Assessing the Effects of Antipsychotics on Parenting

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Received 2017 May 16; Accepted 2017 July 08.

Abstract

Context: Mental health professionals interact with substantial numbers of parents, mainly mothers, who suffer from severe mental disorders and who are treated, acutely or chronically, with antipsychotic medication. The behavior of these clients is affected by their primary illness but also by many other factors, including their drug regimen. The treating team, however, does not always recognize that a drug can profoundly impact cognition and behavior. The aim of this paper is to inform non-medical mental health workers how antipsychotic medication (AP) can influence client cognition and behavior, and thereby impact the safety of the client’s children. Indirectly, APs can also affect the immediate and longer-term behavior of the children.

Evidence Acquisition: This article qualitatively reviews the very sparse literature on antipsychotic effects on cognition and behavior in populations of mentally ill mothers of young children. This narrative review includes case illustrations taken from a clinic for women with psychotic disorders. Also included are references to studies of rodent maternal behavior, as influenced by antipsychotic drugs.

Results: Animal studies have shown that maternal behavior in rodents is impaired by antipsychotic drugs. In humans, drug effects such as sedation, dizziness, indicated thinking, tardive dyskinesia, increased appetite, and sleepwalking, as well as client beliefs about and attitudes toward their drugs, can affect their problem solving, decision-making, and behavior and, thus, play a critical role in child custody determinations. Behavior induced by drugs includes issues of tolerance, withdrawal, and sensitization. Importantly, there are major safety concerns related to APs.

Conclusions: Listening attentively when clients speak about their drugs and understanding potential drug effects help mental health professionals increase their therapeutic efficacy and make sound decisions about clients and their children.

Keywords: Severe Mental Disorder, Parenting, Antipsychotic Agents, Adverse Effects, Maternal Behaviors

1. Context

A recent survey found that 2.7 million parents in the United States, most of them mothers, had suffered from severe mental illness in the preceding year (1). Although many effective strategies have been developed to support parents with serious mental illness (2), one aspect of comprehensive treatment has been largely ignored – the appreciation of the degree to which antipsychotic medication can affect the quality of parenting. Understanding the impact of medication on critical human functions such as parenting is essential because potent therapeutic drugs have the potential to improve, but also to impair, parenting adequacy and, consequently, the wellbeing of children. This review is mainly intended for non-medical mental health workers whose background and training may not have sufficiently equipped them to assess the role that antipsychotic drugs play in their clients’ parenting behaviors and, potentially, in the subsequent behavior of their offspring. Because non-medical mental health workers are usually the ones charged with making child custody determinations, they need to understand in depth how medications such as APs can affect parental function.

2. Evidence Acquisition

This paper is a non-systematic narrative literature review of medication-related issues with which health care professionals need to be familiar when caring for mothers with psychotic illnesses; the review focuses on issues most capable of influencing child custody decisions. It includes case illustrations taken from a clinic for women with psychotic disorders. The article also references studies of rodent maternal behavior, as influenced by antipsychotic drugs.

3. Findings

Non-medical mental health workers generally assume that doctors always prescribe appropriate medication in appropriate doses, that the medication their clients take is free of adverse effects and that clients always take their drugs as prescribed. None of these assumptions turn out
to be totally true. An additional problem sometimes described in the literature is the inherent distrust that some mental health workers have for all forms of medication, a distrust that can be tacitly communicated to patients and that encourages non-adherence to prescribed APs. An important mistake that mental health workers can make is to attribute to medication problems that result not from drugs but from the patient’s illness. Mental confusion, for instance, can be drug-related, but it can also be an undertreated symptom of psychosis. Client attitudes toward medication are almost never sufficiently probed during therapy, and yet they can be determinants of long-term health and effective parenting. It is the basic premise of this paper that it is important for non-medical mental health workers to know as much as possible about the drugs their clients are prescribed, their intended and unintended effects, the degree to which their clients adhere to their drug regimens, and the underlying reasons behind any non-adherence. A further premise is that factors such as cultural attitudes toward drug-taking, as well as lifestyle factors such as cigarette smoking, substance use, diet, and the use of complementary herbal medicines all potentially interact with APs and influence behavior. The drugs mothers take can also affect the behavior of children, although there is little solid evidence for this assertion. While there are accumulating research data on the potential cognitive and behavioral effects of maternal antipsychotics on the neonate and developing child (3-5), there is very little research on the secondary effects on growing children of maternal behaviors that are induced by antipsychotics.

3.1. Recognizing Side-Effects

Distinguishing among client personality problems, illness symptoms and drug side effects is a fundamental issue (Figure 1). Examples of difficulties that have arisen in the past are taken from the Women’s Clinic for Psychosis, Toronto, Canada. Client and worker details have been altered to ensure anonymity.

3.2. Examples

A vocational therapist, initially intent on helping a young woman who was being treated for schizophrenia find gainful employment, soon gave up trying. She explained that her client was not interested in pursuing the recommended course of study because “the client spent all her time flirting with the men in the group instead of attending to the class.” It turned out that the client, who was often observed winking and grimacing, was suffering from tardive dyskinesia, a side effect of her antipsychotic drug (6). She was not flirting.

A nurse visiting a young postpartum woman being treated with clozapine, an AP, was concerned that the client might have suffered a stroke because she had suddenly begun to stutter. The nurse did not realize that stuttering was a relatively common but not widely-reported side effect of clozapine (and other antipsychotics) and that the dose, therefore, needed adjustment (7). The client had not suffered a stroke.

A woman treated with antipsychotics knew that she was sleepwalking at night so she barricaded her front door with furniture every evening to prevent her leaving the apartment. She did not want to put herself at risk, nor to leave her young children unattended. Her case worker misunderstood the situation and attributed the client’s barricading behavior to paranoia. She recommended that her antipsychotic dose be raised, which only made the sleepwalking worse (8, 9).

A young mother being treated with olanzapine (an AP) received increasing criticism from her social worker for continuously putting on weight. Neither the client nor her care provider realized that the heightened appetite and subsequent weight gain were attributable to the AP she was taking (10). A change of medication was required, not a scolding.

One worker advised a client, also on olanzapine, to purchase a series of expensive shampoos to try to counteract hair loss because clumps of hair fell out each time she brushed. The worker was not aware of the fact that hair loss can occur as a reaction to antipsychotic medication (11). The client could have used her money to better purposes.

Another worker, whose client began taking anticholinergic medication to help counteract muscle contractions caused by the AP she was on, noticed that the client had become more confused. The worker attributed this to an exacerbation of illness and suggested an increase of her AP dose, but it turned out to be due, instead, to the cognitive impairment induced by the anticholinergic drug (12).

Partially clouded consciousness and dizziness due to the sedative and hypotensive effects of APs have several times been mistaken for intoxication at the Women’s Clinic for Psychosis. Distinctions are often difficult to make accurately because of the reportedly strong association between substance abuse and serious mental illness (13).

The non-recognition of side-effects may be short-lasting and trivial, but neglecting the common side effect of AP sedation can sometimes have far-reaching consequences, interfering as it does with arousal, attention, memory, and fine motor skills. Mothers newly treated with antipsychotics may be so sedated that they do not wake in the night when their baby is crying or may fall asleep during the day and fail to appropriately monitor their child’s activities. Childcare workers can miss the fact that this is an AP side effect and can consider such mothers as alco-
holic, neglectful or apathetic, evaluations that sometimes lead to loss of child custody (14, 15). Maternal sedation during an infant’s early weeks can constitute a serious impediment to mother-child bonding and attachment (16) and can become a critical safety issue, especially for single mothers who live alone with their infants, which is not unusual in the context of serious mental illness (17). Individuals usually adapt to acute AP-induced sedation after a short period (18) but, in the longer term, the chronic use of antipsychotics increases the risk of sleep apnea (19), which itself leads to daytime sedation. AP-induced sedation is a significant problem that interferes with most parenting tasks.

3.3. Effects on Parenting Tasks

Human parenting behaviors are so complex that it is difficult to study the effects of antipsychotics on any one individual parenting behavior. The effect is clearer in rodents where antipsychotics have been shown to substantially interfere with maternal behaviors such as pup retrieval, pup licking, nest building and pup nursing (20-23). By extension, there is every reason to believe that the medication that mothers with psychosis need to take makes their parenting tasks more difficult than they would otherwise be. They need to work very hard to overcome both their illness symptoms and their medication side-effects in order to fulfill the tasks of motherhood. Mothers with severe mental illness constantly worry that AP side-effects such as slow movements, clouded thinking, delayed responses, and emotional blandness will cause their child care workers to conclude that they are not able to care for their children. For these reasons, they may stop taking their drugs, exposing themselves to the dangers of reactivated psychotic illness.

3.4. Example

When a mother who had temporarily lost custody of her daughter was told by her Children’s Aid worker, “You
cannot have your daughter back yet. You are still on too much medication," the client immediately stopped her medicine and, unfortunately, relapsed into a psychotic state. The amount of medication one takes should have nothing to do with the assessment of function.

3.5. Drug Interactions

Side-effects are relatively straightforward to identify if they start when the offending drug is first taken and stop when it is removed. It is, however, much more difficult to associate a drug and its effects when first drug use and adverse effect occur asynchronously as in the examples described earlier of tardive dyskinesia and of hair loss. In both the instances, the side-effect was delayed. A major source of such delays are drug interactions that emerge only when a second interacting factor is added to the original drug. The second factor can be a new drug or it can be an auxiliary condition.

3.6. Examples

A young woman treated with a long-acting antipsychotic complained of stiff muscles from time to time. Her occupational therapist did not believe this was a side-effect of her long-acting depot antipsychotic drug because it only occurred sporadically. She thought the patient was using stiff muscles as an excuse to not take part in a recommended parenting group. But the stiff muscles were, in fact, an extrapyramidal side effect of the antipsychotic that emerged only after exercise, whenever extra drug from the muscle injection site was released into the blood stream (24).

Another patient’s complaints of extrapyramidal side effects (EPS) were also initially dismissed because she had been taking the same medication at the same dose for years without EPS. What the treatment team did not initially take into account, however, was that the client had aged and that age exerts a powerful effect on drug metabolism. Her antipsychotic dose now needed to be reduced (25).

Antipsychotic drug levels vary not only with age and exercise but also with smoking (and smoking cessation), with substance abuse, and, in certain cases, with diet (e.g. caffeine, grapefruit juice). The prescribed drug can interact with herbal supplements to cause side effects or, very commonly in women, with contraceptives and with other medicines (26-30). The metabolism of some antipsychotic drugs is also powerfully affected by variation in estrogen levels (31) over the course of reproductive cycles – menstrual phase, pregnancy, postpartum, menopause. Episodic or late-appearing side-effects are difficult to recognize for what they are. Consultations are in order whenever the cause is unclear.

3.7. Tolerance, Dependence, Withdrawal, Sensitization, and Rebound

There are mental health professionals who view all drugs as potentially addictive and consider concepts such as tolerance, dependence, withdrawal effects and sensitization applicable to antipsychotic drugs. In some ways, they are right. Tolerance means the need for higher and higher doses over time to achieve the same results. Although higher doses of drug are often prescribed over time to individuals with schizophrenia to prevent the return of psychotic symptoms, this is not necessarily tolerance but, rather, a progressive loss of responsiveness due to known and unknown factors, one known factor being the loss of estrogen at menopause (32). In humans it is almost impossible to dissociate tolerance to drug effects from the contribution of the many factors capable of decreasing the responsiveness of antipsychotic symptoms to antipsychotic drugs. Animal experiments, however, have been able to show evidence of true tolerance to antipsychotics (33). Too often, care providers attribute breakthrough psychotic symptoms to the client’s stopping medication, but there is a variety of other explanatory possibilities.

3.8. Example

A woman with schizophrenia, a divorcée with an adolescent son, had been successfully treated for many years with a low dose of the AP, perphenazine. As she approached menopause, her dose was constantly increased because of increasing psychotic symptoms. When dose escalation was unable to control the symptoms, different antipsychotics were tried. The patient responded to none and had to be hospitalized because of mounting dysfunction. Her ex-husband took over the care of their son. She was eventually discharged from hospital on an intramuscular depot injection with her symptoms under control. Looking back, it was not possible to know whether she had developed progressive tolerance and now required a higher drug blood level or whether, because of menopausal changes, she was no longer absorbing oral drugs.

Sensitization is the opposite of tolerance. It refers to altered sensitivity to a drug that increases rather than decreases some (not necessarily all) of the effects of the drug (33). Many people taking antipsychotic drugs report worsening adverse effects as time goes on. This can be the result of drug accumulation and subsequent release of drug previously sequestered in fatty tissue.

3.9. Example

A young woman who had been taking antipsychotics for several years went on a strict diet and lost 20 pounds...
in four months. Her antipsychotic dose remained unchanged. As proud as she was of losing weight, she was made miserable by the sudden appearance of extrapyramidal symptoms, something she had not experienced prior to her weight loss. Weight loss had released accumulated drug from her lipid stores.

Tardive dyskinesia is a side effect of APs that has been hypothesized to result from the sensitization of dopamine receptors after long-term exposure to antipsychotics (34).

Withdrawal from antipsychotics (whether from lowering the dose or discontinuing the drug or switching to a new drug) may result in physical withdrawal effects such as difficulty falling or staying asleep, mood changes, increases in anxiety/agitation, difficulty concentrating/completing tasks, headaches, memory loss, nightmares, nausea, and vomiting (35). These effects do not mean that the client is physically dependent on or “addicted” to the drug. There is no accompanying craving for the drug, but there may be a psychological dependence, the effect of learning from previous discontinuation experience that one’s wellbeing depends on regular intake of the AP.

3.10. Supersensitivity Psychosis

Rebound or supersensitivity psychosis refers to increased psychotic symptoms after a dose reduction or a drug discontinuation (34, 36-39). Taking a dopamine blocker over a long stretch of time multiplies postsynaptic receptors on dopamine neurons so that, when the drug is stopped, endogenous dopamine floods the receptors and triggers psychotic symptoms (40). The lesson for mental health workers is that an increase in psychotic symptoms does not necessarily mean non-adherence on the part of the client nor does it signal a downhill course of illness. It may be a temporary and readily fixable drug-related phenomenon. On the other hand, stopping drugs can, on rare occasions, lead to irreversible non-responsiveness.

3.11. Example

A young woman was diagnosed with schizophrenia in High School but her illness was well controlled on a small dose of the AP, olanzapine. She successfully completed post secondary studies, married, and maintained steady employment. She was doing so well that she was recruited for a study in which olanzapine was administered every second day and then every third day (41). At the end of the study, this young woman continued to experience no psychotic symptoms so decided to stop olanzapine altogether. Within four months she was back in hospital with a full-blown psychosis only, this time, olanzapine did not work no matter how high the prescribed dose. She was tried on a number of other treatments but, tragically, after another two years of being in and out of hospital with persistent threatening hallucinations, she took her own life by jumping out of a bathroom window.

3.12. Meaning of Medication to Client

Non-medical mental health workers sometimes feel unqualified to talk to clients about their medications and, when the issue surfaces, refer them instead to their doctors. But there are many aspects of taking drugs that need to be sorted out repeatedly in discussion; listening to individual concerns about drugs is therapeutically important. Depending on past experience and cultural tradition, all individuals hold strong beliefs about drugs, endowing medications with a personal meaning (42). Some people with schizophrenia view their antipsychotic medication as a shield against stress; some see the drug as an unwelcome imposition by powerful others; some see needing to take medication as a character weakness; some see it as a crutch; some see it as a effective weapon against tormenting voices. A potentially useful therapeutic intervention is to help clients untangle the complex weave of symbolic meaning that can attach to medications (42).

Depending on the precise definition of adherence, between 20% - 89% of clients with schizophrenia are said to be non-adherent from time to time (43). This is important because the maintenance of health, especially in the context of parenting, is critical in schizophrenia and health usually means faithful adherence to one’s medication schedule. It is important to try to understand why individuals often stop medication or omit some of their doses. Some do it because they are afraid to gain weight, some do it to try to maintain control over decision-making, some feel medication interferes with creativity, some stop because they don’t like the prescriber, some believe that medication interferes with their relationships. Mothers, for instance, may sense that drugs spoil their rapport with their children.

The reason for abandoning medication may be unresolved issues in the client’s relationship with the prescriber. It may also be a result of friends or family members sharing fears that the drug is “addictive”. Many stop their drugs because they experience specific side-effects that they find especially distressing. Very commonly in the context of schizophrenia, the aversion to a drug can be traced to feeling coerced to take it, not being given a choice in deciding treatment. It is noteworthy that many individuals are willing to take alternative rather than prescribed medicines (44) because they feel they have chosen it for themselves. Time spent listening to and discussing such feelings is valuable; it clarifies important issues for both client and care provider.
3.13. Safety

A medication-related safety issue is pills that are accessible to small children (45, 46). House hazards such as these are important to the health of children; this means that periodic home visits are recommended to check on matters of safety.

The literature also mentions late-appearing hazards of parental medication for offsprings. For instance, the increased appetite and sedentary life style of a mother on antipsychotic medication may be mimicked by children as they grow up (47-49). Child obesity may be a result. Behavioral mimicry may make it more likely that children who see their parents taking pills will also want to self-medicate when distressed. In a review paper on self-medication in adolescents, Shehnaz et al. (50) found that one of the risk factors for self-medication in adolescents was use of medication within the family. The literature encourages parents and care providers to talk to children about the pros and cons of medication and how best to balance health needs against addiction risks.

4. Conclusions

The literature on the subject of APs affecting parental behavior is sparse. Animal studies show that early maternal behavior in rodents is definitely impaired by antipsychotic medication, strongly suggesting that this could be the case for humans. Drug-related sedation interferes with mother-child secure attachment and with mother’s energy levels and cognitive sharpness. It also interferes with parents’ ability to provide consistency, stimulation, and socialization for their children. Other important findings are that tardive dyskinesia signs can be easily misinterpreted and that drug-induced appetite and metabolic changes can lead to obesity, the risk of which can be transmitted to the next generation. Sleepwalking secondary to antipsychotics is a neglected potential danger to clients and their children. An important issue in child custody determination is the accurate assessment of maternal behavior that might be drug-induced. Concepts such as tolerance, withdrawal, dependence and sensitization may sometimes be applied to the use of antipsychotic drugs and need to be understood more fully than they are at present. Listening attentively to client concerns about the drugs they take facilitates understanding of drug effects and helps mental health professionals increase their therapeutic efficacy.

References

1. Stambaugh LF, Forman-Hoffman V, Williams J, Pemberton MR, Ringelstein H, Hedden SL, et al. Prevalence of serious mental illness among parents in the United States: results from the National Survey of Drug Use and Health, 2008-2014. Am Epidemiol. 2017;27(3):222-4. doi:10.1016/j.annepidem.2016.12.005. [PubMed: 28081894].
2. Biebel K, Nicholson J, Woolsey K, Wolf T. Shifting an agency’s paradigm: Creating the capacity to intervene with parents with mental illness. Am J Psychiatr Rehabil. 2016;19(4):315-38. doi:10.1080/15487768.2016.1239164.
3. Guillemot J, Laborie C, Dutrieu-Castello I, Maron M, Deloef S, Lesage J, et al. Could maternal perinatal atypical antipsychotic treatments program later metabolic diseases in the offspring? Eur J Pharmacol. 2011;657(1-3):13-6. doi:10.1016/j.ejphar.2011.05.076. [PubMed: 21664905].
4. Oyebode F, Rastogi A, Berrisford G, Coccia F. Psychotropics in pregnancy: safety and other considerations. Pharmacol Ther. 2012;133(1):71-7. doi:10.1016/j.pharmthera.2012.03.008. [PubMed: 22483705].
5. Singh KP, Singh MK. In utero exposure to atypical antipsychotic drug, risperidone: Effects on fetal neurotoxicity in hippocampal region and cognitive impairment in rat offspring. Prog Neuropsychopharmacol Biol Psychiatry. 2017;75:35-44. doi:10.1016/j.pnpbp.2016.12.006.
6. Asnis GM. Tardive dyskinesia: is it or is it not? A review of the problems in diagnosis and a case study. Dis Nerv Syst. 1977;38(10):856-9. [PubMed: 908251].
7. Murphy R, Gallagher A, Sharma K, Ali T, Lewis E, Murray J, et al. Clozapine-induced stuttering: an estimate of prevalence in the west of Ireland. Ther Adv Psychopharmacol. 2015;5(4):232-6. doi:10.1177/2045125315590060.
8. Seeman MV. Sleepwalking, a possible side effect of antipsychotic medication. Psychiatr Q. 2011;82(3):59-67. doi:10.1007/s11126-010-9149-8. [PubMed: 20734137].
9. Tamanna S, Ullah MI, Pope CR, Holman G, Koch CA. Quetiapine-induced sleep-related eating disorder-like behavior: a case series. J Med Case Rep. 2012;6:380. doi:10.1186/1752-1947-6-380. [PubMed: 22939910].
10. Stip E, Lungo OV, Anselmo K, Letourneau G, Mendrek A, Stip B, et al. Neurocognitive changes associated with appetite information processing in schizophrenic patients after 16 weeks of olanzapine treatment. Transl Psychiatry. 2012;2:e128. doi:10.1038/tp.2012.53. [PubMed: 2274121].
11. Leung M, Wixon K, Remick RA. Olanzapine-induced hair loss. Can J Psychiatry. 2002;47(9):891-2. doi:10.1177/070674770204700925. [PubMed: 12500765].
12. Seeman MV. Atypical antipsychotics and sleep: A review. Sleep Med Rev. 2012;16(2):69-75. doi:10.1016/j.smrv.2011.10.006. [PubMed: 22886686].
13. Seeman MV. Antipsychotic-induced somnolence in mothers with schizophrenia. Psychiatr Q. 2012;83(1):83-9. doi:10.1007/s11126-010-9085-x. [PubMed: 22739209].
14. Seeman MV. Intervention to prevent child custody loss in mothers with schizophrenia. Schizophr Res Treatment. 2012;2012:796763. doi:10.1155/2012/796763. [PubMed: 22966446].
15. De Falco S, Emer A, Martini L, Rigo P, Pruner S, Venuti P. Predictors of mother-child interaction quality and child attachment security in at-risk families. Front Psychol. 2014;5:389. doi:10.3389/fpsyg.2014.00389. [PubMed: 25091287].
16. Dolman C, Jones I, Howard IM. Pre-conception to parenting: a systematic review and meta-synthesis of the qualitative literature on motherhood to women for severe mental illness. Arch Womens Ment Health. 2013;16(3):173-96. doi:10.1007/s00737-013-0336-0. [PubMed: 23525788].
17. Miller DD. Atypical antipsychotics: sleep, sedation, and efficacy. Prim Care Companion J Clin Psychiatry. 2004;6(Suppl 2):3-7. [PubMed: 16001094].
20. Li M. Antipsychotic drugs on maternal behavior in rats. Behav Pharmacol. 2015;26(6):516-26. doi: 10.1097/FBP.0000000000000688. [PubMed: 26228123].

21. Li M, Davidson P, Budin R, Kapur S, Fleming AS. Effects of typical and atypical antipsychotic drugs on maternal behavior in postpartum female rats. Schizophr Res. 2004;70(1):69-80. doi: 10.1016/j.schres.2003.09.013. [PubMed: 15246446].

22. Pereira M, Farrar AM, Hockemeyer J, Muller CE, Salamone JD, Morrell MJ. Effect of the adenosine A2A receptor antagonist MSX-3 on motivational disruptions of maternal behavior induced by dopamine antagonism in the early postpartum rat. Psychopharmacology (Berl). 2011;213(1):69-79. doi: 10.1007/s00213-010-2015-4. [PubMed: 20840806].

23. Wu R, Gao J, Chou S, Davis C, Li M. Behavioral, pharmacological and neuroanatomical analysis of serotonin 2C receptor agonism on maternal behavior in rats. Psychoneuroendocrinology. 2016;72:252-62. doi: 10.1016/j.psyneuen.2016.08.017. [PubMed: 27566448].

24. van Baak MA. Influence of exercise on the pharmacokinetics of drugs. Clin Pharmacokinet. 1990;19(3):32-43. doi: 10.2165/00003088-199019010-00003. [PubMed: 2199126].

25. Uchida H, Mamo DC, Mulsant BH, Pollock BG, Kapur S. Increased antipsychotic sensitivity in elderly patients: evidence and mechanisms. J Clin Psychiatry. 2009;70(3):397-405. [PubMed: 19924746].

26. Davuluri S, Dharmarajan TS. Complementary and alternative medicine: Herbs and supplements: A review for the primary care physician. Cureus. 2014 doi: 10.7759/cureus.184.

27. Desai HD, Seabolt J, Jann MW. Smoking in patients receiving psychotropic medications: a pharmacokinetic perspective. CNS Drugs. 2001;15(6):469-94. [PubMed: 11524025].

28. Hagg S, Spigset O, Mjorndal T, Dahlqvist R. Effect of caffeine on clozapine pharmacokinetics in healthy volunteers. Br J Clin Pharmacol. 2000;49(1):59-63. [PubMed: 10606838].

29. Kennedy WK, Jann MW, Kutscher EC. Clinically significant drug interactions with atypical antipsychotics. CNS Drugs. 2013;27(12):1021-48. doi: 10.1007/s40263-013-0114-6. [PubMed: 24170642].

30. Lu ML, Lane HY. Clinically Significant Interactions with Antipsychotics. Springer International Publishing; 2016.

31. Urichuk L, Prior T, Duraz S, Baker G. Metabolism of atypical antipsychotic: involvement of cytochrome p450 enzymes and relevance for drug-drug interactions. Curr Drug Metab. 2008;9(5):410-9. [PubMed: 18537577].

32. González-Rodríguez A, Catalan R, Penades R, Ruiz Cortes V, Torra M, Seeman MV, et al. Antipsychotic Response Worsens With Postmenopausal Duration in Women With Schizophrenia. J Clin Psychopharmacol. 2016;36(6):580-7. doi: 10.1097/JCP.0000000000000571. [PubMed: 27628286].

33. Li M. Antipsychotic-induced sensitization and tolerance: Behavioural characteristics, developmental impacts, and neurobiological mechanisms. J Psychopharmacol. 2016;30(8):749-70. doi: 10.1177/026988116654697. [PubMed: 27714988].

34. Chouinard G, Chouinard VA. Atypical antipsychotics: CATIE study, drug-induced movement disorder and resulting iatrogenic psychiatric-like symptoms, supersensitivity rebound psychosis and withdrawal discontinuation syndromes. Psychother Psychosom. 2008;77(2):169-77. doi: 10.1055/s-0028-1082883. [PubMed: 18230939].

35. Salomon C, Hamilton B, Elsom S. Experiencing antipsychotic discontinuation: results from a survey of Australian consumers. J Psychiatr Ment Health Nurs. 2014;21(10):597-23. doi: 10.1111/jpm.12178. [PubMed: 25294092].

36. Cerovecki A, Musil R, Klimke A, Seemuller F, Hain E, Schennach R, et al. Withdrawal symptoms and rebound syndromes associated with switching and discontinuing atypical antipsychotics: theoretical background and practical recommendations. CNS Drugs. 2013;27(7):545-72. doi: 10.1007/s40263-013-0079-5. [PubMed: 23821019].

37. Goudie AJ, Cole JC. Switching antipsychotics. Antipsychotic tolerance, withdrawal and relapse: unresolved issues and research implications. J Psychopharmacol. 2008;22(2):858-7. doi: 10.1077/026988110782904. [PubMed: 18751274].

38. Moncrieff J. Does antipsychotic withdrawal provoke psychosis? Review of the literature on rapid onset psychosis (supersensitivity psychosis) and withdrawal-related relapse. Acta Psychiatr Scand. 2006;114(1):3-13. doi: 10.1111/j.1600-0447.2006.00787.x. [PubMed: 16774455].

39. Yin J, Barr AM, Ramos-Miguél A, Procyslyn RM. Antipsychotic Induced Dopamine Supersensitivity Psychosis: A Comprehensive Review. Curr Neuropharm. 2017;15(1):174-83. [PubMed: 27264948].

40. Seeman MV, Seeman P. Is schizophrenia a dopamine supersensitivity psychotic reaction? Prog NeuroPsychopharmac Biol Psychiatry. 2014;48:556-60. doi: 10.1016/j.pnpbp.2013.10.003. [PubMed: 24126868].

41. Remington G, Seeman P, Feingold A, Mann S, Shammi C, Kapur S. “Extended” antipsychotic dosing in the maintenance treatment of schizophrenia: a double-blind, placebo-controlled trial. J Clin Psychiatry. 2011;72(4):1042-8. doi: 10.4088/JCP.09m05866yel. [PubMed: 20868339].

42. Seeman MV, Seeman N. The meaning of antipsychotic medication to patients with schizophrenia. J Psychiatr Pract. 2012;18(5):338-48. doi: 10.1097/01.pra.0000419818.60505.95. [PubMed: 22995991].

43. 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. [PubMed: 12416599].

44. Thorne S, Paterson B, Russell C, Schultz A. Complementary/alternative medicine in chronic illness as informed self-care decision making. Int J Nurs Stud. 2002;39(7):671-83. [PubMed: 12230244].

45. Cobaugh DJ, Erdman AR, Booze LL, Scharman EJ, Christianson G, Manoguerra AS, et al. Atypical antipsychotic medication poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila). 2007;45(8):918-42. doi: 10.1080/1556926708665442. [PubMed: 18163325].

46. Love JN, Smith JA, Simmons R. Are one or two dangerous? Pheno- nothiazine exposure in toddlers. J Emerg Med. 2006;31(1):53-9. doi: 10.1016/j.jemermed.2005.08.011. [PubMed: 16798156].

47. Hermans RC, Lichtwarck-Aschoff A, Bevelander KE, Herman CP, Larsen JK, Engels RC. Mimicry of food intake: the dynamic interplay between eating companions. Plos One. 2012;7(2):e31027. doi: 10.1371/journal.pone.0031027. [PubMed: 22324438].

48. Sharps M, Higgs S, Blissert J, Nouwen A, Chechclacz M, Allen HA, et al. Examining evidence for behavioural mimicry of parental eating by adolescent females. An observational study. Appetite. 2015;89:56-61. doi: 10.1016/j.appet.2015.01.015. [PubMed: 25624020].

49. van Schaik JE, Hunnius S. Little chameleons: The development of so- cial mimicry during early childhood. J Exp Child Psychol. 2016;147:71- 81. doi: 10.1016/j.jecp.2016.01.003. [PubMed: 27060418].

50. Shehnaz SI, Agarwal AK, Khan N. A systematic review of self- medication practices among adolescents. J Adolesc Health. 2014;55(4):467-83. doi: 10.1016/j.jadohealth.2014.07.001. [PubMed: 25245937].