SMOKING IN MENTAL DISORDERS – BETWEEN THE RIGHT TO HEALTH AND A PUBLIC HEALTH PROBLEM

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Abstract: *There is an association between smoking and many mental illnesses. Smoking prevalence in all patients with psychiatric pathology is between 35% and 54%. The prevalence of smoking among patients with schizophrenia is between 74% and 92%, much higher than the one between 22% and 30% concerning the general population. Male patients with schizophrenia are at increased risk for smoking. Smoking is implicated in the pathogenesis of many diseases and it is responsible for 90% of lung cancer deaths, 75% of those in chronic bronchitis and emphysema and around 25% of those involving cardiovascular diseases. Tobacco is a strong inducer of cytochrome P450 enzyme, the metabolizing pathway for many antipsychotics. This leads to decreased levels in plasma concentrations of antipsychotic agents. Higher doses of antipsychotic agents are administered to smoking patients with schizophrenia to achieve similar therapeutic effects as in non-smoking patients with schizophrenia. The higher the doses of antipsychotic agents administered, the greater the risk of adverse events. In case of sudden smoking cessation, the plasma concentrations of antipsychotic agents may exceed the therapeutic range and may cause side effects. Thus, there is an added risk of adverse reactions to antipsychotics to the general health risk of smoking. Patients with schizophrenia smoke because nicotine improves the cognitive symptoms of the disease. Smoking is a habit for patients with schizophrenia and sometimes this activity is the only source of pleasure. Smoking-related concessions are motivating factors that increase compliance in patients with schizophrenia. It is well known that compliance rates are low for this category of patients. It would be preferable to try phasing out smoking in patients with schizophrenia, as well as in any other patient.*

Smoking is common in psychiatric medical practice and it worries patients, psychiatrists, caregivers and family members. Epidemiological data show a large discrepancy between the prevalence of smokers in the general population and among patients with schizophrenia. World Health Organization indicates that smoking prevalence in the adult population worldwide is 30%, with a gender distribution of 48% in men and 12% in women. In 2007, smoking prevalence in the adult population in Romania was 30%, according to a study conducted by the Center for Health Policies and Services (1), and in 2011 the prevalence was 22.1%.(2) Many psychiatric disorders are associated with smoking and, for smoker patients, with massive amount of cigarettes consumed.(3) Smoking prevalence among all patients with psychiatric disorders is 35-54%.(4) The situation worsens when we analyze patients with schizophrenia because studies show smoking prevalence of 70% to 92%.(5,6) Schizophrenia is a risk factor for smoking in men.(7) Patients with schizophrenia smoke an average 19 cigarettes daily.(4) For the general population of Romania, only 12-29% of smokers smoke 10-20 cigarettes daily (2), with the remaining smokers consuming less.

It is estimated that smoking is responsible for 90% of lung cancer deaths, 75% of those in chronic bronchitis and emphysema and around 25% of those with cardiovascular disease.(1) The relative risk for lung cancer is 7.8 higher for smokers than for non-smokers.(1) It is well documented that smoking is involved in the pathogenesis of many diseases.

Smoking is an important factor for the dosage of antipsychotics, due to the polycyclic aromatic hydrocarbons, byproducts of tobacco burning, which are inducers of the cytochrome P450 and UDP-glucoroniltransferase.(3) An extensive meta-analysis (8) that consulted the scientific literature for a long period of time between 1950 and 2009 revealed changes in pharmacokinetics in smokers versus nonsmokers; it was also demonstrated that higher doses of drugs were administered to smoker patients. Significant differences in sex ratio plasma level concentrations of olanzapine (9) can be explained by the fact that smoking prevalence is higher in male patients, and smoking is an inducer of CYP1A2 metabolic pathway of olanzapine.(10) So, lower plasma level concentrations of olanzapine are obtained in males. Haloperidol plasma level concentration in oral administration is significantly lower in smoker patients.(11) Smoker patients with schizophrenia receive higher doses of antipsychotics than non-smoker patients, i.e., 1160 mg chlorpromazine equivalent daily compared with 542 mg daily (4), due to the increased metabolism induced by smoking. Consequently, to achieve the same therapeutic effect in smoker patients as in non-smokers, higher doses of drugs should be administered.

There are several types of side effects of antipsychotics: neurological, metabolic, endocrine and cardiovascular. Neurological effects (12) consist of reversible extrapyramidal effects such as acute dystonia, akathisia and parkinsonism, and irreversible extrapyramidal effects such as tardive dyskinesia. Metabolic and endocrine effects are represented by hyperprolactinemia (13) with amenorrhoea or gynaecomastia, obesity - between 40% and 62% of patients with schizophrenia are

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obese (14) antipsychotics being incriminated in weight gain;(15) the cardiovascular side effects are represented by orthostatic hypotension (16), ventricular arrhythmias, extended QTc interval.(17,18) Other adverse effects include sedation (16), M-cholinolitic phenomena (19), jaundice, leukopenia and agranulocytosis (20) and neuroleptic malignant syndrome (21), metabolic syndrome (22), hyperlipidemia (23,24) diabetes mellitus.(25) There may also occur disorders of sexual dynamic (26,27), with serious implications to decreased compliance rates, because approximately 43% patients complain of these side effects.(28)

Ever since 1981 Linnoila et al. have shown that smoking can have implications in pharmacokinetics and pharmacodynamics in patients with schizophrenia, by lowering plasma level concentrations of antipsychotics. Consequently, abrupt cessation of smoking may increase plasma level concentrations of antipsychotics and potentiating the occurrence of extrapyramidal adverse effects. It is necessary to reduce the dose by 30-40% to achieve plasma level concentrations similar to those of the period previous to smoking cessation.(8) Atypical antipsychotics can reduce the urge to smoke in some patients with schizophrenia, particularly due to their special pharmacodynamics.

In 2009, Prochaska (29), advocated for the treatment of nicotine addiction in chronic mentally ill inpatients, as this would be the key to a proper management of the disproportionate morbidity and mortality of these patients, more over that there are evidence-based therapies in smoking cessation.

Smoking ban is now legally regulated in the healthcare facilities, so this would represent an excellent opportunity for smoking cessation due to the consequences of law infringement. Romania aligned its legislation to the European Community's policy concerning smoking ban in enclosed spaces and with clear indications on smoking ban in the public health system and so smoking is prohibited in all healthcare facilities. These regulations are contained in Law no. 349/2002 on preventing and combating the effects of tobacco products, as amended and supplemented. Seeing that they are not allowed to smoke, psychiatric inpatients can use nicotine transdermal therapeutic systems. Smoking ban would motivate patients to stop smoking and would encourage them in maintaining abstinence after discharge.

When patients quit smoking, time, human and financial resources are saved, both for the benefit of the patient and of the healthcare system, because these resources can be relocated to some poor sectors of the system. It is said that patients can stop smoking without adverse effects on mental recovery, requiring only antipsychotic dose adjustment to prevent side effects for the antipsychotics influenced by smoking. In principle, quitting smoking is beneficial for patients' health, but, as noted above, may cause neuropsychological effects of variable intensity. Some patients experience a worsening of negative symptoms and /or Parkinsonism or become more irritable. Others, as presented by West and Hajek, express a decrease in anxiety, although further research is needed to confirm.

However, smoking cessation should occur gradually. If psychiatric inpatients are not capable to quit smoking during hospitalization there is a high risk of resumption after discharge with all the negative aspects of this practice.

Authors state that smoking large amount of cigarettes is not considered an unhealthy habit anymore for patients suffering of schizophrenia Instead it is regarded as a self-medication against clinical symptoms and side effects of antipsychotics.(6)

The successful therapy of schizophrenia involves certain factors regarding the treatment, the patient and the healthcare system. One of the most prominent factors related to patient is adherence (Buckley, 2008). Adherence to treatment in patients with schizophrenia is reduced. More than 50% of patients with schizophrenia are not compliant to treatment.(30) A therapeutic break of only 1 to 10 days per year increases the risk of hospitalizations for patients with schizophrenia.(31)

The common goal for doctors, caregivers and family members is to insurance and/or to increase adherence. Concessions related to smoking are made to the patient: cigarettes are offered to increase cooperation to accept the medication in the psychiatric wards, caregivers and family members take care that during hospitalization or at home, the patient should have cigarettes at his disposal. Given that smoking is a strong motivation factor for patients with schizophrenia, there is a widespread practice of using cigarettes as positive reinforcement factor for the administration of medication, presentation to the medical examination and other behaviours important to control the therapy.

Although a must, occupational therapy cannot be carried out in all psychiatric wards, so patients' boredom is cast away by smoking cigarettes. For some of the chronic patients this activity may be their one true pleasure. This fact is well known by many organizations that care for outpatients suffering from schizophrenia. The social life of these patients is poor, some may not be able to establish new social contacts, and as the disease progresses maintaining previous social relationships suffer. Thus, smoking plays a social role, offering the patient a chance to interact with the medical staff, with other patients even if suffering from different pathologies or, to an extent, with passersby.

The lifestyle of patients suffering from schizophrenia is sedentary. Obesity goes hand in hand with the chronicity of the disease partially as a side effect of the antipsychotic medication and physical activities are carried out with difficulty. Under these conditions, smoking has a comforting role. In addition to the subjective benefits that have already been presented, we must stress on the objective benefits: nicotine temporarily relieves the cognitive and sensory symptoms of schizophrenia, by binding the nicotinic receptors in the brain. Thus, smoking is relieving for patients with schizophrenia. The mechanism appears to be simple: the nicotine contained in the cigarettes is absorbed in the lungs, enters the bloodstream, penetrates the blood-brain barrier and it binds the neuronal nicotinic receptors that modify neuronal response to relieve symptoms. Cognitive deficits in schizophrenia are common and serious things. Unfortunately, these deficits may lead to functional disability.(32) This would represent the way in which nicotine contained in the cigarettes can improve symptoms of schizophrenia.

The conclusion is that nicotine may improve cognitive deficits observed in psychiatric diseases.(33) Another possible explanation for the increased chronic cigarette intake in patients with schizophrenia may be the self-medication hypothesis, according to which patients smoke to reduce the cognitive deficits, part of the disease, but also part of antipsychotic side effects.(34,35) However, smoking may improve attention and working memory, but in a modest way similar to that of atypical antipsychotics. Antipsychotics can cause sedation, may reduce the ability to concentrate and can affect memory, and nicotine could prevent these things from happening.(36) Current directions in research involve deciphering the mechanisms of action of nicotine in the systems involved in schizophrenia. It is expected that one day researchers' strives be rewarded by creating new drugs (37) with high efficiency, to improve the lives of patients with schizophrenia. Mental health professionals should be aware that smoking is an important activity for many chronic psychiatric patients in general and for those suffering from schizophrenia in particular. Given the patient's needs, it is desirable to encourage the reduction of smoking in these patients, as well as in any patient, and to concern about creating a therapeutic environment

that is warm, welcoming and intimate in order to strengthen the doctor-patient relationship.

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REFERENCES

1. http://www.stopfumat.eu/index.php?s=page&id=7.
2. Institutul de Pneumoftiziologie Marius Nasta București. Impactul politicilor de control al tutunului asupra consumului produselor din tutun - Studiu de prevalență a fumatului în România – Raport sintetic TOTEM Communication; 2011.
3. De Leon J. Psychopharmacology: Atypical Antipsychotic Dosing: The Effect of Smoking and Caffeine. Psychiatric Services. 2004;55:491-493.
4. Goff DC, Henderson DC, Amico E. Cigarette smoking in schizophrenia: relationship to psychopathology and medication side effects. Am J Psychiatry. 1992;149:1189-1194.
5. De Leon J, Becona E, Gurpegui M, et al. The association between high nicotine dependence and severe mental illness may be consistent across countries. J Clin Psychiatry. 2002;63:812-816.
6. Winterer G. Why do patients with schizophrenia smoke? Current Opinion in Psychiatry. 2010;23(2):112-119.
7. Johnson et al. Gender-specific profiles of tobacco use among non-institutionalized people with serious mental illness. BMC Psychiatry. 2010;10:101
8. Lowe EJ, Ackman ML. Impact of Tobacco Smoking Cessation on Stable Clozapine or Olanzapine Treatment. Annals of Pharmacotherapy. 2012;44(4):727-732.
9. Kelly DL, Conley RR, Tamminga CA. Differential olanzapine plasma concentrations by sex in a fixed-dose study. Schizophr Res. 1999;40:101-104.
10. Carrillo JA, Herraiz AG, Ramos SI, Gervasini G, Vizcaino S, Benitez J. Role of the smoking-induced cytochrome P450 (CYP)1A2 and polymorphic CYP2D6 in steady-state concentration of olanzapine. J Clin Psychopharmacol. 2003;23:119-127.
11. Shimoda K, Someya T, Morita S, Hirokane G, Noguchi T, Yokono A, Shibasaki M, Takahashi S. Lower plasma levels of haloperidol in smoking than in nonsmoking schizophrenic patients. Ther Drug Monit. 1999;21:293-296.
12. Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics: differential risk and clinical implications. CNS Drugs. 2007;21(11):911-936.
13. Kleinberg DL, Davis JM, de Coster R, Van Baelen B, Brecher M. Prolactin levels and adverse events in patients treated with risperidone. J Clin Psychopharmacol. 1999;19(1):57-61.
14. Haupt DW. Differential metabolic effects of antipsychotic treatments. Eur Psychopharmacol. 2006;16(3):149-155.
15. Allison DB, Casey DE. Antipsychotic-induced weight gain: a review of the literature. J Clin Psychiatry. 2001;62(7):22-31.
16. Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs: a critical overview. CMAJ. 2005;172(13):1703-1711.
17. Glassman AH, Bigger JT Jr. Antipsychotic drugs: prolonged QTc interval, torsade de pointes, and sudden death. Am J Psychiatry. 2001;158(11):1774-1782.
18. Ray WA, Chung CP, Murray KT, Hall K, Stein CM. Atypical antipsychotic drugs and the risk of sudden cardiac death. N Engl J Med. 2009;360(3):225-235.
19. Chew ML, Mulsant BH, Pollock BG, et al. A model of anticholinergic activity of atypical antipsychotic medications. Schizophr Res. 2006;88(1-3):63-72.
20. Alvir JM, Lieberman JA, Safferman AZ, Schwimmer JL, Schaaf JA. Clozapine-induced agranulocytosis. Incidence and risk factors in the United States. N Engl J Med. 1993;329(3):162-167.
21. Leucht S, Burkard T, Henderson J, Maj M, Sartorius N. Physical illness and schizophrenia: a review of the literature. Acta Psychiatr Scand. 2007;16(5):317-333.
22. Newcomer JW. Metabolic considerations in the use of antipsychotic medications. J Clin Psychiatry. 2007;68(1):20-27.
23. Koro CE, Meyer JM. Atypical antipsychotic therapy and hyperlipidemia: a review. Essent Psychopharmacol. 2005;6(3):148-157.
24. Meyer JM, Koro CE. The effects of antipsychotic therapy on serum lipids: a comprehensive review. Schizophr Res. 2004;70(1):1-17.
25. Rubio G, Gomez-de-la-Camara A, Ledesma F, et al. Therapy with antipsychotic drugs as a risk factor for diabetes in schizophrenia: a case-control study. Med Clin. 2006;126:441-444.
26. Ghadirian AM, Chouinard G, Annable L. Sexual dysfunction and plasma prolactin levels in neuroleptic-treated schizophrenic outpatients. J Nerv Ment Dis. 1982;170(8):463-467.
27. Wirshing DA, Pierre JM, Marder SR, Saunders CS, Wirshing WC. Sexual side effects of novel antipsychotic medications. Schizophr Res. 2002;56(1-2):25-30.
28. Wallace M. Real progress - the patient's perspective. Int Clin Psychopharmacol. 2001;16(1):S21-S24.
29. Prochaska JJ. Ten Critical Reasons for Treating Tobacco Dependence in Inpatient Psychiatry. J Am Psychiatr Nurses Assoc. 2009;15(6):404-409.
30. Hashimoto Y, Uno J, Miwa T, Kurihara M, Tanifuji H, Tensho M. Effects of antipsychotic polypharmacy on side-effects and concurrent use of medications in schizophrenic outpatients. Psychiatry Clin Neurosci. 2012;66(5):405-410.
31. Weiden PJ, Kozma C, Grogg A, Locklear J. Partial compliance and risk of rehospitalization among California Medicaid patients with schizophrenia. Psychiatric Services. 2004;55(8):886-891.
32. Harvey PD. Pharmacological Cognitive Enhancement in Schizophrenia. Neuropsychol Rev. 2009;19:324-335.
33. Burda K, Czubak A, Nowakowska E, Kus K, Metelska J, Nowakowska A. Interactions of nicotine and drugs used in the treatment of mental illnesses with respect to cognitive functions. Arzneimittel-Forschung-Drug Research. 2010;60(9):527-543.
34. Matthews AM, Wilson VB, Mitchell SH. The Role of Antipsychotics in Smoking and Smoking Cessation. CNS Drugs. 2011;25(4):299-315.
35. Segarra R, Zabala A, Eguiluz JI, Ojeda N, Elizagarate E, Sanchez P, Ballesteros J, Gutierrez M. Cognitive performance and smoking in first-episode psychosis: the self-medication hypothesis. European Archives of Psychiatry and Clinical Neuroscience. 2011;261(4):241-250.
36. Yale University. Nicotine Helps Schizophrenics With Attention And Memory. ScienceDaily, 11 Jul. 2005. Web. 20 Feb. 2013
37. Foster DJ, Jones CK, Conn PJ. Emerging approaches for treatment of schizophrenia: modulation of cholinergic signalling. Discov Med. 2012;14(79):413-20.