The Disease Burden of Hepatitis C in Belgium: development of a realistic disease control strategy

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Abstract

Background: Novel direct antiviral agents (DAAs) will become available soon with higher sustained viral response (SVR), fewer side-effects and higher compliance. Our aim was to evaluate different realistic strategies to control the projected increase in HCV-related disease burden in Belgium.

Methods: Based on literature review, expert opinions and historical assumptions, HCV-disease progression and mortality in Belgium was modeled to 2030. Strategies exploring the impact of increased treatment rate, treatment delay, and treatment restrictions were developed.

Results: Although the overall HCV prevalence is decreasing in Belgium, the burden of advanced stage HCV, including cirrhosis and hepatocellular carcinoma (HCC), is expected to increase under current treatment and cure rates. By increasing SVR to 90% from 2016 onward and the number of treated cases (from 710 to 2,050), in 2030 the cases with cirrhosis, decompensated cirrhosis and HCC would be significantly lower than in 2013. This strategy was found most efficient when applied to F2-F4 cases. To obtain comparable outcomes with F0-F4 cases, 3,490 patients should be treated. A two year delayed access to the DAAs increased HCV-related morbidity and mortality by 15% relative to our strategy.

Conclusions: Considering the evolving burden of HCV disease and the need for efficacious usage of healthcare resources, primary application of new DAAs in Belgium should focus on patients with significant and advanced fibrosis (F2-F4), providing these new drugs without delay upon availability and increasing access to therapy. (Acta Gastroenterol. belg., 2014, 77, 280-284).

Background

Chronic hepatitis C virus (HCV) infection heralds a significant clinical, societal and economic burden (1). As the population ages more patients with end stage HCV liver disease are seen, substantially adding complexity to treatment (e.g. decompensated liver cirrhosis, hepatocellular carcinoma (HCC) and liver transplantation) (2,3). Long-term disease progression, suboptimal therapies and an aging population also contribute to increasing burden on the Belgian healthcare system (1,4).

Once diagnosed, the standard of care (SOC) therapy for patients chronically infected with HCV infection has, until recent years, been dual therapy with pegylated interferon α (Peg-IFN) and ribavirin (5). In 2011, the United States Food and Drug Administration and the European Medicines Agency approved first generation direct acting antivirals (DAAs), Telaprevir (6) and Boceprevir (7), for the treatment of chronic HCV genotype (G) 1 infection. The addition of first generation DAAs to the SOC was associated with an increase in sustained viral response (SVR) rate, as well as an increase in the number and severity of side effects (8). Telaprevir and Boceprevir were approved for reimbursement in Belgium in mid 2012. However, due to the known adverse effects, they have limited adherence and restricted eligibility.

In the coming years second and third generation DAAs are expected to become the primary treatment for HCV in Belgium as they achieve regulatory approval. Once available they are anticipated to increase patient eligibility and decrease HCV disease burden through higher SVR rates, shorter treatment duration, better compliance and fewer side-effects. Novel DAAs with pangenotypic activity may also boast higher cure rates across all genotypes. Our aim was to evaluate various efficient and realistic strategies to control the projected increases in HCV-related disease burden and to examine the effects of delayed treatment access on disease burden.

Methods

Historical data were trended using non-linear polynomial extrapolation for years 2012-2030 with the Belgian population handled as stocks whereas transition probabilities were handled as flows. The population was allowed to age through 36 age cohorts by gender. This model was developed to provide maximum flexibility in changing inputs over time. The factors considered involve HCV incidence rate, transition probabilities, new case incidence, background mortality, treatment rate, transplantation rate, cost per complication of advanced liver disease and overall cost. As such, trends in epidemiology, disease progression and healthcare costs can be simulated, as was the impact of future therapies on the HCV infected population and on the associated healthcare costs. A detailed description of the model and methodology can be found in the methods paper (9).
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Modeled scenarios, and baseline treatment assumptions

Baseline: The current SOC in Belgium calls for the treatment of all patients between 15 and 84 years of age. Treatment was restricted in patients infected with G1, G3 and G4 to those with a METAVIR stage ≥ F2. Treatment was unrestricted for G2 patients. Approximately 40% of patients were contraindicated for treatment or refuse treatment altogether. Each year an estimated 710 patients were treated, with estimated SVR rates as follows: G1/4 = 60%, G2 = 65%, G3 = 40%.

Increased Treatment Efficacy: To assess the effect of projected increases in treatment efficacy, a strategy was developed in which the SVR changed, but treatment (including the subset of the population treated and the number of patients seen) remained constant. Estimated increases in SVR were developed by an expert panel using clinical trial results and projections of real world experiences. In Belgium SVR increases were projected to occur in 2015 (G2 = 85%, G3 = 70%) and 2016 (G1/2/3/4 = 90%) as Peg-IFN was removed from use and as regimens become easier to tolerate.

Disease Control Strategy: To control the disease burden it was postulated that the number of patients treated should approach the annual number of newly diagnosed viremic patients (~2,000). Consequently a strategy was developed in which SVR increased as previously described, and the number of ≥F2 patients treated increased to ~2,000 annually by 2019. This increase in treated patients correlated with a 50% reduction in mortality.

To further explore the impact of treatment, this strategy was modified to achieve 30% and 80% reductions in mortality by changing the number of patients treated and by changing the segment of the population eligible for treatment (from ≥F2 to ≥F0 or ≥F3). Finally, to explore the impact of time, the date of second and third generation DAA reimbursement was delayed by two years.

Results

Base Case

There were an estimated 67,100 (24,800-78,600) viremic cases in Belgium in 2013. Peak viremic prevalence of chronic HCV infection was reached in 2003 with 72,800 infected individuals and the overall prevalence has been declining since (estimated to be 47,700 in 2030) (Fig. 1). Compensated cirrhosis, decompensated cirrhosis and HCC were projected to peak in 2030 at 11,500, 1,400 and 650 cases respectively (Table 1). Under the current SOC, liver related mortality was forecasted to increase by 95% by 2030, to an estimated 570 liver related deaths annually.

Scenario 1: Increased Treatment Efficacy

Under the scenario to increase SVR to 90% by 2016 and maintain treatment of 710 patients annually, HCV related mortality was forecasted to peak and level off earlier than under the base case, equating to approximately 320 liver-related deaths averted by 2030. Annually, this equates to a 10% decrease in liver-related deaths, as compared with the base case of 570 deaths, by 2030.

Viremic prevalence was forecasted to decrease at a slightly faster rate than under the base case with a remaining 44,900 viremic cases in 2030 (a 10% improvement over the base case) (Fig. 2). Although the number of individuals with late stage disease will continue to increase, it will occur more slowly than under the base case. Compared to the base case forecast, SVR increases will avert 1,130 cases of cirrhosis, 140 cases of decompensated cirrhosis, and 60 cases of HCC from 2013 to 2030.

Scenario 2: Disease Control Strategy

As compared with the base case, a scenario that increases SVR to 90% and treats 2,050 F2-F4 cases beginning in 2017 was estimated to decrease liver related deaths by 50% by 2030. The number of cases of decompensated cirrhosis and HCC were also expected to decrease by 50%. By 2030 this strategy was projected to decrease the total number of viremic cases to 31,400, a 35% improvement from the base case (Fig. 2).

By extending this scenario to F0-F4 cases, it was forecasted that 3,490 patients will have to be treated annually by 2019 to obtain a similar benefit concerning reduction of mortality, decompensated cirrhosis or HCC. Further the total number of infected, viremic patients would decrease by an additional 50%, with 16,000 viremic infections remaining in 2030.

The disease control strategy was then modeled with a two year delay (implementation in 2018). By 2030 the delay resulted in a 5% increase in the total number of

| Table 1. — HCV-related sequelae projections, 2013, 2030 and year of peak estimate |
|-----------------------------------------------|---------------|----------------|---------------|-------------|---------------|
| Base Case | 2013 Estimate | 2030 Estimate | Percent Change | Peak Year | Peak Estimate |
| Total viremic infections | 67,100 | 47,800 | -30% | 2003 | 72,800 |
| Compensated cirrhosis | 7,000 | 11,500 | 65% | 2030 | 11,500 |
| Decompensated cirrhosis | 810 | 1,400 | 70% | 2031 | 1,400 |
| HCC | 300 | 640 | 115% | 2031 | 650 |
| Liver-related deaths | 290 | 570 | 95% | 2032 | 580 |

viremic HCV cases and 460 additional HCV liver-related deaths (15% increase), as compared to the 2016 implementation. Delayed implementation increased the number of cases of HCC and cirrhotic decompensation by 10%.

Limiting the strategy objective to a 30% reduction in mortality and treating only F2-F4 cases, the number of patients to be treated would decrease to 1,390 patients (Fig. 3). As a consequence, the benefit on the different disease outcomes observed with the disease control strategy would be reduced by 40%. Extending this strategy to F0-F4 patients, which implies treating the same number of patients as in the disease control strategy considering only F2-F4 cases for treatment, will not attenuate the loss in benefit which remains at a 40% magnitude.

Discussion

The present study contributes to a better understanding of the burden associated with HCV infection in Belgium by modeling the base case and several strategies with varying treatment rates. The results from this exercise suggest that it is possible to decrease HCV related complications and mortality by increasing treatment efficacy and the number of patients treated. Increased treatment efficacy alone was not projected to have a large effect on the burden of HCV; therefore improvements in screening and increased access to therapy are recommended.

Though not presented in detail here, previously published analyses indicate that control or limitation of HCV
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Fig. 2. — HCV-related morbidity and mortality, by scenario-Base; Increased SVR; Increased SVR with increased treatment with and without a 2-year delay.

Fig. 3. — Sensitivity Analysis – The impact of fibrosis score on the cumulative number of treated patients necessary to achieve 30%, 50% and 80% reductions in mortality.
circulation in Belgium is possible with aggressive treatment and screening strategies (10). A substantially higher number of patients (nearly 5,000 annually) would have to be treated with higher SVR therapies to reduce HCV prevalence below 6,000 viremic cases. Additionally, for this scenario to be successful, all ≥ F0 patients would have to be treated. If implemented, however, an 88% decrease in viremic patients, together with an 80% reduction in mortality could be possible by 2030. By contrast, limiting this strategy solely to F2-F4 cases was unlikely to achieve the goal of controlling the circulation of HCV by 2030. Furthermore, this scenario would require targeted screening and case-finding programs, as it is currently estimated that half of the infected population in Belgium is unaware of their infection.

Limitations associated with the model have been described in detail elsewhere (10), however it is important to note that just because a scenario can be modeled does not mean that it will be realistic to implement. The goal of this exercise was to show that significant reductions in disease burden, or the control of disease circulation are possible, and to inform the direction of the strategy chosen. For example, a goal of decreasing mortality is best addressed by treating late stage patients, while a goal of control or limitation of HCV circulation is only possible if treatment is expanded to all infected patients. Either way, delay of access to higher SVR treatments increases the overall burden of HCV in Belgium.

This analysis demonstrated that timely administration of treatments with high SVR can result in the reduction of patients with HCV related end stage liver disease and its complications. Delaying treatment access by as little as two years results in significantly higher HCV related morbidity and mortality.

References