Dream anxiety and early response to treatment in depressive disorder: A prospective analytical study

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Summary. Early response to treatment in depressive disorder is a predictor for duration of illness, full response and remission. Dream anxiety is a common complaint about which patient is distressed and reports to the clinician frequently. There are no studies assessing the relationship between dream anxiety and early response to treatment. The aim was to assess whether change in dream anxiety levels was related to early response to treatment in patients with depressive disorder. 106 patients with depressive disorder were assessed using HAM-D, Van dream anxiety scale at baseline and at follow-up after 1 week. Patients' adherence to treatment was evaluated by Morisky medication adherence scale-4 and those with high adherence were included for further assessment at follow-up. 41.5% of the study population had early response to treatment. There was 24.7% reduction in the dream anxiety levels after treatment. Improvement in dream anxiety scores (OR = 1.321, 95% CI = 1.079 - 1.618, p-value = 0.007) was significantly associated with early response to treatment. The improvement in dream anxiety was associated with early response to treatment in depressed individuals. Clinical assessment of change in dream anxiety levels could indicate to the early response to treatment, thereby helping in planning the management strategies.

Keywords: Depressive disorder, dream anxiety, early response

1. Introduction

Depression is a major public health problem contributing to significant morbidity, disability as well as mortality, along with significant socioeconomic losses. According to WHO 2017 report, Depression is the single largest contributor to non-fatal health loss globally. In certain circumstances, depression can provoke an individual for suicidal attempts, generally in first few weeks of the episode, which is one of the top 20 leading causes of death in 2015 world-wide.

Normally, anti-depressants take 4-6 weeks to show full response to treatment which makes the clinician lose the early crucial time (Kats et al., 2004; Machado-Vieira et al., 2010). Currently early response is gaining rise in emphasis as it helps in predicting the full response (78.3%) (Ciftci, Ulas, Topuzoglu, & Tunca, 2016) and planning treatment strategies. Though there are various other definitions, most commonly, early response to treatment has been defined as a 25% decrease in Hamilton depression rating scale (HAM-D) scores with respect to the initial scores after the first week of treatment (Cifiti et al., 2016, Crimson, 1999). Early response is the predictor of total duration of the illness, probability of remission and relapse (Machado-Vieira et al., 2010). As reported by Kats et al. (2004) and Mume (2009), the percentage of early response to anti-depressants ranges from 34% to 46%.

Dream anxiety (Nightmare) is the most common parasomnia occurring in depression (Beauchemin, & Hays, 1996), and frequently with poor self-image, loss of property and death which worsens their sleep quality and thereby socio-occupational functioning causing poor quality of life (Li, Zhang, Li, & Wing, 2010 and Mume, 2009). As reported in the literature, dream anxiety in depressed individuals' ranges from 17.5%- 28.4% (Mume, 2009 and American Academy of Sleep Medicine, 2015). Clinician encounters patients with dream anxiety frequently and it also cause significant distress in them (Akkaoui, Lejoyeux, d'Ortho, & Geoffroy, 2020). There is inconsistency in the studies regarding change in intensity and frequency of nightmares following use of anti-depressants.

Kerkhofs, Hoffmann, De Martelaere, Linkowski and Mendlewicz (1985) have studied the pattern of EEG in depressed individuals and described that increased REM density and sleep disturbance are considered as state markers for depression more evident during a particular episode. Similar changes in REM sleep (increased REM density) have been associated with nightmares or dream anxiety. There is no published literature available regarding the relation between dream anxiety and early response to treatment. Hence, we hypothesized and aimed at studying whether improvement in dream anxiety is related to early response to treatment in patients with depressive disorder.

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2. Method

It was a prospective - analytical study conducted in the Department of Psychiatry of a tertiary care hospital, South India. An approval from the Institutional Ethics Committee was obtained.

2.1. Participants

A total of 106 patients with depressive disorder were included in the study by convenient sampling. All patients aged between 18-59 years, with the diagnosis of depressive disorder (F32 and F33) according to ICD-10 (WHO, 1992), who were willing to give informed consent were included. Patients with any other psychiatric illness or mental retardation or those who were already on anti-depressants or other psychotropics or those who were unable to give informed consent due to severity of illness were excluded.

2.2. Assessment

Semi-structured proforma including the socio-demographic details and clinical parameters were assessed for all the patients satisfying the inclusion criteria. International classification of diseases – 10th edition (ICD-10) was used to diagnose depression in the patient. Hamilton depression rating scale (HAM-D) was used to assess the severity of depression. HAM-D 17 item questionnaire with score range of 0-50 was used in this study (Hamilton, 1960). Van Dream Anxiety Scale (VDAS) is a self-rated questionnaire with 17 questions (Agargun, Mehmet & Kara, H. & Bilici, Mustafa, 1999). Four questions are used only for clinical information. Thus, thirteen question scores are summed to yield a global VDAS score, which has a range of 0-52. Morisky medication adherence scale – 4 (MMAS-4) is a self-reporting scale with 4 items , each answered yes or no with score ranging from 0-4 (Morisky, Green, & Levine,1986).

2.3. Procedure

The participants were interviewed and a semi-structured proforma was used to record information about socio-demographic characteristics, clinical parameters and treatment details. They were assessed and diagnosed of having a depressive episode by a psychiatrist clinically using ICD-10 diagnostic criteria and the severity was assessed by Hamilton depression rating scale (HAM-D) and medication was started as per decision of treating psychiatrist. All the participants were evaluated for dream anxiety using Van dream anxiety scale (VDAS).

Patients were followed up after 1 week of treatment and treatment adherence was assessed by Morisky Medication Adherence Scale (MMAS). Patients with low adherence were excluded from the study. Patients with high adherence were further reassessed with HAM-D and VDAS. Changes in dream anxiety levels in patients with early response and in patients who did not show early response were compared. Severity of depression scores and dream anxiety scores were assessed separately by two psychiatrists both at baseline and during follow-up. Details of the study procedure were given in Figure 1.

Table 1. Means and standard deviations and percentages for the total sample and for each age group

Parameter	Early Response Yes (N=44)	Early Response No (N=44)	p value
Age (Mean ± SD)	29.52 ± 9.58	31.98 ± 10.03	0.244
Gender			
Male	13 (29.54%)	16 (36.36%)	0.463
Female	31 (70.45%)	28 (63.63%)	
Education			
Up to high school	14 (31.81%)	18 (40.90%)	0.275
Intermediate	13 (29.54%)	7 (15.90%)	
Above Graduate	17 (38.63%)	19 (43.18%)	
Location			
Rural	23 (52.27%)	22 (50%)	0.83
Urban	21 (47.72%)	22 (50%)	
Occupation			
Unemployed	27 (61.36%)	21 (47.72%)	0.61
Up to skilled	10 (22.72%)	10 (22.72%)	
Above Skilled	7 (15.90%)	13 (29.54%)	
Family type			
Nuclear	40 (90.90%)	39 (88.63%)	1.00
Others	4 (9.1%)	5 (11.4%)	
Socio Economic Status			
Upper-lower	9 (20.45%)	6 (13.64%)	0.64
Lower-middle	18 (40.90%)	15 (34.09%)	
Upper-middle	17 (38.64%)	23 (52.26%)	
Marital status			
Married	23 (52.27%)	20 (45.45%)	0.18
Others	21 (47.7%)	24 (54.5%)	
Duration of current episode (months)	6.14 ± 8.17	10.78 ± 11.97	<0.001*
Improvement in Dream Anxiety	4.68 ± 2.83	3.11 ± 2.05	<0.001*
Past episodes	10 (22.72%)	6 (13.63%)	0.269

Note. *p <0.05 is considered statistically significant. SD = Standard deviation

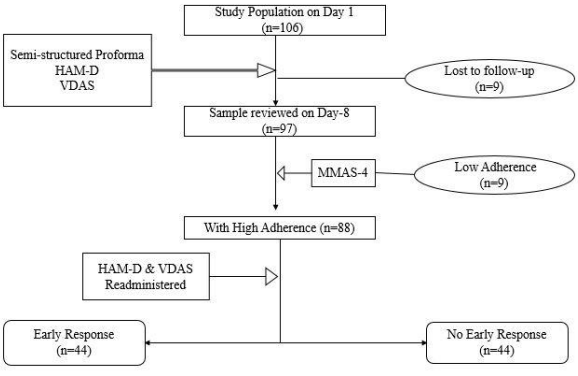

Figure 1. Outline of the study procedure

2.4. Statistical analysis

Frequencies with percentages were calculated for categorical variables, and mean and standard deviation were calculated for continuous variables. Shapiro- wilk test was conducted to assess normal distribution (p value of >0.05). For normally distributed quantitative parameters the mean values were compared between the study groups using Independent sample t-test. For non-normally distributed quantitative parameters, Medians and Interquartile range (IQR) were compared between the study groups using Mann Whitney u test. Categorical outcomes were compared between study groups using Chi square test or Fisher's exact test based on the cell size. Logistic regression analysis was applied to analyze the association between different variables with early response to treatment. A p-value < 0.05 was considered statistically significant. The Statistical Package for the Social Sciences version 22.0 (SPSS 22.0) for Windows was used for statistical analysis (Machines IBM, 2013)

3. Results

The mean age of the study population (n = 106) was 32.50 ± 10.60 years. Majority of them were females (66.98%), married (53.77%), living in nuclear families (90.57%), had graduate or postgraduate education (40.57%), unemployed (54.72%) and 14.5% of them had family history of depression. After the initial assessment, the study population were started on anti-depressants, mostly SSRIs (93.3%). Benzodiazepines (49.1%) and anti-psychotics (3.7%) were given as adjuvants. There is no significant difference of use of benzodiazepines between the two groups.

Early response to treatment was considered as the primary outcome. Among the study population, 88 (83.02%) participants had high adherence to treatment, of which, 44 (41.5%) participants showed early response. For the purpose of statistical analysis, the study population was divided into two groups, one with early response to treatment and the other without early response to treatment. There is no significant difference in age at presentation and other socio-demographic or clinical details in both the groups except for duration of current episode and improvement in dream anxiety which is significantly more in the group with early response to treatment (Table 1).

The mean scores of Hamilton Depression Rating Scale and Van Dream Anxiety Scale were significantly less after 1 week of treatment in the group with early response when compared to the group without early response (p-value <0.001 and 0.002) (Table 2). In our study, none of the participant had increase in the dream anxiety levels after 1 week of treatment.

Improvement in dream anxiety levels (OR = 1.321; CI = 1.079–1.618; p-value = 0.007) and duration of current episode (OR = 0.950; CI = 0.905 – 1.000; p-value = 0.050) were significantly associated with early response to treatment. The odds of early response to treatment increased 1.321 (CI = 1.079 – 1.618) and 0.95 (CI = 0.905 - 1.000) times with each unit increase in dream anxiety level and duration of current episode respectively (see Table 3).

4. Discussion

This is the first study to consider the relationship between improvement in dream anxiety and early response to antidepressant treatment in depressive disorder. In our study, early response to treatment was found to be 41.5% which is in comparison with other studies which showed early response being in the range of 34 to 46 % (Kats et al, 2004; Li et al, 2010). The baseline mean Dream anxiety (VDAS) scores in our study were found to be 18.69 ± 4.775, which is similar to that of a study done by Bilici, Yazici, Ozer, Kavakci (2002). In this study, duration of current episode is lower in the group with early response to treatment, which is statistically significant and associated with the early response. This finding was similar to the results of previous literature in this area (Çiftçi et al., 2016).

Though the effect of Anti-depressants on dream anxiety is inconsistent, a systematic review by Tribl, Wetter and Schredl (2003) revealed that antidepressants reduce the dream recall frequency, thereby reducing the dream anxiety. Previous studies suggested that the level of Dream anxiety might be used to predict the severity of illness in depressed individuals (Bilici et al., 2002; Schredl, & Engelhardt, 2001). In contrast to finding in our study, few other studies revealed that there is an increase in dream anxiety or intensity of dreams after the use of anti-depressants (Kierlin, & Littner, 2011; Pace-Schott et al., 2001). But in most of these studies, the study duration was 2 weeks unlike our study in which we had followed up after 1 week. This difference in the duration of follow-up along with variations in the study population, sample size and cultural factors could be the reasons for the contrast of the results obtained in the present study regarding improvement in dream anxiety.

Our study focused on the changes in Dream anxiety levels, which can be monitored clinically, being a possible predictor of early response to treatment. There is no significant difference in baseline Van Dream Anxiety scale scores in both the groups in our study. However, there is significant improvement in Hamilton depression rating scale scores and Van dream anxiety scores after 1 week of treatment in the patients with early response and significant association

Table 2. Baseline and follow-up scores of depression and dream anxiety in both the groups

	Parameter	Early Response Yes (N=44) (Mean ± SD)	Early Response No (N=44) (Mean ± SD)	p value
Baseline (Day 1)	**HAM-D**	18.23 ± 3.05	18.8 ± 4.16	0.467
	VDAS	18.41 ± 4.58	19.75 ± 4.89	0.188
After 1 week of treatment (Day 8)	**HAM-D**	11.55 ± 2.54	15.55 ± 3.61	<0.001*
	VDAS	13.73 ± 4.49	16.64 ± 4.22	0.002*

Note. *p <0.05 is considered statistically significant. SD = Standard deviation

Table 3. Association between the factors determining early response in the study population (N = 88)

Parameter	Odds ratio	95 % CI# of odds ratio Lower	95 % CI# of odds ratio Upper	p value
Age	0.971	0.930	1.031	0.172
Gender (Base line = Male)				
Female	1.363	0.558	3.327	0.497
Education (Base line = Above graduate)				
Up to high school	0.869	0.334	2.264	0.774
Intermediate	2.076	0.672	6.413	0.204
Location (Base line = Urban)				
Rural	1.095	0.475	2.527	0.831
Occupation (Base line = Above skilled)				
Unemployed	2.388	0.810	7.014	0.115
Up to skilled	1.857	0.522	6.612	0.339
Family type (Base line=Others)				
Nuclear	1.282	0.320	5.131	0.725
Socio Economic Status (Base line= Upper-middle)				
Upper-lower	2.029	0.606	6.794	0.251
Lower-middle	1.624	0.641	4.110	0.306
Marital status (Base line = Others)				
Married	1.314	0.569	3.038	0.523
Age of depression	0.974	0.932	1.018	0.242
Duration of current episode (months)	0.950	0.905	1.000	0.050*
Family history of depression (Base line = No)				
Yes	1.296	0.476	3.528	0.611
Improvement in Dream Anxiety (Base line = No)				
Yes	1.321	1.079	1.618	0.007 *
Past episodes (Base line=No)				
Yes	1.863	0.612	5.668	0.273

Note. *p <0.05 is considered statistically significant. SD = Standard deviation

was found as mentioned. There is extensive research being done on relation between Dream anxiety as early indicator of depression and its treatment response, by American Academy of Sleep Medicine (AASM, 2015 and Sandman et al., 2015). This can help us to determine dream anxiety as an indicator of early response, thus help in the management and reducing delays in treatment decisions.

However, our study has few limitations. Sample size is small to generalize the results. We did not follow-up the patients for full response in this study. We did not consider the age of onset of illness or response to past treatment (in those with recurrent depressive disorder).We reassessed dream anxiety within a week using the rating scale (VDAS), which would have reduced the sampling interval, there by having effect on the scores. We did not take into account other variables of dreams, like recall frequency or content of the dream.

Further studies can include these factors, with more sample size and following up the patients for entire response period for generalizability of results. A detailed evaluation of dream anxiety, considering all the confounding factors (improvement in sleep, general clinical improvement and improvement in the dream content) can be the scope of future research in this area.

5. Conclusion

This study suggests that improvement in dream anxiety is associated with early response to anti-depressant treatment. This can help clinician to identify the patients showing early response, thereby reducing the initial waiting period to monitor the response and planning management strategies accordingly.

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