Interferon Treatment of Viral Hepatitis
Practical Recommendations

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Summary

Since the end of the 1980s, interferons have been widely used to treat viral hepatitis B and C. Numerous therapeutic regimens involving different dosages, administration frequencies and therapy durations have been used in various clinical and virological situations. The mode of administration and treatment modalities remain similar whatever the type of viral infection.

Absolute contraindications to giving interferon are few. Nevertheless, this treatment should not be considered in the presence of severe cardiovascular, pulmonary, endocrine or neurological disturbances. Disruption of haematological and thyroid functions may limit treatment, and markers of autoimmunity must be carefully monitored because they can be either virologically induced or coexist with a viral infection. Clinical tolerance is assessed through regular follow-up which aims to detect any significant decline in the patient’s general status or the presence of neuropsychiatric manifestations, skin disorders or, more rarely, pulmonary or cardiovascular problems that might justify a dosage reduction or discontinuation of therapy.

Biological monitoring of therapy aims first to evaluate haematological and thyroid tolerance and secondly to evaluate biological and virological efficacy.
Serum transaminases should always be monitored, and beyond this the quantitative follow-up of viral replication markers is the most useful means to monitor virological efficacy of treatment. These markers allow rapid judgment of the response and optimal adaptation of treatment after taking into account the various biological and virological clinical parameters.

Since the end of the 1980s, the interferons have been the antiviral molecules most widely used in the treatment of viral hepatitis B (HBV) and C (HCV), and these agents are licensed for this purpose in many countries.

Widespread use has enabled precise assessment of the responses expected to therapy according to the virus involved and various prognostic factors. Furthermore, more is now known about the medium-term clinical and biological evolution of treated patients. Finally, the large number of patients treated according to various schedules of dosage and duration now enables evaluation of the general tolerability of the interferons and of various adverse effects that were not readily appreciated in the early years of interferon treatment. These observations now allow specific recommendations for the clinical and biological monitoring necessary during follow-up of patients treated with interferon.

1. General Principles of Interferon Therapy

1.1 Types of Interferons

Leucocyte interferon-α (IFNα) and fibroblast interferon-β (IFNβ) are both used in the treatment of chronic viral hepatitis. Recombinant or lymphoblastoid interferons are available in different countries for both types of molecule.

In Europe and North America, recombinant IFNα is the most widely used. Lymphoblastoid IFNα is usually used in Southern Europe, whereas IFNβ is widely used in Asia and Japan. IFNα is administered subcutaneously or intramuscularly, whereas IFNβ is injected intravenously or subcutaneously.

1.2 Administration

IFNα is administered subcutaneously or intramuscularly, sometimes by a nurse, but more frequently by the patient after a short training. It is usually an ambulatory treatment, injections being made in the evening to avoid disruption to everyday life. Injections are usually made 3 times weekly, sometimes daily in some regimens. Intravenous IFNβ injections require more medical or paramedical involvement.

1.3 Dosage and Treatment Duration

In viral hepatitis, doses usually vary between 3 and 10MU, with an injection frequency of 3 to 7 times weekly.

Treatment duration varies according to the situation, but is at least 6 months unless therapy has obviously failed. Maximal duration varies according to indication, response and tolerance of treatment. Longer term treatment is sometimes beneficial, especially to prevent relapse or severe viral reactivation.

1.4 Adverse Effects

The nature of the interferon molecule and its pleiotropism explains the wide diversity of possible adverse effects which must be monitored for during follow-up (table 1).

At the doses currently recommended for the treatment of chronic hepatitis B or C, adverse effects are generally mild. Most are dose-dependent, but a dosage reduction or discontinuation is rarely justified.\(^{1,2}\)

1.4.1 'Flu-Like Syndrome'

This often occurs at the beginning of treatment with a 3MU dose and tends to become universal with higher dosages. Fever, myalgia, arthralgia and chills may be reported.

The intensity of these symptoms usually decreases or disappears after some weeks. They can be alleviated with paracetamol (acetaminophen)