Opioid-induced Hallucinations: A Review of the Literature, Pathophysiology, Diagnosis, and Treatment

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Abstract

Despite their association with multiple adverse effects, opioid prescription continues to increase. Opioid-induced hallucination is an uncommon yet significant adverse effect of opioid treatment. The practitioner may encounter patient reluctance to volunteer the occurrence of this phenomenon because of fears of being judged mentally unsound. The majority of the literature concerning opioid-induced hallucinations arises from treatment during end-of-life care and cancer pain. Because the rate of opioid prescriptions continues to increase in the population, the rate of opioid-associated hallucinations may also conceivably increase. With a forecasted increase in the patient-to-physician ratio, opioid therapy is predicted to be provided by practitioners of varying backgrounds and medical specialties. Hence, knowledge of the pharmacology and potential adverse effects of these agents is required. This review seeks to increase awareness of this potential complication through a discussion of the literature, potential mechanisms of action, diagnosis, and treatment strategies. (Anesth Analg 2016;123:836–43)

Opioid prescription for both chronic cancer and non-cancer pain has been steadily increasing over the past few decades.\textsuperscript{1,2} Although the use of opioid therapy for noncancer pain remains controversial, it is utilized in the treatment for a multitude of conditions. With a forecasted increase in the patient-to-physician ratio, opioid therapy is predicted to be provided by practitioners of varying backgrounds and medical specialties. Hence, knowledge of the pharmacology and potential adverse effects of these drugs is required. Treatment of pain conditions is at the forefront of public debate. The economic loss of pain conditions to the

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United States in 2007 was estimated to be a total of $55.7 billion with workplace costs accounting for $25.6 billion (46%) and health care costs accounting for $25.0 billion (45%).

Opioid therapy may be associated with adverse effects. At the extreme, 16,235 of 22,235 (71.3%) pharmaceutical over-dose deaths in 2013 involved opioid analgesics. The most common adverse effects are gastrointestinal and central nervous system-related. Up to 80% of patients treated with opioids experience a minimum of 1 adverse event. Common adverse events noted across multiple studies include xerostomia (42%), constipation (20%–41%), diaphoresis (34%), weight gain (29%), somnolence (14%–29%), sleep disorders (25%), memory deficits (24%), decreased appetite (23%), nausea (17%–33%), concentration deficits (19%), fatigue (19%), sexual dysfunction (18%), dizziness (12%–22%), emesis (11%–15%), pruritus/dry skin (10%), and urinary retention (4%–18%). Other adverse effects whose incidences are more difficult to quantify include hyperalgesia, muscle rigidity, myoclonus, immunologic and hormonal dysfunction, physical dependence, tolerance, and addiction.

Opioid-induced hallucination is an uncommon yet significant adverse effect of opioid treatment, frequently attributed to underlying psychiatric disease or personality disorder rather than a direct neurobiologic effect of opioids. This phenomenon is likely underreported because of the tolerable intensity of many hallucinations and fear associated with the stigma of being labeled as psychologically unstable. This review seeks to increase awareness of this potential complication through a discussion of the literature, potential mechanisms of action, diagnosis, and treatment strategies.

**METHODS**

A search was conducted using MEDLINE/PubMed, MeSH, Cochrane Review, and Google Scholar. The search words included “opioid” and “hallucinations” combined with “neurotoxic,” “delirium,” “neuroexcitatory,” “adverse effects,” “hallucinosis,” “fentanyl,” “morphine,” “pentazocine,” “hydromorphone,” “oxycodone,” “naloxone,” “methadone,” “tramadol,” “remifentanil,” “sufentanil,” “alfentanil,” “buprenorphine,” or “meperidine.” No language restrictions or date limits were applied. Although a sweeping number of case reports were identified, the paucity of prospective studies, despite the broad search criteria applied, limits the definition of conclusive recommendations regarding diagnostic and treatment options. Articles were included if they related hallucinations to opioid treatments. The reference lists of the articles selected for review were also scrutinized to identify the additional studies not found using the original search terms.

**RESULTS**

One thousand two hundred fifty-three articles were identified after the database search using the aforementioned methods. After a manual review of their abstracts, most articles were rejected because they did not identify hallucinations with concurrent opioid administration. Fifty-six articles met search criteria for hallucination development linked to opioid treatment.
Review of the Literature

The word “hallucination” has its origin in the Latin root *hallucinari* or *allucinari*, which translates to “wander in mind.” The following is the *Diagnostic and Statistical Manual of Mental Disorders*’ definition of a hallucination: “a perception like experience with the clarity and impact of a true perception but without the external stimulation of the relevant sensory organ.”

Numerous reports exist of hallucinations attributed to opioids, which have been typically described as auditory, visual, or rarely tactile hallucinations. The majority of the literature arises from treatment during end-of-life care and cancer pain. Many of these reports involve high-dose opioid regimens, both planned and accidental. They are often reported in patients with comorbidities that may predispose to hallucinations, yet they are also seen in patients without any underlying confounders. Most reports have cited morphine as the causative agent, but there is also a multitude of reports implicating fentanyl, methadone, tramadol, hydromorphone, buprenorphine, pentazocine, and oxycodone. Conversely, there have been reports of opioid-induced hallucinations, which are reversed by rotation to oxycodone.

The first reports of opioid-induced hallucinations in the literature were associated with the use of pentazocine, a mixed agonist/antagonist opioid belonging to the synthetic benzomorphan class. A report of 57 cases linked to acute pentazocine overdose collected over 10 years included 3 patients with neuroexcitatory symptoms, 2 of whom reported visual hallucinations, delusions, and paranoid ideation. Earlier studies had attributed these symptoms to the agonist action of pentazocine on sigma opioid receptors. Pentazocine-associated hallucinations are now reported much less frequently reflective of its diminished use in favor of other opioids.

Morphine remains the opioid most commonly associated with opioid-induced hallucinations. This may be attributed to its long history of use and widespread availability. The association between morphine and hallucinations was reported on multiple occasions in *The Lancet* several decades ago. A study conducted over 14 months by Caraceni et al involving 161 patients with cancer-related chronic pain who were administered opioids for at least 1 week reported that 9 of these patients developed hallucinations with morphine administration, 8 of which were categorized as primarily visual. The accumulation of morphine metabolites, particularly morphine-3-glucoronide, has been linked to the development of neurologic phenomena. Morphine has also been linked to the development of musical (auditory) hallucinations, although this occurs less frequently than visual symptoms.

Bruera et al reported 4 cases of patients developing organic hallucinosis of a total 55 patients receiving chronic opioids for cancer pain. He defined the term organic hallucinosis to describe the development of hallucinations in individuals without pre-existing cognitive impairment. All 4 of these patients were receiving hydromorphone and described their hallucinations as visual. These hallucinations subsequently resolved with opioid rotation to diamorphine or morphine and concomitant administration of haloperidol.
A single report appears to be the first describing oxycodone-induced musical hallucinations. There is also a single report of oxycodone-induced visual hallucinations in the context of serotonin syndrome associated with that opioid and acute dose escalation. Notably, most of the literature involving oxycodone and hallucinations involves its use in opioid rotation as a treatment for opioid-induced hallucinations.

Hallucinations with fentanyl use have been reported to occur at a rate as high as 6% (5 of 82 patients) during its use in patient-controlled intravenous analgesia for postoperative acute pain management. Case reports link fentanyl and hallucinations with the high doses used in the context of cancer pain management. A patient with gastric adenocarcinoma described the development of visual hallucinations after accidental administration of 5000 μg fentanyl instead of a scheduled 100-μg dose. Because the hallucinations ceased immediately after administration of 0.1 mg naloxone, it was postulated that these were caused by fentanyl and that opioid toxicity may result in neuroexcitation as opposed to its more traditionally noted depressant effects. Fentanyl-induced hallucinations have been reported within a few days of initiation when this drug has been administered through a transdermal patch. This increased incidence was hypothesized to occur because of the variability in transdermal absorption, which can lead to increased peak plasma concentrations. Norfentanyl, a metabolite of fentanyl, has been noted to share structural similarities with normeperidine and may cause neuroexcitation through a similar mechanism as that known to occur with normeperidine accumulation.

The frequency of hallucinations with methadone use appears to be rare with 1 retrospective review finding an incidence of 4 in 3000 patients on a chronic methadone maintenance program. There also exist only 2 case reports associating methadone with hallucinations with 1 seen in the pediatric literature and the other noted in the management of an adult with gastric carcinoma. Although morphine metabolism relies on glucuronidation, methadone is metabolized by the type I cytochrome P450 group of enzymes. Thus, toxicity may be related to polypharmacy affecting these same enzymes. The mechanism of methadone-induced hallucinations may also differ because, in addition to its affinity for opioid receptors, it is also an N-methyl-d-aspartate antagonist and inhibitor of monoamine reuptake.

A study using the French Pharmacovigilance Database, which recorded 469,181 reports of adverse effects between 1985 and 2013, found that 482 patients reported hallucinations of the total 12,184 patients who had received opioids. Although the duration of opioid therapy was not standardized, these data provide suggestion to the overall incidence of opioid-induced hallucinations. Tramadol was involved most often with an incidence of 240, an odds ratio of 6.3, and 95% confidence interval of 5.5 to 7.2, whereas morphine was next with an incidence of 143, an odds ratio of 4.4, and 95% confidence interval of 3.7 to 5.2. The increased incidence associated with tramadol may occur because along with its opioid-agonist properties, it also inhibits reuptake of norepinephrine and serotonin. In an earlier report of 2 cases, hallucinations occurring 6 days after flu immunization and chronic tramadol administration were hypothesized to occur through antigen-specific production of interferon-γ by lymphocytes that interfered with CYP3A4 activity and expression.
Musical hallucinations have also been reported shortly after starting tramadol when it was used as a part of a palliative treatment regimen. 21

This review did not reveal any reports that attribute hallucinations to the use of remifentanil, sufentanil, or alfentanil. Plausible explanations for this lack of association include their preferential agonism of the κ and δ opioid receptors, often short duration of treatment, short elimination half-lives, and the frequent concurrent use of other sedatives and hypnotics, which may mask hallucinations.

Buprenorphine is frequently chosen as a therapeutic agent because of its low side effect profile and the ceiling on its depressant action because it functions as a mixed opioid agonist/antagonist. Initial case reports described the development of visual hallucinations within 2 days after epidural administration of buprenorphine after spine surgery in a series of 5 patients. 44 Another case report described near fatal auditory hallucinations because of suicidal ideation after receiving a single dose of sublingual buprenorphine. 45 Subsequent case reports have additionally reported tactile, visual, and auditory hallucinations with chronic intravenous administration. 46, 47 Neurotoxicity appears to be related to the accumulation of buprenorphine metabolites, N-desalkyl buprenorphine and buprenorphine-3-O-glucuronide. 47 Another study linked hallucinations to a more direct excitatory or disinhibiting effect than other opioids on the limbic and extrapyramidal systems. 44

Normeperidine, an active meperidine metabolite, has significant effects, which include confusion, anxiety, nervousness, seizures, and hallucinations. 48 A retrospective study examining 355 records identified a 2% incidence of neurotoxicity after approximately 2 days of treatment, which directly correlated with plasma normeperidine levels. 49 Meperidine is primarily metabolized through N-demethylation by the hepatic cytochrome P450 system to produce normeperidine. 50 Subsequently, elimination of normeperidine occurs by both the liver and the kidneys. 51 Normeperidine accumulation can occur as a result of enzyme-inducing drugs, hepatic failure, or renal failure. 50–52 Some authors have suggested that the anticholinergic properties of meperidine and normeperidine are causative for hallucinations, because concomitant administration of cimetidine exacerbates neurotoxicity, whereas physostigmine is alleviating. 53

Pathophysiology

Many hypotheses have been advanced to explain the etiology of opioid-induced hallucinations. One common feature of these hypotheses involves opioid-induced dopamine dysregulation. 54–58 There is neuropsychiatric literature similarly associating schizophrenia with dopamine dysregulation. In particular, the mesolimbic dopaminergic system has been implicated in many of the central side effects. 56 Along with hallucinations, other central adverse reactions include drowsiness, confusion, and nightmares. 59 This system projects from the ventral tegmental area (VTA) to the nucleus accumbens (NAc). 58 An overactivation of the dopaminergic pathways is thought to result in auditory and visual hallucinations. Opioid metabolites may have similar activity to the parent compound and, thus, enhance toxicity with accumulation. 60 It is also possible that metabolites act through alternate receptors with alternate effects, as noted in the example of morphine metabolites having
differential affinity for μ receptor subtypes and nonopiate receptors. Differing mechanisms of action may make some metabolites more likely to produce hallucinations than their parent compounds.

A previous study involving Sprague-Dawley rats demonstrated a positive dose-related correlation between opioids, specifically heroin, and dopamine concentration in the NAc. Conflicting reports have noted that opioid agonists potentiate this pathway, whereas others have found that agonist activity decreases dopamine release. However, the reported site of action differs, because κ-opioid agonist action at the NAc decreases dopamine release, whereas μ-opioid agonist action at the VTA increases dopamine release from the NAc. The release of dopamine by μ-receptor agonists has been postulated to occur through an indirect mechanism that involves hyperpolarization and subsequent inhibition of interneurons that normally provide γ-aminobutyric acid-mediated synaptic input to the dopamine cells. Thus, opioids potentiate disinhibition of dopamine cells. A previous study similarly demonstrated that μ-receptor binding in the VTA was not altered by destruction of dopamine-containing cells.

There is no definitive answer as to whether metabolites or the parent compounds are more likely to produce hallucinations, and this may vary with the properties of each particular opioid. Although some metabolites act through different receptors than their parent compound, others exhibit similar agonist properties at the same receptors. Examples of well-studied metabolites exhibiting neurotoxicity include morphine-3-glucuronide, normeperidine, and hydromorphone-3-glucuronide. It remains to be determined whether the agonism of a particular subset of opioid receptors is more likely to prompt the development of hallucinations.

The dopamine neurons of the midbrain, including the VTA, have been linked to activity in the prefrontal cortex with a possible role for cognitive prefrontal cortex inhibition of dopamine release in the NAc. The NAc also receives ascending sensory input through multiple pathways including the hippocampus, amygdala, and hypothalamus. A phasic dopamine system has been linked to reward-based learning and the assignment of salience to sensory stimuli. Thus, it has been surmised that prefrontal cognitive function can alter salience to sensory stimuli by inhibiting dopamine release in the NAc. The altered salience of sensory stimuli can contribute to the development of hallucinations whereby internal representations are perceived as reality.

Diagnosis

To make a diagnosis of opioid-induced hallucinations, it is first necessary to rule out other possible etiologies. These include psychiatric disease, substance abuse, metabolic derangements, electrolyte disorders, infection, brain neoplasm, neurologic disease, ophthalmologic disease, inner or middle ear disease, toxins, vascular insult, endocrinopathies, and substance or psychiatric medication withdrawal. A thorough history and clinical examination can help differentiate opioid-induced hallucinations from other etiologies. Standard laboratory analysis may eliminate the most common electrolyte
disorders and impaired metabolism because of hepatic or renal insufficiency. Impaired metabolism because of altered cytochrome P450 enzyme function may be suspected clinically with the examination of concurrently administered medications, although genetic variation can also account for differences in function.\textsuperscript{76,77} Numerous other genetic variations outside of the scope of this article can also alter opioid metabolism or action.\textsuperscript{59,78} Emergency situations may involve cerebrovascular accidents, neuroinfectious processes including meningitis and encephalitis, or suicidal ideations.\textsuperscript{79,80} These conditions require immediate evaluation and treatment.

The duration of hallucinations appears to be highly variable and, without treatment, it is likely to depend on the elimination properties of each particular opioid. Situations in which metabolism or excretion of either the parent compound or neurotoxic metabolites is impaired may lengthen the period of neurotoxic symptoms.\textsuperscript{81} Hallucinations are likely to be continuous until serum concentrations decrease; however, intermittent hallucinations have been observed with repeat opioid dosing after hallucination abatement or with the use of short-duration opioid antagonists.\textsuperscript{34,38}

A challenging circumstance involves concomitant neuropsychiatric disease. The prevalence of hallucinations in Parkinson disease has been reported to be as high as 39.8\% when all types of hallucinations are included.\textsuperscript{15} Initiation or dose escalation of dopamine agonists used in the treatment of Parkinson disease is particularly notable for its association with hallucinations.\textsuperscript{82,83} In schizophrenia, auditory hallucinations are most common with a prevalence of 74.8\% followed by visual hallucinations (39.1\%), cenesthetic hallucinations (28.9\%), and tactile, olfactory, and gustatory hallucinations (1.3\%–6.6\%).\textsuperscript{84} Hallucinations have also been noted to occur with numerous other psychiatric illnesses. Despite these numbers, a patient with pre-existing psychiatric disease can develop hallucinations primarily attributable to opioids; furthermore, this population can be particularly susceptible. This may especially be the case in patients whose psychiatric disease had been stable before opioid dosing. It is not uncommon for a diagnosis of opioid-induced hallucinations to be discarded in favor of an exacerbation of a psychiatric disease resulting in the subsequent adjustment of psychotropic medications. In addition, cessation of antipsychotics or alteration of psychiatric medications should be suspected if the timing coincides with the development of hallucinations.

Although there are factors that increase the likelihood of this diagnosis, treatment is often based on clinical judgment rather than any specific test result. Similar clinical discretion is seen in the diagnosis of numerous other conditions such as in the treatment of anaphylaxis before receiving confirmatory serum tryptase levels.\textsuperscript{85} Exclusion of the aforementioned differential diagnoses, recent opioid administration, rapid opioid dose escalation, or eradication of hallucinations with opioid antagonists are all criteria that support the diagnosis of opioid-induced hallucinations.

Treatment

If a diagnosis of opioid-induced hallucinations is made, there are a number of potential treatment options that may be considered. The simplest perhaps is to consider discontinuing opioid therapy if practical. However, this solution may not be possible in many situations.
Opioid rotation or dose reduction can serve as an alternative to complete discontinuation. High-dose opioids administered intentionally or unintentionally have been reported to more likely result in neurotoxic effects including hallucinations.\textsuperscript{18,86,87} A dose reduction of 10\% to 50\% or increase in the frequency of administration for the same total dose has been applied previously to treat opioid neurotoxic effects.\textsuperscript{86–88} The addition of adjuvant pain medications utilizing a multimodal approach may help facilitate decreased opioid dosing. Efforts to reduce the likelihood of developing hallucinations may be made by conservative initial dosing and slow titration to achieve analgesia; nevertheless, clinical discretion with patient suffering under consideration may prompt a hastened speed of titration.

Opioid rotation has been utilized to help with suboptimal analgesia or adverse effects associated with the use of a particular opioid.\textsuperscript{89} There also exists weak evidence that changes in administration route can ameliorate side effects as seen with the reports of using parenteral or rectal routes instead of oral.\textsuperscript{86,88,90} The mechanism has been attributed to varying bioavailability or metabolism.\textsuperscript{90} Decreased dosing through epidural and intrathecal administration may also decrease the potential for accumulation of neurotoxic metabolites.\textsuperscript{88,91}

The particular opioid suspected of inducing toxicity may also be switched to another opioid. A retrospective chart review reported that 81\% of patients were able to obtain an effective balance of analgesia and side effects when up to 5 trials of substitution were consecutively performed with different opioids until successful.\textsuperscript{92} Rotation of an opioid from another class was previously suggested in a case where fentanyl, a piperidine derivative, was rotated out for hydrocodone, a phenanthrene derivative, with the successful elimination of the hallucinations.\textsuperscript{19} This same report further suggested the use of an NMDA antagonist such as ketamine to treat fentanyl-induced hallucinations.\textsuperscript{19} Nevertheless, this may not be advisable because ketamine is a known hallucinogen.\textsuperscript{93} Reduction or elimination of hallucinations through opioid substitution has been attributed to genetic variations in response to specific opioids among patients, clearance of the original opioid and its metabolites, or essentially decreased dosing of the new opioid because of incomplete cross-tolerance.\textsuperscript{88,94,95}

Opioid antagonists are well known to reverse many opioid-associated adverse reactions.\textsuperscript{96} There are reports describing the successful use of naloxone and \kappa selective opioid antagonists in the treatment of hallucinations associated with schizophrenia.\textsuperscript{97–99} Naloxone is the most studied antagonist available for the treatment of schizophrenic hallucinations with a wide range of reported initial intravenous doses from 0.4 to 10 mg.\textsuperscript{98} Although this study noted increasing efficacy with higher dosing, caution is mandated because their use may be associated with adverse effects including acute withdrawal symptoms in chronic opioid users, pulmonary edema, seizures, arrhythmias, and hypertension.\textsuperscript{98,100} Furthermore, precipitated opioid withdrawal has been noted to cause hallucinations.\textsuperscript{101} The duration of action of the antagonists must be considered to avoid recurrence of hallucinations if these agents are deemed to be clinically indicated. Based on the elimination half-life of a particular opioid, a continuous antagonist infusion may be necessary as noted in the case of fentanyl-induced hallucinations, which were successfully treated with repeated intravenous dosing of 0.1 to 0.2 mg/h of naloxone followed by an infusion of 0.2 mg/h for 7 hours.\textsuperscript{38}
Symptomatic management of hallucinations is an option that may include the use of antipsychotics, acetyl-cholinesterase inhibitors, and benzodiazepines. These treatments do not directly address the root cause of the hallucination but rather have been used in situations of urgency or refractory symptoms. Acetylcholinesterase inhibitors have been administered for the treatment of hallucinations of various etiologies such as schizophrenia and Parkinson disease. These studies report a similar hallucinatory mechanism among these disease processes involving anticholinergic activity. It has been hypothesized that opioids also exert multiple inhibitory effects on cerebral cholinergic activity. The successful use of physostigmine in the treatment of opioid-induced neurotoxicity, including hallucinations, has been reported as well.

Antipsychotics, also known as neuroleptics, function as dopamine antagonists, whereas those classified as atypical antipsychotics also antagonize serotonin receptors. It is this dopamine antagonism, which is posited to alleviate hallucinations, because of limbic and frontal lobe dopamine release induced by opioids. Atypical antipsychotics may be preferred because they are less associated with extrapyramidal side effects. Interestingly, risperidone has been associated with antagonism of opioid action, even precipitating withdrawal, although the exact mechanism is unclear. Antipsychotics have commonly been used for the treatment of hallucinations because of numerous disease processes including schizophrenia, iatrogenic dopaminergic neurotoxicity, Bonnet syndrome, and Parkinson disease. Haloperidol has been noted to rapidly resolve opioid-induced hallucinations and accordingly it has been widely used.

Psychostimulants such as methylphenidate, dextromethorphan, pemoline, and modafinil have been successfully used to treat many of the neurodepressant adverse effects associated with opioids. However, their use in treating opioid-induced hallucinations is not recommended because this stimulatory drug class can exacerbate neuroexcitatory effects including hallucinations. If these medications are taken concurrently with the development of suspected opioid-induced hallucinations, dose reduction or discontinuation may be considered.

Benzodiazepines may be considered if the hallucinations are refractory to dose reduction or rotation and harm to the patient or others is predicted. The ability of these agents to decrease agitation and anxiety may be desirable. This drug class has been noted to be particularly effective in treating hallucinations in schizophrenics when used in combination with neuroleptics. Higher doses of benzodiazepines, particularly oral diazepam, starting at 15 mg, may alleviate hallucinations, whereas lower doses serve to reduce agitation. If necessary, repeat dosing of diazepam may be given based on its elimination half-life of 44.2 hours. Although not well studied, it is likely that equivalent dosing of other benzodiazepines may be similarly effective. Withdrawal symptoms including hallucinations have occurred with the discontinuation of benzodiazepines after repeated dosing over a prolonged period. The synergistic interaction of opioids and benzodiazepines increases the risk of adverse cardiorespiratory events, and patients should be monitored closely.

The treatment of opioid-induced hallucinations may be approached in a stepwise manner (Figure). At any point during treatment, the use of symptomatic management with opioid...
antagonists, antipsychotics, acetylcholinesterase inhibitors, or benzodiazepines may be considered. If hallucinations develop because of opioids, cessation of the opioids may be considered on an individualized basis. Opioid dose reduction, rotation, or altered routes of administration are the next steps in those patients not deemed candidates for opioid cessation. Furthermore, the use of multimodal pain management may be implemented with the use of adjuvant pharmacotherapeutics, rehabilitative and psychobehavioral treatments, or interventional modalities.

CONCLUSIONS

Opioid-induced hallucinations are an infrequent, yet significant potential adverse effect of pain therapy. It has been the goal of this review to raise awareness of this potential complication through a review of the literature and discussion of possible etiologic mechanisms, diagnosis, and treatment. Because prospective studies are lacking, which makes it difficult to draw definitive conclusions, a limitation of this review is that it primarily focuses on case reports. Patients may be reluctant to divulge the presence of hallucinations because of fears of being judged mentally unsound, and this should be kept in mind when patients discuss their displeasure with any opioid treatment program. As the rate of opioid consumption continues to increase, the rate of opioid-associated hallucinations may also increase. Future research focusing on the identification of genetically susceptible populations may hopefully decrease the incidence of opioid-induced hallucinations.

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REFERENCES


Figure.
Treatment algorithm for opioid-induced hallucinations.