Orzeł Anna, Janeczko Dominika, Klatka Barbara, Hołowczuk Magdalena, Neścior-Piech Małgorzata, Tchórz Michał. Acute overdose of antipsychotics and antidepressants by patient with paranoid schizophrenia - a case report. Journal of Education, Health and Sport. 2019;9(9):578-588. eISSN 2391-8306. DOI http://dx.doi.org/10.5281/zenodo.3445078
http://ojs.ukw.edu.pl/index.php/johs/article/view/7468

The journal has had 5 points in Ministry of Science and Higher Education parametric evaluation. § 8. 2) and § 12. 1. 2) 22.02.2019.

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 01.09.2019. Revised: 18.09.2019. Accepted: 18.09.2019.

Acute overdose of antipsychotics and antidepressants by patient with paranoid schizophrenia - a case report

Anna Orzeł 1, Dominika Janeczko 1, Barbara Klatka 1, Magdalena Hołowczuk 1, Małgorzata Neścior-Piech 1, Michał Tchórz 2

1. Students' Research Group at the Department of Toxicology, Medical University of Lublin

2. Department of Toxicology, Medical University of Lublin

Abstract

Introduction

Despite developing strategies for treatment of people with schizophrenia, earlier mortality rate is still observed in this group of patients. One of the major causes remains suicides due to drug overdose. Main approach to the treatment of schizophrenia is pharmacotherapy that is based on antipsychotics. Yet, in order to sustain patients well being, medicaments from other groups may be introduced. Pharmacological treatment should be accompanied by psychotherapy to prevent suicidal attempts.

A 28 years old woman diagnosed with paranoid schizophrenia was brought by the ambulance and admitted to the Clinical Toxicology Department due to deliberate drug overdose. Her history indicated previous suicidal attempt. A patient took all her psychiatric medications that included 240 tablets of quetiapine (Ketrel a 200 mg), 100 tablets of zuclopenthixol (Clopixol a 25 mg), 100 tables of chlorprotixen, several tablets of escitalopram (Aciprex) and 12 tablets of bisoprolol (Bibloc a 5 mg) - in summary around 470 tablets. This suicidal attempt was probably the cause of abrupt drugs withdrawal after discharge from recent hospitalization in psychiatric department. Complications involved allo- and autodisorientation, enhancement of imperative auditory hallucinations and psychotic symptoms, respiratory failure and aspiration pneumonia. After admission, intensive symptomatic treatment was introduced in order to sustain living functions of the patients. Due to respiratory failure, she was in need of external mechanical ventilation. The end of hospitalization was followed by implementation of new drug (perazine) and transportation to Neuropsychiatric hospital for further diagnosis and treatment.

Conclusion

Process of pharmacotherapy in case of patients with schizophrenia should be continuously and precisely monitored by psychiatrists. Such control would minimize the chance of suicidal attempt. What is more, patient should not limit the therapy to drugs and psychiatric appointments, but also should attend to community health services.

Key words: drug overdose, schizophrenia, antipsychotics, suicide

Introduction

Suicidal risk due to drug overdose contribute to increased mortality rate of patients with schizophrenia. As abrupt onset of the disorder considers late adolescence to early adulthood, the average age of patients mortality is lower than in case of general population [1]. Moreover, the research of Carsten Hjorthøj et al. indicated that people with schizophrenia, bipolar disorders or major depression show higher rate of substance use disorder (mainly including alcohol, hard-drugs and cannabis) [2]. Pharmacological treatment of schizophrenia involves various groups of medications with differentiated strength. Although main therapeutic approach is an introduction of first generation antipsychotics (FGA) or second-generation antipsychotics (SGA) [3] also a wide range of other medicaments such as antidepressants or anticholinergic agents may be implemented according to patients needs [4].

Secondly, medications have to be adapted to patients condition. Quetiapine is a SGA that inhibits differentiated receptors mainly focusing on serotonin receptors (anti-HT2A action) and in lower range on dopamine receptors (D2) [3]. Generally, SGAs are characterized by smaller risk of side-effects occurrence than in case of FGAs. Yet, one of them are suicidal thoughts and actions that may be enhanced after implementation of the drug [5]. Concerning patients with suicidal tendencies and high risk of quetiapine overdose, different medicament from SGAs should be provided [6].

Complex treatment creates the need of easy access to great amount of drugs. This situation itself may be a risk factor of suicidal incidence in case of psychiatric instability. Psychiatrist that prescribe drugs should regularly control if patient follows their indications concerning the treatment.

According to the studies, patients recently discharged after being hospitalized in psychiatric hospitals have increased risk of suicide. This risk is also enhanced when patients history includes severe mental illness or previous suicidal attempt [7]. Secondly, there exist a correlation between number of hospital admission and probes of suicide. Additionally, majority of suicides occur during first weeks after discharge. The pattern indicates that patients were prematurely discharged, their therapy was limited or implementation of therapeutic follow up was inadequate [7].

Substantial issue of proper pharmacotherapy of patients with recurrent schizophrenia is constant intake of medications. The studies of De Hert et al. indicated that continuous treatment lowers the risk of relapses and guarantees longer relapse free period than in case of placebo or intermittent treatment [8].

Materials and methods

The information about the patient was gathered from the hospital documentation available at the Clinical Toxicology department. Moreover, we conducted the research regarding antipsychotics overdose and suicidal attempts in case of patients with schizophrenia. References connected with our subjects were obtained using PubMed and Science Direct website.

Case report

We present a case report of 28 years old woman that was brought by the ambulance and admitted to the Clinical Toxicology Department due to deliberate drug overdose. The patient was diagnosed with paranoid schizophrenia. Her history card indicated that she was previously hospitalized in the department due to drug poisoning (four times). Moreover, it should be underlined that the patient had spent almost two months in Neuropsychiatric hospital due to exacerbation of schizophrenia symptoms. Her admission to Clinical Toxicology Department happened around 1,5 weeks after her discharge.

According to relation of emergency medical team, patient took all her psychiatric medications that included 240 tablets of quetiapine (Ketrel a 200 mg), 100 tablets of zuclopenthixol (Clopixol a 25 mg), 100 tables of chlorprotixen and several tablets of escitalopram (Aciprex). She also took available cardiological drugs:12 tablets of bisoprolol (Bibloc a 5 mg). In summary, patient took around 470 pills. In moment of admission to the department, she was unconscious and her state was severe. She did not react to painful stimuli yet she was cardiovascularly and respiratorily stable. With anesthesiological assistance, the patient was intubated, had stomach probe implemented and gastric lavage conducted. Moreover, she in took activated carbon. There was no detection of blood pressure drop nor bradycardia during admission. In course of further treatment these deviations were also not observed due to applied treatment.

Tab. 1. Laboratoty tests

TOXYCOLOGY	
PARAMETER	RESULT
Valproic acid [µg/ml] (therapeutic range of 50–100 µg/mL)	3.93
Tricyclic antidepressants (TCA) [ng/ml]	277.01
Ethyl alcohol [g/ml]	0.00
Carbamazepine [µg/ml]	<0.50
Benzodiazepines [ng/ml]	150.09

As indicated in the table, laboratory tests show no sign of intoxication. Even elevated level of tricyclic antidepressants (TCA; 277.01 ng/ml) does not exceed the harmful value (Tab 1.). In case of TCA, the poisoning level is estimated to >300 ng/ml while considering intoxication >500 ng/ml [9]. Unfortunately, the abilities of hospital laboratory in indication of new generation of antipsychotics were limited. Such performance may be obtained using chromatography. No alcohol level was detected (Tab. 1).

Tab. 2. Saturation and CRP levels in biochemistry results

BIOCHEMISTRY RESULTS						
PARAMETER	**DAY 1**	**DAY 4**	**DAY 5**	**DAY 6**	**DAY 8**	**DAY 9**
CRP [mg/l]	12.11	127.09	201.13	168.63	39.6	-
Saturation [%]				87.0;99.3		72.6;98.9

Additionally, the patient revealed pneumonia of the left lung. The symptoms included developing respiratory failure, characteristic consolidations on RTG image and parameters of inflammation in laboratory tests (Tab 2.). The empiric antibiotic therapy was implemented - ceftriaxone and levofloxacin (Biotraxon+Levoxa). In order to prevent possible complications, computer tomography (CT) was performed to exclude possible head injuries or bleeding. Although patient was extubated in second day of hospitalization, due to increasing respiratory failure and saturation drop to 87.0% (Tab 2.), on fifth day she had to be intubated again and had respiratory therapy using life-support machine for next three days. Then therapy with antibiotics ended successfully. Severe condition of the patient was a complex combination of both intoxication and developing pneumonia. Yet, her treatment involved intensive symptomatic therapy that aimed to sustain and balance out living parameters. It needs to be underlined that there is no specific antidote to second generation of antipsychotics (SGA). Implied therapy enabled sufficient improvement of somatic state of the patient.

During the stay at the department, the psychological state of the patient was assessed three time. Due to severe condition during admission, the first consultation could not be performed correctly. Second consultation revealed that patient was disoriented auto- and allo-psychologically. Contact with the patient was illogical. She was depressed, suffering from anxiety and suicidal thoughts- for her safety she was immobilized in safety bed. Patient was awarded of her illness and claimed that she stopped therapy with prescribed medications. She admitted that it had been her fourth suicidal attempt and regretted of being alive. Moreover, her problem were imperative auditory hallucinations and she presented psychotic symptoms (talking to imagined people). After last consultation, the patient was qualified for further treatment in Neuropsychiatric hospital. What is more, a psychiatrist prescribed a therapy with perazine (Pernazinum).

Discussion

Presented case report underlines the importance of monitoring and control of pharmacotherapy of people with schizophrenia. The history of the patient indicated that previously she had four hospitalizations due to suicidal attempts and drug overdose. Described stay in hospital began 1,5 weeks after the discharge from almost two months stay in psychiatric clinic. According to the report patient took 240 tablets of kwetiapine (Ketrel 200 mg). Total value of the substance intake equaled to 48 000 mg. It shows that patient gathered at least 4 packages of the drug (each package possesses 60 tablets) that may be prescribed during the discharge or accumulated before. Such action supports the contradiction that quetiapine should not be implemented in group of people with suicidal attempts [10].

Recommended administration of quetiapine in therapy of schizophrenia is 50 mg in first day, 100 mg in second day, 200 mg in third day and 300 mg in fourth day. From day four, the effective daily dose varies between 300-450 mg. The maximum recommended dose per day is estimated to 750 mg [10]. It is clearly visible that our patient exceeded this with more than 60 times bigger value of a daily intake. A half-life of quetiapine is approximated to 7 hours. In majority the drug binds to serum proteins and reaches maximum concentration in plasma after around 2 hours. The primary route of metabolism is via hepatic elimination [11]. It may explained why quetiapine should be carefully administered in patients with permanent diseases.

Typical symptoms of acute overdose of this substance include drowsiness, tachycardia and coma [12]. The depression of central nervous system (CNS) may be explain by inhibition of histamine receptors (H1) and by quetiapine [13]. Moreover, the comparison of quetiapine overdoes with other antipsychotic drugs revealed that the substance is more likely to enhance side effects such as hypotension, respiratory depression and death [12]. In case of our patient, coma and respiratory failure was so intensive (saturation at level of 87%, Tab 2.) that she had to be intubated two times. The reason for second intubation was probably the imposition of both - inflammatory changes (pnemonia) and respiratory depression.

Intake of such significant dose of the drug creates the problem with initiation of the hospital treatment. Due to limited capabilities of indication of SGAs, their concentration in the organism is hard to determined. Most of psychiatric drugs cannot be marked using simple laboratory tests. To evaluate the concentration of all medicaments that our patient took, the method of gas chromatography- mass spectrophotometry (GC-MS) should be used [14]. Regrettably, such diagnostic equipment was not available at the department. An analysis of drug concentration is not only issue in case of intoxication but also in terms of restoration of the therapy. Due to unknown level of the previously medicament, consecutive introduction of SGA has to be very careful.

Another important issue is abrupt withdrawal of medications. Within the period between the discharge and suicidal attempt, our patient did not continue recommended pharmacotherapy. As in her case, such behavior in exacerbation and relapse of schizophrenia [15]. She admitted constant suicidal thoughts, imperative auditory hallucinations and was disoriented auto- and allo-psychologically. Additional symptoms that can occur during withdrawal of neuroleptics involve nausea, tachycardia and general autonomic dysregulation. Regarding quetiapine withdrawal, it is a result of dopamine (D2), serotonin (5-HT1A), and histamine (H1) receptors stimulation. As these receptors influence chemoreceptor trigger zone, a medullary site that cause the emergence of nausea and emesis. Moreover, serotonin and dopamine act on brainstem nuclei that is in charge of autonomic control [16]. Undoubtedly, withdrawal of quetiapine increases the risk of suicidal attempt as the relapse may occur abruptly and is accompanied by negative symptoms. That is why, this drug should not be implemented in case of patients that are in risk group of suicide [10].

Regarding antipsychotics, apart from quetiapine, zuclopenthixol, chlorprotixen and escitalopram were taken in increased quantity. Zuclopenthixol (Clopixol) is a member of thioxanthene derivatives and possesses high affinity towards dopaminergic receptors, D1 and D2, a1-adrenergic receptors and 5-hydroxytryptamine receptor, 5-HT2. Moreover, it also acts on histamine receptors, H1, with smaller extent [17, 10]. Although zuclopenthixol belongs to different chemical group, it stimulates same receptors as quetiapine. That is why, the overall effect of drugs intoxication may be enhanced. The maximum dose of zuclopenthixol equals to 150 mg [18]. According to medical history, our patient took 2500 mg of the drug (100 tablets of 25 mg Clopixol), so she exceeded the maximum dose by almost 17 times. Moreover, the maximum concentration of ziclopenthixol depends on the form of the substance - in case of zuclopenthixol dihydrochloride it is after1 hour whereas considering zuclopenthixol acetate - 36 hours [19]. The half life of medicament is assessed to 20 hours (range from 12-28 hours) [20].

Appearance of zuclopenthixol side effects are dependent on the dosage of the medicament. Regarding overdose, the symptoms are similar to quetiapine (as previously mentioned- it works on same receptors) yet including transient dose-dependent sedation and hyper- or hypokinesia [21]. Such significant drug overdose creates the risk of rare yet life-threatening complication zuclopenthixol- induced neuroleptic malignant syndrome (NMS). This condition is characterized by fever, altered mental status, autonomic instability, extrapyramidal righty and changes in laboratory parameters. Mortality rate of NMS varies between 10-20% so intensive life supporting treatment has to follow progressing symptoms [22]. Fortunately, our patient did not develop NMS. Moreover, the interaction between zuclopenthixol, chlorprotixen and escitalopram results in decreased metabolism of the substances that elongates the effect of their overdose.

The primary goal in treatment of overdose is aggressive supportive therapy. In order to prevent CNS depression and respiratory failure, patient needs to be supported by mechanical ventilation (intubation and life-support machine). Hypotension should be treated by intravenous fluids with use of direct acting vasopressors. Our patient had injected Natrium Bicarbonicum 8.4%. Additionally, she obtained Midazolam from group of benzodiazepines that are used for seizures [23]. In further treatment, she had injected selective β1 receptor blocker type, metoprolol in order to support cardiac functions. Quetiapine overdose enhances the possibility of serious side effects such as cardiac failures such as QTc interval prolongation, and torsade de pointes [24]. Three EKGs revealed QTc integrals as presented in the table (Tab 3.).

Tab 3. EKG evaluation

	EKG RESULTS	
Date	Rhytm	QTc interval (ms)
18.07.2019	Sinus rhytm	500
24.07.2019	Sinus rhytm	430
29.07.2019	**Sinus rhytm**	**460**

Normal values of QTc intervals for women should be smaller than 450 ms [25]. In presented table, the elongated intervals occurred during two examinations. Prolongation of QT interval due to intake of medications creates the predisposition to torsades de points or ventricular fibrillation [26]. In case of corrected QT interval exceeding 500 milliseconds intravenous magnesium may be provided [23]. Such conduct was proceeded in our patient.

Hard condition of the patient may be also a result of developing pneumonia (Tab 2.). These inflammatory changes may be a result of potential choke. Great number of taken drugs that act depressively on central nervous system (CNS) and reflexes could contribute to aspiration pneumonia [27]. Moreover, observing the pattern, it is clearly visible that CRP level was gradually increasing from the beginning of admission. That is why, two antibiotics, ceftriaxon and levofloxacin, were introduced to work within wide range of bacteria.

Definitely, after hospitalization, she had to be transported to Neuropsychiatric hospital. What is more, after clinical therapy, she should follow the course of treatment that includes pharmacotherapy and psychotherapy with controlled psychiatric appointments. Undoubtedly, the substantial aid for patients with recurrent schizophrenia would be community mental health services (CMHS) that sustains the goals of therapy, helps to prevent relapses and deals with society exclusion. Current situation in Poland indicates that people with schizophrenia have better chances for effective therapy. Although within 5 years (2010-2014), the number of diagnosed cases increased by 3.4%, it was observed that number of hospitalizations in the hospitals decreased by 10%. Such tendency underlines the fact that the model of CMHS is more common in Poland. In case of our patient, the important role plays a guardian. Usually, the guardian is a family member that supports person financially and emotionally [28].

Last strategy that would prevent the suicidal attempt of patients with schizophrenia is prescription drug monitoring programs (PDMPs). In future it may be an important tool to both prevent non-medical use of medicaments and decrease mortality rate caused by overdose. Yet, recent researches conducted in US are not yet satisfying [29].

Outcome

The risk of suicide in group of people with schizophrenia is increased 12 times than in common society. Suicidal attempts and more frequent cardiovascular disorders are definitely two major factors contributing to earlier mortality in this group [30]. Regarding suicides, overdose of medicaments is significant issue.

Although SGAs are commonly used in treatment of schizophrenia, quetiapine should not be implemented for patients with suicidal thoughts. This substance enhances the risk of harmful attempts by the patient. At the beginning of the therapy, quetiapine and other antipsychotics intake should be strictly and frequently controlled. Also, it is not recommended to prescribe medicaments in increased amount as it also creates the risk of deliberate drug overdose. Thirdly, drugs may be prescribed with postponed time of buying out in pharmacy. It would help to control the amount of medicaments taken that should be also checked by psychiatrist during regular appointments.

Remarkably important period in therapy of patient with schizophrenia is the time after discharge. As discussed before, the highest rate of suicidal attempts fall on the first weeks after the end of hospitalization.

Conclusion

Treatment of patients with schizophrenia should be constant and involve differentiated institutions: hospital, community psychiatry and psychiatric therapy. While choosing pharmacotherapy, all aspects including contradictions, side effects and general state of the patient should be taken under consideration. Only complex approach to this kind of patient enables the successive yet fluent improvement of persons health and comfort. Moreover, multi institutional approach sustains permanent course of treatment, supports the family and prevent from society exclusion.

References

1. Cagliostro D. Paranoid schizophrenia. Accessed: https://www.psycom.net/paranoid-schizophrenia last updated: May 14, 2019 (22.08.2019).

2. Hjorthøj C, Østergaard ML, Benros ME, Toftdahl NG, Erlangsen A, Andersen JT, Nordentoft M. Association between alcohol and substance use disorders and all-cause and cause-specific mortality in schizophrenia, bipolar disorder, and unipolar depression: a nationwide, prospective, register-based study. Lancet Psychiatry (2015), 2(9):801-8.

3. Schizofrenia. Perspektywa społeczna, sytuacja w Polsce. Accessed: www_janssen_com_polandfileraport_schizofrenia_perspektywa_spoleczna._sytuacja_w_polsce.pdf (01.09.2019).

4. Hausmann A, Fleischhacker W. Differential diagnosis of depressed mood in patients with schizophrenia: a diagnostic algorithm based on a review. Acta Psychiatrica Scandinavia (2002), 106(2), 83–96.

5. MEDGUIDE SECTION, Medication Guide SEROQUEL (SER-oh-kwell) (quetiapine fumarate). Accessed: https://www.fda.gov/files/drugs/published/Seroquel-Medication-Guide.pdf (15.08.2019).

6. Kwetiapina, quetiapine. Medycyna Praktyczna. Accessed: https://indeks.mp.pl/leki/desc.php?id=1017 (15.08.2019).

7. Lynskey MT, Kimber J, Strang, J. Drug-related mortality in psychiatric patients. The Lancet Psychiatry (2015), 2(9): 767–769.

8. De Hert M, Sermon J, Geerts P, Vansteelandt K, Peuskens J, Detraux J. The Use of Continuous Treatment Versus Placebo or Intermittent Treatment Strategies in Stabilized Patients with Schizophrenia: A Systematic Review and Meta-Analysis of Randomized Controlled Trials with First- and Second-Generation Antipsychotics. CNS Drugs (2015), 29(8):637-58.

9. Zapalska-Pożarowska K, Szponar J, Tchórz M, Kostek H, Pożarowski W. Ciężkie zatrucie trójcyklicznymi antydepresentami - opis przypadku. Przegląd Lekarski (2012), 69(8): 621-623.

10. Ketrel (kwetiapina). Medycyna Praktyczna. Accessed: https://www.mp.pl/pacjent/leki/lek/61144,Ketrel-tabletki-powlekane (21.08.2019)

11. DeVane CL, Nemeroff CB. Clinical Pharmacokinetics of Quetiapine. Clinical Pharmacokinetics (2001) 40(7): 509.

12. Ngo A, Cranny M, Olson KR. Acute Quetiapine Overdose in Adults: A 5-Year Retrospective Case Series. Annals of Emergency Medicine (2008), 52(5): 541–547.

13. Pollak PT, Zbuk K. Quetiapine fumarate overdose: clinical and pharmacokinetic lessons from extreme conditions. Clin Pharmacol Ther. (2000), 68:92-97.

14. http://www.imp.sosnowiec.pl/files/wykaz_toksykologa.pdf (accessed: 12.09.2019)

15. Gilbert PL. Neuroleptic Withdrawal in Schizophrenic Patients. Archives of General Psychiatry (1995), 52(3): 173.

16. Kim DR, Staab JP. Quetiapine Discontinuation Syndrome, American Journal of Psychiatry.(2005), 162(5): 1020.

17. Bryan EJ, Purcell MA, Kumar A. Zuclopenthixol dihydrochloride for schizophrenia. Cochrane Database of Systematic Reviews (2017), 11: Art. No.: CD005474.

18. Zuklopentyksol (dekanian zuklopentyksolu) (opis profesjonalny). Medycyna praktyczna. Accessed: https://www.mp.pl/pacjent/leki/subst.html?id=3381 (12.09.2019)

19. Aaes-Jørgensen T, Pharmacokinetics of three different injectable zuclopenthixol preparations. Progress in Neuro-Psychopharmacology and Biological Psychiatry (1989), 13(1-2): 77-85.

20. Zuclopenthixol. Drugbank. Accessed: https://www.drugbank.ca/drugs/DB01624 (12.09.2019)

21. Clopixol-Acuphase. Accessed: https://www.lundbeck.com/upload/il/files/pdf/patient_and_doctor_information/Clopixol_Acuphase_leafelt_pcr_approval.pdf (12.09.2019)

22. Varoglu AO, Ates O, Gundogdu OL, Aksoy A, Deniz O. Zuclopenthixol-induced neuroleptic malignant syndrome presenting as fever of unknown origin, hyperglycaemia and acute myocardial infarction in a 60-year-old man. The World Journal of Biological Psychiatry (2009), 10(4-2): 644–647.

23. Levine M, Ruha AM. Overdose of Atypical Antipsychotics. CNS Drugs (2012), 26: 601-611.

24. Hasnain M, Vieweg WR, Howland RH, Kogut C, Breden-Crouse EL, Koneru JN, Hancox JC, Digby GC, Baranchuk A, Deshmukh A, Pandurangi AK.Quetiapine, QTc interval prolongation, and torsade de pointes: a review of case reports. Ther Adv Psychopharmacol. (2014), 4(3): 130–138.

25. Sawicka-Parobczyk M, Bieganowska K. Odstęp QT/QTc w elektrograficznym zapisie – ważny parametr, trudna ocena. „Forum Medycyny Rodzinnej" (2010), 4: 17–25.

26. Dąbrowska B, Dąbrowski A. Podręcznik elektrokardiografii. PZWL (1993), 60-61.

27. Bardino DM, Wunderink RG. Aspiration pneumonia: a review of modern trends. Journal of Critical Care (2015), 30(1): 40–48.

28. Schizofrenia. Rola opiekunów w kreowaniu współpracy. Accessed: https://www.janssen.com/poland/sites/www_janssen_com_poland/files/raport_schizofrenia._rola_opiekunow_w_kreowaniu_wspolpracy.pdf (12.09.2019).

29. Paulozzi LJ, Kilbourne EM, Desai HA. Prescription Drug Monitoring Programs and Death Rates from Drug Overdose. Pain Medicine (2011), 12: 747–754.

30. Chesney E, Goodwin GM, Fazel S. Risks of all-cause and suicide mortality in mental disorders: a meta-review. World Psychiatry (2014), 13(2):153–160.