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Original Article

Depression scores of delta hepatitis patients treated with pegylated interferon alfa

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Abstract: The aim of this study is to evaluate and compare depression scores in chronic hepatitis delta patients during treatment with pegylated interferon by using Beck Depression Inventory-II. Between year 2010-2017 in two hospitals; Bursa Yuksek Ihtisas Research and Training Hospital and Gaziantep 25 Aralık State Hospital, 28 patients with delta hepatitis who were treated with pegylated interferon alfa and had completed the 48 weeks treatment period with negative HDV RNA values were included in the study. Beck Depression Inventory-II was applied to patients before treatment and at 1st, 3rd, 6th month and at the end of the treatment. The subjects average age was 41.21±11.04. Compared to the initial treatment, in the first month, 3rd month, 6th month and at the end of treatment, increases in Beck depression scores of 9.25, 14.00, 3.93 and 2.54 respectively were found to be statistically significant (P = 0.001; P<0.01). In patients with chronic delta hepatitis treated with pegylated interferon there were high scores of depression especially in the first 3 months of treatment. Patients should be followed closely during the treatment period for the possible development of depression.

Keywords: Hepatitis delta virus, depression, interferon alfa

Introduction

Hepatitis D (delta) virus (HDV) is a unique nuclear antigen in the hepatocytes of patients who have chronic hepatitis B infection (HBV) [1]. HDV is a worldwide infection with a prevalence of 5% in HBV carriers leading to nearly 20 million cases [2]. It is highly endemic in developing nations where HBV remains poorly controlled especially in northern parts of South America, Central Africa, and the Middle East regions [3]. Intermediate prevalence is seen in much of Eastern Europe, Turkey, and Central and South America [4]. HDV leads to fulminant hepatitis and further disease progression among hepatitis B infected patients [5]. HDV worldwide is the least common and most severe form of the chronic viral hepatitis and ironically the one for which new and effective treatments have been slowest to develop. The only treatment choice available is interferon-α (IFN-α). Nucleoside and nucleotide analogs, are not effective in the treatment of HDV infection [6, 7]. Serious side effects of interferons may lead to withdrawal of the therapy [8]. Interferon alpha (IFN) treatment is frequently associated with psychiatric side effects leading to significant depressive symptoms in 30-70% of patients. Therefore treatment discontinuation can occur in some cases [9]. If IFN-related depression can be identified early, patients outcomes might be improved significantly [10]. The Beck Depression Inventory II [11] is a 21-item self-report questionnaire for investigating depressive symptomatology. The BDI-II has cutoff scores for severity of symptoms: 0-13 = minimal, 14-19 = mild, 20-28 = moderate and 29-63 = severe. Significant depressive symptoms are especially important for a cutoff score of ≥17. BDI-II has been supported in many studies and it is one of the most common measurements of depression [12, 13]. One reliable predictor of IFN-related depression is the severity of depressive symptoms prior to the start of IFN treatment [14]. Assessing patient tendency to depression can help the clinician to take precautions for early psychiatric consultation and treatment of the patient while taking IFN [15]. The most important methods of determining the patients at risk of developing IFN-induced

Table 1. Distribution of demographic features

Age (year)	Min-Max (Median)	21-67 (41)
	Average ± Sd	41.21±11.04
Sex	Female	12 (42.9)
	Male	16 (57.1)
Education	Illiterate	1 (3.6)
	Literate	1 (3.6)
	Primary School	4 (14.3)
	Middle School	8 (28.5)
	High School	9 (32.1)
	University	5 (17.9)
Marital Status	Single	5 (17.9)
	Widow	7 (25.0)
	Married	16 (57.1)
Income level	0-1500	9 (32.1)
	1500-2500	10 (35.8)
	2500-5000	3 (10.7)
	≥5000	6 (21.4)

depression are interviews and clinical evaluation of the patient rather than expensive analyses and examinations [16]. In this study, we aimed to assess patients depression scores before, during and at the end of the treatment by using Beck Depression Inventory-II.

Material and methods

Between 2010-2017 in two hospitals, both belonging to ministry of health; Bursa Yuksek Ihtisas Research and Training Hospital and Gaziantep 25 Aralık State Hospital; 28 patients with delta hepatitis who were treated with pegylated interferon alfa and had completed the 48 weeks treatment period with negative HDV RNA values were included in the study. Beck Depression Inventory-II was applied to patients before treatment and in the 1st, 3rd, 6th month and at the end of the treatment. Approval of ethics committee was received. Participants provided written informed consent and information about age, gender, education, marital status and income. Medical records were also reviewed.

Statistical methods

For statistical analysis, NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) programme was used. Mann Whitney U test was used for two group quantitative data comparison. Kruskal Wallis test was used for three or more group comparison. Friedman Test was used for inside group comparison and Wilcoxon Signed Ranks Test was used for evaluation of binary comparisons. Spearman's Correlation Analysis was used for evaluation of correlation among variables. $P<0.05$ was considered significant.

Results

This study included 12 females (42.9%) and 16 male males (57.1%), which makes it a total of 28 patients from the Gaziantep State Hospital and Bursa Yuksek Ihtisas Research and Training Hospital. The average age of the patients was 41.21±11.04 between 21 and 67. While the education level of the patients that were illiterate, literate, primary school, middle school high school and university had rates of 3.6%, 14.3%, 28.5%, 32.1%, 17.9% respectively. 57.1% of the cases were married. The income level of the patients were; 32.1% 0-1500 TL (Turkish Liras), 35.8% 1500-2500 TL, 10.7% 2500-5000, 21.4% 5000 and more (**Table 1**). The average Beck depression scores before treatment and at 1st, 3rd, 6th months, and at the end of the treatment were 9.14±5.22, 18.39±5.96, 23.14±8.84, 13.07±4.22, 11.68±4.00 respectively. Changes in these scores according to follow up were found statistically significant ($P = 0.001$; $P<0.01$). In order to evaluate these significant differences, binary comparisons were made statistically. When compared to pre-treatment for the average Beck depression score; 9.25 increase in the 1st month, 14.0 increase in the 3rd month, 3.93 increase in the 6th month 2.54 at the end of the treatment were found statistically significant ($P = 0.001$; $P<0.01$) (**Table 2**). For the female patients the average increase in Beck depression score at the end of the treatment compared to pre-treatment was 2.92 whereas for the male patients it was 2.25. This difference was not found statistically significant ($P>0.05$). As far as education level is concerned, in patients below high school education the Beck depression scores increased 2.71 units after treatment compared to pre-treatment. Whereas this score was 2.36 for the patients with higher level education. The difference was not statistically significant ($P>0.05$). In single and married patients the average increase in the Beck depression score post-treatment compared to pre-treatment was 2.33 and 2.69

Table 2. Evaluation of Beck depression scores

	Beck Depression Scores		*P*
	Min-Max (Median)	Avr ± Sd	
Before Treatment	0-20 (9)	9.14±5.22	*0.001*[a,**]
1st Month	7-32 (19)	18.39±5.96	
3rd Month	10-51 (21)	23.14±8.84	
6st Month	1-21 (14)	13.07±4.22	
After treatment	3-18 (12)	11.68±4.00	
Differences			
1st Month-Before Treatment	1-16 (10)	9.25±4.33	*0.001*[b,**]
3rd Month-Before Treatment	2-47 (12.5)	14.00±9.16	*0.001*[b,**]
6th Month-Before Treatment	-10-11 (4)	3.93±4.21	*0.001*[b,**]
After-Before Treatment	-3-8 (2)	2.54±2.56	*0.001*[b,**]

[a]Friedman Test, [b]Wilcoxon Signed Ranks Test, **P<0.01.

Table 3. Evaluation of changes in Beck depression scores according to demographic features

		n	After T.-Before T. Change of Beck Depression		*P*
			Min-Max (Median)	Avr ± Sd	
Sex	Female	12	0-8 (2.5)	2.92±2.15	*0.464*[c]
	Male	16	-3-7 (2)	2.25±2.86	
Education	Below High School	14	-3-8 (2.5)	2.71±3.12	*0.944*[c]
	Above High School	14	-2-6 (2)	2.36±1.95	
Marital Status	Single	12	-3-8 (2)	2.33±2.99	*0.944*[c]
	Married	16	-1-7 (2)	2.69±2.27	
Income Level	0-1500	9	1-7 (3)	3.22±2.11	*0.611*[d]
	1500-2500	10	-1-8 (2)	2.40±2.27	
	≥2500	9	-3-6 (2)	2.00±3.32	

[c]Mann Whitney U Test, [d]Kruskal Wallis Test.

Table 4. Relation of changes in age and Beck depression scores

		After T.-Before T. Change of Beck Depression
Age (year)	r	-0.250
	P	0.199

r: Spearman's Correlation Coefficient.

respectively without reaching statistical significance (P>0.05). In low income level with 0-1500 TL (Turkish Liras), the average Beck depression score increased 3.22 units in patients after treatment compared to before treatment. This score was 2.40 and 2 units in patients with 1500-2500 TL and over 2500 TL income level respectively which has no statistical significance (P>0.05) (**Table 3**). Negative relation of 25% level between age and change of Beck depression score before and at the end of treatment was not statistically significant (r: -0.250; P = 0.199; P> 0.05) (**Table 4**).

Discussion

Chronic HDV appears to be a long-lasting infection with a relatively high tendency to evolve to cirrhosis [17]. It is the most severe form of chronic hepatitis and and the only treatment option is interferon-α (IFN-α) which has also been used for treatment of chronic hepatitis B and C. IFN-α in patients receiving treatment for HCV leads to the emergence of a major depressive episodes in a meaningful subset of patients [6, 7, 18]. Depressive symptoms during IFN treatment has fluctuations leading to a need for examination of early and later onset of depression. This can help the clinician to guide treatment decisions [19, 20]. In a previous study in HCV patients receiving pegylated interferon, patients had severe depression from the first weeks but without receiving any psychiatric drug treatment in some of the patients, spontaneous remission occurred. Therefore, delaying antidepressant treatment according to this observation for interferon related depression is not ethical [21]. In a previous study, higher age, lower education level, being unmarried, and poor social support did not appear to be risk factors for the development of depression in elderly healthy subjects [22]. A sex difference in prevalence of depression with twice as much women as men having a life time diagnosis is observed in community samples [23]. Sex, age, educational, and marital status were considered potential demographic correlates of major depression onset. Marriage is a protective factor for development of depression [24]. A meta-analysis by Lorant et al indicated a stronger relation of

depression with income than with education [25]. Socioeconomic characteristics, such as low income, low education level, debt and unemployment, are generally associated with higher rates of having mental health problems [26]. For the time being, the only management available for Chronic Hepatitis Delta is treatment with interferons. Potential treatment targets and strategies need testing in the human condition [27]. Therefore in the near future, interferon still seems to be the preferred drug in clinical use for the treatment of hepatitis delta, observations on the aforementioned side effect is worth studying. In our study, we found the opportunity to reach 28 hepatitis delta patients treated with pegylated interferon alpha. When compared to before treatment, for the average Beck depression score, the 9.25 increase in the 1st month and 14.0 increase in the 3rd month, was the most important observation of this study indicating that development of possible depression is most likely in first 3 months of the treatment period. Towards the end of the treatment period, this score becomes lower. Sex, education, marital status and income of the patients did not reach to a statistically significant difference for Beck depression scores. In summary, our study indicates that for the development of depression in patients treated with pegylated interferon alpha only important effect is the drug side effect itself independent from sex, education, marital status, income and laboratory values. Therefore all delta hepatitis patients who are scheduled to be treated with pegylated interferon should be closely followed during the treatment period, especially in the first 3 months.

Disclosure of conflict of interest

None.

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