Archives of Psychiatry and Psychotherapy, 2009 ; 3 : 5–9

Current trends in pharmacological treatment of schizophrenia presented on the XIV World Congress of Psychiatry

Adam Wysokiński, Monika Talarowska, Agata Orzechowska, Krzysztof Zboralski, Piotr Gałecki, Antoni Florkowski

Summary

The authors present the summary of current trends in the pharmacological treatment of schizophrenia presented during the XIV World Congress of Psychiatry (Prague, Czech Republic, 19-25 September 2008). The results of studies presented during the Congress, recommendations and new trends may be divided into two groups of actions: (1) aimed at increasing patients' compliance and adherence; and (2) aimed at promoting depot antipsychotics. The problem of the metabolic syndrome was also stressed as it remains a significant clinical complication of the treatment with antipsychotics, particularly with atypical ones. Moreover, it was also emphasized that clinical tools used to evaluate treatment efficacy should include scales which evaluate quality of life, for example SWN (Subjective Well-being under Neuroleptics) scale.

schizophrenia / antipsychotics / compliance / adherence

The XIV World Congress of Psychiatry was held in Prague, Czech Republic, on 19-25 September 2008. The objective of this paper is to present current trends in the pharmacological treatment of schizophrenia on the basis of information presented during the Congress.

According to data presented by Sturgeon [1], mental disorders affect more than 14% of the general population. At the same time it is emphasized that despite the fact that according to current state of medical knowledge, these disorders are curable, one third of all countries have no mental health policy or separated budget for care and treatment of mental disorders, while in 25% of the remaining countries less than 1% of the total health care budget is allocated for the care of mentally ill patients. As a result, according to Sartorius [2], 40% of the patients with schizophrenia remain untreated. It is of significant importance because the course of disease and introduction of treatment during the first two years predict long-term outcomes. Approximately half (40-60%) of the remaining 60% of patients who have an antipsychotic treatment initiated, discontinue the treatment. It stresses the importance of propagating and introducing new diagnostic and therapeutic techniques in the treatment of schizophrenia, particularly aimed at promoting patients' compliance and adherence.

Problems associated with the treatment of schizophrenia and schizophrenia-like psychoses do not result only from economical and political conditions. This issue is strongly associated

Adam Wysokiński, Monika Talarowska, Agata Orzechowska, Krzysztof Zboralski, Piotr Gałecki, Antoni Florkowski: Clinic of Adult Psychiatry, Medical University of Łódź, Poland. Correspondence address: Adam Wysokiński, Clinic of Adult Psychiatry, Medical University of Łódź, Unit XIB, Szpital im. J. Babińskiego, 159 Aleksandrowska Str., 91-229, Łódź, Poland, E-mail: adam.wysokinski@gmail.com

This paper was not sponsored.

with a high heterogeneity of this group of mental disorders, which affects diagnostic and therapeutic processes. Jablensky [3] from the Centre for Clinical Researches in Neuropsychiatry, University of Western Australia, presented several causes of schizophrenia heterogeneity. These include: (1) polygenic transmission, (2) incomplete penetrance and variable phenotype expression, (3) phenocopies, (4) latent disease subtypes that may be aetiologically different, (5) population (ethnic) admixture in study samples, (6) epigenetic phenotype modification, and (7) measurement or classification errors. Moreover, he emphasized that psychiatrists should abandon "rigid" classical (phyletic) categories for classification systems based on dimensions (quantitative assessment of certain features or symptoms) and prototypes (general and comprehensive "models" of particular disease or disorders), which make elimination of artificial problem of comorbidity possible and enable diagnosis of "subthreshold" (sub-clinical) disorders.

Early diagnosis of schizophrenia and introduction of treatment should remain the primary objective of diagnostic and therapeutic actions. Duration of untreated psychosis (DUP) is thought to have a direct effect on prognosis, treatment outcomes, as well as severity of psychosocial deficits [4].

Psychiatrists observe (and studies prove these observations) that the level of compliance is low. Moreover, a low level of patients' compliance and high discontinuation rates remain as a significant obstacle for achieving optimal treatment outcome. According to data presented by David [5], patients treated with atypical antipsychotics (SGA, second generation antipsychotics) have a higher level of compliance as compared to patients treated with typical antipsychotics. However, even in the former group, the level of compliance and adherence is unsatisfyingly low. Certain factors were listed as having a negative influence on patients' compliance: (1) level of insight/attitude towards the treatment; (2) low level of cooperation with a therapist; (3) low level of family and relatives support; (4) abusing psychoactive substances; (5) low level of compliance in the past; (6) symptoms duration; (7) cognitive deficits; (8) complexity of treatment schedule; (9) symptoms intensity; (10) affective disorders; and (11) various demographic factors, such as age, gender and level of education [6].

Numerous study results presented by David [5] confirmed that a certain group of actions is associated with a higher level of compliance, assessed for example using the number of re-hospitalizations or disease relapse. Cognitive-behavioral psychotherapy and motivational techniques were listed among such actions. Interestingly, Zygmunt et al. [7] suggested that psycho-educational actions are in most cases ineffective and a higher number of sessions with a patient is not more efficacious when comparing to shorter interventions. From the other hand, results of the QUATRO study [8] indicate that therapies focused on improving compliance may not have a significant effect, although due to the fact that the studies evaluating their effectiveness have certain methodological restrictions (for example the fact that the patients participating in clinical studies usually cooperate to a higher extent), it is possible that in the future psychiatrists will be able to identify groups of patients in which such interactions would be significantly more effective. Finishing his presentation David emphasized that the low level of compliance is the main obstacle in achieving optimal treatment results in patients with schizophrenia.

Among the factors influencing the level of patients' compliance, specific properties of administered antipsychotics, such as formula and administration route, side effects and dosing schedule play an important role. The importance of depot forms of antipsychotics was repeatedly underscored [5, 9]. Numerous studies [6, 10, 11, 12, 13] demonstrated that depot formulas are superior to antipsychotics administered by the oral route in terms of mental condition improvement, percentage of patients continuing the treatment, risk of relapse and the number of relapses. Moreover, its use enables psychiatrists to detect patients incompliance early. These results are also confirmed by the studies presented during the poster session, which evaluated, among others, the efficacy of depot forms of risperidone and olanzapine (the latter is currently not available in Poland) [14, 15, 16]. It was also emphasized that the only contraindication for depot forms of antipsychotics is ineffectiveness or intolerance of an oral form of an antipsychotic.

Liew et al. presented the results of a study in which the efficacy of atypical antipsychotics (risperidone and olanzapine) was compared with typical antipsychotics (haloperidole and trifluoperazine) [17]. These results indicate that up to 90% of the study participants discontinued the treatment before 18 months of the treatment (primarily due to intolerable adverse effects) – 96%, 93%, 86% and 86% for haloperidole, trifluoperazine, risperidone and olanzapine, respectively. The authors found that the patients treated with typical antipsychotics discontinued their treatment more often and the lowest discontinuation rate was found among the patients treated with olanzapine. Risperidone was found to be more effective than haloperidole in terms of longer treatment duration. Vrdoljak et al. [18] demonstrated that the use of atypical antipsychotics is associated with better social functioning when compared to patients treated with typical ones. Consequently, it confirms the necessity of promoting modern guidelines for the treatment of schizophrenia, according to which atypical antipsychotics should be used as the first-line medicines and their usage should not be limited to treatment-refractory patients.

Considering significant importance of the use of depot forms of antipsychotics, the fact that studies evaluating the number of psychiatrists administering depots indicate that this group of antipsychotics is still thought to be more stigmatizing and an old-fashioned therapeutic method, which limits the patient's autonomy and the use of which should be limited mainly to forensic patients, remains unaccountable [19]. Low percentage of patients treated with depot antipsychotics proves this negative "image" of this form of antipsychotic treatment. The results presented by Patel et al. [9] show that psychiatrists proposed the treatment with depots to 36% of patients, while only 14% of them had depots administered. Moreover, Patel also presented results which indicate that during the last 5 years almost half of the studied psychiatrists declared that they limited the usage of depots in a moderate or high degree. As it was underscored, controversy of these opinions consist not only in the fact that they are contradictive with the results over the efficacy of depots cited above, but also because they are incompatible with patients' opinions on these medicines. Patel et al. [20] did not find any significant differences in patients' opinions about depots and oral antipsychotics that these patients were treated with. David [5] emphasized that these results may suggest that psychiatrists are wrong about the negative assessment of depots by patients' treated with this forms of antipsychotics. He also noticed that the most important factor that would persuade psychiatrists to use depots more often is the availability of depot forms of other atypical antipsychotics [21]. It is an important information for pharmaceutical companies as it indicates one of the important directions in which further developments and researches over new antipsychotics should be carried.

Another issue associated with the treatment of schizophrenia, which was particularly taken into consideration during the poster session, was the problem of the metabolic syndrome – frequent consequence of chronic treatment with antipsychotics, especially with atypical ones [22]. Yoon et al. [23] presented results of the study, which indicate that the frequency of the metabolic syndrome in the group of 269 patients was 22.9% and, what is interesting, it was not associated with treatment duration or currently administered antipsychotics. The frequency of metabolic syndrome observed by these authors is not higher comparing to the general population (for example 19.4% in Poland [24]) and is more than two times lower comparing to the results of other researchers for the population of patients treated with antipsychotics [25, 26]. Moreover, Yoon et al. [27] proved that a programme of exercises aimed at reducing body-weight, lasting for 12 weeks reduced not only the BMI value, but also significantly improved patients' quality of life. Similar results were presented by Hou and Hsuan [28]. Therefore it may be assumed that such procedures should become a part of routine clinical practice.

It was also noticed, that criteria of treatment efficacy that are currently in use, including PANSS (Positive and Negative Syndrome Scale) and Simpson-Angus rating scale (used to assess extrapiramidal symptoms), should be extended by methods that enable psychiatrists to evaluate patients' quality of life (QoL). Naber [29] presented results which indicate that the SWN (Subjective Well-being under Neuroleptics) scale may be a very effective clinical tool, as it allows not only to

evaluate quality of life, but also is the strongest studied predictor of compliance and adherence. It was also emphasized that the level of insight is important for long-term treatment outcomes. Better insight is associated with a higher level of compliance. Therefore, improvement of insight should become one of the primary objectives of pharmacological and psychotherapeutic treatment of patients with schizophrenia. However, it should be noticed that patients with restored insight are exposed to a risk of lowered quality of life and occurrence of depressive symptoms and have a higher risk of the development of post-schizophrenia depression. Therefore, such patients should be monitored for affective disorders.

With reference to atypical antipsychotics it is worthwhile to notice that the importance of these medicines in the treatment of treatment-refractory depression was repeatedly underscored during the Congress. Kasper [30] presented results of studies over combined treatment with antidepressants and atypical antipsychotics: risperidone + citaloprame [31], olanzapine + fluoxetine [32], aripiprazole and ziprazidone [33] and quetiapine + SSRI/SNRI [34], which prove that atypical antipsychotics significantly improve the clinical condition in patients with depression. The fact that this improvement occurs in the first week of combined treatment is even more interesting. Consequently, it was suggested that a combined treatment of antidepressant and second-generation antipsychotic should become a first-line method in the treatment of treatment-refractory depression.

To summarize, in the current trends in the treatment of schizophrenia two group of actions may be distinguished. The first group include paying attention to an alarmingly low level of compliance and adherence and a very high prevalence of treatment discontinuation. Therefore, actions aimed at improving modifiable factors of non-compliance should be implemented. The other group of actions include activities focused on promoting the use of depot forms of antipsychotics as being as effective as antipsychotics administered orally, which have an advantage in terms of better compliance and adherence.

REFERENCES

1. Sturgeon S. Mental health advocacy – the way forward. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session SL–47.
2. Sartorius N. Recalibrating our clinical expectations in the long–term treatment of schizophrenia. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session SaS–04.
3. Jablensky A. The nosology of psychoses: categories, dimensions and prototypes. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session SeS–020.
4. Saavedra I, Teixeira P, Verissimo F. Relationship between Duration of Untreated Psychosis and outcome in first–episode psychosis. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–02–157.
5. David A. Will novel atypical depots make a difference? Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session SaS–04.
6. Lacro JP, Dunn LB, Dolder CR, Leckband SG, Jeste DV. Prevalence of and risk factors for medication nonadherence in patients with schizophrenia: a comprehensive review of recent literature. J Clin Psychiatry 2002; 63(10): 892–909.
7. Zygmunt A, Olfson M, Boyer CA, Mechanic D. Interventions to improve medication adherence in schizophrenia. Am J Psychiatry 2002; 159(10): 1653–1664.
8. Gray R, Leese M, Bindman J, Becker T, Burti L, David A, Gournay K, Kikkert M, Koeter M, Puschner B, Schene A, Thornicroft G, Tansella M. Adherence therapy for people with schizophrenia. European multicentre randomised controlled trial. Br J Psychiatry 2006; 189: 508–514.
9. Patel M, Chaudhry I, Husain N, McLaughlin S, Cunningham P, David A, Haddad P. Psychiatrists' attitudes to antipsychotic depot injections: changes over 5 years. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session NRR–03–04.
10. Adams CE, Fenton MK, Quraishi S, David AS. Systematic meta-review of depot antipsychotic drugs for people with schizophrenia. Br J Psychiatry 2001; 179: 290–299.
11. Hogarty GE, Schooler NR, Ulrich R, Mussare F, Ferro P, Herron E. Fluphenazine and social therapy in the aftercare of schizophrenic patients. Relapse analyses of a two-year controlled study of fluphenazine decanoate and fluphenazine hydrochloride. Arch Gen Psychiatry 1979; 36(12): 1283–1294.
12. Lauriello J, Lambert T, Andersen S, Lin D, Taylor CC, McDonnell D. An 8–week, double–blind, randomized, placebo–controlled study of olanzapine long–acting injection in acutely ill patients with schizophrenia. J Clin Psychiatry; 2008, 69(5): 790–799.

13. Tiihonen J, Walhbeck K, Lönnqvist J, Klaukka T, Ioannidis JP, Volavka J, Haukka J. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: observational follow-up study. BMJ. 2006, 333(7561): 224–224.
14. Detke H, McDonnell D, Kane J, Naber D, Sethuraman G, Lin D. Olanzapine long–acting injection for maintenance treatment of schizophrenia. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–03–264.
15. Olivares J, Rodriguez–Morales A, Diels J, Povey M, Lam A, Jacobs A, Zhao Z. Impact of risperidone long-acting injection versus oral antipsychotic treatments on hospitalization in schizophrenia. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–04–189.
16. Pecenak J, Tuma I, Povey M, Lam A, Zhao Z. Remission in patients with schizophrenia treated with risperidone long acting injection (RLAI): 18-month follow-up of the electronic schizophrenia treatment adherence registry (E–STAR) in Czech Republic and Slovakia. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–04–136.
17. Liew A, Poon L, Vaingankar J. Comparing effectiveness of second–generation antipsychotic vs. first-generation antipsychotic medications in patients with schizophreniaspectrum disorders. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–03–259.
18. Vrdoljak M, Ivezic S, Jukic M. Atypical antipsychotics and social functioning in schizophrenic patients. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–03–259.
19. Patel MX, Nikolaou V, David AS. Psychiatrists' attitudes to maintenance medication for patients with schizophrenia. Psychol Med. 2003, 33: 83–89.
20. Patel MX, De Zoysa N, Bernadt M, David A. Depot and oral antipsychotics: patient preferences and attitudes are not the same thing. J Psychopharmacol. 2008. [Epub ahead of print].
21. Haddad PM, Chaudhry IB, Husain N, McLaughlin S, Cunningham P, David AS, Patel MX. Psychiatrists' attitudes to antipsychotic depot injections (I): Preferences and choice. European Psychiatry. 2008, 23(suppl 2): S160.
22. Wysokiński A, Orzechowska A, Strombek M, Gruszczyński W. Zespół metaboliczny – przegląd piśmiennictwa. Psychiatria w Praktyce Ogólnolekarskiej 2007, 7(4): 170–175.
23. Yoon B, Min K, Shin Y, Bae A, Bahk W. Prevalence and Characteristic of Metabolic Syndrome in Schizophrenic Inpatients. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–03–311.
24. Szurkowska M, Szafraniec K, Gilis-Januszewska A, Pach D, Krzentowska A, Szybinski Z, Huszno B. [Prevalence of the metabolic syndrome and its components in adult inhabitants of Krakow]. Przegl Lek. 2006, 63(9): 733–737.
25. Correll CU, Frederickson AM, Kane JM, Manu P. Metabolic syndrome and the risk of coronary heart disease in 367 patients treated with second–generation antipsychotic drugs. J Clin Psychiatry 2006, 67(4): 575–583.
26. De Hert MA, van Winkel R, Van Eyck D, Hanssens L, Wampers M, Scheen A, Peuskens J. Prevalence of the metabolic syndrome in patients with schizophrenia treated with antipsychotic medication. Schizophr Res. 2006, 83(1): 87–93.
27. Yoon B, Min K, Shin Y, Bahk W, Jon D, Bae A, Kim M. Effects of weight loss on obesity-related quality of life in schizophrenic inpatients. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–03–310.
28. Hou Y, Hsuan C. Weight management activities in outpatients with antipsychotic treatment. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Poster P–04–235.
29. Naber D. Barriers to Good Long-Term Prognosis. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session SaS–04.
30. Kasper S. Second generation antipsychotics (SGA) in treatment resistant depression. Presented at the XIV Congress of Psychiatry, September 20–25, 2008, Prague, Czech Republic. Session RS–58.
31. Rapaport MH, Gharabawi GM, Canuso CM, Mahmoud RA, Keller MB, Bossie CA, Turkoz I, Lasser RA, Loescher A, Bouhours P, Dunbar F, Nemeroff CB. Effects of Risperidone Augmentation in Patients with Treatment–Resistant Depression: Results of Open-Label Treatment Followed by Double–Blind Continuation. Neuropsychopharmacology 2006; 31(11): 2505–2513.
32. Shelton RC, Tollefson GD, Tohen M, Stahl S, Gannon KS, Jacobs TG, Buras WR, Bymaster FP, Zhang W, Spencer KA, Feldman PD, Meltzer HY. A novel augmentation strategy for treating resistant major depression. Am J Psychiatry 2001; 158(1): 131–134.
33. Papakostas GI, Petersen TJ, Nierenberg AA, Murakami JL, Alpert JE, Rosenbaum JF, Fava M. Ziprasidone augmentation of selective serotonin reuptake inhibitors (SSRIs) for SSRI–resistant major depressive disorder. J Clin Psychiatry 2004; 65(2): 217–221.
34. McIntyre A, Gendron A, McIntyre A. Quetiapine adjunct to selective serotonin reuptake inhibitors or venlafaxine in patients with major depression, comorbid anxiety, and residual depressive symptoms: a randomized, placebo–controlled pilot study. Depress Anxiety 2007; 24(7): 487–494.

PSYCHOTHERAPY

No 2 (149) 2009

CONTENT

Abstracts in English

Editor: Polish Psychiatric Association Editorial Committee
31-138 Cracow, Lenartowicza 14, Poland
e-mail: psych@kom-red-wyd-ptp.com.pl
http://www.kom-red-wyd-ptp.com.pl