L. Gutiérrez Rojas[1]
P. Molero Santos[2]
F. Ortuño Sánchez-Pedreño[3]

Performance in WCST in schizophrenic patients: influence of clinical variables in manual laterality

[1] District Mental Health Team
Complejo Hospitalario of Jaén
Servicio Andaluz de Salud

[2] Psiquiatry Departament and Clinical Psychology
Clínica Universitaria de Navarra
Spain

SUMMARY

Introduction. The authors review the neuropsychological evaluation of schizophrenia diagnosed patients. The fundamental characteristics of the most useful and effective tests are summarized.

Method. A study of cases and controls was performed. The sample had a total of 53 subjects (23 controls and 30 schizophrenics according to the ICD-10). The participants were evaluated by PANSS, WCST and the Annett test of manual preference.

Results. Schizophrenic patients had a significantly worse performance in number of total errors and T score, conceptual answers and the total completed categories of the WCST in comparison with the group control. There are statistically significant differences in the schizophrenic group between right handed and left-handed subjects in the variables: number of errors (total score), number of errors (T score), total % of perseverative answers and perseverative errors, conceptual answers (total % and % T). On the contrary, no statistically significant «p» values were found in the case of the controls. Those having more positive symptoms are those who commit a greater number of errors (correlation of 0.394 for a p = 0.042).

Conclusions. It has been confirmed that performances on the WCST in schizophrenics are worse than in healthy subjects. These differences are not due to the difference in the educational level. Schizophrenic patients with left-handed manual preference patterns have a greater tendency to perservation (perseverative answers and perseverative errors) than right-handed patients. To study the relationship between symptom seriousness and WCST performance, larger samples must be studied and we must focus on individual symptoms of the PANSS. The limitations of this study are mainly the reduced sample and the non-randomization of the control group.

Key words:
Schizophrenia. WCST. Manual preference. Neuropsychological test.

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Correspondence:
Luis Gutiérrez Rojas
Av. de Madrid, 1, 4.º
18012 Granada (Spain)
E-mail: luisgutierrezrojas@eresmas.com

Ejecución del WCST en pacientes esquizofrénicos: influencia de variables clínicas y de la lateralidad manual

RESUMEN

Introducción. Los autores revisan cómo es la evaluación neuropsicológica de pacientes diagnosticados de esquizofrenia. Se resumen las características fundamentales de las pruebas más útiles y eficaces.

Método. Se realizó un estudio de casos y controles. La muestra tenía un total de 53 sujetos (23 controles y 30 esquizofrénicos según la CIE-10). A los participantes se les pasó la PANSS, el WCST y el test de preferencia manual de Annet.

Resultados. Los pacientes esquizofrénicos han tenido un rendimiento significativamente peor en número de errores totales y en la puntuación T, respuestas de nivel conceptual y en las categorías totales completadas del WCST en comparación con el grupo control. Dentro del grupo de esquizofrénicos hay diferencias estadísticamente significativas entre diestros y no diestros en las variables: número de errores (puntuación total), número de errores (puntuación T), porcentaje total de respuestas perseverativas y de errores perseverativos, respuestas de nivel conceptual (% total y % T). Por el contrario, en el caso de los controles no se han encontrado «p» estadísticamente significativas. Los que tenían más sintomatología positiva son los que cometían un mayor número de errores (correlación de 0,394 para una p = 0,042).

Conclusiones. Se confirma que los rendimientos en el WCST en esquizofrénicos son peores que en los sanos. Estas diferencias no son debidas a la diferencia en el nivel educacional. Los pacientes esquizofrénicos con patrones de preferencia manual no diestra presentan una mayor tendencia a la perseveración (respuestas perseverativas y errores perseverativos) que en pacientes con preferencia diestra. Para estudiar la relación entre la gravedad de la sintomatología y los rendimientos en el WCST es preciso estudiar muestras más amplias y centrarnos en síntomas individuales de la PANSS. Las limitaciones de este estudio son principalmente la muestra reducida y la no aleatorización del grupo control.

Palabras clave:
Esquizofrenia. WCST. Lateralidad manual. Test neuropsicológico.

INTRODUCTION

Brief summary of schizophrenia

The present concept of schizophrenia has been developing thanks to the contributions of three authors: Emil Kraepelin, Eugen Bleuler and Kurt Schneider. All of them based their contributions on the description of clinical manifestations, that is the psychopathological symptoms, in the study of the evolution and prognosis.

Thus, above all, Kraepelin[1] was interested in that concerning the disease course and prognosis: he defined its early onset and the marked deterioration it produces as well as its chronic course and adverse prognosis. Bleuler[2] basically focused on the fundamental symptoms. He rebatized the disorder with the term «schizophrenia» («split mind»). He emphasized thought fragmentation and the fact that its course developed with a complete «restitutio ad integrum». For Bleuler, the fundamental symptoms were the following: altered associations, emotional blunting, abulia (apathy), autism, ambivalence and reduced attention. Schneider was interested in detecting pathognomonic symptoms of schizophrenia and emphasized the psychotic nature of the disorder - that is the presence of delusions and hallucinations - on the contrary to disorders of another nature, such as neurosis or psychopathies. To do so, he defined the First Rank Symptoms, that he considered specific to schizophrenia: thought insertion or diffusion, delusions of control, voices conversing on the patient's actions and voices arguing.

We now know that schizophrenia is a serious mental disorder that generally begins in adolescence or early youth. It generally has an insidious onset, with gradual development of the symptoms, or acute onset, with an important alteration of behavioral conduct. Both genders are affected equally, although the onset is earlier in males. Between 0.5 and 1 percent of the population is affected by schizophrenia.

Although in initial stages, in general, intellectual capacity is conserved, cognitive deficits frequently appear in the disease course. It was, above all, beginning in the decade of the 80's, when dichotomic classifications of schizophrenia, such as that of Andreasen[4] and Crow[5], that divided the symptoms into two groups (positive and negative symptoms), began to appear.

At present, the positive symptoms are considered a consequence of hyperdevelopment of normal emotional or cognitive functions. The negative symptoms are a consequence of a decrease in normal functions.

Neuropsychology of schizophrenia

It is necessary to differentiate between classical neuropsychology, that is derived from the study of patients with specific and localized brain lesions and cognitive neuropsychology that consists in recognizing which mental functions are affected.

Neuropsychology and schizophrenia: methodological aspects

We must consider some aspects to perform studies that aim to evaluate cognitive deficits that appear in schizophrenia. In the first place, when the studies are performed, many patients are taking drugs (neuroleptics, benzodiazepines, anticholinergics) that act as a confounding factor when interpreting the test performance. In the second place, institutionalization (remaining hospitalized for a long time) may give rise to cognitive deterioration that acts as a confounding factor of the test results.

If we divide the patients by groups, according to intelligence quotient, there would be more possibilities of finding specific areas of deterioration. Given the heterogeneicity existing in the test performance, it is good to group them into homogeneous groups (schizophrenics with negative symptoms, with positive symptoms, with the same treatment, etc.) and to compare them. This process is easier and may reveal the psychological conditions that underlie a specific symptom.

Neuropsychology of schizophrenia- some findings

There are no conclusive results that explain in which hemisphere (laterality) or in which cerebral lobe the damage is found. Cognitive studies have found that schizophrenics have multiple deficits in different areas. They are not capable of maintaining attention in vigilance tasks, they tend to become distracted and find it difficult to retain inappropriate answers. They suffer memory deterioration and tend to not organize the random lists of material. They understand what is said to them, but find it difficult for people to understand what they say. Abnormalities appear in speech planning and use of language for communication.

Some frequently used cognitive tests

1. General tests:
   - The WAIS-R[7,8] and the Raven Progressive Matrices[9] measure intellectual function. The Multilingual Aphasia Battery evaluates language functions and the Mini-mental Status Exam examines mental state.
   - Executive function: Wisconsin Card Sorting Test, Stroop Test[10], Porteus Mazes[11] and Tower of London[12].
2. Fluency: Controlled Oral Word Association Test and Category Fluency Test.
3. Memory verbal: Logical Memory (Wechsler Memory Scale), Rey Auditory Verbal Learning Test and Paired Associate Learning.

4. Visual reconstructive memory: Rey-Osterreith Complex Figure[13] and Benton Visual Retention Test.
5. Motor function: The Finger Oscillation Test and Purdue Pegboard.

Wisconsin card sorting test (WCST)

This is a test that measures the so-called «executive» function. Specifically, it evaluates the subject's capacity to change schemes as well as planning strategies for which the dorsolateral prefrontal cortex is hypothetically responsible.

It has the advantage that it can be administered to a very wide age range (between 6.5 and 89 years). In the beginning, the subject must have normal eyesight or eyesight corrected with glasses and sufficient auditory capacity to understand the instructions. If this is not possible, the reliability of the results will depend on the examiner's skill.

The original test form was established in 1948 by Grant and Berg[14]. The present version, and the one we use in this study, was designed by Heaton et al.[15]. The design of the cards and their presentation order were standardized. In 1993, a manual version that included the scales obtained from a standardized sample with 899 subjects divided by ages was published[15].

Utility of the WCST in schizophrenia

Using the basis that the WCST evaluates the executive function and frontal functioning, we apply this test to the study of schizophrenia. Neuroimaging studies state that there is hypoactivity of the frontal cortex in patients with this disease when different tests such as the WCST are performed. Thus, we could establish a relationship between a low score on the WCST and frontal hypoactivity in schizophrenic patients. Comparing this activity by SPECT in patients and controls, it is verified that the results are similar for both groups during «mental rest», however when the test is performed, the controls have an adequate response of the frontal cortex but the patients do not succeed in activating it adequately. In addition, the PET makes it possible to verify an increase in blood flow in this brain region under normal conditions, on the contrary to what occurs in schizophrenics.

The relationship between disease and low score on the WCST is also shown when adding D-serine (NMDA receptor agonist, which is hypofunctioning in schizophrenics) to the antipsychotic treatment of these patients and on verifying that not only do the positive, negative and cognitive symptoms improve but also the scores obtained on the test.

The question arises if the performance of this test may temporally improve in patients with training, which would speak in favor of the usefulness of neuropsychology in mental disorder rehabilitation. Equally, the question arises if neuroleptic treatment can worsen, improve or not modify cognitive performances in the test.

The importance of the genetic factor in the etiology of schizophrenia makes us think that the low score on the WCST in first degree relatives of patients and in theoretically normal persons can be considered an indicator of vulnerability to this disease.

An aspect that has not been examined is the comparison of the executive functions in schizophrenia, based on the presence of a possible development abnormality marker. In this sense, in recent years, the possible greater prevalence of left-handed manual preference (left-handed, mixed or both) in schizophrenic patient samples emerges as a marker of the abnormal process of hemispheric lateralization in this disease16.

All the previously mentioned data invite us to consider three questions in this study. Do schizophrenic patients perform worse when taking the WCST than those of the healthy control group with comparable age and cultural level? Is the intensity of the positive and negative symptoms of schizophrenia related with the test performance? Does the test execution differ in patients according to their manual preference?

METHOD

Objectives

Verify the following hypothesis:

- The execution of WCST in schizophrenic patients is more defective than in healthy volunteers.
- Performances on the WCST in patients with left-handed manual preference patterns (left-handed or mixed) differ from those of patients with right-handed manual preference.
- WCST performances are inversely related with intensity of negative symptoms of schizophrenia.

Subjects

The study subjects were included during a complete year. The patients were seen in the out-patient clinic or were hospitalized. The control group participants were generally students from the Medicine School of the University of Navarra.

The study sample was formed by a total of 53 subjects, distributed into two groups. The control group was made up of 23 health subjects (16 men and 7 women) whose mean

age was 25.74 years (SD: 5.81). The patient group was made up of 30 subjects (25 men and 5 women) diagnosed of schizophrenia according to ICD-10 diagnostic criteria[3]. Their mean age was 27.13 years (SD: 8.41). The patients had studied a mean of 14.93 years of school (SD: 4.14) and the controls 18.86 years (SD: 0.35).

Material

The material used for assessment consisted in an initial interview that collected sociodemographic data (age, gender, civil status, number of children, years of study and profession) and different questionnaires were administered.

- *PANSS.* The positive and negative syndrome scale of schizophrenia (PANSS) elaborated by the Kay work group[6] consists in a standardized clinical interview that includes 30 operational items defined to evaluate the patient's psychopathology grade. It was designed as an instrument capable of providing a representation of the relative importance of the negative and positive symptoms within the general clinical picture of each specific schizophrenic patient. It is made up of three scales that measure positive and negative syndromes, their differences and the general severity of the disease. A study with 101 schizophrenics6 demonstrated that the four scales had a normal distribution, together with high statistical reliability and validity.

  In this study, we have used the adaptation to Spanish made by Peralta and Cuesta[17]. In 1990, Kay et al.[6] demonstrated that this adaptation had psychometric properties equivalent to those of the PANSS, and thus that it could be used in the Spanish speaking population without this leading to less certainty in the diagnosis.
- *Annett's manual preference test[18] adapted to Spanish.*
- *WCST15 adapted to Spanish by De la Cruz[15].* The test consists in four cards-stimulus (CS) and 128 cards-response (CR) divided into two blocks of 64 and numbered. Each card has one or several figures that can be classified according to three parameters: color, form and number. Each parameter has four different variables for each category: red, green, yellow and blue for the category of color, triangle, star, cross, circle for the form category and between one and four figures for the number category.

The four CT are presented in an ordered way to the subject and the subject is requested to pair up each CR with a CT in that way that he/she feels is the most correct. As the individual places the cards, he/she will be told if it is correct or not, without explaining the criterion followed by the examiner. The subject must make 10 correct answers consecutively in each category in order to go on to the next one. The order is generally color, form, number. When there have been 10 correct answers, the subject will go from one variable to another without being advised. When the individual fails in the same variable several times consecutively, he/she commits a perservative error.

The scores obtained are recorded on a special note page and are compared with those of reference based on the age of the subject being evaluating.

In some cases, the cultural level is considered. On the note pages, there is a space to fill out the color-form-number sequence at least twice. In addition, there is a place for the most relevant data of the patient's history. Anyone with minimum experience can administer the WCST. In our study, it was administered by medical students who worked as intern students of the psychiatry department.

The parameters that we have used are: number of correct answers, number of cards applied, perseverative errors, non-perseverative errors, number of complete categories. In turn, both the direct scores as well as the standardized values were studied for each one of them. The standardized values are expressed adding a –T suffix in each one of the direct score variables. They are obtained with the normalized value that corresponds to the direct score, looking at the corresponding table (included in the WCST manual appendix) according to age and study years. Thus, these T scores have the advantage that they supply information on how the test result has been in relationship with the normative group of age and cultural level.

This test is generally considered as an important test to evaluate the problem solving capacities and the capacity to change the group of answers. The test means classifying cards according to color, form or number. The subject, without being told, is «corrected» while he/she uses a classification criterion and he/she should recognize at this time that it is necessary to change the response group. In our study, this test constitutes the main tool, so that we dedicate a separate chapter later on.

Statistical analysis

The statistical analysis has been performed with the SPSS version 9.0 program. To compare the two groups that form the sample in the quantitative variables, the Student's *t* test for independent samples was used when the variable followed a normal distribution and the Mann-Whitney U test when this was not the case. To study the association of qualitative variables, (χ^2 contingency tests and Fisher's exact test (when necessary) were performed. To study the association between the WCST and PANSS scale variables, an analysis of correlation was performed with Spearman's test (r_s) due to the ordinal nature of the latter ones. The results are presented as mean (standard deviation). A bilateral p value less than 0.05 was defined as significant.

RESULTS

Sociodemographic analysis of the sample

No statistically significant differences have been observed in age (p = 0.057), but there were differences in study years (p = 0.0001). We attribute this difference to the incapacity caused by schizophrenia to continue a normal school life.

Comparison of the execution of WCST between schizophrenic patients and healthy controls

Table 1 shows that the scores obtained by schizophrenic patients in the WCST are inferior to those obtained by the controls. We have obtained especially significant differences in number of total errors and in the T score, conceptual responses (both in the total percentage as well as T score percentage) and in the total categories completed. There are also statistically significant differences in the total percentage of perseverative response and in that of the perseverative errors.

Comparison of performance in the WCST in patients and controls with undefined manual preference patterns vs patients and controls with defined manual preference (right-handed left-handed)

As can be seen in tables 2 and 3, there are statistically significant differences in schizophrenic patients between right-handed and left-handed subjects in the variables: no. of errors (total score), no. of errors (T score), total % of perseverative responses and perseverative errors, conceptual responses (total % and T %). On the contrary, a statistically significant «p» has not been found in the case of the controls. Thus, these data suggest that the manual preference pattern is indifferent on the performance in the WCST in healthy subjects while it has a value in the case of schizophrenic patients. Specifically, performance in non-right-handed subjects is poorer.

Comparison between the PANSS scale and the WCST

Table 4 shows the relationship between positive symptoms of the schizophrenic patients and the results on the WCST: there are two significant correlations. There is one negative correlation between intensity of positive symptoms and the number of total errors. In turn, those who have less positive symptoms are those who commit the least errors. No other correlations are observed between the *p* score and performance on the WCST. Subsequent studies should include samples with a larger number of subjects

CONCLUSIONS

Regarding the first hypothesis, it is confirmed that the performances on the WCST obtained by schizophrenic patients are noticeably worse than those obtained by healthy

Table 1 Comparison of the execution of WCST between schizophrenic patients and healthy controls

WSCT	Patients (n = 29)	Controls (n = 23)	p
Total no. correct	68.24 ± 17.95	69.26 ± 6.55	0.507
Total no. of errors	51.41 ± 24.76	21.22 ± 14.39	0.000
T. no. of errors	33.00 ± 14.31	47.61 ± 13.39	0.000
Total % of perseverative responses	27.16 ± 5.27	12.80 ± 6.91	0.022
T % of perseverative responses	38.72 ± 15.84	42.61 ± 8.74	0.187
Total % of perserverative errors	21.91 ± 19.01	11.56 ± 5.64	0.036
T % of perseverative errors	39.93 ± 16.21	42.39 ± 8.64	0.391
Total of non-perseverative errors	15.24 ± 12.43	9.89 ± 7.66	0.197
T % of non-perseverative errors	44.62 ± 17.39	47.87 ± 7.78	0.376
Total no. of categories completed	3.21 ± 2.41	5.70 ± 0.88	0.000
Failure to maintain set	1.18 ± 1.56	0.61 ± 1.03	0.114

Table 2 Performance in WCST in patients

WSCT	Right-handed (n = 17)	Non-right handed (n = 6)	Mann Whitney U test (p)
Total no. correct	73.88 ± 16.31	63.67 ± 17.87	0.293
Total no. of errors	40.35 ± 23.10	63.50 ± 18.72	0.042
T. no. of errors	39.12 ± 9.87	28.33 ± 7.66	0.039
Total % of perseverative responses	18.15 ± 21.43	28.24 ± 14.55	0.046
T % of perseverative responses	45.65 ± 14.44	33.33 ± 15.74	0.093
Total % of perserverative errors	15.47 ± 16.12	23.92 ± 11.83	0.042
T % of perseverative errors	47.12 ± 15.10	33.17 ± 15.18	0.073
Total % of non-perseverative errors	16.73 ± 13.4	18.27 ± 12.29	0.649
T % of non-perseverative errors	41.24 ± 18.60	43.00 ± 14.16	0.916
Number of categories completed	4.12 ± 2.23	2.33 ± 2.58	0.161

Table 3 Performance in WCST in healthy controls

WSCT	Right-handed (n = 14) X ± DS	Non-rigth-handed (n = 6) X ± DS	U de Mann Whitney (p)
Total no. correct	71.00 ± 7.02	67.17 ± 4.92	0.215
Total no. of errors	22.50 ± 15.27	20.83 ± 16.38	0.804
T. no. of errors	48.14 ± 17.23	46.33 ± 8.57	0.590
Total % of perseverative responses	12.42 ± 7.33	12.32 ± 5.40	0.805
T % of perseverative responses	42.93 ± 9.19	42.83 ± 7.76	0.967
Total % of perserverative errors	11.11 ± 5.68	11.45 ± 5.38	0.934
T % of perseverative errors	42.93 ± 8.71	42.50 ± 8.78	0.8.36
Total % of non-perseverative errors	10.70 ± 8.89	10.13 ± 6.16	0.680
T % of non-perseverative errors	47.21 ± 8.92	47.50 ± 6.98	0.803
Total categories completed	5.71 ± 0.83	5.50 ± 1.22	0.842

subjects. These differences are not due to the difference in the education level.

Schizophrenic patients with left-handed manual preference patterns present a greater tendency to perseveration (perseverative responses and perseverative errors) than patients with right-handed preference. This difference speaks in favor of the relationship between the greater deficit in the executive functions and the abnormalities in the hemispheric lateralization process.

The hypothesis of the relationship between the seriousness of positive or negative symptoms and performances in WCST in schizophrenia is not supported or ruled out. However, the results suggest that it is necessary, on the one hand, to study larger samples and on the other to study individual symptoms of the PANSS instead of the positive and negative global scales in order to approach this hypothesis in future investigations.

DISCUSSION

Regarding the first hypothesis, the results agree with the previous studies[19,20] that indicate that patients with schizophrenia as well as those with frontal lobe deficit obtain lower scores than those of the healthy subjects in the WCST.

The second hypothesis on the differences obtained in the performance of WCST based on manual preference agrees

Table 4 Relationship between positive symptoms of the schizophrenic patients and results in WCST

Spearman's Rho	PANSS-P score	PANSS-N score	PANSS-PG score
Total no. correct			
Sig. correlation coefficient	−0.064	0.061	−0.030
(bilateral)	0.751	0.763	0.881
Total number of errors			
Sig. correlation coefficient	0.394	0.217	0.315
(bilateral)	0.042	0.278	0.110
T no. of errors			
Sig. correlation coefficient	−0.399	−0.206	−0.316
(bilateral)	0.039	0.303	0.109
Total % of errors			
Sig. correlation coefficient	0.348	0.221	0.289
(bilateral)	0.066	0.267	0.144
T % of errors			
Sig. correlation coefficient	−0.364	−0.163	−0.244
(bilateral)	0.067	0.426	0.229
Total perseverative responses			
Sig. correlation coefficient	0.030	0.216	0.150
(bilateral)	0.518	0.278	0.455
T perseverative responses			
Sig. correlation coefficient	−0.035	−0.114	−0.130
(bilateral)	0.503	0.570	0.518
Total % perseverative responses			
Sig. correlation coefficient	0.110	0.597	0.116
(bilateral)	0.585	0.325	0.563
T % perseverative responses			
Sig. correlation coefficient	−0.055	−0.188	−0.157
(bilateral)	0.785	0.347	0.433
Total perseverative errors			
Sig. correlation coefficient	0.152	0.209	0.157
(bilateral)	0.449	0.295	0.435
T perseverative errors			
Sig. correlation coefficient	−0.087	−0.183	−0.167
(bilateral)	0.667	0.361	0.404
Total % perseverative errors			
Sig. correlation coefficient	0.114	0.201	0.128
(bilateral)	0.571	0.315	0.125
T % perseverative errors			
Sig. correlation coefficient	−0.068	−0.199	−0.162
(bilateral)	0.736	0.320	0.418
Total non-perseverative errors			
Sig. correlation coefficient	−0.107	0.235	0.071
(bilateral)	0.595	0.239	0.723
T non-persever errors			
Sig. correlation coefficient	0.050	−0.303	−0.174
(bilateral)	0.803	0.124	0.386
Total % of non-perseverative errors			
Sig. correlation coefficient	−0.137	0.221	0.051
(bilateral)	0.494	0.269	0.179
T % of non-perserverative errors			
Sig. correlation coefficient	0.079	−0.258	−0.137
(bilateral)	0.696	0.195	0.497
Number of categories completed			
Sig. correlation coefficient	−0.250	0.323	−0.385
(bilateral)	0.208	0.101	0.047

with the only study that has analyzed this question up to date[21]. In this study, it is concluded that the patients with a right-handed manual preference pattern obtain better results than the left-handed subjects.

The results obtained with the intension of verifying the third hypothesis have not made it possible to establish any statistically significant relationship between the high score on the negative symptoms scale of the PANSS and low score on the WCST. We have only found a relationship, although limited, between the total number of errors and the seriousness of the positive symptoms. However, this finding suggests that some of the seven symptoms that make up the positive scale can be more related with the executive functions. Thus, an individual analysis of these symptoms must be made. This same thing extends to the seven negative symptoms of the PANSS's N scale. Another possibility is to perform a factorial analysis of the PANSS scale in order to detect the grouping of some cognitive type factor, since some authors observed that a factor integrated by a positive symptom (conceptual disorganization) and two negative symptoms (difficulties in abstract thought and lack of spontaneity and fluency in conversation) that presented an inverse relationship with the low score on all the WCST variables.

This study has several limitations, such as its reduced size and restricted nature of the sample in addition to the cross-sectional and open evaluations that have been used. In addition, the control group was not randomized so that it is probably not representative of the general population. This could limit the generalization of the results of other patient populations with similar diagnoses.

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