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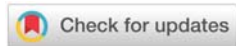
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Research Article

The application of Kubler-Ross model in Newly Diagnosed Patients with Relapsing-Remitting Multiple Sclerosis

Abstract

Background: Anxiety and depressive disorders affect Multiple Sclerosis (MS) patients since the early stages of the disease. Although the presence of these symptoms is widely recognized, the beginning and the psychological mechanisms at the basis of these disorders have rarely been examined in detail. This observational study aims to assess the presence of emotional distress in the early stages of the disease in patients with relapsing-remitting MS (MS-RR) and to check similarities and dissimilarities with a shared conceptual framework: the “curve of change” of the Kübler-Ross model.

Thirty-six RR-MS patients were examined at 1 and 24 months after the diagnosis, and they were asked to answer to the questionnaire “State-Trait Anxiety Inventory (STAI X-1 and X-2) for the evaluation of anxiety, Beck Depression Inventory 2nd Edition (BDI-II)”, for the assessment of depressive symptoms.

Results: STAI X-1 scores were significantly higher than the BDI II during the first 6 months, while the mean BDI II resulted higher from the 18th to the 22th month, especially on the cognitive domain.

Conclusions: The study showed that psychological symptoms follow a clearly time course in newly diagnosed patients. During the first six months we found high levels of anxiety with a decrease until the first year of MS disclosure. From the first year on depressive symptoms begin to increase with a significant involvement of the cognitive domain. During the 20th month the depressive symptomatology reaches its highest level. The time course of the anxiety and depression symptoms in RR-MS patients is in accordance with the Kübler-Ross model.

Introduction

Multiple Sclerosis (MS) is a chronic, degenerative disease of the central nervous system which is commonly presents in young adults in their 20s and 30s and affects women 2–3 times more often than men [1,2].

The MS diagnosis is a moment of a complex and distressing experience for the patient and sometimes for their physicians [3,4]. Since the early stages of MS, the patients revalue many aspects of their lives and the disease disclosure induces them to a new self-knowledge processes. Anxiety, stress and depression symptoms are frequent [5–8] and they may be severe enough to interfere with their daily life [9–10] and the course of the disease [11]. Indeed, they are associated with reduced adherence to disease modifying therapies (DMTs) [12,13]. Although the presence of these psychological disorders in MS is well-recognized, the beginning and the underlying

mechanisms of these symptoms were rarely investigated or evaluated in detail [14].

Until today the targets of psychological interventions for the newly diagnosed MS patients have been centered on the satisfaction of informational needs [15–17] and the emotional impact [7,18–20], but there are no studies about a shared reference model regarding how to support patients in the early stages of MS.

The application of the “Kubler-Ross model” [21], could provide some insight into how the MS patients experience the communication of diagnosis in time. This conceptual framework has been introduced and researched in several chronic illness, such as type 1 diabetes mellitus [22], renal disease [23] and cancer [24–27].

The “Kubler Ross’s Change Curve”, and its associated emotions, is explained into transitional stages [28,29]:

- ❖ **Stage 1: Shock and denial**–The first reaction to the change is usually a shock. It is often due to the lack of information, the fear of the unknown [29]. Later individuals can experience the denial, since they believe the diagnosis is somehow incorrect [28,30].
- ❖ **Stage 2: Anger and depression**–When the patient recognizes that he cannot continue to deny his conditions, he gets angry. The awareness of the disease increases, so this period can be associated with depression, apathy and isolation [29].
- ❖ **Stage 3: Acceptance and integration**–A more optimistic mood begins to emerge, individuals accept that the change is inevitable. The final steps involve the integration of feelings of hope and trust [28,30].

These stages do not necessarily come in order, nor are all stages experienced by all patients. They may pass through one stage for a few days, remaining in another for months [26]. These stages manifest as the “normal reactive responses” facing a MS diagnosis, otherwise they could take a pathological condition if the psychological symptoms have a profound impact on the daily activities of living, employment, income, relationships, social and leisure activities, and life goals.

This paper summarizes the results of psychological assessments on a group of Newly Diagnosed Patients with Relapsing-Remitting Multiple Sclerosis (RR-MS). The purpose of our work was to assess if the MS patients showed signs of psychological distress in early stages of disease, to diagnose possible pathologies and to define similarities and dissimilarities with the “Change Curve” reported by the Kübler-Ross model [28,30].

Materials and Methods

This cross-sectional study were conducted on patients with Relapsing-Remitting Multiple Sclerosis according to the 2010 McDonald criteria [31], followed at the “Multiple Sclerosis Center” of the “A. Cardarelli Hospital” between September 2014 and August 2016.

The group was composed by 36 adults MS patients receiving diagnosis for no more than 24 months. They were interviewed about their psychological symptoms. All subjects gave their informed consent to the study, which was approved by the local ethics committee. The observational study included an interview in which it was administered the following set of questionnaires:

- ❖ **State-Trait Anxiety Inventory (STAI X-1 and X-2)** [32]. The self-report questionnaire was adopted for measuring anxiety. The form X includes 2 dimensions - a) State Anxiety (Form X-1), which evaluates the emotional state of an individual in a particular situation; b) Trait Anxiety (Form X-2), a relatively stable characteristic of personality.
- ❖ **Beck Depression Inventory 2nd Edition (BDI-II)** [33]. It is a

21-item self-report instrument designed to assess the severity of depression in adults. The BDI-II was designed to act as an indicator of depressive symptoms based on diagnostic criteria in the DSM-IV. It is not a diagnostic instrument. The BDI-II evaluates 21 symptoms of depression, 9 of which cover cognitive symptoms and the others cover somatic-emotional reactions. Total score of 0–13 is considered the minimal range, 14–19 is considered a mild depression, 20–28 is considered a moderate depression and 29–63 is considered a severe depression.

Descriptive statistic was used to summarize demographic and clinical data. The observation time was divided in three periods according to Maciejewski classification [28]. For the BDI index an alternative classification according to the data distribution was proposed. One way ANOVA was used to compare index data between the periods. Bonferroni correction was applied in case of posthoc analysis. Predicted curves were estimated and graphed to evaluate data distribution and consequently a possible time classification. The best fitted model was chosen between a series of regression (linear, quadratic, cubic and quartic) considering each indicator as a dependent variable and time as an independent one. The model with the lower Akaike’s Information Criterion (AIC) was selected. STATA 14.2 was used for all analysis and a p value inferior to 0.05 was considered statistically significant.

Results

The demographic characteristics of the participants are listed in Table 1. The median age of patients at the diagnosis time was 29 years (IQ range 18–54 years) (Table 1). The Median EDSS was 1.5 and only the 13% of the patients had an EDSS higher than 2.0 at the time of the questionnaires.

Table 1: Demographic and baseline characteristics.

Patients' sociodemographic and disease-related characteristics	
	Patients (n = 36)
Age at onset, median (IQ range)	28 (17-51)
Age at diagnosis, median (IQ range)	29 (18-54)
Gender	
Females, number (%)	19(52.8)
Males, number (%)	17(47.2)
Years of education, median (IQ range)	13(8-18)
Work, number (%)	
Full time	16(46)
Part time	2(5)
Housewife	4(10)
Student	9(26)
Unemployed	5(13)
Marital status	
Single (never married)	23(65)
Married/cohabiting	11(30)
Separated/divorced	2(5)
Actual disease, number (%)	
SM Relapsing-Remitting	36(100)
EDSS, median (IQ range)	1.5 0 – 4.0)

All patients were submitted to DMTs (Table 2) No patients presented relapses during the observational period.

STAI X-1 scores were significantly higher during the first 6 months (Table 3) and increased slightly after the 16th month (Figure 1).

X-2 scores were also lower in the period ranging from the 7th to 12th month, but the difference was not statistically significant.

The mean BDI II was higher from the 18th to the 22th month (Table 4). The two subscales of BDI II (cognitive and somatic-emotional symptoms) followed the same trend, which was more evident for the cognitive domain ($p < 0.001$).

Table 2: DMTs distribution in MS population.

DMT	Dosage	Number patients (%)
Interferon beta-1 a	30 mcg	1(3)
Interferon beta-1 a	22 mcg	15(42)
Interferon beta-1 a	44 mcg	5(13)
Fingolimod	0.5 mg	1(3)
Natalizumab	300 mg	1(3)
Teriflunomide	14 mg	2(5)
Dimetilflumarato	480 mg	9(26)
Peginterferone beta-1a	125 mg	2(5)

Table 3: Mean and standard deviation of STAI X-1/-2 scores.

Period	n	STAIX-1			STAIX-2		
		mean	SD	P*	mean	SD	P*
1-6	10	46.4	12.2	0.028	43.9	10.9	0.384
7-12	7	31.4	9.7		36.4	8.1	
13-24	19	39.2	10.4		42.6	12.6	

*Oneway anova

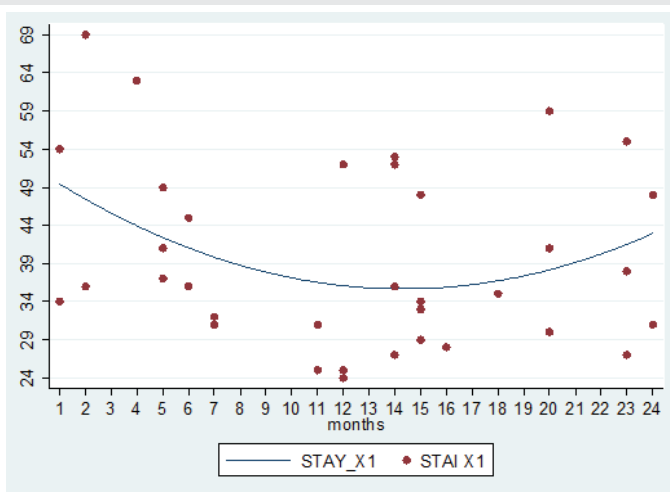


Figure 1: STAI X-1 as function of the time: raw data are presented as single points; a predicted curve based on quadratic regression model is reported as a continuous line.

Table 4: Mean and standard deviation of BDI-II scores.

Month	N	BDI Total		P	Somatic-emotional Symptoms		P	Cognitive symptoms		P
		mean	SD		mean	SD		Mean	SD	
1-6	10	10.9	8.1	0.003	7.4	5.7	0.024	3.2	3	<0.001
7-12	7	4.7	4.6		2.9	2.7		1.9	2.3	
13-17	9	10.9	13		7.6	8.2		3.3	4.5	
18-22	5	29.4	14		16.4	9.1		13	5.4	
23-24	5	12	7.4		8.4	4.5		3.6	3.2	

Discussion

This study showed that in newly diagnosed patients psychological symptoms follow a precise time course. During the first six months we have found high levels of anxiety with a decrease until the first year from MS diagnosis. Among the observed symptoms most subjects suffered from a condition characterized by hyper-vigilance, rumination and fear of their own future. In the same period mild depressive symptoms were present, as it is showed by BDI II scores, however these are largely associated with the somatic symptoms (agitation, crying, sleeping disorders, problems of attention). All these psychological manifestations are related to anxiety disorders rather than an onset of depressive condition. From the first year on, the depressive symptoms begin to increase with a significant involvement of the cognitive domain. The irritability and the loss of interest are stable conditions in this phase, often accompanied by low self-esteem, sense of guilt and uselessness. The depressive symptomatology reaches its highest level during the 20th month.

The development of anxiety and depression symptoms in MS patients are in accordance with the stage 1 and stage 2 of Kübler-Ross model. During the first stage we observe the initial reaction of shock and hyper-vigilance. These manifestations have a timing of about 6 months. year after the MS diagnosis, the awareness of the disease begins to appear, so the patients experience a state of frustration and anger. This condition is followed by the loss of interest toward the others and himself that causes a deep state of depression and isolation. This condition persists until the second year of observation, with a peak around the 20th month. Although the depressive condition continues, we observe a decrease in the last two months: this suggests that the patient probably is moving towards a partial mood improvement. Nevertheless in our study the “acceptance and integration” phase (stage 3) is not confirmed because of the short observational time-frame.

According to this model a “stage-specific” psychological support might be useful to improve the coping to prevent future consequences and to facilitate the re-organization process [11].

The Figure 2 shows the possible psychological interventions that follow the communication of MS diagnosis (Figure 2).

This study present some limitation such as the small sample size, the lack of relapses during the observational period and its

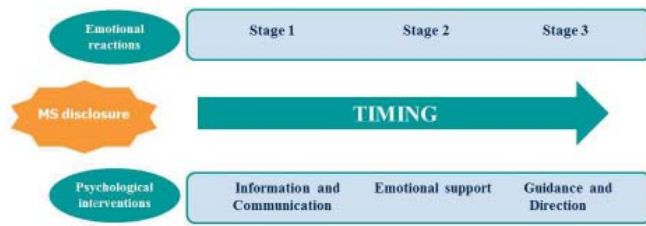


Figure 2: The stages of Kübler-Ross model in MS patients and the respective modes of intervention.

cross-sectional structure. So our group is carrying out a study with a longitudinal design and a larger population.

Conclusion

In our observational study MS patients show psychological symptoms according to the “Kübler-Ross model”. These findings can contribute to increase the understanding of the psychological mechanisms experienced by MS patients, and to implement psychological intervention and, if needed, rehabilitation programs.

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