Original Article

Effect of Interferon on Prevalence of Insomnia in Chronic Hepatitis C Patients.

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Abstract:

Objective: The goal of this study was to estimate the impact of treatment response on prevalence of insomnia in chronic hepatitis C patients. **Methods:** This is a survey performed to hepatitis C patients using a representative sample of 354 patients aged 20 years or older from Mansoura specialized hospital and from Mansoura general hospital at start and end of treatment with interferon, laboratory and radiological assessment were done, Interviews were conducted using the Berlin insomnia scale. The questions were related to the risk of having sleep apnoea. **Results:** 18.67% (66 patients) of the sample reported insomnia during the study, 28.8% (102 patients) had insomnia both at the start and at the end, so 47.5% (168 patients) had insomnia total, the prevalence was higher in females than in males at start 53.9% vs. 46.1% (55 vs. 47 patients) and increased with age but at end males were more and no effect for age. **Conclusion:** Insomnia is frequent in hepatitis C patients, affecting 47.5% of patients. Results showed that insomnia is differently affected by sex with treatment.

Key Words: Insomnia and hepatitis C.

Introduction:

Hepatitis C Virus (HCV) infection is a major health problem in Egypt, where the prevalence is (10–20) folds higher than that in the USA. Egypt has the highest prevalence of HCV worldwide, ranging from 6% to more than 40% across regions and demographic groups.(1) Insomnia has been studied both as a symptom and as a sign.(2) Insomnia is studied in a variety of ways in the medical literature and popular press. Insomnia is defined by the presence of an individual's report of difficulty with sleep.(3) Insomnia is common and includes symptoms such as difficulty falling asleep or staying asleep, early morning wakening, and sleep dissatisfaction, as well as daytime consequences such as tiredness.(4) Several risk factors for insomnia were reported by the State-of-the-Science conference in June 2005, age and gender are the most clearly identified demographic risk factors, with an increased prevalence in women and older adults. The cause of this increased risk in the elderly is not well defined, it may be due to the partial decline in functionality of sleep control systems that may contribute to insomnia in this older population, the presence of comorbid medical conditions is also a significant contributor to the increased prevalence of insomnia in the elderly, in females insomnia is more prevalent with both the onset of menses and menopause. (5)Many studies investigating prevalence of insomnia in the USA and Europe, including the UK, however less is known about the onset and natural history of insomnia. These studies have highlighted factors associated with prevalent insomnia, and it is not clear what is cause and effect or whether the factors are linked with the onset or persistence of the problem. (6) 60% of chronic untreated HCV patients had sleep problems

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and 30% of patients on interferon therapy also had sleep problems, the non-pharmacological treatment of it includes:

1. Go to sleep when you are sleepy .If you cannot fall asleep within 20 minutes, get up and do something boring until you feel sleepy.
2. Naps as your doctor advises.
3. Have a regular sleep-wake schedule even on weekends.
4. Do regular exercise four hours before bedtime at least.
5. Innovate sleep rituals (listening to music, etc.) as cues to your body to sleep.
6. Use your bed for sleeping and intimacy only.
7. Stop caffeine containing beverages foods and medications nicotine and alcohol at least 4-6 hours before bedtime.
8. Eat a light snack before bed with a glass of milk, which contains sleep promoting tryptophan.
9. Have a hot bath before bedtime, as a drop in the body temperature will promote sleep.
10. Keep your bed and bedroom quiet and comfortable for example a cooler room is recommended and you can use a humidifier if the air is too dry.

The pharmacological treatment includes:

1. Benzodiazepines but has risks like tolerance, dependence, withdrawal, impaired cognition, respiratory depression and disrupted sleep: reduced slow wave sleep and rapid eye movement, it may give short term benefit in the acute phase of treatment of comorbid anxiety or mood disorders, in HCV patients lorazepam, oxazepam and temazepam are preferred as eliminated by glucoronidation which is spared in liver disease. Lorazepam and temazepam are better in maintenance insomnia as they have intermediate half-life.
2. Second generation antipsychotics for a variety of psychiatric disorders, it may be tempting to use sedating antipsychotics for treating primary insomnia but the metabolic risks included: weight gain, diabetes and hyperlipidemia also its great effects on sustained virological response rates during IFN and ribavirin combination therapy. [7]

Aim of this study:

The aim of this study was to study the effect of interferon on prevalence of insomnia in chronic hepatitis C patients.

Patients and Methods:

Study design: Cohort study.

Settings: This study was carried out at the Liver Unit of Mansoura University Hospital and Mansoura General Hospital.

Sample and sampling technique:

The study was carried out on 354 adult patients with chronic hepatitis C, of them 258 were males (72.88%) and 96 were females (27.11%). Informed consent to be included into the study was obtained from each patient.

Inclusion criteria: age > 20 years, Positive HCV antibody and HCV- RNA, Patients with liver biopsy proven chronic hepatitis, HBsAg negative.

Exclusion criteria: Age<20 years, co-infection with HBV, active alcohol consumption, HBsAg positive, pre-existing psychiatric condition, pregnancy or breast feeding and co-morbidities.

All patients have been subjected to thorough history taking and complete clinical examination, Laboratory investigations including: CBC (WBCs, hemoglobin & platelets), Bleeding time (BT), Alanine amino transferase (ALT) (U/L), Aspartate amino transferase (AST) (U/L), Serum bilirubin (mg/dl), Serum albumin (g /dl), Alkaline phosphatase (U/L), International normalized ratio (INR), Viral markers including HCV- antibody, HCV- RNA (IU/m1) and Hepatitis B surface antigen, ANA titre, SMA, AMA and LKM, TSH level, α fetoprotein (ng/dL), and pregnancy test for females**.**

Data collection and ethical considerations:

Consent to participate was implied by the return of the completed Berlin questionnaire[8], it was performed in the period between April 2012 and April 2013. completed by respondents on a voluntary choice and they were assured of confidentiality of their response, it was done for all patients after translation to Arabic and replied either by the patient directly or his relative asked him if he can't read, patients answered 3 groups of questions related to the risk of having sleep

apnoea, patient was considered low risk if one or no categories with positive score and he was considered high risk if two or more categories with positive score. The questionnaire includes: height (m), weight (Kg), age, sex and request to choose the correct answer

Group 1:

1. Do you snore?

a. yes

b.no

c. don't know

If you snore:

2. How your snoring is?

a. slightly louder than breathing.

b. as loud as talking

c. louder than talking.

d. very loud-can be heard in adjacent rooms.

3. How often do you snore?

a. nearly every day.

b. 3-4 times a week.

c. 1-2 times a week.

d. 1-2 times a month.

e. never or nearly never.

4. Has your snoring ever bothered other people?

a.yes

b.no

c.don't know

5. Has anyone noticed that you quit breathing during your sleep?

a.nearly every day.

b.3-4 times a week.

c.1-2 times a week.

d.1-2 times a month.

e.never or nearly never.

Group 2:

6. How often do you feel tired or fatigued after your sleep?

a. nearly every day.

b. 3-4 times a week.

c. 1-2 times a week.

d. 1-2 times a month.

e. never or nearly never.

7. During your waking time, do you feel tired, fatigued or not up to par?

a. nearly every day.

b. 3-4 times a week.

c. 1-2 times a week.

d. 1-2 times a month.

e.never or nearly never

8. Have you ever nodded off or fallen asleep while driving a vehicle?

a. yes

b. no

if yes:

9. How often does this occur?

a. nearly every day.

b. 3-4 times a week.

c. 1-2 times a week.

d. 1-2 times a month.

e. never or nearly never

Group 3:

10. Do you have high blood pressure?

a.yes

b. no

c.don't know

Group 1:

Question number 1: if yes 1point

Question number 2: if c or d 1point

Question number 3: if a or b 1 point

Question number 4: if a 1 point

Question number 5: if a or b 2 points, add points

Group 1 is positive if total score is 2 or more points.

Group 2:

Question number 6: question number 3: if a or b 1 point

Question number 7: if a or b 1 point

Question number 8: if a 1 point

Question number 9: noted separately, add points

Group 2 is positive if total score is 2 or more points.

Group 3: is positive if question number 10 is yes or the BMI is greater than 30/m^2

Statistical analysis:

Collected data were entered and analyzed using SPSS software version 17 qualitative data were expressed as count and percent and compared with Chi square or Fisher exact test quantitative data were expressed as Mean ±Standard deviation (SD) or Median and compared using Independent sample T test if normally distributed or Mann-Whitney test if not.

Results:

As shown in table (I) 18.67% (66 patients) had insomnia during the study, 28.81% (102 patients) had insomnia both at the start and at the end, 47.5% (168:66&102) had insomnia total, 52.5 %(186 patients) had no insomnia all through, the prevalence was higher in females than in males at start 53.9% vs. 46.1% (55 vs 47) but at end males were more 81.8%vs18.2%(54 vs 12)

As shown in table (II) there is significant increase of insomnia with age at start of treatment.

As shown in table (3) there is no significant changes of insomnia with age at end of treatment.

Table (I): Insomnia Groups:

	No Insomnia althrough	Insomnia althrough	No Insomnia at start but develops on treatment	Total	X^2	P value
Male	84.4% 157	46.1% 47	81.8% 54	258	52.247	<0.0001
Female	15.6% 29	53.9% 55	18.2% 12	96		
Total	52.5% 186	28.81% 102	18.67% 66	354		

Table (II): Age versus Insomnia groups before starting therapy

	No significant sleep disorder	Significant sleep disorder	Total	X^2	P value
Age between 20 and 30	30	0	30	17.74	<0.0001
Age between 30 and 40	93	33	126		
Age between 40 and 50	105	51	156		
Age between 50 and 6	24	18	42		
Total	252	102	354		

Table (III): Age versus Insomnia groups at end of therapy

	Age between 20 and 30	Age between 30 and 40	Age between 40 and 50	Age between 50 and 60	Total	X^2	P value
No significant sleep disorder	18	69	81	18	186	2.52	<0.47
Significant sleep disorder	12	57	75	24	168		
Total	30	126	156	42	354		

Discussion:

Insomnia needs to be assessed as such because it is multidimensional.[4] Patients with insomnia had greater loss of function than patients with congestive heart failure in reported pain, emotional effects, and mental health effects. Also, those patients reported more physical problems than patients with depression. During the daytime consequences of insomnia, the increased occurrence of accidents poses the greatest health risk. Insomniacs are 2.5 to 4.5 times more likely than controls to have an accident .The most common complications associated with insomnia are psychiatric disorders. It is estimated that 40% of all insomnia patients have a coexisting psychiatric condition. Among these psychiatric disorders, depression is the most common, heart rates were increased and variability was decreased in all stages of sleep in insomnia patients compared to healthy normal sleepers.[2]

Our study showed that 47.5% of patients had insomnia: 18.67% (66 patients) had insomnia during the study, 28.81% (102 patients) had insomnia both at the start and at the end, 52.5% (186 patients) had no insomnia all through, consistent with Roth who stated that insomnia is widely prevalent and affects approximately 30% of the population.[2]

The study showed that 18.67% (66 patients) had insomnia during the study, 28.81% (102 patients) had insomnia both at the start and at the end, 52.5% (186 patients) had no insomnia all through, The prevalence was higher in females than in males at start 53.9% vs. 46.1% (55 vs 47) but at end males were more 81.8% vs 18.2% (54 vs 12) which is consistent with Ohayon and Sagales[4] who stated that the prevalence was higher in females than in males (23.9% vs. 17.6%).

And also we found that insomnia increased with age which is consistent with Weyerer, Klink and Ohayon[9,10,11] who found a clear relationship between increasing age and insomnia.

At end of study we found that males had more insomnia than females which may be either due to good response of female to treatment or due to more stresses males are exposed to.

Conclusion:

Insomnia is frequent in hepatitis C patients, affecting up to half individuals (47.5%). Results showed that insomnia is differently affected by sex with treatment.

Recommendations:

More wide scale studies are needed to explain the insomnia in HCV patients

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