

APPROACH TO EMERGENCIES IN SCHIZOPHRENIA IN UNIVERSITY HOSPITAL "VRAPČE"

Ante Silić, Aleksandar Savić, Ilaria Čulo, Suzana Kos, Jakša Vukojević,
Daška Brumen & Draženka Ostojić

University Psychiatric Hospital Vrapče, Zagreb, Croatia

SUMMARY

Background: An emergency in psychiatric setting is any disorder in thought process, feelings and/or behavior of the patient that requires urgent therapeutic intervention. In general, we can observe an increase in numbers of psychiatric emergencies throughout the world and in Croatia as well. Agitation and aggression are one of the most common causes of emergency in psychiatry. Agitation is common and frequent in patients suffering from schizophrenia. Patient can be agitated in various levels such as: mild, moderate or severe and can alternate between these levels in the same presentation. Agitated patients often require hospitalization that includes pharmacotherapy and sometimes physical restraining, in order to treat the cause of agitation and prevent auto and/or heterodestructive behavior.

Subjects and methods: In this paper we focus on patients suffering from schizophrenia that were admitted in University Hospital "Vrapče" in 2017, and assess the numbers through the criteria of voluntary vs. involuntary admissions and physical restraint usage.

Results: Out of total observations, 130 (35.6%) were patients admitted for the first time and 179 (49%) were patients later diagnosed with schizophrenia spectrum and other psychotic disorders. Court ordered involuntary hospitalization was ordered for 35 (2.8%) patients out of total admitted patients, and 68.6% (N24) of them were diagnosed with schizophrenia spectrum and other psychotic disorders. Physical restraint was used for 122 patients out of total admissions and 28.7% (N35) of restrained patients were diagnosed with schizophrenia spectrum and other psychotic disorders.

Conclusions: Emergencies in patient suffering from schizophrenia are extremely delicate and demanding situations in every-day clinical practice of psychiatrist. There is an increased risk involved for the patient but for the staff as well. All interventions should be individualized and patient should carefully monitored throughout the entire process. All professionals involved in care for a patient should be up to date with medical and legal issues.

Key words: schizophrenia - psychotic disorders - psychomotor agitation - violence

* * * * *

INTRODUCTION

An emergency in psychiatric setting is any disorder in thought process, feelings and/or behavior of the patient that requires urgent therapeutic intervention. In general, we can observe an increase in numbers of psychiatric emergencies throughout the world and in Croatia as well (Ostojić & Čulo 2018, Silić 2018). Agitation and aggression are one of the most common causes of emergency in psychiatry. Agitation is common and frequent in patients suffering from schizophrenia. Patient can be agitated in various levels such as: mild, moderate or severe and can alternate between these levels in the same presentation. Agitated patients often require hospitalization that includes pharmacotherapy and sometimes physical restraining, in order to treat the cause of agitation and prevent auto and/or heterodestructive behavior (Allen 2000, Allen & Currier 2004). Agitation is always related to the underlying disease and when patient presents with agitation we always have to consider the possible cause such as schizophrenia, bipolar disorder, substance abuse disorders, iatrogenic etc (Buckley 2006, Leventhal & Zimmerman 2010, Fiorentini et al. 2011). Data from the United States (US), suggests close to two million emergency department visits per year that involve agitated patients, with schizophrenia being an underlying cause for 21% of

these visits (Sankaranarayanan & Puumala 2000, Marco & Vaughan 2005). 52% of presented patients in the Psychiatric ER were agitated and 45% of them were hospitalized and received specific psychopharmacotherapy in order to reduce agitation (Boudreaux 2009).

Schizophrenia spectrum and other psychotic disorders are grouped together in recent classifications - DSM 5 (American Psychiatric Association 2013). Psychiatry redefined the term "psychosis" in numerous occasions so far and it is safe to say that we did not achieve generally accepted definition (Sadock et al. 2015). In context of emergencies in psychiatry we can define psychosis as a disturbance of the perception of reality which may or may not include hallucinations and delusions. We can define delusions as false, fixated beliefs and hallucinations as sensory perceptions (in all sensory modalities) in the absence of real external stimuli. Neither hallucinations nor delusions should be considered as diagnosis rather as a symptom (Goldberg & Murray 2006, Gelder et al. 2007, Black & Andreasen 2014). Every psychotic patient should be approached to as having a potential for psychiatric emergency whether it is patient's first or repeated contact with psychiatric services. Differential diagnostic procedures should be started as soon as possible in order to clarify the pathophysiology and etiology underlying presented symptoms. All psychotic patients must be monitored closely

during their evaluation. Not all psychotic patients will become agitated and can be treated without difficulties, but we should anticipate and when possible prevent agitated and violent outbursts routinely in a management of psychotic patient. Agitation is very often preceded by verbal or behavioral hints but may also emerge without warning (Sadock et al. 2015).

Diagnostic and therapeutic decisions should be made in good clinical practice manner by a team of educated professionals. All involved professionals (psychiatrists, nurses...) should be up to date with medical and legal aspects of care for management of psychiatric emergencies (Allen et al. 2005). In medicine in general there are few clinical situations that can be as complicated as are those emerging with management of psychotic patients. During the process of management of each individual psychotic patient we must achieve delicate balance between care (intervention) and safety of the patient and staff while respecting patient's human rights. Recognizing and preventing violent behavior is one of the most important priorities in psychiatric emergencies (Chanmugam et al. 2013).

SUBJECTS AND METHODS

In this paper we focus on patients suffering from schizophrenia that were admitted in University Hospital „Vrapče“ in 2017, and assess the numbers through the criteria of voluntary vs. involuntary admissions and physical restraint usage. We analyzed data on file in retrospective manner.

RESULTS

In 2017, total number of admissions in University hospital "Vrapče" was 7.167. Out of total admissions, 2.244 (31.3%) were diagnosed with schizophrenia spectrum and other psychotic disorders. Number of admissions in Department for urgent psychiatry was 1.235. Number of patients that were admitted for the first time was 579 (46.9%) and number of patient that were admitted (and discharged) prior to 2017 was 656 (53.1%). 439 (35.5%) admitted patients were discharged with diagnosis of schizophrenia spectrum and related psychosis. Out of total admissions 870 (70.4%) valid informed consents were obtained during admission process and 365 (29.6%) patients were admitted for the observation (up to 48 hours), according to Croatian law for psychiatric patients – ZZODS (Kos 2018).

Out of total observations, 130 (35.6%) were patients admitted for the first time and 179 (49%) were patients later diagnosed with schizophrenia spectrum and other psychotic disorders.

Court ordered involuntary hospitalization was ordered for 35 (2.8%) patients out of total admitted patients, and 68.6% (N24) of them were diagnosed with schizophrenia spectrum and other psychotic disorders.

Physical restraint was used for 122 patients out of total admissions and 28.7% (N35) of restrained patients were diagnosed with schizophrenia spectrum and other psychotic disorders. Every physically restrained patient diagnosed with schizophrenia spectrum and other psychotic disorders was administered with parenteral therapy in the acute setting (within 48 hours upon admission). We used haloperidol, olanzapine, promazine and ziprasidone i.m and/or diazepam i.m. (Table 1).

DISCUSSION

According to our data, diagnosis of schizophrenia spectrum and other psychotic disorders was strong predictor of need for involuntary treatment if patient did not give valid informed consent upon admission and not a strong predictor for usage of physical restraint.

Here we state some clinical facts and recommendations based on our experience and available guidelines.

Clinical facts crucial to recognition and avoidance of violent behavior (Savic 2018)

- It is difficult to predict violent behavior but it is most often related to:
 - Intoxication with alcohol or other psychoactive substances (Alkhoury et al. 2010);
 - Neuro cognitive disorders such as dementia, delirium or brain injuries;
 - Schizophrenia spectrum and other psychotic disorders;
 - Personality disorders.
- Patient must be approached in a calm manner:
 - Involved professional must not present in intimidating, authoritative or provoking manner;
 - Clinician must address patient quietly from a "passive position" while respecting personal space of the patient which can be wider than usual in a psychotic patient – usually two arm lengths;
 - Neither clinician nor patient must not feel "cornered".

Table 1. Analysis of total number of admissions in Department for Urgent psychiatry in 2017

Total no of admissions	First admission	Repeated admission	Sch* - admission	Observation	Observation-first
1235 (7167)	579 46.9%	656 53.1%	439 35.5%	365 29.6%	130 35.6%
Sch-observation	Court**	Court - sch	Restraint	Restraint - sch	Perenteral – sch
179 49%	35 2.8%	24 68.6%	122 9%	35 28.7%	35 100%

*schizophrenia spectrum and other psychotic disorders; **court ordered involuntary hospitalization

Table 2. Advantages and disadvantages of different routes of administration (adopted from Zeller et al. 2016)

Administration route	Advantages	Disadvantages	Examples	Time to peak plasma concentration
Intramuscular	Rapid systemic entry; patient cooperation not necessary	Invasive; can damage patient - physician relationship	Haloperidol Olanzapine Aripiprazole* Ziprasidone	~20 minutes 15–45 minutes 1–3 hours 60 minutes
Inhaled	Less invasive than intramuscular route and can improve patient experience. Enters alveoli for rapid entry into arterial circulation	Requires patient cooperation Bronchospasm/ respiratory distress	Loxapine*	2 minutes
Oral				
Standard tablets/ capsules/ solution	Less invasive than intramuscular route and can improve patient experience	Require patient cooperation; slow onset of action; enter systemic circulation via portal system resulting in potential for erratic absorption; can be diverted (“cheeking”)	Haloperidol Olanzapine Risperidone Aripiprazole Ziprasidone	2–6 hours 5–8 hours ~1 hour 3–5 hours 6–8 hours
Orally disintegrating tablets	Less invasive than intramuscular route and can improve patient experience. Less potential for diversion (“cheeking”) vs standard tablets/capsules; suitable for patients with dysphagia	Slow onset of action; enter systemic circulation via portal system resulting in potential for erratic absorption	Olanzapine Risperidone Aripiprazole	~6 hours 1–2 hours 3–5 hours
Buccal/ sublingual	Less invasive than intramuscular route and can improve patient experience; rapid absorption; avoids first-pass metabolism	Requires patient cooperation; needs to be taken correctly so that it is not swallowed, mitigated in part by the friability of the tablet	Sublingual asenapine*	0.5–1.5 hours
Intranasal	Less invasive than intramuscular route and can improve patient experience; rapid absorption; avoids first-pass metabolism	Requires patient cooperation.	Intranasal midazolam*	10 minutes

* Currently not available in Croatia

Table 3. Other psychopharmacs that can be used in emergencies in patient suffering from schizophrenia spectrum and other psychotic disorders (Stahl 2014)

Group	Target symptoms
Antiepileptic / mood stabilizer	Positive symptoms
Na-valproate	Agitation
Carbamazepine	Aggression
Lamotrigine	Negative symptoms
Topiramate	Affective symptoms
Gabapentine	
Lithium	
Benzodiazepines	Agitation
Diazepam	Anxiety
Clonazepam	Insomnia
Lorazepam	
Alprazolam	
Bromazepam	
Oxazepam	
Flurazepam	
Midazolam	
Nitrazepam	

▪ Clinician should calmly ask the patient “What seems to be wrong?” or “What is going on?” or state “You seem to be angry, can I know why?....”

▪ Violent patients need to be hospitalized because in that way we can ensure their safety and safety of people surrounding them.

▪ If and when needed violent or agitated patient should be restrained according to good clinical practice and law (ZZODS).

▪ Underlying cause of psychotic symptoms should be intensively treated.

▪ Outpatients should be reassessed for violent behavior on every visit.

Therapeutic interventions in management of agitation in patient suffering from schizophrenia can be summarized in two groups: behavioral (non-pharmacological) and pharmacological (Zeller & Citrome 2016).

Behavioral intervention

Verbal de-escalation – should be attempted with all patients.

Quiet unlocked room - patients in whom de-escalation alone was insufficient to reduce dangerousness enough to allow to remain in general care areas, and/or may need more time to regain control away from other patients

Locked seclusion - if patients are considered an imminent danger to others but not themselves, and cannot tolerate or remain in a quiet unlocked room.

Restraint - if patients are considered an imminent danger to themselves, and cannot remain in a locked seclusion room without actively trying to injure themselves.

Non pharmacological interventions should be preferred but there are some advantages and disadvantages of such interventions for agitation (Savić 2018)

Advantages: facilitates better short- and long-term patient–physician relationships, reduces staff and patient injuries associated with restraint and sedation and can reduce resource (clinical and staff) use.

Disadvantages: may not be effective in all patients and most importantly it requires at least some co-operation from the patient.

Pharmacological intervention

First line of treatment in psychiatric emergencies is psychopharmacotherapy. Mechanism of action is primarily blockage of dopamine D2 receptors in mesolimbic projections of dopaminergic neurons. That effect in cascade reaction leads to psychomotor calming of the patient in the acute phase of treatment but is also important in the long run. (Zeller & Citrome 2016, Savić 2018).

Antipsychotic drugs represent highly heterogeneous group of drugs interacting with various types of receptors other than dopaminergic (serotonergic, cholinergic, noradrenergic, histaminergic...) (Fruyt & Demyttenaere 2004, Zeller & Rhoades 2010).

Which drug will be drug of choice in psychiatric emergencies depends on various factors:

- Leading symptom(s): auto or heterodestructive behavior, hallucinations, delusions, anxiety, agitation, insomnia...
- Potential side effects: EPS, sedation, hypotension, QT effect...
- Earlier response to therapy;
- Earlier developed side effects;
- Psychiatric and non psychiatric co morbidities;
- What patient prefers (when possible, respecting patient's wishes regarding formulation, brand-name and type of therapy can lead to better long-term outcomes).

Whenever it is possible we should administer monotherapy. Combining two or more drugs is often necessary but should be avoided if possible. There are different formulations of psychopharmacotherapy available for the management of emergencies in schizophrenia. We should always prefer peroral route of administration if possible thus avoiding intrusive ways of administering a drug (Ostinelli et al. 2017).

First line therapy in acute setting can be inhaled Loxapine. Loxapine is a first-generation antipsychotic structurally similar to clozapine. Recommended dosage via inhalation (approved by FDA for agitation in schizophrenia and manic phase of bipolar disorder) is 10 mg and should not be exceeded through 24 hours. It can be administered only for in patients (Keating 2013, Popovic et al. 2015). At this moment Loxapine is not available in-patient.

In psychiatric emergencies with agitated or violent behavior in addition to antipsychotic we can administer parenterally benzodiazepines such as lorazepam (currently not available in-patient in parenteral formulation) or diazepam (Beckman & Haas 1980, Citrome 2013).

Recommendations on dosages and combinations of drugs are not generally accepted but there are some general rules (Gugger 2011, Citrome 2013, Huang et al. 2015):

- All drug to drug interactions should be considered as well as possible interactions with psychoactive substances on individual basis;
- We must not exceed maximal recommended daily dose;
- Simultaneous administration of parenteral formulation of olanzapine and any benzodiazepine is not allowed;
- If i.m. therapy does not achieve desired effect, exception can be made and it is possible to administer slow intravenous application of haloperidol or diazepam with rigorous monitoring of vital functions.

Given the heterogeneity of presentation in psychiatric emergencies in schizophrenia patients, we can be faced with necessity of administering other group of psychopharmacs (Ostojić et al. 2017, Silić 2017).

CONCLUSIONS

Emergencies in patients suffering from schizophrenia spectrum and related psychoses are extremely delicate and demanding situations in every-day clinical psychiatric practice. There is an increased risk involved for the patient but for the staff as well. All interventions should be individualized, carefully timed and patient should carefully monitored throughout the entire process. All professionals involved in care for a patient should be up to date with medical as well as with legal issues involved.

Contribution of individual authors:

Ante Silić: conception and design of the paper, analysis and interpretation of data;

Aleksandar Savić: conception and design, participated in drafting and revising article;

Ilaria Čulo & Suzana Kos: analysis and interpretation of data, critical revision;

Jakša Vukojević: analysis and interpretation of data, data search

Daška Brumen: acquisition of data;

Draženka Ostojić: conception and design, participated in drafting and revising article.

Acknowledgements: None.

Conflict of interest: None to declare.

References

1. Allen MH: *Managing the agitated psychotic patient: a reappraisal of the evidence.* *J Clin Psychiatry* 2000; 61(S14):11-20
2. Allen MH & Currier GW: *Use of restraints and pharmacotherapy in academic psychiatric emergency services.* *Gen Hosp Psychiatry* 2004; 26:42-9
3. Allen MH, Currier GW, Carpenter D, Ross RW & Docherty JP: *Expert Consensus Panel for Behavioral Emergencies 2005. The expert consensus guideline series. Treatment of behavioral emergencies.* *J Psychiatr Pract* 2005; 11(S1):5-108
4. Alkhoury I, Gibbons P, Ravindranath D & Brower K: *Substance-Related Psychiatric Emergencies.* In: Riba MB & Ravindranath D (eds): *Clinical Manual of Emergency Psychiatry.* Washington, DC, London, England: American Psychiatric Publishing, 2010
5. *American Psychiatric Association: Diagnostic and statistical manual of mental disorders (5th ed.).* Arlington, VA: American Psychiatric Publishing, 2013
6. Beckman H & Haas S: *High dose diazepam in schizophrenia.* *Psychopharmacology (Berl)* 1980; 71:79-82
7. Black DW & Andreasen NC: *Introductory textbook of Psychiatry.* 6th ed. American Psychiatric Publishing, 2014
8. Boudreaux ED, Allen MH & Claassen C: *The psychiatric emergency research collaboration - 01: methods and results.* *Gen Hosp Psychiatry* 2009; 31:515-22
9. Buckley PF: *Prevalence and consequences of the dual diagnosis of substance abuse and severe mental illness.* *J Clin Psychiatry* 2006; 67(S7):5-9
10. Chamugam A, Triplett P & Kelen G: *Emergency psychiatry.* Cambridge University Press, 2013
11. Citrome L: *Limited evidence of effects of haloperidol alone for rapid tranquilization in psychosis-induced aggression.* *Evid Based Ment Health* 2013; 16:47
12. Fiorentini A, Volonteri LS & Dragogna F: *Substance-induced psychoses: a critical review of the literature.* *Curr Drug Abuse Rev* 2011; 4:228-40
13. De Fruyt J & Demyttenaere K: *Rapid tranquilization: new approaches in the emergency treatment of behavioral disturbances.* *Eur Psychiatry* 2004; 19:243-9
14. Gelder M, Harrison P & Cowen P: *Shorter Oxford Textbook of Psychiatry.* 5th ed. Oxford University Press, 2007
15. Goldberg D & Murray R: *The Maudsley Handbook of Practical Psychiatry.* 5th ed. Oxford University Press, 2006
16. Gugger JJ: *Antipsychotic pharmacotherapy and orthostatic hypotension: identification and management.* *CNS Drugs* 2011; 25:659-71
17. Huang CL, Hwang TJ, Chen YH, Huang GH, Hsieh MH, Chen HH et al.: *Intramuscular olanzapine versus intramuscular haloperidol plus lorazepam for the treatment of acute schizophrenia with agitation: An open-label, randomized controlled trial.* *J Formos Med Assoc* 2015; 114:438-45
18. Keating GM: *Loxapine inhalation powder: a review of its use in the acute treatment of agitation in patients with bipolar disorder or schizophrenia.* *CNS Drugs* 2013; 27:479-89
19. Kos S: *Zakonski okviri zbrinjavanja hitnih stanja u psihijatriji (Croatian laws on management of emergencies in psychiatry).* In Jukić V & Ostojić D (eds): *Hitna stanja u psihijatriji*, 125-30. Medicinska naklada, Klinika za psihijatriju Vrapče, 2018
20. Leventhal AM & Zimmerman M: *The relative roles of bipolar disorder and psychomotor agitation in substance dependence.* *Psychol Addict Behav* 2010; 24:360-5
21. Marco CA & Vaughan J: *Emergency management of agitation in schizophrenia.* *Am J Emerg Med* 2005; 23:767-76
22. Ostinelli EG, Brooke-Powney MJ, Li X & Adams CE: *Haloperidol for psychosis-induced aggression or agitation (rapid tranquilization).* *Cochrane Database Syst Rev* 2017; 7
23. Ostojić D & Čulo I: *Hitni psihijatrijski bolesnik - agitacija i agresija (Emergency in psychiatry - agitation and aggression).* In Jukić V & Ostojić D (eds): *Hitna stanja u psihijatriji*, 18-30. Medicinska naklada, Klinika za psihijatriju Vrapče, 2018
24. Ostojić D, Silić A, Kos S, Čulo I & Savić A: *Terapija prve psihotične epizode (Treatment of First episode psychosis).* *Medicus* 2017; 26:151-60
25. Popovic D, Nuss P & Vieta E: *Revisiting loxapine: a systematic review.* *Ann Gen Psychiatry* 2015; 14:15
26. Sadock BJ, Sadock VA & Ruiz P: *Kaplan & Sadock's Synopsis of Psychiatry.* 11th ed. Wolters Kluwer, 2015
27. Sankaranarayanan J & Puumala SE: *Epidemiology and characteristics of emergency department visits by US adults with psychiatric disorder and antipsychotic mention from 2000 to 2004.* *Curr Med Res Opin* 2007; 23:1375-85
28. Savić A: *Načini procjene rizika i primjena intervencija (preventivnih/deeskalacijskih, farmakoterapijskih) (Risk assessment and interventions - preventive/de-escalation, pharmacotherapy).* In Jukić V & Ostojić D (eds): *Hitna stanja u psihijatriji*, 78-87. Medicinska naklada, Klinika za psihijatriju Vrapče, 2018
29. Silić A: *Hitna stanja kod psihotičnih bolesnika (Emergencies in psychotic patients).* In Jukić V & Ostojić D (eds): *Hitna stanja u psihijatriji*, 51-60. Medicinska naklada, Klinika za psihijatriju Vrapče, 2018
30. Silić A: *Psihofarmakoterapijske specifičnosti u liječenju prvih psihotičnih poremećaja (Psychopharmacotherapy specificities in treating first episodes of psychotic disorders).* In: Ostojić D (ed): *Suvremeni pristup prvim psihotičnim poremećajima*, 49-56. Zagreb: Medicinska naklada, Klinika za psihijatriju Vrapče, 2015
31. Stahl SM: *Stahl's essential psychopharmacology. Prescriber's guide.* 5th ed. Cambridge university press, 2014
32. Zeller SL & Citrome L: *Managing Agitation Associated with Schizophrenia and Bipolar Disorder in the Emergency Setting.* *West J Emerg Med* 2016; 17:165-72
33. Zeller SL & Rhoades RW: *Systematic reviews of assessment measures and pharmacologic treatments for agitation.* *Clin Ther* 2010; 32:403-25

Correspondence:

Ante Silić, MD, PhD
University Psychiatric Hospital Vrapče
Bolnička cesta 32, 10 000 Zagreb, Croatia
E-mail: ante.silic@gmail.com