Clinical Outcomes improvement of refractory Obsessive compulsive disorder by use Olanazapine

Hafidh Mohammed Farhan*

الخلاصة

أكثر من نصف المرضى الذين يعانون من الوسواس القهري لا تتحسن حالتهم الصحية بالاستخدام مثبطات أعادة الامتصاص مادة السيروتونين .

أن الهدف من هذه الدراسة هو فحص مادة اولانزيبم كمادة إضافية إلى مادة الاسيرتالين في معالجة الوسواس القهري الذي لا يستجيب إلى مثبطات إعادة امتصاص السيروتونين وتمت الدراسة بطريقة:

1. عشرون مريض تم تشخيصهم بمرض الوسواس القهري وفق (DSM-IV-TR) حيث أنهم لم يستجيبوا إلى العلاج بمادة الاسيرتالين بجرعة 100-150 ملغم يوميا.
2. تستخدم مادة اولانزيبم كمادة تضاف لعلاج السابق بجرعة 2.5 ملغم خلال العلاج ولمدة شهر ثم تزداد الجرعة إلى 5 ملغم لشهرين المتبقية من الدراسة.
3. يتم تقيم الاستجابة لعلاج باستخدام معيار (Yale-Brown Obsessive-Compulsive Scale (YBOCS) .

كانت النتائج هي ستة عشر مريض من مجموع عشرون تم إخضاعهم لدراسة اظهروا استجابة لعلاج اولانزيبم كمادة تزيد من فعالية الاسيرتالين في معالجة الوسواس القهري حيث يظهر نزول معدل الخط الأساسي لمعيار (YBOCS) لدى الذكور من(32,75) إلي (21,75) أي بنسبة 12,81% . بينما يبدأ نزول معدل الخط الأساسي من (33,83) الي (21,67) لدى الإناث أي بنسبة 17,06%.

استنتج ان هنالك فائدة من إضافة مادة اولانزيبم إلي مادة الاسيرتالين في معالجة الوسواس القهري المتعنت لعلاج.

مفتاح الكلمات : الوسواس القهري " اولانزيبم " الاسيرتالين" YBOCS

Abstract

More than half of the patients with obsessive- compulsive disorder (OCD) remain unimproved by Serotonin-Reuptake inhibitors(SSRI).

objective of this study was to examine whether addition of atypical antipsychotic (olanzapine) to Sertraline is useful for patients with OCD who do not respond to SSRI monotherapy.

1. According to (DSM IV-TR criteria) , 20 patients are diagnosed as OCD and did not responded to Sertraline at dose 100-150mg/day
2. Olanazapine was additional treatment , start 2.5mg/day at first month then 5 mg/day for last two months of study .

***Kufa College of Medicine**

3. Treatment response was assessed using the Yale-Brown Obsessive-Compulsive Scale (YBOCS) at end of each months of study

16 of 20 patients respond to the olanzapine augmented sertraline therapy . The mean baseline YBOCS score of 32.75 dropped to a mean of 21.75 at endpoint for male with reduction 12.81% from baseline.
While in female, the mean baseline YBOCS score of 33.83 dropped to a mean of 21.67 at endpoint with reduction 17.06% from baseline.
Treatment-refractory OCD Patients may benefit from addition of olanzapine to ongoing SSRI therapy.

Key word : OCD, Olanazapine, Sertraline ,YBOCS

Introduction

Selective Serotonin Reuptake Inhibitors (SSRIs) are the most effectual drug treatment accessible for obsessive-compulsive disorder (OCD) [1]. Clomipramine, citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline have been proved to be effective against obsessive and compulsive symptoms independent of their antidepressant activity [2, 3, 4].
50%-60% of patients with OCD fail to respond to a single trial of an SSRI, and 20-40% does not respond sufficiently after several medication trials [1]. Moreover, although the Selective Serotonin Reuptake Inhibitors (SSRIs) are generally considered to be secure and well tolerated, still a proportion of subjects does experience intolerable side effects and discontinue treatment prematurely. Also, no single drug acting on different neurotransmitter systems has yet proved an absolute efficacy against obsessive-compulsive symptoms. Therapeutic strategies in these resistant cases usually consist of augmentation therapies with, tryptophan, buspirone, clonazepam and lithium or the addition of antipsychotic drugs. But the final results with these tactics were not encouraging so far and have remained somewhat experimental than crucial. The addition of low-dose antipsychotics to standard antidepressant treatment has shown to be effective in some cases, but extrapyramidal side effects have limited the use of typical antipsychotics. Therefore treatment with atypical antipsychotic that

shows fewer extrapyramidal symptoms might be a useful alternative for treatment-refractory OCD patients. Beneficial effects of adding risperidone to SSRIs have been observed in some cases of treatment-resistant obsessive- compulsive disorder [5, 6]. In prior four open [7, 8, 9, 10] and one Double-blind [11] studies, there had been seen positive results with the addition of olanzapine to the regular antidepressant treatment of the patients.

Materials and Methods

Twenty clients whose visit psychiatric unit of Al-Hakeem General Hospital entered the study and after meeting following criteria:-

1. obtaining signed informed consent,.
2. explanation the procedure of augmentation.
3. Patients were diagnosed as OCD according to the DSMIV-TR criteria. Inclusion criteria in this study were:

A.OCD symptoms resistant to Sertraline at maximum dose and enough duration (12 weeks).

B.A score on the Yale- Brown Obsessive compulsive Scale (YBOCS)[12] can be divided into:-

0 - 7: not worth treating
8 - 15: mild
16 - 23: moderate
24 - 31: severe
32 - 40: extreme

In an open, 12-week trial, all patients continued to take their current SSRI (Sertraline) at the dose (100-150mg/day) during addition. Olanzapine addition was initiated at a dose of 2.5 mg/day in the first 4 weeks then increased to 5 mg was held at 8 weeks of study.

3. Subjects were followed up at the end of weeks 4, 8 and 12, at which times clinical response and adverse events were evaluated. The rater was not blind to treatment and its goals.
4. The primary efficacy parameter was (DSM IV TR) for OCD [12]. The significant to treatment was prospectively defined as p-value is less than 0.05 in endpoint YBOCS score. Adverse events were assessed at each visit by means of patients' spontaneous

reports and clinical examination by psychiatrist.

Results

In table 1 the results show the mean age is(32.85 and Std. deviation 8.3), with mean of baseline YBOCS is (33.4 and Std deviation 3.9),while the endpoint YBOCS (21.7 and Std. deviation 3.3).There is obvious difference between mean of age ,baseline and endpoint YBOCS between male and female

Table 1: Number of clients, Mean, std of mean, std deviation of age, Baseline YBOCS and Endpoint YBOCS according to gender

Gender	Statistical Measures	Age	Baseline YBOCS	Endpoint YBOCS
Female	N	12	12	12
	Mean	32.42	33.83	21.67
	Std. Error of Mean	2.372	1.236	1.082
	Std. Deviation	8.218	4.282	3.750
	% of Total N	60.0%	60.0%	60.0%
Male	N	8	8	8
	Mean	33.50	32.75	21.75
	Std. Error of Mean	3.202	1.278	1.048
	Std. Deviation	9.055	3.615	2.964
	% of Total N	40.0%	40.0%	40.0%
Total	N	20	20	20
	Mean	32.85	33.40	21.70
	Std. Error of Mean	1.866	.887	.754
	Std. Deviation	8.343	3.966	3.373
	% of Total N	100.0%	100.0%	100.0%

Table 2 revealed statistical values difference between baseline and endpoint YBOCS. In (95% confidence interval 31-35),the baseline YBOCS before augmentation show (t-test=37.6 ,df=19, p-value=0.000), after augmentation there is drop in statistical value show (t-test=28.7, df=19, p-value=0.000) .

Table 2 : Statistical values before and after augmentation by Olanazapine

YBOCS	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Baseline YBOCS	37.666	19	.000	33.40	31.54	35.26
Endpoint YBOCS	28.769	19	.000	21.70	20.12	23.28

***P-value* significant <0.05**

Table 3 show four cases with endpoint YBOCS =18 are significant response with (p-value = 0.001, df=3,and t-test=13.6), while there are three case are more significant response to augmentation with (p-value=0.000,df=3,t-test=89). Two cases are nearly significant to response augmentation with (p-value=0.47,df=1,t-test=33.6). there are four of twenty cases not responding to augmentation with (p-value-0.53 and 0.66, df=1 , t-test= 36 and 33.5) respectively.

Table 3 : Comparative statistical values between Endpoint and Baseline of YBOCS of cases.

Endpoint YBOCS	Baseline YBOCS	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
						Lower	Upper
18	Baseline YBOCS	13.663	3	.001	33.00	25.31	40.69
19	Baseline YBOCS	89.000	2	.000	29.67	28.23	31.10
20	Baseline YBOCS	12.932	2	.006	33.67	22.47	44.87
21	Baseline YBOCS	13.400	1	.047	33.50	1.73	65.27
22	Baseline YBOCS	14.924	3	.001	35.00	27.54	42.46
25	Baseline YBOCS	12.000	1	.053	36.00	-2.12	74.12
26	Baseline YBOCS	9.571	1	.066	33.50	-10.97	77.97

***P-value* significant <0.05**

Table 4 : percentage of response for each cases.

Age	Gender	Type OCD	SSRI	Dose	Baseline YBOCS	Endpoint YBOCS	% 0f response
20	Male	Contamination	sertraline	150	29	22	24.1%
21	Female	Contamination	sertraline	150	31	18	41.9%
22	Female	Contamination	sertraline	150	34	20	41.2%
24	Female	Contamination	sertraline	150	33	25	24.2%
26	Male	Sexual impulse	sertraline	150	39	25	35.9%
27	Male	Checking	sertraline	150	32	18	43.8%
27	Female	Contamination	sertraline	150	38	20	47.4%
29	Female	Contamination	sertraline	150	40	22	45.0%
30	Female	Contamination	sertraline	150	37	22	40.5%
33	Female	Contamination	sertraline	150	36	21	41.7%
34	Male	Checking	sertraline	150	34	22	35.3%
35	Male	Blasphemous	sertraline	150	37	26	29.7%
36	Female	Contamination	sertraline	150	29	19	34.5%
38	Female	Blasphemous	sertraline	150	30	26	13.3%
38	Male	Counting	sertraline	150	31	21	32.3%
39	Male	Contamination	sertraline	150	30	19	36.7%
41	Female	Blasphemous	sertraline	150	29	18	37.9%
44	Female	Contamination	sertraline	150	29	20	31.0%
44	Female	Contamination	sertraline	150	40	18	55.0%
49	Male	Blasphemous	sertraline	150	30	19	36.7%

Discussion

This study provides supplementary evidence that adding of olanzapine to ongoing SSRI treatment may be efficacious for therapy-refractory OCD patients. There are, however, limitations to the data presented due to the small sample size and open-label design. In all, the results of current study are consistent with the findings of previous addition trials with risperdone and olanzapine [5, 6, 7, 8, 9, 10, and 11]. More patients (80%) in the current trial had responded positively to the aforesaid augmentation, in comparison with Koran.LM (30%) [8] and Bogetto.F (43%) [9], although it was smaller than Weiss.El (70%) [7] and Francobandiera.G (60%) [10]. But this diversity is the outcome of dissimilarities between intervening factors, like the kind of prescribed SSRI, duration of study, patient's gender, and the criteria

of response. The main problem here is that there is some inconsistency in the definition of treatment refractoriness. Most studies included patients who had failed to respond to only one SSRI trial. Also there is not yet any universal agreement on the definition of responsiveness or resistance in the realm of OCD in comparison with, for example, schizophrenia. For instance, Weiss et al. [7] used a cutoff of 50% decrease in YBOCS score as responders, while Francobanderia [10] chose a cutoff of 25%. On the other hand, McDougle et al [6] and Pallanti [11], preferred cutoff of 35% for YBOCS decrease and a final score of 16 on the YBOCS in combination with a final Clinical Global Impressions scale rating of much improved or very much improved. Partial response, also, is defined as 23-35% improvement in YBOCS score [11]. In this regard relapse was defined as a 25% worsening in YBOCS (or a CGI score of 6) after a period of remission and the term treatment-refractory has reserved for those who do not respond to all available treatments [11]. Such differences make difficult the comparison of effect sizes between studies. Unlike other studies, in this one, weight gain (18%) was not the most common side effect of olanzapine and dizziness and dyspepsia had the same prevalence too among our patients. Somnolence was the most prevalent side effect (27%). Additionally, all of them were mild to moderate and did not cause serious problem for the patients.

Atypical antipsychotics may enhance the action of SSRIs through serotonin receptor blockade. The broader range of effective treatment with the addition of atypical antipsychotics may be due to D2 blockade or a combined serotonergic- dopaminergic blockade, particularly a 5-HT2A and D2 antagonism [5]. The addition of atypical antipsychotics to SSRIs seems a promising pharmacotherapy intervention for treatment refractory OCD patients.

Conclusion

Treatment-refractory OCD Patients may benefit from addition of olanzapine to ongoing SSRI therapy.

Suggestion

Further investigations on the mechanism of Olanazapine of these addition strategies for OCD are warranted.

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