NCBI Bookshelf. A service of the National Library of Medicine, National Institutes of Health.

StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-.

Buprenorphine

Authors

Rachna Kumar; Abdolreza Saadabadi[1].

Affiliations

[1] Western University/ Kaweah Delta

Last Update: September 30, 2019.

Indications

Buprenorphine, a synthetic opioid, treats pain and opioid addiction. It underwent development in the late 1960s. It a synthetic analog of thebaine, an alkaloid compound derived from the poppy flower. It is a schedule III drug, which means that it has some potential for moderate or low physical dependence or high psychological dependence.[1][2][3][4][5]

Buprenorphine is FDA-approved for acute pain, chronic pain, and opioid dependence. It is used in agonist substitution treatment, which is a process for treating addiction through the use of a substance (such as buprenorphine or methadone) to substitute for a stronger full agonist opioid (such as heroin). The substitute is then tapered down, and the patient withdraws from the opiate addiction with minimal discomfort. Buprenorphine substitute treatment allows the patient to focus on therapy instead of uncomfortable withdrawals. It is an effective option to treat opioid dependence and reduces cravings and improves the quality of life for patients undergoing addiction treatment. It allows the patient to circumvent many of the uncomfortable symptoms of opioid withdrawal, creating a treatment plan that patients are more likely to adhere to, thereby decreasing reducing morbidity and mortality.

Off-label, use includes withdrawal for heroin-dependent, hospitalized patients. This use is only by injection.

Additional Uses Buprenorphine

Other kinds of addiction may also find a role for buprenorphine use. There is an experimental drug that is a combination of buprenorphine and naltrexone, and its role in cocaine addiction is under investigation. Naltrexone is an antagonist of mu and kappa opioid receptors, and when used in conjunction with buprenorphine, it results in stimulation of only kappa receptors without stimulating the opioid receptors. Theoretically, this combination may result in decreased compulsive cocaine use without resulting in opioid addiction.

The Drug Addiction Treatment Act of 2016 now allows physicians to provide office-based treatment for opioid addiction (DEA, 2018). This Federal legislation permits physicians to prescribe schedule III, IV, or V "narcotic" medications that are approved by the US Food and Drug Administration (FDA) for patients with opioid addiction. In 2002, the FDA-approved buprenorphine and combination of buprenorphine/naloxone to manage opioid dependence.

Indications

- For managing opioid-dependent patients who have a contraindication to methadone
- No available methadone facilities or healthcare providers or there is a long waitlist of more than three months to join a methadone clinic
- For opioid-dependent patients with intolerance to or have failed methadone treatment
- Other individuals who may benefit from buprenorphine are those with a short history of opioid dependence and/or have lower needs for opioid agonists

Mechanism of Action

Buprenorphine is a partial agonist at the mu receptor, meaning that it only partially activates opiate receptors. It is also a weak kappa receptor antagonist and delta receptor agonist. It is a potent analgesic that acts on the central nervous system (CNS). The partial agonism at the mu receptor is a unique quality to buprenorphine and the feature that gives it its many unique properties, specifically that its analgesic effects plateau at higher doses, and then its effects become antagonistic. Buprenorphine exhibits ceiling effects on respiratory depression, which means that it is safer than methadone for agonist substitution treatment in addiction.

Buprenorphine has high-affinity binding to the mu-opioid receptors and slow-dissociation kinetics. In this way, it differs from other full-opioid agonists like morphine and fentanyl, which allows withdrawal symptoms to be milder and less uncomfortable for the patient.

When administered orally buprenorphine has poor bioavailability because of the first-pass effect. The majority of the drug is broken down by the liver and intestine. Sublingual administration is the preferred route of administration. The absorption is fast, and this route also avoids the first-pass effect. Upon placing the tablet under the tongue, it has a slow onset of action with the peak effect occurring at 3 to 4 hours after administration.

Once in the body, buprenorphine is broken down by the cytochrome CYP 34A enzymes to an active metabolite (norbuprenorphine) with weak intrinsic activity. The average half-life of buprenorphine is about 38 hours (25 to 70 hours) following sublingual administration. Strong inhibition of the 3A4 enzyme by drugs (such as ketoconazole or protease inhibitors) may cause increased levels of buprenorphine, while inducers of this enzyme (such as carbamazepine, topiramate, phenytoin, or barbiturates) may cause lower levels.

The majority of the drug and the metabolite get excreted in the feces, and the kidneys excrete less than 20%. Because of the slow onset of action and prolonged duration of action, the drug is used to treat opioid dependence. It may be prescribed on alternate days once the patient has stabilized on the daily dose.

Administration

Buprenorphine administration is possible via many means. For chronic pain relief, a transdermal patch is an option. Oral forms include a buccal film and sublingual tablets. Parenteral routes include a subdermal or subcutaneous implant, and intravenous (IV) or intramuscular (IM) injections.

Buprenorphine is also available combined with naloxone in a sublingual tablet. Naloxone is not absorbed orally, so when taking the combination drug, the effect is predominantly of buprenorphine. Naloxone is added to buprenorphine to reduce its abuse potential when injected. When taking the combination in an IV form, the naloxone is absorbed as well and works to prevent the high of buprenorphine and may even precipitate a withdrawal; this is why buprenorphine alone has a higher potential for abuse than Suboxone does.[6][7][8]

Federal Regulations for Prescribing Buprenorphine

Sublingual buprenorphine preparations are helpful in the management of opioid-dependence (such as heroin, oxycodone, hydrocodone, morphine). The use of buprenorphine replacement therapy in the management of opioid dependence is regulated and highly monitored. In the United States, a special federal waiver is required to prescribe buprenorphine on an outpatient basis. Each federally approved physician is allowed to manage only 30 patients on buprenorphine for opioid addiction as outpatients.

Unlike methadone, which must be dispensed in a specialized clinic, buprenorphine/naloxone can be prescribed in an outpatient setting, as permitted by the Drug Addiction Treatment Act of 2000. However, health care workers who wish to prescribe buprenorphine to treat their opioid-dependent patients must undertake some training or extra-education to know more about this agent and obtain a waiver, before offering the drug to patients. Further, most insurers also recommend that health care workers who prescribe this drug must have completed an approved course of buprenorphine treatment for opioid dependence.[9][10][11]

Just like the prescription of other narcotics like morphine, the healthcare worker must maintain good medical records when prescribing buprenorphine. Each time a clinician prescribes the drug, the medical notes should contain the following:

- Reason for prescribing
- Start and end date
- Which pharmacy will dispense the drug?
- Who will supervise the administration?
- Will the drug be taken at home or the pharmacy?
- What type of follow up and who will be in charge of follow up
- How will compliance be monitored?

Further, the prescriber must comply with all the DEA requirements and actively monitor the patient.

DEA Rules

All healthcare workers who prescribe must have an active DEA registration number and a waiver to prescribe buprenorphine. The parenteral formula is not FDA-approved for the management of opioid dependence, and hence Intravenous use is not permitted, except under extraordinary circumstances and with permission; otherwise, such use can be illegal, and the prescriber can lose his or her DEA number and ability to write any future prescriptions for controlled substances.

As stated above, buprenorphine has multiple routes of administration. For chronic pain relief, a transdermal patch can be used (this

formula is only available in Europe). Oral forms include a buccal film and sublingual tablets. Parenteral routes include a subdermal or subcutaneous implant, and IV or IM injections, but are not routinely in use. The sublingual formula is widely used to treat opioid addiction. It contains buprenorphine and naloxone in a 4 to 1 ratio. Buprenorphine is available in 2 mg and 8 mg sublingual formula combined with naloxone 0.5 mg and 2 mg, respectively to deter drug abuse by injection.

Once placed underneath the tongue, the drug formula dissolves in 2 to 10 minutes.

Naloxone is an opioid antagonist, and its use in the formula is to prevent injection of the liquid obtained by dissolving the pills; this may help decrease the misuse of buprenorphine and also limit diversion. Because naloxone is poorly absorbed sublingually, its systemic effects when buprenorphine is taken properly are minimal. However, if the tablet is dissolved and injected, the naloxone blocks mu receptors and prevents receptor activation or precipitates withdrawal in opioid-dependent patients.

Initial Dosing

The initial treatment dose of buprenorphine/naloxone should be at the lowest dose and gradually titrated on a weekly basis until noting a response. The minimum duration of treatment is 8 weeks. In the majority of cases, the drug is administered under supervision by a pharmacist, except when the pharmacy is not open on the weekends, then the patient can receive a take-home dose. Take-home doses are only suitable for patients who are compliant and are clinically motivated to treat their opioid dependence. However, before take-home dosing is agreed upon, the patient must be educated on the consequences of the following:

- Potential for overdose
- Unintended dosing by others
- Diversion
- Consequences of careless storage

If take-home dosing is agreed upon, initially it should be limited to weekend doses only and then gradually increased as the patient shows more reliability. At all times, the patient requires monitoring for compliance. (Ottawa, 2016)

Induction Therapy

Induction with buprenorphine is initiated when the patient is experiencing mild to moderate symptoms of opioid withdrawal. The treatment is usually started 6 to 12 hours after use of short-acting opioids (e.g., heroin, oxycodone) or at least 24 hours or longer after the use of a long-acting opioid (e.g., morphine or oxycodone controlled-release formulations. For those methadone maintenance patients who prefer a switch to buprenorphine, the recommendation is that one wait at least 72 hours or more after the dose of methadone before initiating treatment. The dose of methadone should be tapered down to less than 30 mg before buprenorphine treatment to decrease the risk of precipitating intense withdrawal symptoms.

For patients on the fentanyl patch, at least 48 to 72 hours is necessary after discontinuation before starting treatment.

In most patients with opioid dependence, the initial dose is 2 to 4 mg. For those who are on high doses of opioids or potent agents like oxycodone, an additional dose of 2 to 4 mg may be necessary on the same day. After the supervised dosing, the healthcare provider in the clinic will monitor the patient.

During this time, the patient is monitored for withdrawal symptoms. Tools like the Clinical Opiate Withdrawal Scale is used to determine the presence and intensity of the withdrawal symptoms. Additional doses of buprenorphine may be required for symptomatic management of the withdrawal symptoms. Once the symptoms have subsided, the patient is discharged, and the induction rescheduled the following day. The patient should be encouraged to abstain from opioids while at home.

Maintenance Phase

During this phase, the dose of buprenorphine is gradually increased according to the patient's physical and psychological needs but should not exceed a maximum of 24 mg in one day. Most patients respond to doses between 8 to 12 mg per day. In most patients, the maintenance dose is attainable within 2 to 4 days. Once stabilized, the dosing frequency may be reduced, especially in reliable patients or those who need to travel. Some patients may benefit from alternate dosing by doubling the dose at each visit.

Adverse Effects

Buprenorphine exerts some anticholinergic-like effects and may cause central nervous system depression, hypotension, QT prolongation, and lowering of the seizure threshold. Other side effects of buprenorphine include nausea, vomiting, drowsiness, dizziness, headache, memory loss, sweating, dry mouth, miosis, orthostatic hypotension, sexual side effects, and urinary retention.

Potential for Buprenorphine Abuse

Even though buprenorphine is only a partial opioid agonist and has mild addictive potential, some people still misuse the drug. Buprenorphine tablets are misused by crushing them and either snorting the powder or dissolving the power and using it as an intravenous solution. Also, in the US where buprenorphine is also available in a sublingual formula, concerns have been raised about diversion and abuse; thus, the sublingual formulation is combined with naloxone to prevent IV abuse. Further, most patients undergo supervised daily dosing for the first 2 months of treatment to help lower the risk of diversion. Pharmacists also pay close attention to the patient's compliance to ensure that double doctoring and lost or stolen 'carries' do not occur frequently.

There is always the potential of overdose from the diverted buprenorphine in opioid-naive individuals when combined with benzodiazepines, alcohol, or other centrally acting agents.

Contraindications

The only true contraindication to buprenorphine use is a hypersensitivity reaction to it. Its use requires caution in patients with respiratory depression, gastrointestinal obstruction

Buprenorphine is also not recommended for patients who are currently using full opioid agonists, such as heroin or morphine, because the concurrent use of a full and partial agonist may result in acute withdrawal (see "Monitoring"), thus defeating the purpose of buprenorphine administration.

In patients with renal impairment, the dose of buprenorphine does not require alteration. However, in patients with liver dysfunction, the dose has to be modified to prevent toxicity.[12][13][14]

Buprenorphine Use in Special Populations

Pregnant Patients

It is well-known that in-utero exposure of infants to opioids can result in withdrawal symptoms after birth or what is referred to as the neonatal abstinence syndrome (NAS). Buprenorphine is classified as category C for use during pregnancy, which means that the risk of adverse effects on the fetus cannot be ruled out. Buprenorphine does cross the placenta, and use of opioids during pregnancy may result in neonatal withdrawals soon after birth. Symptoms of this may include irritability, apnea, increased tone, tremor, convulsions, or respiratory depression in the neonate. The onset of withdrawal in a neonate whose mother has taken buprenorphine during the pregnancy could be anywhere from the first day of life to the eighth day of life.

Medication-assisted treatment (MAT), including opioid treatment programs (OTPs), is a combined therapeutic approach using behavioral therapy and medications to treat substance use disorders. There is ample evidence indicating that methadone maintenance does improve maternal and newborn outcomes in pregnant opioid-dependent patients. Similarly, there is evidence suggesting that maintenance with buprenorphine may also improve fetal and maternal and outcomes and that the resultant NAS may be less intense than that observed after methadone. At present buprenorphine is listed as a category C drug in pregnancy; whereas methadone is category B, in pregnant patients. Buprenorphine is classified as category C for use during pregnancy, which means that the risk of adverse effects on the fetus cannot be ruled out. Buprenorphine does cross the placenta, and use of opioids during pregnancy may result in neonatal withdrawals soon after birth. Symptoms of this in the neonate may include any of the following:

- Tremors (trembling)
- Fever
- Irritability
- Sleep problems
- Tachypnea
- Excessive and/or high-pitched crying
- Increased muscle tone
- Hyperreflexia
- Seizures
- Yawning, stuffy nose, and sneezing
- Poor feeding and suck, slow weight gain
- Vomiting

- Diarrhea
- Dehydration
- Sweating

The onset of withdrawal in a neonate whose mother has taken buprenorphine during the pregnancy could be anywhere from the first day of life to the eighth day of life (Nguyen et al., 2018). According to the Substance Abuse and Mental Health Administration (SAMHSA), the following are the recommendations:

- The woman should be informed that experts are undecided as to whether intrauterine exposure to methadone, buprenorphine, or buprenorphine/naloxone leads to lasting developmental issues for the infant. The clinician should further inform her that the benefits of pharmacotherapy for opioid use disorder outweigh the risks.
- There is no evidence to date showing buprenorphine or methadone result in increased birth defects, and it has a minimal long-term impact on neurological development.
- Experts are not in agreement whether a woman in early pregnancy or who states her intention to become pregnant, with opioid use disorder, should be switched from a buprenorphine/naloxone combination to buprenorphine alone, and that any switch from the combination to the buprenorphine-only product should only be made based on the specifics of the case, with the woman's full informed consent.
- The is increasing evidence that newborn outcomes are not adversely affected by the combination product; the decision should remain with the clinician and the patient based on the benefit vs. risk.

Breastfeeding Women

Research has shown that buprenorphine does pass into breast milk, but because it has low bioavailability, it is not well established how much enters the systemic circulation in the breastfed infant. A few case reports indicate that the buprenorphine does not suppress NAS and that the syndrome doesn’t develop even after discontinuation of breastfeeding. While the manufacturers of buprenorphine advise against the use of buprenorphine in breastfeeding women, the limited evidence to date reveals that buprenorphine appears to be safe and discontinuation may not be necessary.

Elderly

So far, there is very little data on the use of buprenorphine in elderly patients. Because geriatric patients do have altered absorption, distribution, and metabolism, one should exercise caution when prescribing buprenorphine to this population. Plus, the potential for drug interactions also exists.

HIV Patients

Common comorbidity in HIV patients is opioid addiction. While highly active antiretroviral therapy (HAART) can prolong life and improve the quality of life, opioid dependency still needs to be treated. In one study, buprenorphine-treated patients were found to be more compliant with HAART compared to untreated patients, but the drug does not change the effectiveness of HAART.

Since many HAART drugs also affect the liver microsomal enzymes, healthcare workers should closely monitor liver function and drug levels in patients who have buprenorphine prescribed at the same time. In some patients, the dose of buprenorphine may require alteration.

Hepatitis

Both hepatitis B and C are common comorbid conditions in opioid-dependent patients. Since buprenorphine is broken down in the liver, these patients should have their liver function and drug levels closely monitored. Patients with hepatitis should be cautioned that intravenous use of buprenorphine has correlations with liver damage.

Patients with Pain

Even though buprenorphine is an opioid, it only has partial analgesic activity at the mu-opioid receptor. The two reasons why buprenorphine has no use as an analgesic is it is only a partial agonist and has a ceiling effect, and it binds tightly to the mu receptors and will prevent the binding of full agonists at the mu receptor and prevent further analysis. Thus, in patients with pain managed with buprenorphine, the options for analgesic include the use of non-steroidal-antiinflammatory drugs. If the patient is on a low dose of buprenorphine (2 to 8 mg), this can be increased to up to 24 mg every day. Other options include regional anesthesia, nerve blocks, or the use of anticonvulsants.

Monitoring

It is important to keep in mind how buprenorphine, a partial agonist, behaves when administered with other opioid receptor agonists. When in the presence of a full agonist, buprenorphine use results in a blockade effect and doesn't allow the high of the full opioid agonist to occur. If taken too soon after a full agonist, the patient may enter into withdrawals, which is why it is important to perform a simple assessment such as the Clinical Opiate Withdrawal Scale, or COWS, before giving buprenorphine. Suggestions are that the patient is in at least mild to moderate withdrawal, which translates to a score of at least 5 to 24 on the COWS. This step ensures that a patient with opioid intoxication will not receive a partial agonist that may push them into withdrawal.[15][16]

Before prescribing buprenorphine, one should closely look at all the medications; the patient is taking because serious drug interactions can occur. When combining buprenorphine with CNS depressants like the benzodiazepines, alcohol, certain antidepressants, antihistamines, hypnotics, or sedatives, it can lead to life-threatening respiratory depression, coma, and even death. The patient should be warned not to combine buprenorphine with other opioids or alcohol.

Buprenorphine is broken down in the liver by the CYP3A4 microsomal enzymes. Hence if the patient is on medications that induce these enzymes (e.g., carbamazepine, phenytoin or rifampin), therapeutic levels of buprenorphine may not be reached. On the other hand, if the patient is on inhibitors of CYP3A4 (e.g., fluvoxamine, ketoconazole, indinavir, erythromycin, saquinavir), levels of buprenorphine will remain elevated, and there is potential for toxicity.

At each clinic visit, the patient's drug list has to be checked to make sure that there are no new drug additions.

Managing Missed Doses

When dealing with opioid-dependent patients and their treatment, one must be prepared to deal with missed doses. Today most pharmacists who dispense buprenorphine keep track of the drug, the dose, time and day. This information is vital as it helps with compliance .anytime the individual misses a dose of buprenorphine; the healthcare provider must be notified since it may be the first sign of instability in the patient. To prevent loss of compliance, the clinician must develop a new treatment plan.

Follow up

As with patients treated with methadone, patients prescribed buprenorphine also need close monitoring from a multidisciplinary group of healthcare professionals as part of a comprehensive opioid dependence treatment protocol. In some parts of the country, pharmacists have also taken an active role in the supervision and monitoring of patients treated with buprenorphine. The pharmacist further communicates with the healthcare providers and plays an active role in dispensing take-home doses (carries).

Cost and Availability of Buprenorphine

The average costs for a 30-day supply of buprenorphine (two 2 or 8 mg tablets per day) are about $300 to $350. Formulas that contain naloxone are slightly more expensive, retailing at $400 to $450 a month.

Toxicity

At each visit to the pharmacy, the patient must undergo assessment for buprenorphine toxicity. The vital signs should be obtained, and the patient's overall physical and mental health status evaluated. Buprenorphine should not be dispensed if the patient appears lethargic or intoxicated. In some cases, the dose of buprenorphine may have to be withheld. The healthcare provider must be notified of these plans as patient safety is paramount. Because buprenorphine has a long half-life, the drug can be withheld for one day without any adverse effect. The patient should then be released the next day. If the patient has signs of respiratory depression and/or hypotension, he or should be evaluated in the emergency room and treated like any other opioid overdose patient.

One of the problems when trying to determine the adverse effects of buprenorphine is the difficulty in differentiating the withdrawal symptoms. The typical withdrawal symptoms after opioid withdrawal include nausea, vomiting, headache, diarrhea, flu-like symptoms, and diaphoresis. These withdrawal symptoms may occur at any dose of buprenorphine. On the other hand, the adverse effects associated with buprenorphine treatment usually relate to the dose. The higher the dose, the more severe are the symptoms. Also, the side effects of buprenorphine can worsen with other CNS depressants and alcohol.

If a patient overdoses on buprenorphine, they may experience confusion, dizziness, pinpoint pupils, hallucinations, hypotension, respiratory depression, seizures, or coma. Respiratory depression is a possibility when using other central nervous depressants, especially benzodiazepines. For example, when using buprenorphine and diazepam together, it resulted in an increased risk of respiratory and cardiovascular collapse.

When a patient overdoses on buprenorphine, they must be given a naloxone bolus dose of 2 mg to 3 mg followed by continuous infusion of 4 mg per hour; this will cause a full reversal of the overdose within 40 to 60 minutes. A bolus dose is needed to overcome the high affinity that buprenorphine has to the mu-opioid receptor.

Reports exist of rare cases of liver damage with jaundice with the use of buprenorphine. For those who receive buprenorphine, the liver function requires regular monitoring. The most severe and serious adverse reaction associated with buprenorphine use is respiratory depression which can be fatal. This situation is particularly problematic with buprenorphine because unlike morphine, there is no effective antidote. The respiratory depression associated with buprenorphine trends occur at high doses and is much more prolonged and difficult to reverse with naloxone, as the binding of buprenorphine to the opioid receptors is very tight. In some cases, the patient may require mechanical ventilation to manage respiratory depression.

Benefits of Buprenorphine compared to Methadone

Use of buprenorphine has been shown to be effective than detoxification in improving outcomes in patients with opioid dependence. When compared to methadone, buprenorphine has the following advantages:

- It is safer even at high doses
- Optional therapeutic doses are achieved relatively quickly
- There is less risk of abuse and diversion
- The drug is easier to taper
- There is less stigma associated with buprenorphine than methadone.
- Patients can get the medication from any healthcare provider and does not have to go to special methadone clinics

Buprenorphine, because of its partial opioid receptor agonist activity is said to cause less euphoria compared to full agonists like methadone or morphine, and thus is less likely to be abused or diverted.

The buprenorphine treatment typically lasts 3-6 months (or sometimes 1 to 2 years); on the other hand, methadone treatment is often lifelong.

Patient Education

The success of buprenorphine/naloxone is dependent on patient education. At each visit, the patient should have counsel about the drug's addiction potential and avoidance of other CNS sedatives. Family members or the caregiver should receive education about the signs and symptoms of buprenorphine toxicity. Patients should also understand what to do if the patient is lethargic and had depressed respiration.

To ensure that there is continuity in care, healthcare workers need to communicate all aspects of the treatment with each other at a weekly meeting; this is to ensure that there are no omissions or overlap in the dosing of buprenorphine. These meetings are vital when a patient gets discharged from jail or a healthcare institution.

Pearls of Wisdom

- Buprenorphine acts as a partial agonist at the mu-opioid receptor and overall is safer than methadone. However, it should not be combined with other CNS depressants like alcohol or benzodiazepines; otherwise, this can lead to respiratory depression.
- If an overdose occurs with buprenorphine, much higher doses of naloxone plus other supportive measures are required
- Because the drug is a partial opioid agonist, it has a much lower potential for dependence and misuse than pure agonists like heroin or morphine; however, misuse still occurs.
- The addition of naloxone to the formula is designed to lower the risk of abuse by injection further but does not always eliminate the risk.
- Unlike methadone, the therapeutic dose of buprenorphine can be titrated to a stable dose within several days, whereas methadone often takes many weeks or even months to reach a therapeutic dose.
- There are some patients in whom despite the maximal dose of buprenorphine, it may not be sufficient to treat the dependence; in such scenarios, one could consider switching the patient to methadone.
- Buprenorphine can induce withdrawal symptoms in patients dependent on opioids if it is administered quickly after the last dose of a pure agonist like fentanyl or oxycodone.

Enhancing Healthcare Team Outcomes

The management of patients addicted to opioids is interprofessional. The success of buprenorphine/naloxone is dependent on patient

education. Thus at each visit, the patient should be educated about the drug's addiction potential and avoidance of other CNS sedatives. Family members, or the caregiver, should receive education about the signs and symptoms of buprenorphine toxicity. Patients and/or caregivers should also receive instruction regarding actions to take in the event of depressed respiration.

Clinicians who prescribe buprenorphine require a waiver, as discussed above. The pharmacists need to work in concert with the prescriber to ensure proper dosing, monitor drug interactions, and counsel the patient on appropriate administration. Nursing should be alert for signs of adverse effects or poor compliance. All professionals must be aware of the potential for diversion, and keep the entire interprofessional team informed should any possible signs present.

To ensure that there is continuity in care, healthcare workers need to communicate all aspects of the treatment with each other at the weekly meeting to ensure that there are no omissions or overlap in the dosing of buprenorphine. This approach is vital when after patient discharge from jail or a healthcare institution. The outcomes depend on compliance with therapy. However, because many patients with substance misuse disorder have other significant comorbidities, the overall effectiveness is poor, marked by remissions and relapses.[17] As with any drug, but perhaps even more so with buprenorphine, the regimen needs to be part of an interprofessional team approach to ensure optimal patient outcomes with minimal harm. [Level V]

Questions

To access free multiple choice questions on this topic, click here.

References

1. Preuss CV, Kalava A, King KC. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): May 10, 2019. Prescription of Controlled Substances: Benefits and Risks. [PubMed: 30726003]
2. Noble F, Marie N. Management of Opioid Addiction With Opioid Substitution Treatments: Beyond Methadone and Buprenorphine. Front Psychiatry. 2018;9:742. [PMC free article: PMC6345716] [PubMed: 30713510]
3. Lyden J, Binswanger IA. The United States opioid epidemic. Semin. Perinatol. 2019 Apr;43(3):123-131. [PMC free article: PMC6578581] [PubMed: 30711195]
4. Molfenter T, Fitzgerald M, Jacobson N, McCarty D, Quanbeck A, Zehner M. Barriers to Buprenorphine Expansion in Ohio: A Time-Elapsed Qualitative Study. J Psychoactive Drugs. 2019 Jul-Aug;51(3):272-279. [PMC free article: PMC6667294] [PubMed: 30732542]
5. Van Zee A, Fiellin DA. Proliferation of Cash-Only Buprenorphine Treatment Clinics: A Threat to the Nation's Response to the Opioid Crisis. Am J Public Health. 2019 Mar;109(3):393-394. [PMC free article: PMC6366517] [PubMed: 30726142]
6. Shi JM, Henry SP, Dwy SL, Orazietti SA, Carroll KM. Randomized pilot trial of Web-based cognitive-behavioral therapy adapted for use in office-based buprenorphine maintenance. Subst Abus. 2019;40(2):132-135. [PMC free article: PMC6874094] [PubMed: 30714880]
7. Joshi P, Shah NK, Kirane HD. Medication-Assisted Treatment for Opioid Use Disorder in Older Adults: An Emerging Role for the Geriatric Psychiatrist. Am J Geriatr Psychiatry. 2019 Apr;27(4):455-457. [PubMed: 30718033]
8. Hollander MAG, Jarlenski MP, Donohue JM, Cole ES, Kelley D, Krans EE. Medical specialty of buprenorphine prescribers for pregnant women with opioid use disorder. Am. J. Obstet. Gynecol. 2019 May;220(5):502-503. [PMC free article: PMC6518408] [PubMed: 30703340]
9. Latif ZE, Solli KK, Opheim A, Kunoe N, Benth JŠ, Krajci P, Sharma-Haase K, Tanum L. No increased pain among opioid-dependent individuals treated with extended-release naltrexone or buprenorphine-naloxone: A 3-month randomized study and 9-month open-treatment follow-up study. Am J Addict. 2019 Feb;28(2):77-85. [PubMed: 30701613]
10. Lake EP, Mitchell BG, Shorter DI, Kosten T, Domingo CB, Walder AM. Buprenorphine for the treatment of posttraumatic stress disorder. Am J Addict. 2019 Feb;28(2):86-91. [PubMed: 30664299]
11. Herring AA, Perrone J, Nelson LS. Managing Opioid Withdrawal in the Emergency Department With Buprenorphine. Ann Emerg Med. 2019 May;73(5):481-487. [PubMed: 30616926]
12. Coe MA, Lofwall MR, Walsh SL. Buprenorphine Pharmacology Review: Update on Transmucosal and Long-acting Formulations. J Addict Med. 2019 Mar/Apr;13(2):93-103. [PubMed: 30531584]
13. Volkow ND, Jones EB, Einstein EB, Wargo EM. Prevention and Treatment of Opioid Misuse and Addiction: A Review. JAMA Psychiatry. 2019 Feb 01;76(2):208-216. [PubMed: 30516809]
14. Quaye AN, Zhang Y. Perioperative Management of Buprenorphine: Solving the Conundrum. Pain Med. 2018 Nov 30; [PubMed: 30500943]
15. Wen H, Hockenberry JM, Pollack HA. Association of Buprenorphine-Waivered Physician Supply With Buprenorphine Treatment Use and Prescription Opioid Use in Medicaid Enrollees. JAMA Netw Open. 2018 Sep 07;1(5):e182943. [PMC free article: PMC6324514] [PubMed: 30646185]
16. Jacobs P, Ang A, Hillhouse MP, Saxon AJ, Nielsen S, Wakim PG, Mai BE, Mooney LJ, S Potter J, Blaine JD. Treatment outcomes

in opioid dependent patients with different buprenorphine/naloxone induction dosing patterns and trajectories. Am J Addict. 2015 Oct;24(7):667-75. [PMC free article: PMC5322942] [PubMed: 26400835]

17. Truong C, Krawczyk N, Dejman M, Marshall-Shah S, Tormohlen K, Agus D, Bass J. Challenges on the road to recovery: Exploring attitudes and experiences of clients in a community-based buprenorphine program in Baltimore City. Addict Behav. 2019 Jun;93:14-19. [PMC free article: PMC6528177] [PubMed: 30682677]

Bookshelf ID: NBK459126 PMID: 29083570