

Hep C factsheets

Treatment side effects



Ribavirin

Interferon

Impairment of cognition

Mood disorders/depression

Assessment

People at risk

Treating side effects

Pharmacological interventions

Antidepressants

Opioid antagonists

Psychostimulants

Also see

Ribavirin

Combination therapy involves the use of pegylated interferon injections, once a week, and daily ribavirin capsules.

A potentially serious side effect of ribavirin is anaemia caused by haemolysis (destruction of red blood cells and resultant release of haemoglobin). Doctors will therefore monitor a person's blood counts very closely, especially in the first few weeks.

Also, ribavirin has been shown to cause birth defects in animal studies. Combination therapy, therefore, is not available to women who are pregnant and/or breastfeeding, or to anyone (both women and men) who do not use adequate contraception during, and for up to six months after, treatment.

Interferon

The most common side effects of interferon treatment (pegylated and standard regimes) are flu-like symptoms such as chills, fever, malaise, myalgias (muscle pain), and anorexia. Other common side effects include depression, paraesthesia (tingling or crawling of the skin), impaired concentration, amnesia, confusion, anxiety, sexual dysfunction such as alibido (lack of sex drive or response to sexual stimulus), failure to gain erection or failure to orgasm; mild dementia with apathy and decreased motivation; and cognitive dysfunction such as memory loss, apathy, and a slowing down of mental processes.

These symptoms are rarely severe and appear to be dose related and reversible. On rare occasions, acute (short term) mental status changes, including delirium, psychosis, and neurologic (nervous system) syndromes will occur.

The significance of these side effects increases, however, when they are chronic (long term) and markedly impact quality of life in people who are otherwise relatively well.

Impairment of cognition (thought, perception & reasoning ability)

Even after a single low dose of interferon, people have reported subjectively reduced alertness and slowed performance on a reaction time test up to 6 and 10 hours after injection.

Toxicity develops after several weeks of ongoing interferon therapy and includes subjective complaints of memory loss, depression, lack of initiative, and generalised slowing of thought process.

Most studies report the resolution of symptoms within 2 to 3 weeks following therapy. However, some people develop side effects that persist after treatment discontinuation, without any intervening change in their disease status.

Mood disorders/depression

The distinction between levels of depression is based on the intensity and duration of depressive symptoms; the presence or absence of associated physical, emotional, and cognitive symptoms; and the course of symptoms over time.

The actual rate of interferon-induced depression is unknown. When cancer patients treated with interferon complain of depression, they typically mean apathy, fatigue, and slowing of mental capabilities. Some people will experience dysphoria (feeling ill at ease and restless) at the beginning of treatment, with onset of other symptoms. For others, dysphoria comes later, possibly because cognitive symptoms become more severe or difficult to tolerate.

These people also may experience other psychological symptoms typical of major depression, including anhedonia (lack of pleasure with previously pleasurable acts) and helplessness. In vulnerable people, symptoms may become more difficult over time or with dose escalations, leading to dose modifications or temporary discontinuation.

There are multiple possible mechanisms by which interferon may cause neuropsychiatric (a psychological approach dealing with the nervous system) side effects; unfortunately, little of which is well understood.

Assessment

All people treated with interferon should be considered at some risk for development of an affective syndrome (mood swings), and for cognitive side effects as well. Although there is no standard method for assessing interferon induced depression, pre-treatment assessment should be done so that changes can be reliably detected and documented.

People at risk

Evidence of current or past depression should not be automatic grounds for exclusion from therapy, but does suggest that the person would be at higher risk for side effects. People currently treated with antidepressants should be monitored for needed dose adjustments or medication changes.

Treating side effects

Attempts to lessen or prevent interferon-induced psychological side effects have been hindered by a number of factors, including lack of recognition of the problem, a poor understanding of how psychological side effects are caused, and a lack of scientific trials of pharmacological interventions ('pills & potions' to prevent side effects).

To intervene effectively it is first necessary to raise a person's awareness of the possible problems. Discussion of possible side effects should take place before treatment.

People treated with interferon are sometimes reluctant to complain of depression or impaired cognitive function. This may be due to the stigma associated with psychiatric illness, or because they fear that they will be given a lower dose or be taken off therapy entirely.

Some people who complain of mood or cognitive side effects can be instructed to either "pace" themselves or alter their demanding work and recreational schedules to help maintain some reasonable amount of participation in normal activities.

For others, these interventions, which often are viewed as concessions, do not help and only add to their frustration and dissatisfaction.

Fatigue and depression encourage sedentary behaviour (low physical activity) that can be self-reinforcing, and people who are not active should be encouraged to maintain some level of physical activity.

In the event of suicidal ideations (thinking about suicide), delusions, or panic, therapy should be discontinued, and the use of anti-psychotic medications may be useful. Whether it is prudent to resume therapy in these cases is a matter of clinical judgment, although it is probably advisable to reduce the dose of interferon and closely monitor side effects.

Pharmacological interventions

Medications to address interferon-induced depression have not been formally studied in controlled clinical trials; however, a number of medications are currently used, and the lessening of psychological side effects appears to be a realistic goal. At least three classifications of drugs have shown some use.

Hep C factsheets

Treatment side effects

Antidepressants

Although single case reports have documented successful use of fluoxetine and nortriptyline in people treated with interferon for hepatitis C, there have been no published studies of the value of antidepressants commonly prescribed for interferon-induced depression.

In the cancer treatment setting, SSRIs (selective serotonin receptor inhibitors) have been used with some success. These medicines may counteract interferon-induced decreases in serum serotonin levels. Antidepressants, such as fluoxetine, may be advantageous because they also may improve the cognitive and behavioural slowing associated with interferon toxicity.

Tricyclic antidepressants are relatively more sedating than SSRIs. These medications increase levels of norepinephrine and, for many, serotonin. The anti-muscarinic effects of some tricyclic antidepressants can aggravate memory dysfunction secondary to interferon therapy itself.

Opioid antagonists

To date, the only study to evaluate opioid antagonists (a drug that opposes the effect of another) in this setting has investigated the opioid antagonist Naltrexone. The majority of people in this pilot study experienced partial or complete resolution of psychological symptoms; however, a consistent domain of psychological improvement could not be identified.

Psychostimulants

The use of psychostimulants to treat secondary depression is increasing. Methylphenidate is currently being investigated to treat interferon neurotoxicity. Their mood-elevating effects could be caused by their neurochemical activity or by a beneficial psychological reaction due to increased energy and improved concentration.

Also see

Treatment overview (factsheet)

Treatment consent (factsheet)

Treatment response (factsheet)

Also contact *The Hep C Helpline* who can provide further information or discuss peer support services:

9332 1599 (Sydney callers)

1800 803 990 (NSW regional callers)

- This article is abridged from "Mood & Cognitive Side Effects of Interferon-alpha Therapy", *Seminars in Oncology*, Vol 25, No 1, Supplement I (February), 1998, pp 39-47 by A. D. Valentine, et al.

It has been reviewed by the Hepatitis C Council of NSW Medical & Research Advisory Panel.

This factsheet was produced by the Hepatitis C Council of NSW and was last reviewed in May 2009

Hep C Helpline and *HepConnect* (peer support): 02 9332 1599 / 1800 803 990

Web info: www.hepatitisc.org.au Web peer support: www.hepcaustralasia.org

The Hepatitis C Council of NSW Inc is a community-based, non-government organisation, funded by the NSW Health Dept.