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artigo original

The effect of gender on the clinical features and therapeutic response in obsessive-compulsive disorder

Efeito do gênero nas características clínicas e resposta terapêutica do transtorno obsessivo-compulsivo

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Abstract

Objective: To investigate the existence of clinical and therapeutic differences that could possibly characterize specific subgroups of patients with obsessive-compulsive disorder (OCD) based on their gender.

Methods: Male (n=32) and female patients with OCD (n=37) were compared with regard to age and mode of onset, duration and course of the illness, number of obsessions and compulsions, and subtype of OCD according to the International Classification of Diseases, 10th edition. The groups were also compared with regard to scores on the Yale-Brown Obsessive-Compulsive Scale, Clinical Global Impression, Beck Depression Inventory and Global Assessment of Functioning, before and after drug treatment for 10 weeks. Chi-square test with Yates correction or Fisher's exact test were employed for comparisons between categorical variables and Student's t or Mann-Whitney tests were used to compare continuous variables. The adopted level of significance was 5%.

Results: Male patients with OCD were characterized by an earlier age of onset and greater global severity. Furthermore, a trend to display greater number of obsessions and compulsions and worse global functioning was found among male patients, whereas a trend to more severe depressive symptoms was observed in female patients. No significant differences between the groups were found with regard to treatment response.

Conclusions: Our findings suggest that there may be OCD subtypes based on gender.

Keywords Obsessive-compulsive disorder. Gender. Sex. Diagnosis, clinical.

Resumo

Objetivo: Investigar a existência de diferentes características clínicas e terapêuticas entre pacientes com transtorno obsessivo-compulsivo (TOC) de gêneros distintos, na tentativa de determinar possíveis subtipos.

Métodos: Pacientes masculinos (n=32) e femininos (n=37), com o diagnóstico de TOC, foram comparados quanto a idade e modo de início, tempo e curso da doença, número de obsessões e compulsões e subtipo do TOC segundo o Código Internacional de Doenças, 10ª edição. Os grupos também foram comparados quanto aos escores na escala de Yale-Brown para avaliação dos sintomas obsessivo-compulsivos, na Impressão Clínica Global, no Inventário de Depressão de Beck e na Avaliação Global do Funcionamento, antes e após o tratamento medicamentoso por dez semanas. O teste do qui-quadrado com correção de Yates ou o teste exato de Fisher foram utilizados para comparação de variáveis categoriais, e o teste t de Student ou o teste de Mann-Whitney foram utilizados para comparar variáveis contínuas. O nível de significado estatístico escolhido foi 5%.

Resultados: Pacientes do gênero masculino se caracterizaram por idade de início do TOC mais precoce e por maior gravidade global. Também foi encontrada uma tendência, não estatisticamente significativa, de maior número de diferentes obsessões e compulsões e de pior funcionamento global dentre pacientes masculinos e de maior gravidade de sintomas depressivos dentre pacientes femininos. Não foi observada diferença significativa entre os grupos em relação à resposta terapêutica.

Conclusões: Os achados são compatíveis com a possível existência de subtipos de TOC baseados no gênero.

Descritores Transtorno obsessivo-compulsivo. Gênero. Sexo. Diagnóstico clínico.

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Introduction

Findings of several studies suggest that obsessive-compulsive disorder (OCD) is a group of syndromes with common characteristics but great clinical,[1-4] biological[5-8] and therapeutic[9-12] heterogeneity. Thus, the identification of homogeneous subgroups of patients is essential to improve the diagnosis and treatment of this disorder. Several attempts to identify subgroups were based on the course of the disease,[1] on the symptoms dimensions,[2] and on the comorbidity with tics[3] and personality disorders.[4] Electroencephalographic,[5] neuroendocrinological,[6] neuroimunological[7] and functional neuroimaging[8] characteristics were also studied to identify more biologically homogeneous subtypes. Under the therapeutic point of view, it has been demonstrated that certain groups of OCD patients may respond preferentially to specific drugs (such as clomipramine,[9] fluoxetine,[10] phenelzine[11] and haloperidol).[12]

One of the clinical subtypes of OCD that has been proposed is that based on the patient's gender. OCD in men has been characterized as a more 'organic' subtype,[13,14] with a more frequent history of perinatal trauma, earlier age of onset, sexual, exactness and symmetry obsessions and bizarre compulsions.[13] Among women, OCD has been considered a more 'depressive' disorder,[14] associated to a later onset, a more frequent history of depression and anorexia nervosa,[14] aggressive obsessions, panic attacks after the onset of the disease and a less frequent history of bipolar disorders.[13]

We aimed to widen the scope of the initial studies and to investigate, in a Brazilian sample, if patients with OCD from different genders would present distinct clinical and therapeutic characteristics reflecting possible subtypes.

Methods

Patients

We have studied 79 consecutive OCD patients, diagnosed according to DSM-IV criteria,[15] that spontaneously sought for assistance at the Anxiety and Depression Program of the Federal University of Rio de Janeiro (Obsessive-Compulsive Disorder Unit). Inclusion criteria were: (1) OCD patients with or without psychiatric comorbidity; when comorbidity was present we only included patients whose OCD was the primary disorder, that is, the first disorder to appear along in their evolutionary history and that responsible for the greatest severity and importance for the clinical condition; (2) age 18 to 65 years; and (3) absence of any neurological disorders, except for tics. Ten patients initially examined were excluded from the final sample due to comorbidity with psychiatric disorders that had greater clinical relevance than OCD: two male patients with antisocial personality disorder, alcohol and cocaine abuse; two male patients with paraphilias; one male patient with alcohol, cocaine and cannabis abuse; one female patient with borderline personality disorder; one male patient with paranoid personality disorder; one female patient with moderate mental retardation and bipolar disorder and one schizophrenic female patient.

The 69 subjects selected had the following clinical variables recorded: age at the onset of OCD, duration of the illness, number of obsessions and compulsions according to the Yale-Brown Obsessive-Compulsive Scale(Y-BOCS) symptom checklist,[16,17] mode of onset (abrupt or insidious), course (chronic or episodic) and OCD subtype according to criteria of the International Classification of Diseases, 10th edition (ICD-10)[18] ['mixed obsessional thoughts and acts'; 'predominantly compulsive acts (obsessional rituals); 'predominantly obsessional thoughts or ruminations'; 'other obsessive-compulsive disorders' and 'obsessive-compulsive disorder, unspecified']. When data were collected, interviewers were blind to the study's hypothesis.

Instruments

The following scales were employed to evaluate the severity of the disorder: Y-BOCS,[16,17] Clinical Global Impression (CGI),[19] Beck Depression Inventory (BDI),[20] and Global Assessment of Functioning (GAF).[15]

Treatment

After the baseline assessment, patients were openly treated with different antidepressants for at least 10 weeks (including selective serotonin reuptake inhibitors, tricyclic antidepressants and venlafaxine). Drugs usually not employed in the treatment of OCD were used in two occasions: (1) as lower-cost alternatives (imipramine), when money shortage limited the acquisition of more expensive drugs; or (2) as a therapeutic alternative (venlafaxine), when there was a history of non-response to the several regularly-used drugs. Doses administered were determined according to the therapeutic efficacy or tolerance to side effects. Some patients used low doses of benzodiazepines, when necessary, mainly to control insomnia. At the end of a 10-week period, patients were reassessed with Y-BOCS, CGI, BDI and GAF. The criterion adopted to define a subject as treatment-responder was a decrease of at least 35 % in the initial Y-BOCS scores or CGI score equal to 1 ("much better") or 2 ("better") at the end of the trial.

Statistical analysis

Chi-square test with Yates's correction or Fisher's exact test were used to compare categorical variables such as gender (male vs. female) and the type of onset (abrupt of insidious), the course (episodic or chronic), OCD subtype ('mixed obsessional thoughts and acts, 'predominantly compulsive acts [obsessional rituals]' and 'predominantly obsessional thoughts or ruminations') and the treatment response (present vs. absent). Student's t test or Mann-Whitney test were used to compare continuous variables between male and female patients, such as age of onset, duration of illness, number of obsessions and compulsions, and Y-BOCS, CGI, BDI and GAF scores. The statistical significance level chosen was 5%.

Results

The mean age at the time of assessment was 34.13±12.97 years

and the mean age of onset of OCD was 21.42±14.26 years. The average duration of the illness, i.e., the time period between the onset of symptoms and the interview in the Anxiety and Depression Program, was 12.86±9.78 years. The average number of clinically significant obsessions and compulsions per patient, identified through the Y-BOCS symptoms checklist, was 2.17 ±1.59 and 2.36 ±1.32, respectively. Thirty-two patients (46.4%) were men and 37 patients were women (53.6%). The course of the disorder was considered as episodic in 7 cases (10.1%) and chronic in 62 others (89.9%). OCD onset was abrupt in 22 patients (31.9%) and insidious in 47 others (68.1%). According to the classification proposed by the ICD-10, 53 patients (76.8%) had 'mixed obsessional thoughts and acts'; 10 patients (14.5%) had "predominantly compulsive acts (obsessional ritual)' and 6 patients (8.7%) had "predominantly obsessional thoughts or ruminations'. No patient was diagnosed as having 'other obsessive-compulsive disorders'or' obsessive-compulsive disorder, unspecified.'

The initial mean scores of Y-BOCS, CGI, BDI and GAF scales were respectively 24.42±8.49; 5.34±.99; 23.25±10.58; and 49.00±10.87. The medications and respective average doses used were: fluoxetine, 52,3mg/day ±31,3mg/day (17 patients); clomipramine, 154,3 mg/day±84,9 mg/day (8 patients); sertraline, 137,5 mg/day±69,4 mg/day (8 patients); paroxetine 47,14 mg/day±17,0mg/day (7 patients); fluvoxamine, 400 mg/day±100 mg/day (3 patients); imipramine, 153,5 mg/day±68,4 mg/day (17 patients); and venlafaxine, 131,25±132,5 (2 patients). Seven patients did not complete the treatment; one for medical reasons, two for unknown reasons and four refused to take the drugs. After the 10-week trial with antidepressants, final scores in the mentioned scales were: Y-BOCS, 16,40 ±10,43; CGI, 3,82±1.72; BDI, 12,64±9,65 and GAF, 65,58±13,81. According to the criteria adopted to define the therapeutic response, 43,1% of the patients responded to treatment. The response rate to each drug was: 75%, clomipramine; 29,4%, fluoxetine; 37,5%, sertraline; 71,4%, paroxetine; 66,7%, fluvoxamine; 50%, venlafaxine; and 35,3%, imipramine. The therapeutic response rate found in the group taking serotonin reuptake inhibitors (clomipramine, fluoxetine, sertraline, paroxetine and fluvoxamine) (48,8%) was not significantly different to that observed in the group taking other drugs (imipramine and venlafaxine) (36,8%) (chi-square = 76; gl =1; p= 40).

The comparison between clinical features and treatment response of male vs. female patients is illustrated in the Table.

Table - Clinical and therapeutic features of the sample: male vs. female gender.

	Male OCD patients (n=32) [%]	Female OCD patients (n=37) [%]	P
Mode of onset			.30
Abrupt	8 [25%]	14 [37.8%]	
Insidious	24 [75%]	23 [62.2%]	
Course			.23
Chronic	27 [84.4%]	35 [94.6%]	
Episodic	5 [15.6%]	2 [5.4%]	
Subtype of OCD			.31
Mixed	26 [81.3%]	27 [73%]	
Predominantly compulsive	5 [15.6%]	5 [13.5%]	
Predominantly obsessive	1 [3.1%]	5 [13.5%]	
Age of onset of OCD	16.53±11.98	25.65±14.86	.007**
Duration of illness	14.06±10.19	11.81±9.41	.34
Number of obsessions	2.59±1.95	1.81±1.10	1.0*
Number of compulsions	2.72±1.37	2.05±1.20	.09*
Initial scores			
Y-BOCS****	25.21±8.24	23.81±8.74	.51
CGI*****	5.72±.81	5.00±1.01	.002**
BDI******	19.57±8.36	26.93±11.55	.06*
GAF*******	45.00±11.09	52.29±9.80	.06*
Final scores			
Y-BOCS****	17.25±10.37	15.71±10.57	.56
CGI*****	4.07±1.76	3.62±1.69	.30
BDI******	11.00±9.24	13.57±10.10	.56
GAF*******	62.27±15.55	68.00±12.36	.30
Rate of treatment response***	37.9% (11/29)	47.2% (17/36)	.61

**p≤1.0; **p≤0.05;*
****Rate of treatment response: ratio between number of treatment-responder patients/number of treated patients;*
*****Y-BOCS: Yale-Brown Obsessive-Compulsive Scale;*
******CGI: Clinical Global Impression;*
*******BDI: Beck Depression Inventory;*
********GAF: Global Assessment of Functioning.*

Discussion

This study describes the clinical features and the treatment response of 69 OCD patients seen in the Anxiety and Depression Program of the Institute of Psychiatry of the Federal University of Rio de Janeiro. We aimed to investigate the existence of different clinical and therapeutic characteristics among OCD patients from different genders in order to determine possible subtypes.

We found an earlier age of onset and a greater severity of symptoms among male OCD patients. Moreover, a non-significant trend to a greater number of different and clinically significant obsessions and compulsions and to a worse global functioning in the male patient subgroup was observed. Similar results were found in the literature. For example, Noshirvani et al,[14] Castle et al[21] and Lensi et al[13] also reported earlier onset of clinically significant symptoms among men with OCD. Bogetto et al[22] described similar data, but referred to the age of onset of subclinical obsessive-compulsive symptoms. Regarding the number of symptoms, we did not find studies describing a greater number of obsessions and compulsions among men, but this trend dovetails with the hypothesis that OCD in this population involves a greater degree of psychopathology. We also have not found other studies reporting a greater severity in obsessive-compulsive symptoms among male adult patients. However, OCD in male children and adolescents has been described as more severe.[23,24] Finally, our finding of a worse global functioning in men, although not statistically relevant, is consistent with other studies in which male patients with OCD were described as being more significantly impaired from the social and occupational point of view [25] and as being more frequently non-married [13, 14, 21, 25].

We noticed a trend towards a greater severity of depressive symptoms among female patients. Even though the effect of gender in psychiatric comorbidity of OCD patients has not been investigated with diagnostic instruments, the rate of comorbid psychiatric disorder among male and female OCD patients has been different in several studies. For example, female patients were found to have greater rates of severe depression,[14, 21] eating disorders [14, 21, 22] and panic attacks after the OCD onset,[13] whereas male patients were characterized

by a greater frequency of bipolar [13] (with hypomanic episodes after the OCD onset)[22] and anxiety disorders (often preceding OCD)[22]. The frequency of personality disorders has been also different between male and female OCD patients. A greater frequency of group A personality disorders, especially schizotypal personality disorder,[25] was found among men, whereas a greater frequency of borderline and dependent personality disorders was described among women.[25] Castle et al[21] found greater frequencies of anxious and meticulous personality traits among male patients.

Although our findings are compatible with a greater severity of OCD among male patients, we did not find statistically significant differences between the severity of obsessive-compulsive and depressive symptoms among men and women at the end of a 10-week treatment with antidepressants. In fact, in several studies about predictors of pharmacological response in OCD patients, the gender has not been associated to a differential therapeutic response.[10, 26, 27] Only DeVeaugh-Geiss et al[28] found a non-significant trend to a worse treatment response of male patients to clomipramine.

One could argue that the use of non-approved drugs for the treatment of OCD, such as venlafaxine and imipramine, is a potential limitation of our study. However, the rate of therapeutic response found in the group using serotonin reuptake inhibitors was not significantly different from that seen in the group using other drugs. In fact, while the findings of a double-blind, placebo-controlled study already suggest the efficacy of venlafaxine in this group of patients,[29] the results of a large multicentric, double-blind study carried out in the 80's were compatible with the antiobsessive equivalence of imipramine when compared to clomipramine.[30] Based on this last finding, Mavissakalian[30] suggested that, to treat OCD patients, physicians should not be limited to more selective or potent inhibitors of serotonin reuptake, in case the circumstances turned these agents scarcely available or practical.

Several neuropsychiatric studies have described findings compatible with the existence of OCD subtypes based on gender. For example, Lensi et al[13] found a more frequent history of perinatal trauma among male patients. Concerning neuropsychological aspects, Aronowitz et al[31] found greater disfunction of visuospatial abilities among men, whereas Zohar et al[32] reported that the correlation between the orbitofrontal cortex function, assessed with the *Objects Alternation Test*, and obsessive-compulsive symptoms was negative among women and positive among men. Furthermore, neuroendocrinological studies found blunt responses of cortisol[6] and prolactin[33] to the administration of fenfluramine in women with OCD, but not in men, suggesting that the first group is associated to a reduction in the serotonergic function. In genetic studies, while Karayorgou et al[34,35] found a positive association between male gender and the genes implied in the dopaminergic and noradrenergic neurotransmission (i.e., genes that synthesize catecol o-metiltransferase and monoamino-oxidase A, respectively), Enoch et al[36] found a link between the female gender and a gene responsible for the 5-HT2A receptor, involved in the serotonergic neurotransmission.

As a whole, our data suggest the likelihood of existence of an OCD patient subgroup according to gender. In male OCD patients, the clinical picture is probably more severe. Further studies, with greater samples and investigating other clinical and biological variables are necessary to elucidate the real effect of gender on OCD.

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