Eur Arch Psychiatry Clin Neurosci (2005) 255 : 48–50 DOI 10.1007/s00406-004-0533-y

ORIGINAL PAPER

Andreas Kordon · Kai G. Kahl · Andreas Broocks · Ulrich Voderholzer · Hildegard Rasche-Räuchle · Fritz Hohagen

Clinical outcome in patients with obsessive-compulsive disorder after discontinuation of SRI treatment: results from a two-year follow-up

Received: 23 December 2003 / Accepted: 10 May 2004 / Published online: 12 November 2004

Abstract *Background* Combined treatment with serotonin-reuptake inhibitors (SRI) and cognitive-behavioral therapy (CBT) is a common therapy approach for obsessive-compulsive disorder (OCD). However, it is a matter of debate whether discontinuation of SRI after combined treatment leads to relapse. *Method* Seventy-four consecutively admitted patients suffering from OCD were included in the study. Thirty-seven patients were treated with CBT alone, and 37 patients received combined CBT and SRI treatment. Of these latter patients, seventeen discontinued SRI treatment during the follow-up period (1 and 2 years after inpatient treatment). OCD symptom severity was determined by Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and mood was assessed by Hamilton Depression Rating Scale (HDRS). *Results* During the initial treatment, scores for Y-BOCS ($p < 0.001$), HDRS ($p < 0.001$) and the Global Assessment of Functioning Scale (GAF) ($p < 0.001$) improved significantly in all groups. Reassessment two years later revealed that a) OCD symptom severity and depression scores were similar between the groups and b) discontinuation of SRI did not prompt by a recurrence of symptoms. *Conclusions* We interpret our results as suggesting that discontinuation of SRI treatment may be considered in formerly combined treated OCD patients after stable remission.

U. Voderholzer, M.D. · H. Rasche-Räuchle, M.A.
Department of Psychiatry and Psychosomatic Medicine
Albert-Ludwig University of Medicine
Freiburg/Breisgau, Germany

Andreas Kordon, M. D. (✉) · K. G. Kahl, M.D. · A. Broocks, M.D. · F. Hohagen, M.D.
Universitaetsklinikum Schleswig-Holstein, Campus Luebeck
Klinik fuer Psychiatrie und Psychotherapie
Ratzeburger Allee 160
23538 Luebeck, Germany
Tel.: +49-451/5002471
Fax: +49-451/5004957
E-Mail: kordon.a@psychiatry.uni-luebeck.de

EAPCN 533

Key words obsessive-compulsive disorder · cognitive behavioral therapy · serotonin reuptake inhibitor · discontinuation

Introduction

Obsessive-compulsive disorder (OCD) is a chronic disabling illness with low rates of spontaneous remission. Pharmacological treatment with serotonin reuptake inhibitors (SRI) and cognitive-behavioral therapy (CBT) have both been proven to be effective. Meta-analysis of studies on the long-term effects of behavioral therapy have shown a significant reduction of OCD symptoms lasting up to six years beyond the end of treatment [1]. Studies investigating the effects of SRI alone found improvement to be continuous when medication was maintained [2]. However, discontinuation of SRI treatment led to different results concerning the relapse rates (45–89 % [3, 4]).

Few studies have investigated the long-term efficacy of combined therapy with CBT and SRI [5]. Furthermore, it is a matter of debate whether SRI may be discontinued in OCD patients after successful combined therapy with stable remission.

Therefore, the purpose of the current study was to investigate whether or not combined therapy including maintenance of SRI treatment is superior to CBT treatment alone at a two-year follow-up, and whether discontinuation of SRI treatment in formerly remitted patients leads to relapse of symptoms.

Methods

After approval by the local ethics committee, 89 patients who fulfilled the DSM-III-R criteria for OCD gave their informed written consent to participate and were treated for ten weeks. Fifteen patients dropped out during the follow-up, 74 patients were assessed one and two years after the treatment with CBT. Exclusion criteria were a current or lifetime diagnosis of psychotic disorder, drug or alcohol abuse, organic mental disorders or acute suicidality. On admission, the

Structured Clinical Interview for DSM-III-R (SCID I/II) was administered and a physical examination, routine blood tests, cerebral computed tomography and electroencephalography were performed to exclude somatic disorders.

Patients were assigned to one of the following treatments on the basis of clinical considerations: a) CBT alone (n = 37), or b) CBT and additional administration of SRI (n = 37) in an inpatient OCD-unit for ten weeks. Patients received anti-obsessional SRI doses (at least: clomipramine 150 mg/d, fluvoxamine 150 mg/d; fluoxetine 40 mg/d; paroxetine 40 mg/d) and no other medication. Patients were assessed before treatment (t0), at the end of treatment (t1), and one (t2) and two years (t3) later. Main outcome criteria were the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the Hamilton Depression Rating Scale (HDRS), and the Global Assessment of Functioning (GAF) Scale (DSM-III-R axis V). Ratings were performed by trained study psychologists. Raters were not involved in treatment and were blinded to the medication status of the patients.

After discharge patients were openly treated in different settings and the treatment modalities were re-assessed. In 17/37 formerly combined treated patients the medication had been discontinued. Reasons for discontinuation were clinical considerations (stable remission and the decision of the patients to discontinue SRI treatment). Adverse events did not lead to discontinuation of pharmacotherapy.

"Response" was defined as a reduction of 30 % or more in the Y-BOCS scores. At the two-year follow-up, "relapse" was documented when a patient no longer met the response criterion.

For statistical analysis patients were divided into three groups: A) treatment with CBT alone (t0–t3); B) CBT combined with continuous SRI treatment during follow-up (t0–t3); C) initially combined therapy with discontinuation of SRI during the follow-up period (at least eight weeks before t3). Demographic and psychometric variables were not significantly different between the dropouts (n = 15) and the completers (n = 74). A last-observation-carried-forward analysis revealed that the outcome criteria did not differ significantly between the dropouts and the completers (Y-BOCS: z = –0.47; p = 0.64; HDRS: z = –1.39; p = 0.17; GAF: z = –1.72; p = 0.09).

At baseline, the demographic parameters and psychometric ratings were compared among the three groups by means of the Kruskal-Wallis test. Differences between the groups with regard to sex distribution, comorbidity and former treatments were calculated with the chi-square test. Treatment effects and changes in clinical symptoms were analyzed with two-factorial repeated measures ANOVA for the three treatment groups (A–C) and the four assessments (t0–t3). Further analysis of the time effects were performed with Wilcoxon tests (Bonferroni correction for six comparisons).

Logistic regression analysis was performed to evaluate whether the initial treatment response correlated with the outcome after 2 years.

Results

There were no significant differences between the three groups with respect to age, sex distribution, age of onset and duration of OCD, comorbidity with other psychiatric disorders, earlier treatments (data not shown) or psychometric ratings at baseline (Table 1). In each group, two patients did not respond to either mode of treatment. Of the 35 (31 %) patients in the group treated with CBT alone 11 suffered a relapse (group A), 4 of the 18 (22 %) patients treated with combined CBT and continuous SRI medication (group B), and 3 of the 15 (20 %) patients treated with initially combined therapy and discontinuation of SRI during follow-up (group C). Non-response and relapse rates did not differ significantly between the groups ($\chi^2 = 1.7$; df = 4; p = 0.81).

ANOVA yielded a significant time effect in each group for scores on the Y-BOCS (F = 76.7; df = 3; p < 0.001), HDRS (F = 57.6; df = 3; p < 0.001), and GAF scales (F = 75.5; df = 3; p < 0.001). No significant group

Table 1 Demographic characteristics and scores on symptom measures of cognitive-behavioral therapy patients with obsessive-compulsive disorder divided according to SRI treatment (t_0 pre-behavioral therapy; t_1 post-behavioral therapy; t_2 one year follow-up; t_3 two year follow-up)

	Total		CBT alone (group A)		Additional treatment with SRI			
					t0–t3 (group B)		discontinuation (group C)	
	mean	SD	mean	SD	Mean	SD	mean	SD
N	74		37		20		17	
age (y)	35	10.6	36	10.9	34	10.8	36	10.0
sex (m/f)	38/36		16/21		12/8		10/7	
Duration (y)	12.8	9.7	14.1	10.3	12.1	9.5	10.6	8.7
Y-BOCS (total)								
t_0	27.6[a, b, c]	5.8	26.6[a, b, c]	5.5	28.4[a, b, c]	4.7	28.9[a, b, c]	7.4
t_1	13.3[a]	7.4	11.6[a, e]	7.4	15.7[a]	6.7	14.2[a]	7.7
t_2	14.9[b]	9.7	14.9[b]	10.4	15.6[b]	8.5	13.9[b]	9.5
t_3	15.1[c]	10.0	15.5[c, e]	10.9	15.6[c]	8.7	13.7[c]	9.9
HDRS								
t_0	18.6[a, b, c]	7.8	17.6[a, b, c]	7.4	19.1[a, b, c]	8.8	20.2[a, b, c]	7.4
t_1	9.0[a]	6.9	7.6[a]	6.1	11.1[a]	8.1	9.4[a]	6.6
t_2	8.9[b]	7.4	9.6[b]	8.9	7.7[b]	5.2	8.7[b]	5.7
t_3	8.5[c]	6.8	9.5[c]	8.3	7.8[c]	4.6	7.4[c]	5.0
GAF Scale (axis V)								
t_0	48.7[a, b, c]	8.8	50.0[a, b, c]	9.7	45.0[a, b, c]	6.2	50.3[a, b, c]	8.3
t_1	66.3[a]	10.7	69.1[a]	10.1	61.5[a]	10.3	65.8[a]	11.2
t_2	66.8[b, f]	15.6	66.3[b]	17.3	64.3[b, f]	13.5	70.7[b]	14.1
t_3	69.8[c, f]	16.0	69.0[c]	17.9	67.8[c, f]	14.4	74.1[c]	13.0

[a] p value of < 0.001, t_0 vs. t_1; [b] p value of < 0.001, t_0 vs. t_2; [c] p value of < 0.001, t_0 vs. t_3; [d] p value of < 0.05, t_1 vs. t_2; [e] p value of < 0.05, t_1 vs. t_3; [f] p value of < 0.05, t_2 vs. t_3

effects or group-by-time interaction were found (Y-BOCS: $F = 1$; $df = 6$; $p = 0.43$; HDRS: $F = 1.9$; $df = 6$; $p = 0.08$; GAF Scale: $F = 1.3$; $df = 6$; $p = 0.27$). Further analysis revealed significantly reduced scores on the Y-BOCS (group A/B/C: $p < 0.001$; A: $z = -5.3$; B: $z = -3.7$; C: $z = -3.6$) and the HDRS (group A/C: $p < 0.001$; A: $z = -5.1$; C: $z = -3.6$; B: $p = 0.006$; $z = -2.8$) scales at the end of treatment (t1), while the scores on the GAF scale had increased significantly (group A/B/C: $p < 0.001$; A: $z = -5.1$; B: $z = -3.7$; C: $z = -3.5$). Significant improvements in symptoms were maintained among all treatment groups for one (t2) and two years (t3).

For logistic regression analysis patients were classified according to the initial improvement in Y-BOCS scores (expressed as the difference in Y-BOCS scores between t0 and t1) being above or below the median –14, and according to the treatment outcome concerning Y-BOCS scores after 2 years (being above or below the median 14). We found a significant association of the treatment outcome after 2 years with the initial treatment response concerning OCD symptoms for the whole study group ($p = 0.036$), but not for either subgroup (group A: $p = 0.08$; group B: $p = 0.14$; group C: $p = 0.9$). Furthermore, no correlations were found between the initial treatment response concerning HDRS and GAF scores with the respective outcome after two years for the whole study group or the subgroups (data not shown).

Importantly, no differences in the scores on the Y-BOCS, HDRS and GAF scales were observed between groups B (continuous SRI treatment) and C (SRI discontinuation) at the one- and two-year follow-ups. More than 60 % of the patients in group C already had discontinued SRI during the first year of follow-up.

Discussion

One major finding of our study is that CBT and combined therapy were similarly effective in reducing OCD symptoms and depression in our study sample. These results are in accordance with a metaanalysis from Kobak and coworkers [6] who found no significant difference between CBT, the SRIs as a class, and a combined treatment. Another finding is that OCD and depressive symptoms remained stable during the two-year follow-up period as did social adjustment in all patient groups with comparable relapse rates. This result is in contrast to the findings of Pato [3], who reported a rapid aggravation of symptoms after discontinuation of SRI; however, these patients had been treated with SRI alone.

In another, earlier, placebo-controlled study, we showed the superiority of combined treatment with CBT and SRI (fluvoxamine) for OCD-patients with comorbid depression or predominantly obsessions in the acute phase of treatment [7]. However, our results on the follow-up of these patients suggest that discontinuation of SRI treatment after successful CBT may be considered in clinically stable patients. We here found a low risk for symptom exacerbation in patients with OCD when SRI medication was discontinued within one or two years after a successful CBT treatment.

Interestingly, we found a correlation between the initial treatment response and the outcome after two years concerning OCD symptoms for the whole study group. This result may be interpreted as an argument for considering discontinuation of SRI treatment in patients with strong initial response to therapy and stable remission. However, subgroup analysis failed to reach significance. This negative result may be explained by the small number of patients included in the study.

Due to our naturalistic study design some limitations have to be considered. One is that patients were assigned to one of the treatment groups according to clinical considerations. The lack of randomization may lead to a distinct interpretation of our results. We can not exclude that the more compliant patients were in the SRI discontinuation group. Furthermore, the small number of patients in the subgroups makes it critical to conclude particular clinical decision-making. However, the naturalistic design of our study may reflect the clinical situation of OCD patients. Future studies with a randomized, double-blind, placebo-controlled cross-over design are needed to confirm our results.

In summary, we found combined treatment and CBT in OCD patients similarly effective even after two years of follow-up. Discontinuation of SRI did not lead to a relapse in formerly combined treated patients. Owing to the preliminary character of this study SRI discontinuation can not be recommended in general. However, our results suggest that in patients with stable remission from OCD SRI discontinuation may be considered. These patients should carefully be followed-up for recurrence of symptoms.

References

1. Van Balkom AJ, Van Oppen P, Vermeulen AWA, Van Dyck R (1994) A meta-analysis on treatment of obsessive-compulsive disorder: a comparison of antidepressants, behavior therapy, and cognitive therapy. Clin Psychol Rev 14:359–381
2. Koran LM, Hackett E, Rubin A, Wolkow R, Robinson D (2002) Efficacy of sertraline in the long-term treatment of obsessive-compulsive disorder. Am J Psychiatry 159:88–95
3. Pato MT, Zohar-Kadouch R, Zohar J, Murphy DL (1988) Return of symptoms after discontinuation of clomipramine in patients with OCD. Am J Psychiatry 145:1521–1525
4. Ravizza L, Barzega G, Bellino S, Bogetto F, Maina G (1996) Drug treatment of obsessive-compulsive disorder: long-term trial with clomipramine and selective serotonin reuptake inhibitors. Psychopharmacol Bull 32(1):167–173
5. O'Sullivan G, Noshirvani H, Marks I, Monteiro W, Lelliott P (1991) Six-year follow-up after exposure and clomipramine for obsessive compulsive disorder. J Clin Psychiatry 52:150–155
6. Kobak KA, Greist JH, Jefferson JW, Katzelnick DJ, Henk HJ (1998) Behavioral versus pharmacological treatments of obsessive-compulsive disorder: a meta-analysis. Psychopharmacology 136(3): 205–216
7. Hohagen F, Winkelmann G, Rasche-Räuchle H, Hand I, König A, Münchau N, Hiss H, Geiger-Kabisch C, Käppler C, Schramm P, Rey E, Aldenhoff J, Berger M (1998) Combination of BT with fluvoxamine in comparison with BT and placebo. Br J Psychiatry 173: 71–78