

# Effect of Olanzapine on Disruptive Behavior in Institutionalized Patients with Severe Intellectual Disability – A Case Series

Stipe Drmić<sup>1</sup> and Tomislav Franić<sup>2</sup>

<sup>1</sup> Psychiatric Hospital »Sveti Ivan«, Zagreb, Croatia

<sup>2</sup> Psychiatric Clinic, University Hospital Center »Split«, Split, Croatia

## ABSTRACT

Considerable number of intellectual disabled people experience some form of disruptive behavior. Antipsychotics are the most common treatment for these behaviors. Numerous patients were efficiently treated with thioridazine, recently withdrawn. The authors describe a case series of »thioridazine responders« treated with olanzapine. Thirty three patients with severe intellectual disability were recruited. All patients were assessed for seven types of disruptive behavior on five point scale. Patients with severe behavior disturbances were included in treatment. The time points of assessment were at day 0, 30, 60 and 180. Twenty one patient accomplished inclusion criteria. A significant decrease occurred at day 30 for all types of behavior. Total score, self injurious behavior, compulsive and destructive behavior showed further decrease at day 60 and became stable until the end of study. Olanzapine appears to be efficacious in the treatment of disruptive behavior in the intellectually disabled and could be substitute for thioridazine treatment.

**Key words:** intellectual disability, disruptive behavior, antipsychotics, olanzapine

## Introduction

Behavior disturbances include cluster of heterogeneous noncognitive symptoms and behaviors which are not included in core features of the definition of intellectual disability like behavior adaptive deficits<sup>1,2</sup>. Despite that fact considerable number of people experiences some of these symptoms with prevalence in community-based population up to 60%<sup>3</sup>. These numbers are proportional higher in patients with more serious disability<sup>4</sup>. The term disruptive behavior encompasses a wide range of behaviors that may be harmful to people or property, may be difficult to manage and may limit access to community facilities. Among these symptoms the most dramatic are aggressive, self-injurious behavior and temper tantrums, with range 9% to 30% and they are among most difficult problems to treat<sup>5-8</sup>.

There is no specific treatment for disruptive behavior. Psychotropic drugs probably have some potential to alleviate certain behavioral disturbances in individuals with intellectual disability<sup>9</sup>, although there is opinion that the

suppression of problematic behavior is often achieved largely through sedation<sup>10</sup>.

Antipsychotics are among the most widely used psychotropic medication in people with intellectual disability both for concurrent psychotic features<sup>11,12</sup> and for disruptive behavior<sup>13</sup>. Previously the conventional antipsychotics were used<sup>9,13,14</sup>. One of frequently used typical antipsychotic was thioridazine.

According to our experience and publicized data thioridazine had long term usefulness for disruptive behaviors of institutionalized mentally retarded patients<sup>15</sup>. Because of unacceptable adverse effects, especially risk of cardiac events thioridazine is withdrawn from approved medications list<sup>16,17</sup>. Emerging of new, atypical antipsychotics with their unique 5-HT<sub>2</sub>/D<sub>2</sub> profile raise a question about their efficacy in treating disruptive behaviors.

There is not clear superiority of atypical antipsychotic over the typical in treating schizophrenic patients, but

they did show less adverse events like extrapyramidal symptoms, withdrawal dyskinesias and tardive dyskinesias<sup>18</sup>. Also typical antipsychotic may have fewer negative cognitive effects<sup>18–20</sup>.

There are some evidence about efficacy of these new drugs in treating disruptive behaviors especially for clozapine<sup>21,22</sup>, risperidone<sup>23,24</sup> and quetiapine<sup>25</sup>. There is some literature finding positive effects of olanzapine in treating behavior disturbances in intellectual disability like single case of 10-year-old autistic patient treated for aggressive and repetitive behaviors<sup>26</sup>. Potenza et al. reported an open label study of treating four children and four adults with pervasive developmental disorder and they found significant improvement in several domains like aggression, hyperactivity, self-injurious behavior, irritability and anger<sup>27</sup>. Williams et al. treated 12 intellectual disabled adult patients with same efficacy as risperidone<sup>12</sup>. Olanzapine also reduced chronic self injurious behavior<sup>28</sup>.

According to present authors opinion, published and available papers are still founded on small numbers of cases or case series, limited pilot studies, heterogeneous clinical entities and severity of intellectual disability. Until present time there is no robust evidence as to whether

antipsychotic medication does or does not help people with intellectual disability and disruptive behavior.

The authors think that there is still necessity to expand available knowledge about efficacy of atypical antipsychotics in treating disruptive behaviors and the aim of present study was to evaluate that efficacy for olanzapine.

## Methods

This was partially prospective, open label case series report. Thirty three patients institutionalized because of intellectual disability, disruptive behavior and absence of appropriate family support were recruited.

Regarding ethical considerations, legal guardians were informed about study and we have their passive consent. All of the patients were previously treated with conventional antipsychotic thioridazine. Olanzapine treatment was introduced after drug free period (up to 4 months) and reevaluation of clinical condition.

The presence of only one type of three following behaviors: attacks to objects/damage to property, self-injurious behavior or temper tantrums were sufficient for in-

**TABLE 1**  
CLINICAL AND PERSONAL DETAILS FOR EACH SUBJECT

Case	Age (years)	Gender	Co-morbidity	Other medication	Total score Day 0	Total score Day 180
A	12	M	None		20	15
B	39	F	None		17	12
C	14	F	Epilepsy	Carbamazepine, Clonazepam, Valproic acid	16	14
D	14	M	Epilepsy	Carbamazepine, Clonazepam	12	10
E	8	M	Epilepsy	Phenobarbitone, Valproic acid	15	11
F	8	M	Epilepsy	Phenobarbitone	15	13
G	19	M	Epilepsy	Valproic acid	20	15
H	24	F	None		11	10
I	34	F	None		23	13
J	27	F	None		12	10
K	20	M	Epilepsy	Phenobarbitone	16	10
L	14	M	Epilepsy	Valproic acid	16	13
M	29	M	None		13	9
N	27	M	None		19	14
O	15	F	None		18	16
P	35	M	None		22	16
R	17	M	Epilepsy	Clonazepam, Carbamazepine, Lamotrigine	10	9
S	29	F	None		16	12
T	25	M	None		18	12
U	21	M	Epilepsy	Valproic acid, Carbamazepine, Clonazepam	19	12
V	36	F	None		21	14

**TABLE 2**  
CAREGIVER SCORES: STATISTICAL DATA FOR EACH TYPE OF DISRUPTIVE BEHAVIOR APART AND TOTAL SCORE

Disruptive behavior	Time of scoring (day)	Mean $\pm$ SD	Median (min–max)	$\chi^2$ ; p*
Self-injurious behavior	0	2.29 $\pm$ 0.85	2 (1–4)	29.0; <0.0001
	30	1.95 $\pm$ 0.67	2 (1–3)	
	60	1.62 $\pm$ 0.59	2 (1–3)	
	180	1.52 $\pm$ 0.60	1 (1–3)	
Attacks to objects/damage to property	0	2.43 $\pm$ 0.81	2 (1–4)	33.8; <0.0001
	30	2.05 $\pm$ 0.50	2 (1–3)	
	60	1.62 $\pm$ 0.50	2 (1–2)	
	180	1.57 $\pm$ 0.51	2 (1–2)	
Refusing cooperation	0	2.38 $\pm$ 0.59	2 (2–4)	21.9; <0.0001
	30	2.05 $\pm$ 0.38	2 (1–3)	
	60	1.86 $\pm$ 0.48	2 (1–3)	
	180	1.71 $\pm$ 0.46	2 (1–2)	
Temper tantrums	0	2.14 $\pm$ 0.85	2 (1–3)	11.2; <0.010
	30	1.90 $\pm$ 0.70	2 (1–3)	
	60	1.81 $\pm$ 0.68	2 (1–3)	
	180	1.81 $\pm$ 0.60	2 (1–3)	
Self-stimulation	0	2.95 $\pm$ 0.50	3 (2–4)	27.7; <0.001
	30	2.48 $\pm$ 0.51	2 (2–3)	
	60	2.29 $\pm$ 0.56	2 (1–3)	
	180	2.29 $\pm$ 0.46	2 (2–3)	
Compulsive behavior	0	2.29 $\pm$ 0.72	2 (1–4)	21.8; <0.0001
	30	2.00 $\pm$ 0.45	2 (1–3)	
	60	1.76 $\pm$ 0.44	2 (1–2)	
	180	1.71 $\pm$ 0.46	2 (1–2)	
Excessive and persistent demands	0	2.14 $\pm$ 0.65	2 (1–3)	14.8; <0.002
	30	1.90 $\pm$ 0.44	2 (1–3)	
	60	1.76 $\pm$ 0.62	2 (1–3)	
	180	1.76 $\pm$ 0.62	2 (1–3)	
Total score	0	16.62 $\pm$ 3.64	16 (10–23)	52.5; <0.0001
	30	14.33 $\pm$ 2.08	15 (10–17)	
	60	12.71 $\pm$ 1.93	13 (10–16)	
	180	12.38 $\pm$ 2.20	12 (9–16)	

\*Friedman ANOVA

roduction of olanzapine treatment after drug free period. There were no other treatment modifications beside pharmacological.

Information was collected on following parameters:

- socio-demographic variables (age, gender)
- co morbidity
- co therapy
- seven type of disruptive behaviors (attacks objects/damage to property, self-injurious behavior, refusing cooperation, temper tantrums, self-stimulation, compulsive behavior and excessive and persistent demands) were scored by caregivers on five point scale (1) never and (5) always<sup>29</sup>. There was four ca-

regiver included in rating and each patient was evaluated by the same caregiver.

- Outcome of treatment as secondary variable was measured using the global improvement and efficacy index measures of the clinical global impression-global improvement (CGI-GI) scale<sup>30</sup>. The CGI scores were assigned by two of the investigators independently.
- time points of evaluation were et day 0, 30, 90, and 180

Collected data were processed by statistical software SPSS for Windows ver. 11. descriptive statistics, Wilcoxon test and Friedman ANOVA were used.

**Results**

The review of medical documentation revealed that thirty three patients were treated with thioridazine because of disruptive behavior. The mean duration of treatment was 18 months (range 8–36 months). After withdrawal of thioridazine the patients were followed throughout four month »drug-free« period.

During the »drug-free« period twenty one patients (63.6%) shown one or more inclusion disruptive behaviors:

- attacks to objects/damage to property 19 patients
- temper tantrums 15 patients
- self injurious behavior 18 patients

The mean duration of drug free period was 29.95 days (range 6–56 days).

Among twenty-one patients which accomplished inclusion criteria 8 (38%) were female and 13 (62%) were male. The mean age of the sample was 22.24 (SD 9.30), 27.25 (SD 9.25) for female and 19.15 (SD 8.19) for male.

Gender, age, co morbidity, co-therapy, total disruptive behavior score at day 0 and day 180 are shown in Table 1.

All cases fulfilled the ICD-10 criteria for severe intellectual disability and were institutionalized because of lack of adequate family assistance.

All included patient were treated with olanzapine. Dosage range of olanzapine achieved during study period was 5–15 mg.

The caregiver rated disruptive behaviors on the five point scale.

Total score and scores for each individual disruptive behavior at days 0, 30, 60 and 180 are shown in Table 2.

Total score declined statistical significantly (Wilcoxon test) between day 0 and day 30 ( $p=0.000$ ), between day 30 and day 60 ( $p=0.000$ ) and stay stable without

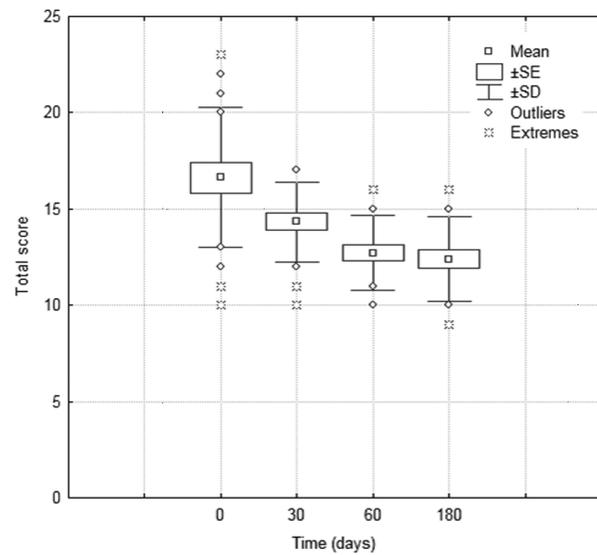


Fig. 1. Caregivers total scores for disruptive behaviors.

statistical significant change until day 180 ( $p= 0.15$ ) Figure 1.

Each of seven observed disruptive behaviors shown statistical significant decline between days 0 and 30 ( $p<0.05$ ).

Two types of disruptive behavior had further decline until day 60:

- Self injurious behavior ( $p = 0.008$ ) Figure 2
- Attacks to objects/damage to property ( $p = 0.0039$ ) Figure 3

There is no statistical significant decline in total score or individual score for any observed behaviors and that scores stay stable between day 60 and day 180 ( $p>0.05$ ).

Clinical outcome was also measured by Clinical Global Impression-Global Improvement (CGI-GI) scale.

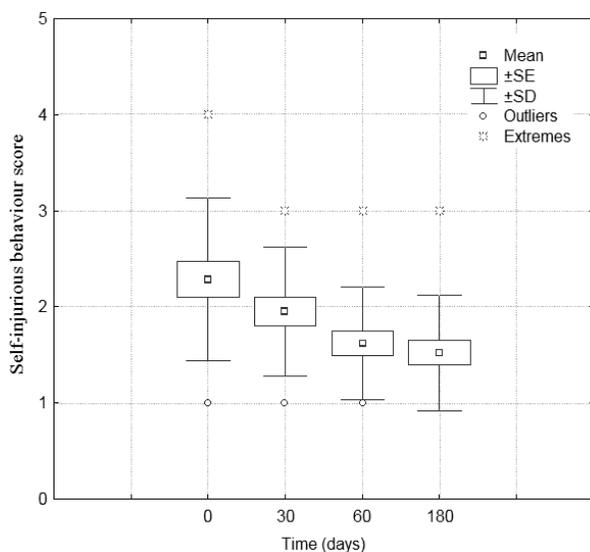


Fig. 2. Caregivers score for self injurious behavior.

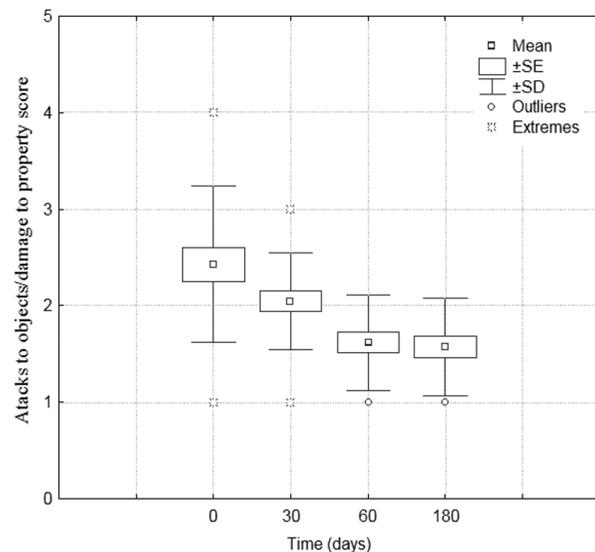


Fig. 3. Caregivers score; attacks to objects/damage to property.

The best improvement was observed in patient with higher score. Although behavior disturbances are not included in core features of intellectual disability they still have remarkable influence on clinical impression and patients with higher disruptive behavior score had higher start CGI score.

## Conclusion

Behavioral symptoms in intellectually disabled people are common and problematic in clinical practice. They represent a significant part of the day-to-day workload of the psychiatry team and caregivers.

The aim of the present study was to evaluate the efficacy of olanzapine treatment on disruptive behaviors in heterogeneous group of patients with severe intellectual disability. The olanzapine is relatively new antipsychotic medication and there is broad spectrum of new indications beside psychotic disorders waiting for eventual affirmation.

The use of olanzapine in treatment of disruptive behaviors in people with intellectual disability is not well established.

The present authors found that olanzapine appeared to have efficacy in reducing disruptive behavior in people with intellectual disability and this is in accordance with some previous findings for antipsychotics in general<sup>7-9</sup>, for olanzapine<sup>12,14,26-28</sup>. This study of 21 patients previously treated with thioridazine indicated that olanzapine was associated with statistical significant improvement on five point scale and CGI scale.

Broadly evaluation on CGI scale showed that 17 patients were rated as minimally improved or better at day 180. This represents some kind of paradox where targeting no-core symptoms results in significant change in perception of patient's clinical presentation.

## REFERENCES

1. AMERICAN PSYCHIATRIC ASSOCIATION, Diagnostic and Statistical Manual of Mental Disorders, 4th eds. (American Psychiatric Association, Washington, DC, 1994).
2. WORLD HEALTH ORGANIZATION, The ICD-10: International Statistical Classification of Disease and Related Health Problems, 10<sup>th</sup> Revision (World Health Organization, Geneva, 1992).
3. DEB S & BRIGHT C, *J Intellect Disabil Res*, 45 (2001) 506.
4. JANSSEN CGC, SCHUENGEL C & STOLK J, *J Intellect Disabil Res*, 46 (2001) 445.
5. ROJAHN J, *Am J Ment Defic*, 91, (1986), 268.
6. REBER M, *Psychiatr Clin North Am*, 15 (1992) 511.
7. AMAN MG, *Ann Clin Psychiatry*, 5, (1993), 171.
8. ROJAHN J, BORTHWICK-DUFFY SA & JACOBSON JW, *Ann Clin Psychiatry*, 5 (1993) 163.
9. REISS S, AMAN MG, *Psychotropic Medication and Developmental Disabilities: The International Consensus Handbook* (Ohio State University Nisonger Center, Columbus, 1998).
10. MATSON JL, BAMBURG JW, MAYVILLE EA, PINKSTON J, BIELECKI J, KUHN D, SMALLS Y, LOGAN JR, *Res Dev Disabil*, 21 (2000) 263.
11. KIERNAN C, REEVES D, ALBORZA A, *J Intellect Disabil Res*, 39 (1995) 263.
12. WILLIAMS H, CLARKE R, BOURAS N, MARTIN J, HOLT G, *J Intellect Disabil Res*, 44 (2000) 164.
13. AMAN MG, MADRID A, *Ment Retard Dev Disabil Res Rev*, 5 (1999) 253.
14. JANOWSKY DS, BARNHILL LJ, DAVIS JM, *J Clin Psychiatry*, 64 (2003) 1258.
15. HEISTAD GT, ZIMMERMANN RL, DOEBLER MI, *Am J Ment Defic*, 87 (1982) 243.
16. GUALTIERI CT, LEFLER WH, GUIMOND M, STAYE JI, *Am J Psychiatry*, 39 (1982)

The study also show that even in population with severe form of intellectual disability there is considerable ratio (nearly 40%) of patients who does not need the continuous treatment with antipsychotic medication. This finding is in accordance with some other studies of clinical outcome in intellectually disabled patients withdrawn from chronic antipsychotic medication<sup>31</sup>.

All of this supports emerging trends to establishing regular reevaluation of antipsychotic treatment of disruptive behavior and which resulted in the development of legislative and procedural controls in Western countries<sup>32</sup>. The sample size of our study is one of largest reported with sociodemographic data somewhat different compared with other reports (lower mean age).

Our study has number of limitation like no placebo controls and no blinding occurred.

The evaluation of previously thioridazine response of disruptive behaviors was retrospective. Diagnostically, our study group was diverse because nine patients had some form of epilepsy and were treated with anticonvulsive drugs.

Antipsychotic treatment of disruptive behavior in intellectually disabled persons is so-called off label indication and according to authors opinion there is no interest among producers of drugs to expand indication on this area. Because of that the vast majority of our knowledge about this gray zone came from studies like this with numbers of limitation.

Further research in this area should involve and include appropriate control groups, double-blind and placebo-controlled methodology, and longitudinal follow-up. There is need for ongoing review and for further research, particularly into the reasons for use and the efficacy of the drugs on target behaviors. Research needs to be conducted to ensure that medication administered to people with intellectual disability is appropriate in type and level.

17. TIMELL AM, *Ann Clin Psychiatry*, 12 (2000), 147.
18. MELTZER HY, *Psychopharmacol Bull*, 22 (2002) 839.
19. HARVEY PD, KEEFE RS, *Am J Psychiatry*, 158 (2001) 176.
20. GREEN MF, MARDER SR, GLYNN SM, MCGURK SR, WIRSHING WC, WIRSHING DA, LIEBERMAN RP, MINTZ J, *Biol Psychiatry*, 51 (2002) 972.
21. RATEY JJ, LEVERONI C, KILMER D, GUTHEIL C, SWARTZ B, *J Clin Psychiatry*, 54 (1993) 219.
22. THALAYASINGAM S, ALEXANDER RT, SINGH I, *J Intellect Disabil Res*, 48 (2004) 572.
23. COHEN SA, IHRIG K, LOTT RS, KERRICK JM, *J Autism Dev Disord*, 28 (1998) 229.
24. VANDEN BORRE R, VERMOTE R, BUTTIENS M, THIRY P, DIERICK G, GEUTJENS J, SIEBEN G, HEYLEN S, *Acta Psychiatr Scand*, 87 (1993) 167.
25. MARTIN A, KOENIG K, SCAHILL L, BREGMAN J, *J Child Adolesc Psychopharmacol*, 9 (1999) 99.
26. HERRIGAN JP, BARNHILL LJ, COURVOISE HE, *J Am Acad Child Adolesc Psychiatry*, 36 (1997) 1166.
27. POTENZA MN, HOLMES JP, KANES SJ & MCDONOUGH CJ, *J Clin Psychopharmacol*, 19 (1999) 37.
28. MCDONOUGH M, HILLERY J & KENNEDY N, *J Intellect Disabil Res*, 44 (2000) 677.
29. N'TTESTAD JA & LINAKER OM, *J Intellect Disabil Res*, 46 (2002) 493.
30. NATIONAL INSTITUTE OF MENTAL HEALTH, *Psychopharmacol Bull*, 22 (1985) 839.
31. MAY P, LONDON EB, ZIMMERMANN T, THOMPSON R, MENTO T, SPREAT S, *Ann Clin Psychiatry*, 7 (1995) 155.
32. MCGILLIVRAY JA, MCCABE MP, *Res Dev Disabil*, 25 (2004) 523.

*S. Drmić*

*Psychiatric Hospital »Sveti Ivan«, Jankomir 11, 10090 Zagreb, Croatia  
e-mail: stipe.drmic@gmail.com*

## **UČINAK OLANZAPINA NA DISRUPTIVNO PONAŠANJE KOD INSTITUCIONALIZIRANIH PACIJENATA SA TEŠKIM INTELEKTUALNIM ONESPOSOBLJENJEM – SERIJA SLUČAJEVA**

### **S A Ž E T A K**

Značajan broj ljudi s intelektualnim poteškoćama pokazuje neki oblik disruptivnog ponašanja. Antipsihotici se najčešće koriste u liječenju takvog ponašanja. Znatni broj pacijenata je liječen tioridazinom, koji je nedavno povučen s tržišta. Autori opisuju seriju slučajeva »tioridazin respondera« liječenih olanzapinom. Trideset i tri bolesnika sa teškim intelektualnim poteškoćama uključena su u studiju. Procjenjivano je sedam tipova disruptivnog ponašanja na skali od pet stupnjeva. Uključeni su i bolesnici s teškim promjenama ponašanja. Vremenske točke ocjenjivanja su bile na dan 0, 30, 60 i 180. Dvadeset i jedan bolesnik je zadovoljio kriterije uključivanja. Značajno poboljšanje je primijećeno 30-ti dan za sve tipove ponašanja. Ukupni zbroj, samoozljeđujuće ponašanje, prisilno i destruktivno ponašanje pokazuju daljnji pad 60-ti dan i ostaju stabilni do kraja studije. Olanzapin se pokazao učinkovitim u liječenju disruptivnog ponašanja kod bolesnika sa intelektualnim poteškoćama, te bi se mogao koristiti kao zamjena za tioridazin.