THE CARLAT REPORT
ADDICTION TREATMENT

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CURRENT COVERAGE OF TOPICS IN ADDICTION MEDICINE

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Editor-in-Chief

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IN THIS ISSUE

Focus of the Month:
Smoking Cessation

Learning Objectives

After reading these articles, you should be able to:

1. Implement strategies to help patients with smoking cessation.
2. Identify the potential benefits and disadvantages of vaping as a replacement for smoking.
3. Summarize some of the findings in the literature regarding addiction treatment.

Using Smoking Cessation Medications in Patients With Mental Illness

Michael Weaver, MD, FASAM. Professor and medical director at the Center for Neurobehavioral Research on Addictions at the University of Texas Medical School.

Dr. Weaver has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

Highlights From This Issue

- Smoking cessation in patients with comorbid mental illness can be particularly challenging, but there are evidence-based strategies that can help.
- Vaping prevalence is on the rise, but not all vaping devices are created equal.
- Quetiapine and olanzapine beat out other antipsychotics for the treatment of methamphetamine-induced psychosis.
- Naltrexone is shown to reduce hospitalization for alcohol-related causes.

As you have likely noted in your practice, smoking is very common among patients with mental illness. Studies have shown that nearly every psychiatric diagnosis is associated with an increased prevalence of smoking, and that there is a growing disparity in smoking rates between patients with mental illness and the general population (Dickerson F et al, *Psychiatr Serv* 2018;69(2):147–153). Smoking cessation rates are lower in patients with mental illness, so getting your patients to quit can be a challenge. But there is good news—studies show not only that nicotine replacement therapy, bupropion, and varenicline work for these patients, but that initial fears of them exacerbating psychiatric illness have been overblown (Evins AE et al, *J Clin Psychopharmacol* 2019;39(2):108–116).

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Q&A With the Expert

A Primer on Vaping: 15 Years On
Sivabalaji Kaliamurthy, MD

Attending psychiatrist, Children's National Medical Hospital, Washington, DC.

Dr. Kaliamurthy has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

CATR: Can you give us your professional background?
Dr. Kaliamurthy: I finished medical school in India followed by an adult psychiatry residency and child psychiatry fellowship at the Institute of Living in Hartford, CT. I then completed an addiction psychiatry fellowship at Yale and am currently an attending psychiatrist at the Children's National Medical Hospital in Washington, DC.
CATR: And vaping has been a particular area of interest for you.
Dr. Kaliamurthy: Yes, my interest got started at an addiction-related conference in 2016. I noticed attendees going outside between talks to use these big devices to blow plumes of smoke. I'm a bit of a technophile, so I

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Using Smoking Cessation Medications in Patients With Mental Illness

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Nicotine replacement therapy

Nicotine replacement therapy (NRT) supplies an alternative source of nicotine without harmful exposure to smoke. NRT comes in a daily long-acting transdermal patch as well as a variety of short-acting formulations. The patch delivers a constant level of nicotine throughout the day, reducing episodes of craving.

The starting dose will depend on the patient's nicotine consumption. As a simple rule of thumb, since a single cigarette delivers about 1 mg of nicotine and there are 20 cigarettes in a pack, patients who smoke a single pack per day (ppd) should start with the 21 mg patch. You can start 2-ppd smokers on two 21 mg patches, and 0.5-ppd smokers should start at 14 mg.

Keep patients on this initial dose for four to six weeks and decrease by 7 mg every four weeks or so until the medication is completely tapered off. Some patients may require longer periods at each dose or may smoke a bit with the patch on. As long as they are smoking less than before, it makes sense to continue treatment as a harm reduction measure. Finally, be sure to have patients remove the patch before bed in order to minimize the possibility of nightmares.

Many patients experience breakthrough cravings while using the patch—if so, they should add one of the short-acting agents. Gum and lozenges are the most common, but there are a variety of formulations that are generally felt to be equivalent (Hajek P et al, *Arch Intern Med* 1999;159(17):2033–2038). One piece of gum delivers 2 or 4 mg of nicotine over 30 minutes.

Combining long- and short-acting formulations, so-called combination NRT (cNRT) is superior to either formulation alone (Lindson N et al, *Cochrane Database Syst Rev* 2019;4(4):CD013308), though light smokers could consider just going with the patch or the gum. cNRT can cause jitteriness, though it usually isn't a problem as long as the patient only takes the short-acting formulation when experiencing cravings. Finally, vaping is not considered NRT, though it is inching closer (www.tinyurl.com/te3ejze; also see Q&A in this issue for more information about vaping).

Varenicline

Varenicline (Chantix) works as a partial agonist at nicotine receptors and, along with cNRT, is the most effective smoking cessation agent. To start, titrate the dose as follows: 0.5 mg daily for days one to three, 0.5 mg twice daily for days four to seven, then 1 mg twice daily for at least 11 more weeks (total of 12 weeks). If your patient has stopped smoking at the end of 12 weeks and is not craving cigarettes, varenicline can be discontinued without tapering. If the patient hasn't achieved abstinence or is still experiencing cravings, varenicline can be continued at 1 mg twice daily for up to a year (Leone FT et al, *Am J Respir Crit Care Med* 2020;202(2):e5–e31).

Typically, patients are instructed to quit smoking on day eight. While this is the most studied approach, the manufacturer insert for Chantix indicates that patients can set a quit date as far out as five weeks after starting the medication or taper smoking over as long as three months (www.tinyurl.com/368va6sr). Even if patients are not ready to set a quit date, experts still recommend starting varenicline since most patients who take it are eventually able to quit (Leone et al, 2020). Although vivid dreams and nightmares aren't very common on varenicline, tell patients about the possibility regardless.

Varenicline's potential psychiatric side effects have been widely covered, but these worries were largely unfounded. A meta-analysis of 39 randomized controlled trials covering 10,761 patients found no difference between varenicline and placebo in rates of depression, suicidal ideation, or aggression (Thomas KH et al, *BMJ* 2015;350:h1109). This makes varenicline safe for patients with stable mental illness and a reasonable first-line treatment, although it is always wise to monitor for possible worsening of symptoms.

Bupropion

Bupropion (Zyban, Wellbutrin) works by inhibiting dopamine uptake in the mesolimbic dopamine system (reward center) of the brain. The manufacturer-recommended smoking cessation dosing is to

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start at 150 mg daily for three days then increase to 150 mg BID (or 300 mg of the XL formulation). It turns out that 150 mg daily is probably just as effective and causes fewer side effects (Hurt RD et al, *N Engl J Med* 1997;337(17):1195–1202). Like varenicline, bupropion can be stopped without tapering.

While superior to placebo, bupropion is not quite as effective as varenicline (Anthenelli RN et al, *Lancet* 2016;387(10037):2507–2520). It is also contraindicated in those with eating disorders or seizure histories because it lowers the seizure threshold. Bupropion may, however, be a particularly good choice for smokers with comorbid depression. It is also safe and effective for patients with schizophrenia (Tsoi DT et al, *Cochrane Database Syst Rev* 2013;2013(2):CD007253) and may have the lowest rate of mood flip among the antidepressants in patients with bipolar disorder who are already on a mood stabilizer (Leverich GS et al, *Am J Psychiatry* 2006;163(2):232–239). Varenicline and bupropion can be safely combined with NRT, which may help some patients—however, the combination might also increase side effects, and we have only mixed data on its efficacy (Baker TB et al, *JAMA* 2021;326(15):1485–1493).

Smoking and the P450 system

Smoking induces a number of P450 enzymes, but the clinically relevant one is CYP1A2, which metabolizes several antidepressants and antipsychotics. Smoking will *decrease* serum levels of medication, while quitting smoking will *increase* medication levels. The relevant antidepressants here are fluvoxamine, duloxetine, mirtazapine, and trazodone (Oliveira P et al, *Ann Gen Psychiatry* 2017;16:17). For antipsychotics, smoking can reduce serum levels of clozapine by 50% and olanzapine by 30% (Tsuda Y et al, *BMJ Open* 2014;4(3):e004216).

There is no standard protocol for how to adjust dosages in smokers vs nonsmokers. As always, dosing should follow the clinical picture—be vigilant for the emergence of side effects in patients who quit smoking and the waning of medication efficacy in patients who start smoking more. For clozapine, we recommend monitoring serum levels as well.

Note that P450 induction is due to polycyclic aromatic hydrocarbons (PAHs) in smoke, not nicotine itself. Therefore, NRT and other smokeless forms of tobacco do not induce medication metabolism. Aerosols from vaping can contain PAHs, though typically at lower amounts than cigarettes (Traboulsi H et al, *Int J Mol Sci* 2020;21(10):3495), so vaping's effects on the P450 system can be unpredictable.

CATR VERDICT: NRT, varenicline, and bupropion are safe and effective cessation agents for smokers with stable mental illness. For most patients, we recommend starting with cNRT or varenicline, since these are both more effective than bupropion. As always, consider comorbid conditions and potential medication interactions when choosing an agent.

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Expert Interview

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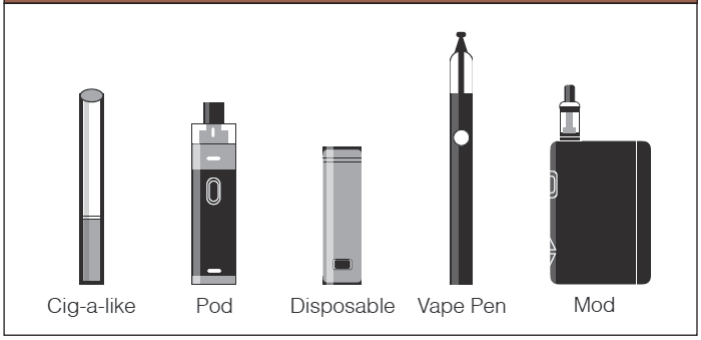
started to learn about them on my own. During my child fellowship, I saw a huge prevalence of vaping among adolescents. Kids being admitted to the hospital would go into nicotine withdrawal, which used to be uncommon. Then in my work at an opioid treatment program, many of my adult patients were switching from combustible cigarettes to vapes.

CATR: What should providers know in terms of how these devices function?

Dr. Kaliamurthy: It's helpful to know the basics so you can understand how patients use and modify these devices, and what some consequences might be. There are a wide variety of products, but all have the same basic components: 1) a battery, which can be rechargeable or disposable; 2) an atomizer, or heating coil, that vaporizes the nicotine; 3) the nicotine source or "e-juice"; and 4) aerosol, the product emitted by the device and inhaled into the lungs. You'll hear the words "cartridge" or "pod" as well, which refers to a self-contained unit that may have the liquid and the atomizer together or is sometimes just an e-juice container.

Examples of Vapes



CATR: And how are these components combined to make different devices?

Dr. Kaliamurthy: For research and clinical purposes, we can classify these devices as "open system" and "closed system." Closed-system products are self-contained units in which the manufacturer predetermines every aspect of the device: battery, power, atomizer, and e-juice. The first closed-system devices were available as early as 2007. They look like traditional cigarettes and are sometimes called "cig-a-likes." There are other more recent closed-system devices that are pod-based; some look like pen drives and others are simple small disposable devices. The open-system devices offer a lot more flexibility to the users. They can change the battery settings, resistance on the atomizer coils, e-juice concentrations, etc. These devices come in different shapes and sizes as well. Devices called "vape pens" look like cylinders with a few interchangeable parts. The more common open-system devices are entirely customizable. These are called "mods" (which stands for modifications) and look like big tanks (see figure above).

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Expert Interview

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CATR: Open-system devices must make it tough to know exactly what a patient is using.

Dr. Kaliamurthy: Yes. New products come out nearly every day, many from small companies, but big tobacco is changing the landscape even further. And some of these companies are clearly targeting children by making devices that are easily concealable. For instance, there was a company creating hoodies where the string around the hood could be put in the mouth and had an e-cigarette device attached! Some flavorings are also clearly being marketed toward the younger generation, which the FDA has begun clamping down on. There are flavors with names like "unicorn puke" or "hulk tears." You hear a name like that and think, "Why would an adult buy a product called unicorn puke?"

CATR: And what should we know about the e-juice?

Dr. Kaliamurthy: E-juice predominantly contains either propylene glycol or vegetable glycerin, as well as nicotine. In closed-system devices, the manufacturer determines all the e-juice components. In open-system devices, users can assemble their own e-juice. They can buy the vegetable glycerin or propylene glycol, nicotine concentrate, flavorants, and mix them together however they want. The nicotine itself is always derived from tobacco but is available in two forms: free-base nicotine (the naturally occurring, nondissolvable form of nicotine) or soluble nicotine salts, which companies began developing about five years ago. Studies showed that, compared to a regular cigarette, salts result in a higher blood-nicotine concentration that then decreases at a faster rate (www.classaction.org/media/colgate-et-al-v-juul-labs-inc-et-al.pdf, Page 19, Figure 4, Juul patent filing). The result is a rapid upward spike in blood nicotine followed by a rapid decline. And we know there is more addictive potential in substances that cause rapid euphoric effects, then leave to quickly create a negative affective state.

"I never recommend vaping as a first-line treatment to help patients quit combustible tobacco. If the goal is to quit smoking altogether, I tell them about evidence-based treatments and recommend that they try those first. But I also tell them at the end of the day, it is their choice, and if they decide to vape, I provide psychoeducation."

Sivabalaji Kaliamurthy, MD

CATR: You mentioned flavorants.

Dr. Kaliamurthy: Yes. There is a multitude of flavors out there, and new ones come out all the time. Early studies show that added flavors increase dopamine release in the nucleus accumbens (Kroemer NB et al, *Eur Neuropsychopharmacol* 2018;28(10):1089–1102). The sweeter the flavor, the bigger that dopaminergic response, which we hypothesize means higher addictive potential. And each flavor confers its own risk in terms of the final aerosol that's produced. We have studies showing that cinnamon and menthol in particular can be cytotoxic to stem cells (Lee WH et al, *J Am Coll Cardiol* 2019;73(21):2722–2737). With flavor compositions constantly changing, it can be hard to offer a sound clinical opinion to patients about specific flavors.

CATR: Can you tell us some of the ways in which open-system devices are modified?

Dr. Kaliamurthy: A common one is called "dripping," in which e-juice is dropped directly onto an exposed heating coil to produce vapor that is then inhaled. Coils can be removed from devices or purchased separately as an "RDA," which stands for rebuildable dripping atomizer. Anecdotally, patients tell me that dripping produces a more flavorful vapor, plus more euphoric effects if the liquid contains cannabis (in which case the term "dabbing" is often used instead of dripping). Modifications to increase smoke volume are popular among the "smoke trick" community in which people blow smoke into unusual shapes. Atomizers are electrical heating elements, so people disassemble devices to increase the electrical resistance, which produces more heat and vapor. But these higher temperatures result in aerosol containing metals from the heating element itself. The higher temperature changes the chemical composition of the aerosol, potentially producing toxic combustion products.

CATR: Do you ever recommend vaping to quit smoking combustible tobacco?

Dr. Kaliamurthy: Never as a first-line treatment. It comes down to the patient's goals: Do they want to quit nicotine completely or just quit combustible cigarettes? If the goal is to quit smoking altogether, I tell them about evidence-based treatments and recommend that they try those first, because they have the most evidence. But I also tell them at the end of the day, it is their choice, and if they decide to vape, I provide psychoeducation.

CATR: What sort of information do you give your patients?

Dr. Kaliamurthy: I advise that they stick to simple devices from established manufacturers and not to modify them, which can lead to unknown harms. I also educate patients about nicotine from cigarettes versus vaping. For example, one cigarette contains about 10 mg of nicotine, so a pack of 20 has 200 mg. Patients may think that a 50 mg pod is cutting down compared to that pack of cigarettes—but that's not necessarily accurate. Cigarettes have a nicotine bioavailability of about 10%, so only 20 mg of nicotine per pack ends up in the bloodstream (Benowitz NL et al, *Handb Exp Pharmacol* 2009;(192):29–60). Depending on the form of nicotine in the e-juice, much more than 20 mg of nicotine per pod may find its way into the patient's bloodstream. So, I recommend to always start at a lower dose and only increase if they feel cravings. I've seen patients switch from cigarettes to vaping in order to quit smoking and go back to cigarettes for one reason or another, and end up smoking more cigarettes than ever before because they now need more nicotine.

CATR: What do you say to patients who are attracted to vaping because it's trendy, as opposed to traditional cigarette smoking?

Dr. Kaliamurthy: I warn patients against "artisanal" vaping, especially the young adults. By artisanal I mean the burgeoning subculture that treats vaping as a hobby, with fancy expensive accessories. It creates a gamification of smoking beyond a simple nicotine delivery system. Not only can it get expensive, but it can lead to high levels of nicotine consumption as well.

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Expert Interview

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CATR: Are there immediate dangers of vaping that patients need to be aware of?

Dr. Kaliamurthy: One is nicotine toxicity, which can happen to inexperienced patients using these high-nicotine products. Initially, nicotine toxicity has stimulatory effects like tachycardia, hypertension, anxiety, GI distress, and can even cause seizures. After the stimulatory effects, patients experience sedation, hypotension, and bradycardia. In severe cases, this later phase can lead to neuromuscular blockade and coma. This level of toxicity is rare from vaping, but can certainly happen if kids get into e-juice and drink it, so safe storage is very important. Treatment is mostly supportive, and patients really need to be treated in a hospital setting. Another danger is that there are cases of batteries catching fire or bursting, causing facial injuries (Jones CD et al, *Burns* 2019;45(4):763–771). Batteries are more likely to malfunction if they are charged often or overnight, or if they overheat. Patients should stop using the devices if they become hot to the touch and always charge them according to instructions. We don't know for sure, but it's probably more likely for batteries to malfunction in open-system modified devices than closed-system devices manufactured by large companies.

CATR: Is there good evidence that vaping products can help patients quit smoking?

Dr. Kaliamurthy: A little. Most evidence comes from the UK's National Health Service. They collected data and published it in a high-profile study that generated a lot of interest (Hajek P et al, *N Engl J Med* 2019;380(7):629–637). The exciting finding was that when patients switched from combustible cigarettes to vaping, at the end of one year most patients had stopped using combustible cigarettes altogether. That finding got lots of fanfare; however, most of the patients were still vaping at the end of the study. Patients did get off combustible tobacco, but they were still using nicotine, possibly in equal or higher doses than before. So, it's difficult to use this study to say whether or not vaping should be recommended as a way to quit smoking. And, unlike the US, the UK has a highly regulated vaping product environment. This raises the question of generalizability of this study outside of the UK, especially in the US where there is not nearly the same level of regulation.

CATR: How do you view switching from cigarettes to vaping from the standpoint of harm reduction?

Dr. Kaliamurthy: The US system is very unregulated, so it's difficult to know long-term risks. We have known about the harms of tobacco for decades, so with vaping we are still very much catching up. There is evidence that, at least over the short to medium term, the harms from vaping are less than that of combustible tobacco products (Kmietowicz Z, *BMJ* 2018;363:k5429). And anecdotally, patients tell me that they are able to breathe better, so subjectively there are improvements in physical health, but that doesn't mean there isn't any harm.

CATR: You mentioned THC and cannabis products being vaped. Are there differences between vaping cannabis and vaping nicotine?

Dr. Kaliamurthy: Not a lot. Any device used to vape nicotine can be used to vape cannabis. These products are available in both medical and recreational dispensaries, as well as on the streets.

CATR: What should clinicians pay attention to if their patients are vaping cannabis?

Dr. Kaliamurthy: I have noticed vaping cannabis is especially popular in adolescents because it is so easily concealable. The paraphernalia is easy to hide and the smoke it emits can be low in volume and less odorous, making it easier to vape THC without facing consequences at school and at home. Another concern is the move toward using cannabis concentrates, which can have THC concentrations over 80%. Some people might seek out high-concentrate products believing that it will result in the use of less cannabis overall. However, a recent study showed that THC blood levels were significantly higher in patients who consumed cannabis by vaping concentrates versus smoking (Bidwell LC et al, *JAMA Psychiatry* 2020;77(8):787–796).

CATR: Vaping THC has been associated with serious lung injury.

Dr. Kaliamurthy: Yes, E-cigarette, or Vaping, product use Associated Lung Injury (EVALI) was a big concern. We saw a rapid uptick in patients presenting with lung injury in August 2019, it peaked in September, and there was a downward trend after that. These patients' injuries had no underlying cause except a recent history of vaping. There was no single ingredient identified as causing EVALI, though in the majority of cases people had used a vape for THC containing vitamin E acetate in the cartridge and bought on the streets, not from a dispensary. It is possible that EVALI is associated with a particular type of device sold on the street under the name "dank vapes," but this is still unclear. The CDC tracked approximately 3,000 total cases with 68 deaths as of February 2020, but we don't have updated data since then (www.tinyurl.com/zmcevyhu). Geography plays a role too; most cases were in Texas and Illinois, followed by California and New York. Since COVID, however, we really haven't been doing a good job of tracking these cases.

CATR: With the limited information available, what advice would you give to a patient vaping THC?

Dr. Kaliamurthy: The CDC says that the only way to definitively avoid vaping-associated lung injury is to not use these devices at all. But if patients are going to vape THC, I recommend that they not use products obtained off the street. I always encourage patients to avoid sources that they don't know and to get devices from dispensaries if possible.

CATR: Do you have recommendations on how providers might keep up with this rapidly evolving field?

Dr. Kaliamurthy: There's a lot of information on the FDA and CDC websites. The American Academy of Child & Adolescent Psychiatry and American Academy of Pediatrics have good informational websites as well (www.tinyurl.com/ne6pdjvm; www.tinyurl.com/mua9r3ay). Unfortunately, there aren't many established resources.

CATR: Thank you for your time, Dr. Kaliamurthy.

Research Updates

PSYCHOSIS

Antipsychotics for Methamphetamine Psychosis

Sanya Virani, MD. Dr. Virani has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

REVIEW OF: Srisurapanont M et al, *Drug Alcohol Depend* 2021;219:108467

STUDY TYPE: Systematic review and network meta-analysis

Methamphetamine psychosis (MAP) is difficult to treat, and there are only so many antipsychotics in our repertoire. Randomized clinical trials (RCTs) to manage MAP are few and far between, and the literature thus far has indicated that no antipsychotic is superior to any other. What is a clinician to do?

In this study, the authors conducted a network meta-analysis of six RCTs with a total of 395 participants. Effectively, they created a head-to-head comparison of six antipsychotics for MAP [risperidone (four trials, n = 129); haloperidol (three trials, n = 93); aripiprazole (two trials, n = 48); paliperidone extended release (ER), quetiapine, and olanzapine (one trial each for a total n = 125)] and examined each medication for their ability to reduce psychotic symptoms.

The evidence in each trial was judged to be of low or very low quality, and none of the trials individually found significant differences between medications. However, when data from all the trials were pooled, the authors were able to establish somewhat of a hierarchy. Comparisons between medications were reported as standardized mean difference, which is a way of standardizing outcomes across studies that measure similar outcomes in various ways. Of all the possible head-to-head medication comparisons, a few significant differences were found. Quetiapine (300 mg/day) and olanzapine (20 mg/day) were the major winners and were superior to risperidone (4–8 mg/day) and aripiprazole (15 mg/day) for psychotic symptoms. Aripiprazole was the big loser—it was inferior to haloperidol (6–20 mg/day) and paliperidone ER (9 mg/day), as well as quetiapine and olanzapine.

The authors acknowledge that only six RCTs met inclusion criteria, and that the total n did not allow for robust conclusions to be drawn in all drug comparisons. Other shortcomings included lack of placebo control and overall study heterogeneity. The authors also point out that the D2 receptor blockade caused by these medications in the setting of methamphetamine withdrawal could heighten anhedonia and theoretically increase risk of return to drug use. Hyperphagia and hypersomnia resulting from methamphetamine withdrawal might compound the side effects from olanzapine and quetiapine. Given that MAP is often self-limiting, the recommendation is to taper off the antipsychotic after resolution of psychotic symptoms, typically a maximum of four weeks after methamphetamine use.

CATR'S TAKE

We recommend considering quetiapine and olanzapine first when treating patients for MAP, and reserving aripiprazole as a third-line treatment only. Be aware of side effect burden and taper these medications off as soon as possible.

AUD

Meds for Alcohol Use Disorders

Mikveh Warshaw, NP. Ms. Warshaw has disclosed no relevant financial or other interests in any commercial companies pertaining to this educational activity.

REVIEW OF: Heikkinen M et al, *Addiction* 2021;116(8):1990–1998

STUDY TYPE: Cohort study

In the US, only 9% of patients diagnosed with alcohol use disorder (AUD) are prescribed AUD medication (Kranzler HR and Soyka M, *JAMA* 2018;320(8):815–824). A Swedish study provides evidence that further illuminates the potential harms from this lack of treatment. The study compares the real-world impact of four medications, three of which—disulfiram, naltrexone, and acamprosate—are FDA approved for AUD.

Researchers used national databases in Sweden to identify 125,556 people (62.5% men) ages 16–64 with a diagnosis of AUD and followed them prospectively for 10 years. They excluded individuals with schizophrenia or bipolar disorder. The researchers recorded whether participants picked up prescriptions for naltrexone, disulfiram, acamprosate, or nalmefene (an opioid antagonist similar to naltrexone that is not available in the US). The primary outcome researchers tracked was hospitalization due to AUD.

Data suggested that naltrexone reduced rates of hospitalization, both as a monotherapy and when combined with disulfiram or acamprosate. For hospitalizations due to alcohol-related causes, naltrexone monotherapy decreased rates by 11%, naltrexone + acamprosate decreased rates by 26%, and naltrexone + disulfiram decreased rates by 24%. The results were nearly identical for all-cause hospitalization.

At first glance, it may seem that naltrexone in combination with another medication is the best option. But the authors point out that even though combinations outperformed naltrexone monotherapy, patients who receive combination medication may also be more likely to be receiving specialist case, and that the lower hospitalization rates might result from the specialist care rather than the medications themselves.

Surprisingly, acamprosate was associated with increased risk of hospitalization. The authors speculate that acamprosate's poor efficacy may partially be explained by the fact that it requires dosing three times daily, and as a result we can surmise that adherence was poorer in the acamprosate

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CE/CME Post-Test

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These questions are intended as a study guide. Please complete the test online at www.carlataddictiontreatment.com. Learning objectives are listed on page 1.

1. According to Dr. Kaliamurthy, which of the following about vaping and/or combustible cigarette use is true (LO #2)?

   [ ] a. Added flavors in e-juice yield lower dopamine release in the nucleus accumbens compared to cigarettes

   [ ] b. Cigarettes have a nicotine bioavailability of about 45%

   [ ] c. Over the short to medium term, the harms from vaping are less than that of cigarettes

   [ ] d. The sweetness of an e-juice flavor has no impact on the magnitude of dopamine release

2. Compared to nonsmokers, smokers have significantly reduced serum levels of which medications (LO #1)?

   [ ] a. Fluvoxamine, mirtazapine, clozapine, and olanzapine

   [ ] b. Sertraline, escitalopram, fluoxetine, and haloperidol

   [ ] c. Citalopram, quetiapine, lurasidone, and aripiprazole

   [ ] d. Phenelzine, nortriptyline, imipramine, pimavanserin, and brexpiprazole

3. According to a 2021 study of methamphetamine psychosis, which two antipsychotics were superior to the others for improving psychotic symptoms (LO #3)?

   [ ] a. Haloperidol and aripiprazole

   [ ] b. Risperidone and olanzapine

   [ ] c. Aripiprazole and paliperidone ER

   [ ] d. Quetiapine and olanzapine

4. Compared to regular cigarette use, how does the use of nicotine salts affect blood-nicotine concentrations (LO #2)?

   [ ] a. Nicotine salts yield lower blood-nicotine concentrations that are sustained longer

   [ ] b. Nicotine salts yield blood-nicotine concentrations equal to that of cigarettes

   [ ] c. Nicotine salts yield higher blood-nicotine concentrations that decrease at a faster rate

   [ ] d. Nicotine salts yield higher blood-nicotine concentrations that are sustained longer

5. In a 2015 study of smoking cessation, what was concluded about the rates of side effects associated with varenicline compared to placebo (LO #1)?

   [ ] a. Varenicline increased rates of depression

   [ ] b. Varenicline did not differ from placebo in rates of depression, suicidal ideation, or aggression

   [ ] c. Varenicline decreased rates of aggression

   [ ] d. Varenicline increased rates of suicidal ideation

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Research Updates

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arm than for other medications. But it's not clear why this would be associated with worse outcomes than no medication at all. Disulfiram and nalmefene monotherapy were not associated with significantly different rates of hospitalization.

Finally, researchers found that benzodiazepines were associated with both an 18% increased hospitalization rate due to AUD and an 11% higher mortality rate. While this result is not unexpected, it does emphasize the dangers of prescribing benzos to patients who are actively drinking or diagnosed with AUD.

CATR'S TAKE

While this study does not investigate the nuances of treatment planning, it does support that naltrexone, both alone and in combination with disulfiram or acamprosate, is one of the most promising medications for AUD. It also emphasizes that we should exercise great caution when prescribing benzodiazepines for these patients.

❖ ❖ ❖

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