Psychiatric Guidelines for Hepatitis C Treatment (Interferon-based)

Introduction

- There is an increased prevalence of psychiatric co-morbidity in patients with chronic HCV infection
- Antiviral combination therapy with interferon-alpha and ribavirin is often associated with significant psychiatric side effects, such as depression (30-70%), fatigue (40-80%), insomnia (18-45%), irritability (16-50%), anxiety, cognitive disturbances and suicidal thoughts
- Depression and cognitive disturbances develop most commonly between week 4-24 and the depressive symptoms are the most intense between week 8-16
- Risk factors for IFN-alpha induced depression include baseline depressive symptoms, baseline sleep disturbance, personal history of major depression, depression during previous treatment with IFN-alpha, early vegetative symptoms (lack of sleep, loss of appetite etc) during treatment
- Between 10-14% of the patients discontinue therapy due to a psychiatric adverse effect

Recommendations for initial pre-treatment assessment

At the time of initial pre-treatment assessment by the BBV specialist professional, the following are recommended:

1. Ask the patient about any past history of depression or other significant psychiatric problems requiring treatment. Also ask about current or former drug use, history of suicide attempts and psychosocial issues (job, family, social circumstances and supports). If history of treated mental illness, suicide attempts or uncertainty then seek information from the GP (or CDPS CPN or Consultant) about patient’s psychiatric history. (Appendix 1).
2. For all patients please complete an initial Hospital Anxiety and Depression Scale (HADS). (Appendix 2)
3. It is advisable to send urine drug screen for patients with a past or current history of substance misuse/dependence including those on stable replacement prescription.
4. Complete a FAST questionnaire (Appendix 3) for all patients.
5. Information about possible psychiatric side-effects should be provided to all patients

Guidance for pre-treatment psychiatric assessment

Based on the information gathered above, some patients will require a formal psychiatric assessment. This should be arranged via the patient’s existing psychiatric team which may include general psychiatry, forensic psychiatry or addictions services. If the patient is currently not in psychiatric care, referral should go to a liaison psychiatrist (Dr Smyth at RIE, contact number: 0131 2421398 or Dr Batra at RIDU).
The flow chart in Table 1 may be used as a guide to decide on the appropriateness of making such a referral. This is not an exhaustive list and when in doubt, discussion with a psychiatrist or other mental health professional is encouraged.

**Recommendations during Hepatitis C treatment**

1. The following questions may be used by the BBV nurse to help screen for common psychiatric side-effects during each patient’s visit to them during Hepatitis C treatment:
   - During the past month (or since the last review) have you often been bothered by feeling down, depressed or hopeless?
   - During the past month (or since the last review) have you often found that you have had little interest or pleasure in doing things you normally enjoy?
   - When people are ill and feeling depressed, they often want to just ‘get it all over with’. Have you felt that way? Have you thought about killing yourself?
   - Have you had any new problems with your sleeping pattern since starting treatment for your Hepatitis C?

   If a patient answers ‘yes’ to any of these questions, it is advisable to repeat Hospital Anxiety and Depression Scale (HADS).

2. For all patients without current psychiatric co-morbidity, repeat HADS every 4 weeks in the first 3 months of treatment with interferon-alpha and then at least every 12 weeks until 12 weeks after treatment finishes.

3. If at any time HADS score is 8-10 in either depression or anxiety subset, repeat in 2-4 weeks time. If it is between 11 and 15, repeat in 1-2 weeks.

4. Patients with current psychiatric co-morbidity should have HADS repeated every 2-4 weeks in first 3 months of interferon-alpha therapy and then every 4-6 weeks until at least 12 weeks after the end of treatment.

**Guidance for psychiatric referral during treatment**

Psychiatric referral or liaison with existing psychiatric supports should be considered in the following group of patients on antiviral Hepatitis C treatment:

1. Any HADS with score greater than 16 in either depression or anxiety.
2. New onset suicidal thoughts or chronic suicidal thoughts that have increased in frequency and intensity.
3. Significant escalation in alcohol use or of other substances of abuse.
4. Suspicion of evolving hypomania or psychotic symptoms.
5. In complex and difficult psychiatric/social situation.
Guidance on prescription of psychotropic medication

- Prophylactic antidepressant should be considered in patients with depression during previous treatment with IFN-α, in those with baseline mild/moderate depressive symptoms (HADS 10-15), those with a past history of major depressive disorder
- Sleep disturbance before treatment and when emerging during treatment with interferon-alpha should be treated with hypnotics (eg zopiclone 3.75-7.5 mg every other night, 4 times/week), or sedative antidepressants (eg mirtazapine 7.5-30 mg at night, trazodone 50-75 mg at night)
- It is recommended to start antidepressant treatment early when indicated during interferon-based HCV treatment. First line agents could include citalopram (20 mg od), escitalopram (5 mg od), sertraline (50 mg od), fluoxetine (20 mg od), mirtazapine (30 mg od)
- Antidepressant should be continued for 12 weeks after discontinuation/completion of interferon combination treatment
- Telaprevir and boceprevir have significant interactions with a number of psychotropic medications. It is recommended to check for these at http://www.hep-druginteractions.org and when indicated adjust medication doses and monitor QTc intervals.

Further information

Please find references of some relevant papers on psychiatric implications of interferon-based hepatitis C treatment (Appendix 4).

I will be happy to discuss any queries relating to this document.

Ravneet Batra
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Table 1: Guidance for pre-treatment psychiatric assessment

Based on information from GP and initial 2 HADS scores

Patients with past psychiatric history

- Current history primarily of substance dependence
  - Link with addiction services or GP to assess stability. In general attendance at appointments and general assessment of stability by CPN or GP means suitable for Hep C treatment even if evidence of ongoing illicit drug use.

- H/O severe mental illness including psychotic illness, bipolar disorder, major depression OR history of deliberate self harm OR current diagnosis of personality disorder
  - Link with current psychiatric team OR concerned forensic team OR liaison psychiatry for patients under no other psychiatric care

- No psychiatric contact for the past 2 years & patient is on no current psychotropic medication
  - HADS (anxiety or depression score) 8 - 10
    - Repeat in 2 – 4 weeks
    - HADS <10
      - No psychiatric concerns for starting Hep C treatment.
      - Re-assess patient in 3 months Hep C treatment. Repeat HADS
      - HADS <10
    - HADS >10
      - Refer to liaison or forensic psychiatry or addiction services appropriately

Patients with no previous psychiatric history

- HADS 11-15
  - Discuss with GP or CDPS worker about starting antidepressants according to protocol below
  - Re-assess patient in 3 months Hep C treatment. Repeat HADS
  - HADS >16 OR ongoing suicidal thoughts OR concerns about serious mental disorder OR current chaotic substance misuse
Appendix 1.

HCV assessment clinic
Request for Information

Re: Name, address
DOB

Has given us permission to contact you regarding any psychiatric history you may be aware of. We are concerned about the possible psychiatric side effects of HCV treatment (interferon-based), in particular depression and we need to ensure we have assessed the above appropriately and have the right support in place if s/he were to be considered for treatment.

Past psychiatric history including drug dependency? Yes No
If yes, please give details...........................................................................................................
..............................................................................................................................................
..............................................................................................................................................
Any history of self harm? Yes No
Please give details..................................................................................................................
..............................................................................................................................................
..............................................................................................................................................
Current depression? Yes No
Antidepressant use? Yes No
If yes, what and how long have they been on these anti depressants for..........
..............................................................................................................................................
..............................................................................................................................................
Any other psychotropic medication including substitute prescription? Yes No
If yes, please give details........................................................................................................
..............................................................................................................................................
Linked in with psychiatric/ other support services? Yes No
If yes, who.................................................................................................................................
Do you have any psychiatric concerns of starting this individual on HCV treatment? Yes No
If yes, please give details........................................................................................................
..............................................................................................................................................
Is there a CPN attached to your practice? Yes No
If yes, please give contact details...........................................................................................

Please could you fill out the above and return it to: ..............................................................
..............................................................................................................................................

Thank you
Appendix 2.

**Hospital Anxiety and Depression Scale (HADS)**

This questionnaire is designed to help your clinician to know how you feel. Read each item below and underline the reply which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire. Don’t take too long over your replies, your immediate reaction to each item will probably be more accurate than a long thought-out response.

<table>
<thead>
<tr>
<th>AD</th>
<th>I feel tense or ‘wound up’</th>
<th>I feel as if I am slowed down</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Most of the time</td>
<td>Nearly all the time</td>
</tr>
<tr>
<td>5</td>
<td>A lot of the time</td>
<td>Very often</td>
</tr>
<tr>
<td>7</td>
<td>From time to time, occasionally</td>
<td>Sometimes</td>
</tr>
<tr>
<td>1</td>
<td>Not at all</td>
<td>Not at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AD</th>
<th>I still enjoy the things I used to enjoy</th>
<th>I get a sort of frightened feeling like ‘butterflies’ in the stomach</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Definitely as much</td>
<td>Not at all</td>
</tr>
<tr>
<td>1</td>
<td>Not quite so much</td>
<td>Occasionally</td>
</tr>
<tr>
<td>2</td>
<td>Only a little</td>
<td>Quite often</td>
</tr>
<tr>
<td>3</td>
<td>Hardly at all</td>
<td>Very often</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AD</th>
<th>I get a sort of frightened feeling as if something awful is about to happen</th>
<th>I have lost interest in my appearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Very definitely and quite badly</td>
<td>Definitely</td>
</tr>
<tr>
<td>2</td>
<td>Yes, but not too badly</td>
<td>I don’t take as much care as I should</td>
</tr>
<tr>
<td>1</td>
<td>A little, but it doesn’t worry me</td>
<td>I may not take quite as much care</td>
</tr>
<tr>
<td>0</td>
<td>Not at all</td>
<td>I take just as much care as ever</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AD</th>
<th>I can laugh and see the funny side of things</th>
<th>I feel restless as if I have to be on the move</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>As much as I always could</td>
<td>Very much indeed</td>
</tr>
<tr>
<td>1</td>
<td>Not quite so much now</td>
<td>Quite a lot</td>
</tr>
<tr>
<td>2</td>
<td>Definitely not so much now</td>
<td>Not very much</td>
</tr>
<tr>
<td>3</td>
<td>Not at all</td>
<td>Not at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AD</th>
<th>Worrying thoughts go through my mind</th>
<th>I look forward with enjoyment to things</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>A great deal of the time</td>
<td>As much as I ever did</td>
</tr>
<tr>
<td>2</td>
<td>A lot of the time</td>
<td>Rather less than I used to</td>
</tr>
<tr>
<td>1</td>
<td>Not too often</td>
<td>Definitely less than I used to</td>
</tr>
<tr>
<td>0</td>
<td>Very little</td>
<td>Hardly at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AD</th>
<th>I feel cheerful</th>
<th>I get sudden feelings of panic</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Never</td>
<td>Very often</td>
</tr>
<tr>
<td>2</td>
<td>Not often</td>
<td>Quite often</td>
</tr>
<tr>
<td>1</td>
<td>Sometimes</td>
<td>Not very often</td>
</tr>
<tr>
<td>0</td>
<td>Most of the time</td>
<td>Not at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AD</th>
<th>I can sit at ease and feel relaxed</th>
<th>I can enjoy a good book or radio or television programme</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Definitely</td>
<td>Very often</td>
</tr>
<tr>
<td>1</td>
<td>Usually</td>
<td>Often</td>
</tr>
<tr>
<td>2</td>
<td>Not often</td>
<td>Sometimes</td>
</tr>
<tr>
<td>3</td>
<td>Not at all</td>
<td>Very seldom</td>
</tr>
</tbody>
</table>

New check that you have answered all the questions.

<table>
<thead>
<tr>
<th>TOTAL</th>
<th>AD</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
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</tr>
</tbody>
</table>
Appendix 3

The FAST Test

1. How often do you have eight or more drinks on one occasion?
   __ Never    __ Less Than Monthly    __ Monthly    __ Weekly    __ Daily or Almost Daily

2. How often during the last year have you been unable to remember what happened the night before because you had been drinking?
   __ Never    __ Less Than Monthly    __ Monthly    __ Weekly    __ Daily or Almost Daily

3. How often during the last year, have you failed to do what was normally expected of you because of your drinking?
   __ Never    __ Less Than Monthly    __ Monthly    __ Weekly    __ Daily or Almost Daily

4. Has a relative or friend, a doctor or other health worker been concerned about your drinking or suggested you cut down?
   __ No    __ Yes, but not in the last year.    __ Yes in the last year.

Scoring the FAST Test

Score questions 1, 2 and 3 as follows:

- Never -- 0 points
- Less than monthly -- 1 point
- Monthly -- 2 points
- Weekly -- 3 points
- Daily or almost daily -- 4 points

Score question 4 as follows:

- No -- 0 points
- Yes, but not in the last year -- 2 points
- Yes, in the last year -- 4 points

The maximum score is 16. A total score of 3 indicates hazardous drinking.

If a person answer "never" on the first question, he or she is not a hazardous drinker and the remaining questions are not necessary.

If a person answers "weekly" or "daily or almost daily" on the first question, he or she is considered a hazardous drinker and the rest of the questions are skipped.

If a person answers "monthly" or "less than monthly" to the first question, the other three questions are needed to complete the screening for hazardous drinking.
Appendix 4.

References


