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Depressive symptoms and preclinical Alzheimer's disease

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Summary: The study investigated the relationship between depressive symptoms and preclinical phase of Alzheimer's disease (AD). 324 non-demented nursing home residents were included. Subjects who entered the study underwent annual follow-up evaluation for up to 6 years. We compared the result of MADRS (Montgomery and Asberg Depression Rating Scale) and GDS (Geriatric Depression Scale) scales at baseline between the demented and non-demented subjects at six years follow-up. The differences were observed in the results of the both depression scales - MADRS and GDS. Comparison between the frequencies of the occurrence of symptoms making up the MADRS reveals differences which apply to some items in terms of frequency and intensity.

Key words: Alzheimer's disease, depression, preclinical stage

Introduction

Depression was suggested as a prodromal symptom in some patients suffering from dementia [1, 2]. Depression was associated with impairment of cognitive functions constituted a significant risk for the development of Alzheimer's disease (AD) [1, 3]. Moreover, the impairment of cognitive functions during the first depressive episode can be an indication of the development of dementia of the Alzheimer type (DAT). However, the clinical picture of depression preceding dementia is atypical and can be influenced by many factors, especially those connected with the somatic state.

We investigated the relationship between depressive symptoms and preclinical phase of AD.

Method

The initial population for this study was made up of all residents (368 subjects) of two Nursing Homes in Gdynia, Poland as of July 1st, 1998. The following criteria were used to screen candidates for this study: 1) Consent to participate in the study, 2) Being over 60 years of age, 3) The subject was non-demented at the baseline evaluation according to DSM-IV criteria, 4) free from serious psychical diseases at the time of

the interview, 4) Candidate's somatic state is adequate and free of illnesses that may hinder performing orders and procedures of the applied scale such as those affecting the organs of movement, vision and hearing, 5) MMSE total score more than 23 points.

Finally 324 non-demented subjects qualified according to these primary criteria and were enrolled in the entire study. The subjects were assessed by a psychiatrist and psychologist with the following instruments: the structured clinical interview and evaluation of the psychopathological status by Montgomery and Asberg Depression Rating Scale [4], moreover social workers and the nursing personnel employed at the Nursing Homes performed the Mini-Mental State Examination (MMSE) [5] and Geriatric Depression Scale (GDS) [6] - the full version of the scale was used in a form of self- evaluation done by the patient. All subjects had the same standardized evaluation. The authors used Polish versions of MMSE and GDS scale.

Prior to starting the study a training program on how to apply the clinical scales was organized for persons taking part in the investigation. Moreover, a pilot study concerning 20 subjects was conducted to work out difficulties connected with the implementation of the protocol and minimize mistakes during the investigation.

Subjects who entered the study underwent an annual follow-up MMSE evaluation for up to 6 years. Those who scored less than 24 points in the MMSE examination underwent a psychiatric evaluation. When dementia was diagnosed during an examination it was classified according to the DSM-IV criteria [7].

Results

Finally 158 subjects were included to statistical analysis out of the 324 patients who were enrolled in the study. We excluded from analyses the remaining 166 subjects for the following reasons: 103 patients died without dementia syndrome; 20 patients had etiologies other than degenerative causes; vascular, mix and unspecified dementia), 21 patients could not be examined due to intensification of somatic symptoms; 10 patients withdrew from the study; 12 patients moved out of the nursing homes included in this study.

Twenty eight subjects were diagnosed with DAT at follow-up. We compared the frequency of depression diagnosis according DSM-IV and the result of the applied scales at baseline between subjects who were demented (n = 28, mean age 74.5) and subjects who remain non-demented (n = 130, mean age 73.08) at six years follow-up.

The differences were observed in the results of the both depression scales - MADRS and GDS. Comparison between the frequencies of the occurrence of symptoms making up the MADRS reveals differences which apply to some items in terms of frequency and intensity (see tabl.).

Statistics

We used two-tailed t tests and the chi-square test to look for group differences between non-demented and DAT groups.

Table 1

The total scores of Montgomery and Asberg Depression Rating Scale (MADRS) and Geriatric Depression Scale (GDS) and frequency and intensity of symptoms making up the MADRS.

Symptoms making up the MADRS	Non-demented group n = 130			Alzheimer type dementia group n = 28		
	frequency (number of subjects)	intensity		frequency (number of subjects)	intensity	
		mean	SD		mean	SD
Apparent sadness	30	0.35	0.73	16 *	1.04 *	1.04
Reported sadness	56	0.79	0.95	17	1.29 *	1.08
Inner tension	76	0.99	0.92	13	0.93	1.02
Reduced sleep	96	1.42	1.60	18	1.32	1.09
Reduced appetite	6	0.12	0.55	5 *	0.32	0.82
Concentration difficulties	97	1.34	1.03	21	2.00 *	1.56
Lassitude	66	0.63	0.70	10	0.54	0.79
Inability to feel	35	0.43	0.76	12	0.82 *	1.06
Pessimistic thoughts	37	0.34	0.60	9	0.32	0.48
Suicidal thoughts	8	0.13	0.55	1	0.04	0.19
Montgomery and Asberg Depression Rating Scale – total score		6.48	4.08		8.61 *	5.11
Geriatric Depression Scale		7.53	4.33		10.68 *	5.13
Mood disorders according to DSM-IV criteria:						
Major Depressive Episode	2		0			
Dysthymia	1		4 *			

* - $p < 0.05$

Discussion

The main goal of this study was to estimate the frequency of occurrence of depressive symptoms in the preclinical phase of DAT. Previous reports show frequent occurrence of depressive disturbances in the process of DAT, especially in its initial stages [8]. Both biological and psychological factors leading to depression were implicated in the process of AD. The emotional responses to difficulties at work, and in social interaction and to memory impairment which are observed in the initial phase of the process constitute the psychological reaction [8]. The neuroanatomic and biochemical background may constitute the biological factors. The connection between

DAT and depression could be explained by the damage of the hippocampus that leads to deterioration of the corticosteroid-level controlling mechanism [9].

Further, hippocampus damage appears in the early, and maybe even in preclinical periods of DAT [10]. Other biological mechanisms may also be responsible for the depressive symptoms in DAT [11, 12]. These observations mainly refer to deep depressive episodes which fulfil the DSM criteria, and were seldom present in our study. However, the symptoms of depression appeared more often in the period preceding AD. Depressive symptoms were more intense both in quantity and quality in the period before the occurrence of AD. The analysis of particular symptoms included in the depression scale according to MADRS (tab.) showed that in the case of later development of DAT the symptoms connected with cognitive function (concentration impairment, narrowing of thinking) and their consequences (social withdrawal, lack of vitality, lowered self-rating) are encountered more often. However, there were no differences in 'endogenic' symptoms (sleep and appetite disturbances) between to the two groups analyzed in this study. It seems that the appearance of the symptoms of depression in the preclinical period of DAT may be conditioned in many ways. In comparison to patients free from dementia, patients with clinical forms of DAT frequently suffered from depressive syndromes (including the ones fulfilling DSM criteria for major depressive episodes) [3, 8]. In the preclinical phase of the illness the psychological mechanisms underlying the appearance of the syndromes or at least the depressive symptoms are more important. Usually a patient experiencing difficulties with cognitive functions is critical about his/her state [13]. In a patient with beginning DAT after many years the lowered self-rating, recorded in the examination at baseline, may be treated as adequate in relation to decreasing psychic efficiency. Withdrawal from social functions and neglect of interests may result from conscious (although not always verbalized) action, as well as it can be an effect of the awakening of unconscious defensive mechanisms.

In conclusion, depressive symptoms often appear in the preliminary - preclinical periods of DAT. Some of the symptoms appear more often in people with an initiating dementia process, and thus can be used in early recognition of DAT. At the same time the observed symptoms seldom make up syndromes that would fulfil the criteria of depression.

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