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Psychotropic Medications and Substances of Abuse Interactions in Youth

Dr. Yifrah Kaminer, MD, MBA, Pablo Goldberg, MD, and Daniel F. Connor, MD

Dr Kaminer is with the Alcohol Research Center at the University of Connecticut Health Center. All authors are with the Division of Child and Adolescent Psychiatry at the University of Connecticut Health Center, Farmington, CT

Abstract

The majority of youth with substance use disorders (SUD) manifest one or more co-occurring psychiatric disorders. Consequently, many of these youths are being prescribed with psychotropic medications. As prescribing rates continue to increase for early onset psychiatric disorders, potential risk for substance of abuse – psychiatric medication interactions may be enhanced. Since this type of drug-drug interaction has received little attention in the scientific literature, we conducted a systematic literature search examining the potential interactive adverse effects between psychotropic medications and substances of abuse in youth. Regardless of the scarcity of psychotropic medications - substance of abuse interactions found, it is important to stay vigilant due to the continued introduction of new classes of medications as well as the ever-changing map of street drugs.

Trends in Drug Misuse

The 2008 Monitoring The Future (MTF) ¹ survey indicates that overall teen drug use is down nationwide. However, more teens misuse prescription drugs and over-the-counter (OTC) medications than any other illicit drug, except marijuana. This trend has been increasing since 2002 and as many as 20% of adolescents, have misused a prescription medication, most commonly pain killers such as opioids. ² Ten percent of seniors reported past year nonmedical use of hydrocodon (i.e., Vicodin) and 4.7 percent report abusing oxycodon (i.e., Oxycontin). ¹ Seven of the top 10 drugs abused, were prescribed or purchased over-the-counter. These prescription and OTC drugs are easy to get and are often free.

According to a review and analysis of the 2005 National Survey on Drug Use and Health, 8.2% of adolescents misused a psychotropic medication and 3% endorsed symptoms of a substance use disorder related to prescription medication misuse in the past year. ³

Schepis and Krishnan-Sarin have reported that past year alcohol, tobacco and other drug (ATOD) use as well as major depression were associated with prescription misuse which included: opioids, stimulants, tranquilizers and sedatives. ⁴ The unsupervised misuse of prescribed and OTC medications in particularly those containing Dextromethorphan (DXM), a cough suppressant with agonist activity at mu-opioid receptors, bear significant risks for adverse effects. ⁵ The majority of deaths reported have been the results of products that combine DXM with other substances that become dangerous in high doses such as alcohol. ^{6–7}

* Address correspondence to Dr Kaminer, Alcohol Research Center, Farmington, CT, 06030-2103, kaminer@psychiatry.uchc.edu.

Psychiatric Co-morbidity

More than seventy percent of adolescents with substance use disorders (SUD) are diagnosed with one or more comorbid psychiatric disorders.⁸ Many of these adolescents believe that substance abuse is the result of self-medication of their psychiatric symptomatology.⁹ A recent meta-analysis concluded that there is little evidence supporting the popular self-medication theory.¹⁰ However, there is empirical support for the rebound effects (i.e., symptom exacerbation) of substance use on symptom severity in youth with psychiatric comorbidity.¹¹ These effects carry added risk for physical and psychological adverse effects.

Not all youth with psychiatric comorbidities need or receive psychotropic medications. However, the treatment of comorbid depression with antidepressants can be effective in reducing the severity of the depressive symptomatology.¹²⁻¹³ Furthermore, it might reduce the elevated risk of suicide attributed to each of the comorbid disorder (i.e., depression and SUD) and to their combined effect.¹⁴⁻¹⁶

Combination of Psychotropic Medications and Substances of Abuse

One would presume that the combination of drugs of abuse and psychotropic medications in youth might increase the probability for the occurrence of adverse effects. Our interest in potential adverse effect interactions between psychotropic medications and drugs of abuse in youth was further stimulated by the growing concerns regarding medication interactions in psychiatry¹⁷ and by two recent publications.¹⁸⁻¹⁹

According to Venkatakrishnan and colleagues, a clinically significant interaction between two drugs is said to have occurred when the therapeutic and/or toxic effects of one drug are altered as a consequence, of co-administration of another drug. Adverse drug reactions are a significant cause of death, with drug interactions being a key contributor. Additionally, with the rapid introduction of new pharmacologic agents there is a concomitant rise in the incidence of polypharmacy and the associated risks of both medication interactions and medication-drugs interactions.¹⁷

A recent review of all U.S. death certificates between 1983 and 2004 reported a steep increase in fatal medication errors (FMEs) with use of alcohol and/or street drugs (Philips et al., 2008).¹⁸ This increase in FMEs applies to persons over the age of nine years both at home (increase by 3196%) and out of home (increase by 555%). This study does not report what type of drugs contributes more to fatal medication errors.

Additionally, and more specifically to psychopharmacological agents, Volkow noted that the necessary treatment of the psychiatric comorbidity raises potential concerns.¹⁹ That is, that undesirable interactions between the drug of abuse and the psychotropic-medication(s) should be considered, with respect both to drugs of abuse interfering with the effectiveness of medications and to the increased risk for side effects of the medications or enhanced toxicity of the drug of abuse. Finally, psychiatric comorbidity as well as drug abuse can each exacerbate the severity of symptoms of the other condition and affect response to treatment of either of the conditions.

Results of A Systematic Literature Search

In order to evaluate the potential interactive adverse effects between psychotropic medications and drugs of abuse in youth, we have conducted a systematic literature search, using the following search engines: PubMed at the National Library of Medicine and Psycinfo. We have used the following keywords in the search: Tobacco and cigarette

smoking, alcohol use, marijuana use, opiate use, Dextromethorphan (DXM), Cocaine, and Methyl-enedioxymethamphetamine (MDMA) use. We combined each one of these keywords with: antidepressants, antipsychotics, stimulants and mood stabilizers (Lithium and Valproate) and with interactions. The age limit set was: All child, 0–18 years. The searches covered the period from 1950 until the end of 2008.

Each of these 79 papers was reviewed and only relevant references were included in the current document. In addition several books on youth pharmacotherapy have been reviewed for medications-substance of abuse interactions. Most of these abstracts have not yielded articles meeting inclusion criteria for the desired 0–18 years of age range. Nevertheless, some of the information retrieved has ancillary value. For example, antidepressant use (especially tricyclics), was associated with higher levels of polydrug use.²⁰ Also, there are some antidepressants that interact more with alcohol than others for example amitriptyline more than reboxetine.²¹ A very interesting report was found considering the interactions between marijuana and treatment with tricyclic antidepressants (TCAs) in youth.²² In this study, Wilens et al, describe adverse effects in four adolescents receiving TCAs after smoking marijuana. These effects included mental status changes consistent with delirium and tachycardia, highlighting a possible drug interaction, which could be attributed to metabolism of both cannabis and TCAs by similar hepatic mitochondrial enzymes. Both cannabis and TCAs have cholinergic and adrenergic properties that could be responsible for the elevated heart rate in all four cases. Finally, it was concluded that treating ADHD in youth with comorbid SUD does not result in worsening of SUD or adverse interactions specific to SUD.²³

Discussion

There could be several explanations for the lack of reports on interactive adverse effects between psychotropic medications and drugs of abuse in youth in general and in dually diagnosed adolescents in particular: First, They either do not happen or they are relatively rare. Newer psychotropic medications have a relatively high therapeutic index and as a class, generally are not victimized by drug interactions that result in impairment of their clearance and an increase in their plasma levels (e.g., Selective Serotonin Reuptake Inhibitors (SSRIs) compared to TCAs and Lithium).¹⁷ Second, it could be attributed to lack of recognition. Unfortunately, such risks are often hidden and may not be readily apparent unless a carefully conducted patient's history is obtained, with specific questions to capture the use of non-prescription products.¹⁷

Third, interactions may be attributed to only one agent (i.e., drug or medication) and not to their potential interaction. Fourth, mild adverse effects may be considered not worthy of reporting. Therefore, leading to a preponderance of false negative results. Fifth, reports of single case studies in the literature are less desirable by peer review journals and consequently less prevalent than in the past. They are mostly published as letters to the editor and may not be included in search engines. Sixth, there might be lack of reports due to compromised ethical considerations. That is, clinical investigators may have concerns that participants in psychopharmacological studies might have to be "terminated" because of substance use that has developed during the study (although originally, eligibility criteria of no drug use have been met or have been ignored). Seventh, based on our clinical experience and community contacts we are aware of cases where legal "gag orders" were issued due to family pressure. These incidents happened in order to prevent release of reports implicating substance abuse, and/or prescription medications use and/or OTC medications use as cause of death of minors.

It is important to note that family members, friends and classmates of youth with prescribed medications might have access to these agents. Similarly, youth may have access to their family members medications.²⁴ Regardless whether the reason for “collateral abuse” is for recreational reasons (e.g., getting high), enhanced academic performance or other there is a potential here not only for adverse effects but also for interactions with either other medications and/or drugs taken by the “collateral”.^{25–26}

CONCLUSIONS

Regardless of the relative scarcity of medications substance of abuse interactions, it is important to stay vigilant due to the continued introduction of new classes of medications as well as the ever changing map of street drugs. It is also prudent to inform the adolescent and their families of the potential risks involved in using substances of abuse, misuse of prescription medications, abuse of OTC medications and of mixing medications with ATOD. Finally, continued research of this topic is highly warranted.

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Table 1

Psychotropic Medication-Substance of Abuse Interaction In Youth (literature review Summary)

Interacting Substances of Abuse	Antidepressant	Anti Psychotics	Stimulants	Mood Stabilizers
Tobacco Smoking	0 abstracts	0 abstracts	0 abstracts	0 abstracts
Alcohol	16 abstracts (942 subjects)	0 abstracts	1 abstract (4896 subjects)	0 abstracts
Marijuana	1 abstracts (4 subjects)	0 abstracts	0 abstracts	0 abstracts
Opioids	11 abstracts (12,796 subjects)	35 abstracts (318 subjects)	2 abstracts (518 subjects)	0 abstracts
DXM	4 abstracts (75 subjects)	1 abstract (24 subjects)	0 abstracts	0 abstracts
Cocaine	1 abstract (0 subjects)	3 abstracts (120 subjects)	1 abstract (0 subjects)	0 abstracts
Ecstasy (MDMA)	2 abstracts (0 subjects)	0 abstracts (0 subjects)	1 abstract (0 subjects)	0 abstracts