Impact of successful hepatitis C treatment on quality of life

Question

- Does successful hepatitis C (HCV) treatment improve quality of life?

Key Take-Home Messages

- People living with HCV who receive treatment and achieve sustained virologic response (SVR) have better health-related quality of life scores than people who do not respond to treatment and people who are untreated (1-11).

- The side effects of interferon — the medication used to treat HCV in the past — were responsible for most of the negative impact on health-related quality of life during treatment (3;12).

- During treatment with interferon-containing regimens, people's physical and mental health-related quality of life get progressively worse (3;13-15). However, once treatment is over, people usually feel better physically and mentally than they did before they went on treatment (3;13;15).

- Depression, fatigue and insomnia are important predictors of patients' quality of life before, during and after treatment (9;12;16;17).

- In clinical trials of the newer drug treatments, patients reported better quality of life outcomes with the modern interferon-free and ribavirin-free regimens with second generation direct-acting antivirals (DAAs). These improvements were sustained post-treatment (18).

- More data are needed to assess whether patients report the same improvements following treatment with interferon-free regimens in real world clinical practice settings (3).

The Issue and Why It’s Important

Health-related quality of life is a broad multidimensional concept

References


that includes self-reported measures of physical and mental health as well as social well-being (3;19;20).

Hepatitis C is a viral infection that damages the liver. Individuals with chronic HCV infection also experience fatigue, depression and anxiety, which affect their health related quality of life (3;9;21). A systematic review of 15 studies that compared health-related quality of life among those with and without chronic HCV found that individuals with HCV reported being in poorer health (22), and their quality of life diminished as their liver disease became more severe (21).

Until recently, people with HCV were treated with interferon-based regimens (with or without ribavirin) and first generation direct-acting antivirals (telaprevir and boceprevir). The side effects of these treatments – which included depression during and after treatment (12;23)— had a negative impact on people's ability to adhere to treatment and on treatment efficacy (3).

Newer HCV treatment regimens using second generation direct-acting antivirals (such as sofosbuvir and ledipasvir) are highly efficacious with significantly fewer side effects (3). This review examines the impact of successful HCV treatment (i.e. achieving SVR) on health-related quality of life taking into consideration rapidly evolving HCV treatment regimens.

What We Found

Measuring health-related quality of life

Three scales are often used to measure health-related quality of life among patients living with HCV (18):

- The Short-Form 36 (SF-36) questionnaire: a generic instrument used to assess health related quality of life. It uses a number of individual scales to measure physical functioning, body pain, general health, vitality, social functioning and mental health (24).

- Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) questionnaire: a fatigue-specific instrument that assesses five individual scales including physical well-being, emotional well-being, social well-being, functional well-being and fatigue (25).

- Chronic Liver Disease Questionnaire–Hepatitis C Virus (CLDQ–HCV) instrument: a disease-specific instrument that assesses the health-related quality of life of patients with chronic HCV in four individual domains: activity and energy, emotional, worry and systemic symptoms (26).


Of these instruments, the SF-36 is the most commonly used (1). It is available in several languages, has demonstrated satisfactory psychometric properties in a variety of populations (including HCV patients), and has shown good validity and reliability (2;27).

Health-related quality of life during treatment with interferon

Historical data from studies on the use of interferon alone or interferon in combination with ribavirin show that patients suffered a significant drop in health-related quality of life scores before treatment, and that those scores continued to fall during treatment (3). Interferon is a cytokine that induces neuropsychiatric symptoms (28): between 12% and 41% of patients without a previously diagnosed mental illness treated with interferon (29) and between 17% and 58% of patients with a history of mental illness developed neuropsychiatric symptoms (29). In some cases, patients continued to complain of cognitive difficulties two years after stopping the interferon-based treatments (30). Depression, fatigue, influenza-like symptoms, anemia and other side effects caused by interferon-containing regimens also have a negative effect on health-related quality of life (3;9;10;14;15;31;32).

Health-related quality of life after treatment with interferon

Despite the significant decrease in health-related quality of life during treatment with interferon and ribavirin, patient-reported outcomes scores generally improved after treatment was finished (3;13). The same pattern applies to HCV patients who fail initial interferon treatment and are re-treated with pegylated interferon and ribavirin (33).

Patients who experienced a sustained virologic response after treatment with interferon had higher health-related quality of life and health utility scores (3;9;10;32), including cirrhotic patients, previous non-responders, relapers, patients in first treatment and patients unaware of treatment response (2;4;5;10;11). Similar results were obtained in: a large trial conducted across nine European countries (6); a large multicentre Canadian cohort (7); a Vancouver cohort (8); a multi-centre setting in the U.K. (32); an outpatient cohort in Sweden (10); and a veterans cohort in New York (11), as well as from Taiwan (34) and Japan (35), indicating no ethnic differences concerning health-related quality of life in HCV patients treated with interferon and ribavirin (34).

A recent systematic review of 16 quality of life studies examining the impact of sustained virologic response confirmed the above findings (1). According to a range of studies, people who achieve a sustained virologic response report an increase in overall health


and vitality and improved mental health outcomes over time – and these improvements in health-related quality of life are sustained more than three years after patients complete therapy (8;36). On the other hand, those who did not achieve a sustained virologic response reported that their capacity to engage in long-term work and leisure activities was significantly compromised (1).

The addition of first-generation direct-acting antivirals (telaprevir and boceprevir) to interferon and ribavirin in 2011 increased the efficacy of the anti-HCV treatment and led to better rates of sustained virologic response. However, the side effects associated with interferon, ribavirin and first-generation direct-acting antivirals were debilitating and adversely affected patient-reported health reported quality of life outcomes (3). For example, a large multi-center trial, ADVANCE, found that telaprevir combination therapy was associated with greater decreases in health-related quality of life during the first 12 weeks (compared to pegylated interferon and ribavirin alone). However, at 72 weeks, those who achieved a sustained virologic response showed significant improvements in health-related quality of life (37).

Health-related quality of life after treatment with second generation direct-acting antivirals without interferon (with or without ribavirin)

Various clinical trials (FISSION, NEUTRINO, POSITRON, FUSION) have examined different sofosbuvir- and ribavirin-containing therapies on different HCV genotypes with different combinations of medications, treatment durations and control strategies (38;39). The fatigue subscale of the FACIT-F remained an independent predictor of health-related quality of life before, during and after treatment even after controlling for important confounders, indicating the importance of fatigue in patients with chronic HCV (12). Depression was another important factor independently associated with patient-reported quality of life (12). A meta-analysis of the clinical trial studies demonstrated the superiority of interferon-free regimens in terms of health outcomes (17).

At the end of 12 weeks of follow-up in the FUSION and NEUTRINO trials, patients treated with the interferon-free regimens showed bigger improvements in their HRQoL compared to those on interferon-containing regimens (12;16).

Recent studies have documented the impact of the latest treatment regimens (second generation direct-acting antivirals sofosbuvir and ledipasvir without interferon and ribavirin) on health-related quality of life (12;40;41). An analysis of 1,952 patients from the three ION trials conducted throughout 2013-14 in the U.S., Spain, Germany, France, the U.K. and Italy showed that patients who achieved a sustained virologic response at 12 weeks after treatment reported significant improvement in their outcomes (up to 18%; 17.


In addition to interferon-free regimens containing sofosbuvir and ledipasvir, the newest direct-acting antivirals such as 3D (also known as Viekira Pak, marketed as Holkira–Pak in Canada – a combination of ombitasvir, paritaprevir, ritonavir, and dasabuvir) and simprevir regimens have minimal negative effects on health-related quality of life (3). While the data from clinical trials are encouraging, fully published peer-reviewed data are not yet available and more information is needed to assess patient-reported outcomes in the real world setting of clinical practice (3).

Health-related quality of life in people living with HIV/HCV co-infection

Similar to the results of studies on individuals living with HCV only, studies including people living with HIV/HCV co-infection also found a positive correlation between sustained virologic response and improvements in health-related quality of life (42;43). For example, a large study among patients of a French hospital found that patients who cleared their HCV (i.e. had a sustained virologic response) had better health-related quality of life than those who did not (42). An Austrian study also found that interferon and ribavirin therapy had a negative effect on health-related quality of life – including more severe fatigue, while a sustained virologic response had a positive impact on health-related quality of life (44).

In a recent multi-centre study of sofosbuvir-containing interferon-free regimens (18) most patient-reported outcome scores improved from baseline levels, with the greatest improvement observed in the worry domain of the CLDQ-HCV instrument (change, +8% on a 0%-100% normalized patient-reported outcome scale; p<0.0001) (18). Among people living with HIV/HCV-co-infection, those who did not achieve a sustained virologic response showed no improvement at week 12 in any patient-reported outcome score (18). Improvements in the scores were similar for individuals living with HCV only and for people living with HIV/HCV co-infection (all p<0.05) (18).

Factors That May Impact Local Applicability

All studies cited in this review were conducted in high income countries in Western Europe (UK, Germany, France, Spain, Sweden), Asia (Japan, Taiwan) as well as in Canada, the U.S. and Australia. Because of similar HCV epidemics and treatment medications across these countries, the review findings are highly relevant and transferable to the Canadian context.
What We Did

We searched Medline using a combination of [Hepatitis C or HCV (text terms) or Hepatitis C or Hepatitis C, Chronic (MeSH terms)] AND Quality of Life (text term or MeSH term). Reference lists of identified literature reviews and systematic reviews were also searched. All searches were conducted on February 2, 2016 and results limited to English articles published from 2005 to present in high income countries. The search yielded 593 references from which 44 studies were included. Sample sizes of primary studies ranged from 18 to 1952.

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