

## Advances in Research on Adverse Drug Reactions and Nursing Interventions for Hepatitis C Patients: Postprint

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### Abstract

Pegylated interferon (PEG-IFN) combined with ribavirin (RBV) regimen and direct-acting antiviral agents (DAA) are currently relatively common clinical treatment options for hepatitis C virus infection. This article reviews the adverse reactions and nursing interventions of these two treatment regimens, aiming to draw attention to and promote renewed understanding of adverse reactions among healthcare professionals and patients, and to provide healthcare professionals with comprehensive nursing intervention measures for reference.

### Full Text

## Research Progress on Drug-Related Adverse Reactions and Nursing Interventions in Hepatitis C Patients

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### Abstract

The combination regimen of pegylated interferon (PEG-IFN) plus ribavirin (RBV) and direct-acting antiviral agents (DAAs) are currently common clinical treatment options for hepatitis C virus infection. This article reviews the adverse reactions associated with these two treatment regimens and corresponding nursing interventions, aiming to raise awareness among healthcare providers and patients regarding adverse reactions and to provide comprehensive nursing intervention strategies for clinical practice.

**Keywords:** hepatitis C; drug-related adverse reactions; pegylated interferon; ribavirin; direct-acting antiviral agents; nursing intervention; complications

Hepatitis C virus (HCV) infection is the fundamental cause of hepatitis C. According to World Health Organization statistics, HCV represents a significant global health burden, with millions of people infected worldwide and hundreds of thousands of deaths annually from hepatitis C-related cirrhosis or hepatocellular carcinoma. China is among the countries with a large number of HCV patients, and a substantial proportion have not received standard antiviral therapy. Treatment guidelines in China have evolved with pharmaceutical advances, with the earlier Guidelines for Prevention and Treatment of Hepatitis C recommending PEG-IFN combined with RBV as the standard regimen, while the updated edition prioritizes interferon-free DAA regimens. Currently, both standard and DAA treatment approaches coexist in clinical practice. This article reviews the adverse reactions and nursing interventions for both regimens.

## 1. Adverse Reactions of Standard Treatment Regimens

The interferon plus ribavirin regimen is associated with numerous adverse reactions, significant side effects, and multiple contraindications, including anemia, leukopenia, autoimmune diseases, hyperthyroidism, and hypothyroidism. Nearly all patients experience at least one adverse reaction during treatment. Some patients develop severe adverse reactions requiring dose adjustment or even treatment discontinuation, which seriously impacts therapeutic efficacy.

### 1.1 Flu-like Symptoms

Flu-like symptoms are the most common adverse reactions in patients receiving interferon therapy, representing the most prominent and earliest side effects of hepatitis C treatment. These symptoms include generalized discomfort, fatigue, fever, myalgia, and varying degrees of arthralgia and headache. Flu-like symptoms typically occur within hours after administration and are dose-related, with severity potentially diminishing after repeated dosing.

### 1.2 Digestive System Symptoms

Patients frequently experience anorexia, loss of appetite, nausea, vomiting, and diarrhea during treatment, leading to weight loss and decreased treatment tolerance. Studies have shown that interferon plus ribavirin therapy affects nutrient intake and reduces body weight. Recent research measuring resting energy expenditure (REE) and predicted REE has demonstrated that antiviral therapy increases energy consumption while decreasing body weight and serum albumin levels, warranting early attention and intervention.

### 1.3 Neurological and Psychiatric Symptoms

Common neurological symptoms during interferon therapy include depression, anxiety, emotional lability, irritability, insomnia, memory impairment, paresthesia, personality changes, and even suicidal ideation. The incidence of depression with PEG-IFN- $\alpha$  and RBV combination therapy can be substantial, with symptoms becoming more pronounced after several weeks of treatment. Irritability, fatigue, and other adverse reactions can exacerbate depressive symptoms.

### 1.4 Hematological and Lymphatic System Symptoms

Frequently observed hematological and lymphatic symptoms include lymphadenopathy, anemia, and changes in peripheral blood platelets, neutrophils, and leukocytes, with some patients developing bone marrow suppression. The anemia associated with combined PEG-IFN and RBV therapy is often termed mixed anemia.

### 1.5 Skin and Injection Site Reactions

Injection site reactions are common during interferon therapy but are typically mild and rarely require treatment discontinuation. The incidence of injection site reactions with PEG-IFN plus RBV is notable, with dermatitis occurring in a subset of patients. Additional manifestations include dry skin, generalized pruritus, rash, eczema, urticaria, photosensitivity, hyperhidrosis, and night sweats.

### 1.6 Other Adverse Reactions

The aforementioned adverse reactions occur in the majority of patients receiving PEG-IFN plus RBV standard therapy. Other notable adverse reactions with lower incidence include infections (herpes simplex, urinary tract infection, bronchitis, oral candidiasis), ocular abnormalities (blurred vision, dry eye, ocular inflammation, eye pain), ear and inner ear abnormalities (vertigo, ear pain), cardiac abnormalities (palpitations, tachycardia), vascular abnormalities (flushing), chest pain, dry mouth, and oral ulcers.

## 2. Adverse Reactions of DAA Regimens

Direct-acting antiviral therapy for hepatitis C can achieve cure rates exceeding 90%, with some regimens approaching 100%. DAAs represent the currently recommended treatment approach, ushering in a pan-genotypic era for antiviral therapy in chronic HCV infection. Sofosbuvir (SOF)-based regimens are widely used in clinical practice, demonstrating high sustained virological response rates and good tolerability.

However, comprehensive evaluation of DAA adverse reactions remains limited. One literature analysis of SOF-based DAA therapy identified adverse reaction cases with onset ranging from minutes after administration to weeks following

discontinuation, with a median time of several weeks. Adverse reactions primarily involved the hepatic system, followed by the hematological, digestive, and immune systems. Common manifestations included fatigue, nausea, and headache. Studies have indicated that SOF-based anti-HCV therapy may cause myocardial enzyme abnormalities, severe bradycardia, and conduction block, often associated with concomitant amiodarone use, though the mechanism remains unclear. A meta-analysis by Caldeira et al. found that SOF-based regimens did not increase the incidence of cardiac adverse events, though the overall quality of evidence was low. In summary, co-administration with amiodarone is not recommended during DAA therapy to avoid serious adverse cardiac events.

Endocrine dysfunction, including hypothyroidism and hyperthyroidism, represents another concern with interferon-based therapy that requires monitoring.

### **3. Nursing Interventions**

#### **3.1 Pre-treatment Intervention**

Comprehensive communication with patients and families before hepatitis C therapy is essential. Discussion should cover treatment objectives, duration, costs, policy support, efficacy expectations, and potential adverse reactions. Healthcare providers should assess patients' family and social support systems, emphasizing that most adverse reactions are reversible and predictable. This preparation enhances psychological readiness and promotes treatment adherence.

#### **3.2 Management of Flu-like Symptoms**

Many patients develop fever and chills within hours after PEG-IFN administration, sometimes accompanied by headache, myalgia, and generalized malaise. Nurses should proactively explain these reactions before injection to prepare patients mentally. Patients should rest in the ward after injection to facilitate observation of reaction severity. Antipyretic analgesics may be administered when necessary. To minimize discomfort, interferon can be injected at bedtime or accompanied by analgesic medication. Physical cooling measures should be implemented for high fever, with prompt drying of sweat, fluid replacement, and linen changes to maintain cleanliness.

#### **3.3 Dietary Intervention and Nutritional Guidance**

Adverse reactions from both standard and DAA regimens commonly affect the digestive system, causing varying degrees of anorexia, reduced food intake, and weight loss, increasing malnutrition risk and potentially compromising antiviral efficacy. Previous research indicated that total caloric requirements increase during treatment weeks, necessitating additional calories, primarily from carbohydrates. Patients should be encouraged to have a carbohydrate-rich snack before bedtime. During flu-like episodes, adequate hydration is crucial. Pa-

tients should be advised to arrange meals according to their condition, emphasizing light, vitamin-rich foods with increased high-quality protein intake (lean meat, eggs, fish). Protein supplements may be used when necessary, with easily digestible foods preferred. Alcohol, high-sugar foods, and excessive legumes should be avoided. Dietary intervention helps reduce weight loss and improve interferon tolerance. As appetite improves during later treatment stages, resting energy expenditure gradually normalizes, allowing gradual reduction in caloric intake.

### 3.4 Psychological Care

Limited public understanding of hepatitis C, including misconceptions, leads to social stigma and isolation, causing significant psychological burden, shame, and humiliation. Patients also worry about disease progression and financial costs, exacerbating anxiety and depression. In addition to thorough communication, healthcare providers can use assessment tools such as the Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) to evaluate psychological status and provide early intervention. For high-risk patients, selective serotonin reuptake inhibitors (SSRIs) such as paroxetine, fluoxetine, sertraline, nortriptyline, citalopram, or imipramine may be prescribed before treatment to prevent or mitigate depression. If severe psychological issues such as self-harm or suicidal ideation emerge despite interventions, medication adjustment or discontinuation should be considered, with enhanced family involvement and safety monitoring.

### 3.5 Activity and Rest

Balanced activity and adequate rest are essential for hepatitis C patients. Activity levels should be tailored to individual tolerance, avoiding overexertion and heavy physical labor. When liver function tests are markedly abnormal, patients should maintain regular schedules and avoid staying up late. After several months of normalized liver function, activity may be gradually increased, though overexertion should still be avoided. Moderate aerobic exercise such as walking, jogging, or yoga is recommended, with each session lasting approximately 30 minutes and adjusted according to physical condition.

### 3.6 Skin and Oral Care

Patients should maintain skin cleanliness using warm water and mild, non-irritating cleansers, avoiding prolonged chemical exposure. Sun protection and moisturization are important, with soft, loose cotton clothing recommended. For rashes, patients should seek medical care rather than self-medicate to avoid increasing hepatic burden. Oral hygiene should be maintained with gentle brushing using soft-bristled toothbrushes to reduce bleeding and infection risk.

### 3.7 Injection Site Care

Long-term subcutaneous interferon injection can cause local pain, bruising, and induration. Nurses should provide thorough explanation to reduce patient anxiety. Injection sites should include the abdomen and outer thighs, avoiding the umbilicus. Painless injection techniques following the “two fast, one slow” principle should be employed. Post-injection pressure should be maintained for 3-5 minutes. Induration results from repeated injections at the same site, superficial injection, and poor local circulation. To promote absorption and prevent induration, injection sites should be rotated. Warm compresses and topical agents may be applied to alleviate local symptoms.

### 3.8 Management of Complications

**Hair Loss:** Interferon-induced alopecia should be explained as reversible, with recovery after treatment discontinuation. Patients should be advised on hair care methods, including vitamin E, traditional Chinese medicine supplements, and natural shampoos.

**Cytopenias:** Interferon can cause reductions in platelets and neutrophils, requiring dose adjustment or discontinuation when necessary. Patients should avoid fatigue, prevent colds, and limit exposure to crowded places. For anemia, iron supplementation and iron-rich foods (black fungus, red dates) are recommended. Patients with severe anemia should rest and avoid sudden movements to prevent dizziness and falls.

### 3.9 Health Education

No vaccine currently exists for hepatitis C prevention, making transmission interruption the primary control measure. Studies have shown that health education significantly improves patient knowledge about the disease. Healthcare providers should emphasize the preventable and controllable nature of hepatitis C to alleviate concerns and improve adherence. Targeted education based on patients' interests and educational levels enhances disease adaptation and coping abilities.

### 3.10 Information Technology Applications

With rapid development of information technology, telemedicine and digital follow-up methods are increasingly optimized. Research has demonstrated that mobile APP combined with WeChat follow-up is superior to traditional models. Healthcare providers can deliver health knowledge through digital platforms, enabling real-time learning for patients and families. This approach facilitates communication, allows timely monitoring of patient conditions, reduces hospital visits, conserves medical resources, and aligns with modern information-seeking behaviors. Daily tracking of patient engagement provides supervision while enabling continuous knowledge acquisition, enhancing self-care awareness and treatment adherence.

#### 4. Conclusion

Comprehensive, multidimensional nursing interventions should be implemented from the initial stages of hepatitis C pharmacotherapy. The treatment process involves various adverse reactions of differing severity, including psychological changes and abnormal laboratory values, which may lead to treatment interruption. These warrant serious attention from healthcare providers. Providing professional guidance and support to patients and families throughout the treatment course ensures completion of full therapy, improves adherence, and enhances prognosis.

#### References

- [1] TIAN S, HAO J L, HAN J, et al. Clinical application of hepatitis C drugs in China[J]. *Cap Food Med*, 2017. (in Chinese)
- [2] WORLD HEALTH ORGANIZATION. Global hepatitis report, 2017[EB/OL]. (2017). <https://www.who.int/publications/i/item/9789241565455>
- [3] HOU Y H, LIU T F, ZHAO X Q, et al. Impact of different direct-acting antivirals on the clinical outcome of genotype 1b chronic hepatitis C and compensated hepatitis C cirrhosis[J]. *J Clin Hepatol*, 2020. (in Chinese)
- [4] HEPATOLOGY BRANCH OF CHINESE MEDICAL ASSOCIATION, INFECTIOUS DISEASES BRANCH OF CHINESE MEDICAL ASSOCIATION. Updated Edition of Guidelines for Prevention and Treatment of Hepatitis C[J]. *J Pract Hepatol*, 2020. (in Chinese)
- [5] HEPATOLOGY BRANCH OF CHINESE MEDICAL ASSOCIATION, INFECTIOUS DISEASES BRANCH OF CHINESE MEDICAL ASSOCIATION. Guidelines for Prevention and Treatment of Hepatitis C, 2019[J]. *Chin J Hepatol*, 2019. (in Chinese)
- [6] NEGISHI H, TANIGUCHI T, YANAI H. The interferon (IFN) class of cytokines and the IFN regulatory factor (IRF) transcription factor family[J]. *Cold Spring Harb Perspect Biol*, 2018.
- [7] SILVA SACERDOTE A BDA, FILGUEIRA N A, DE BARROS BARRETO S, et al. Long-term persistence of anti-rod and rings antibodies in patients with chronic hepatitis C after antiviral treatment[J]. *J Exp Med*, 2019.
- [8] LANGNESS J A, NGUYEN M, WIELAND A, et al. Optimizing hepatitis C virus treatment through pharmacist interventions: identification and management of drug-drug interactions[J]. *World J Gastroenterol*, 2018.
- [9] DIETERICH D T. Treatment of hepatitis C and anemia in human immunodeficiency virus-infected patients[J]. *J Infect Dis*, 2019.
- [10] GUO F, DOU J, XU Q, et al. The efficacy of sofosbuvir-based DAAs treatment on chronic hepatitis C patients with pan-genotypic hepatitis C viral infection[J]. *Chin Hepatol*, 2020. (in Chinese)

- [11] LIANG X Y, CAO M X, HUANG J, et al. Literature analysis of adverse reactions caused by direct-acting antiviral agents based on Sofosbuvir in the treatment of viral hepatitis C[J]. Clin Med J, 2020. (in Chinese)
- [12] GHEMBAZA M E L A, LOUNICI A. Bradyarrhythmia induced by amiodarone-sofosbuvir co-administration[J]. Indian J Gastroenterol, 2018.
- [13] SEYAMM S, FRESHWATER D A, O' DONNELL K, et al. Weight loss during pegylated interferon and ribavirin treatment of chronic hepatitis C[J]. J Viral Hepat, 2018.
- [14] CALDEIRA D, RODRIGUES F B, DUARTE M M M, et al. Cardiac harms of sofosbuvir: systematic review and Meta-analysis[J]. Drug Saf, 2019.
- [15] SUWANTARAT N, TICEA D, KHAWCHAROENPORN T, et al. Weight loss, leukopenia and thrombocytopenia associated with sustained virologic response to Hepatitis C treatment[J]. Int J Med Sci, 2018.
- [16] JIANG H, ZHANG W, CHEN X. Peginterferon-alpha and ribavirin combination in treatment of patients with chronic hepatitis C and its impact on resting energy expenditure and nutritional status[J]. J Pract Hepatol, 2019. (in Chinese)
- [17] ZHAO J, LIU Y Z, DAI L, et al. The effect of interferon and ribavirin combination antiviral therapy on energy metabolism in patients with chronic hepatitis C[J]. Parenter & Enter Nutr, 2018. (in Chinese)
- [18] LIU Y, WANG X, SUN N, et al. Health education to improve cognition of hepatitis C patients[J]. World Latest Med Inf, 2019. (in Chinese)
- [19] DING L H. Observation and nursing care of peginterferon in the treatment of hepatitis C[J]. World Latest Med Inf, 2018. (in Chinese)
- [20] SUN Z J. Research progress on treatment and nursing of hepatitis C[J]. Shanxi Med J, 2019. (in Chinese)
- [21] ZHOU Y. Nursing measures for chronic hepatitis B treated by subcutaneous injection of interferon[J]. Guide China Med, 2018. (in Chinese)
- [22] YUE Y Y. Effect of APP combined with WeChat follow-up on compliance behavior and quality of life of patients with hepatitis C cirrhosis[J]. Clin Res, 2020. (in Chinese)
- [23] LIU Y, LI Z Y, WANG J N, et al. Effects of hepatitis C virus infection on the safety of chemotherapy for breast cancer patients[J]. Breast Cancer Res Treat, 2018.
- [24] HERNANDEZ N, MELKI I, JING H, et al. Life-threatening influenza pneumonia in a child with inherited IRF deficiency[J]. J Exp Med, 2018.
- [25] HAMER C. The impact of combination therapy with peginterferon alpha-2a and ribavirin on the energy intake and body weight of adult hepatitis C patients[J]. J Hum Nutr Diet, 2018.

[26] FIORAVANTE M, et al. Weight loss and resting energy expenditure in patients with chronic hepatitis C before and during standard treatment[J]. Nutrition, 2018.

[27] GAO Y J. Common drugs for anti-hepatitis C virus[J]. Clin Med J, 2017. (in Chinese)

[28] HEPATOLOGY BRANCH OF CHINESE MEDICAL ASSOCIATION, INFECTIOUS DISEASES BRANCH OF CHINESE MEDICAL ASSOCIATION. Guidelines for Prevention and Treatment of Hepatitis C, 2015[J]. Chin J Hepatol, 2015. (in Chinese)

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