Ethnicity	Treatment Naïve	Prior Regimen Name 1	Prior Therapy Response 1	HIV Coinfection	Hepatitis B Coinfection	Comorbid Proton Pump Inhibitor use	History of Illicit Drug Use	History of Alcohol Use

Comorbid Anxiety	Comorbid Chronic Kidney Disease	Comorbid Depression	Comorbid Diabetes	Comorbid Hepatocelluar Carcinoma	Comorbid Hyperlipidemia	Comorbid Hypertension	Medication list:

Appendix 1: Data collection form