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Eliminating Opioid Use in the Treatment of Chronic Lower-Back Pain

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ABSTRACT

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Treatment of Chronic
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Opioid use is an epidemic in the US costing millions annually. Chronic lower-back pain (CLBP) affects people world-wide and is frequently treated with opioids long-term. Long-term opioid use leads to negative health related consequences, increased risk for depression, negative unintended opioid related side-effects, overdose, and death. The purpose of this article is threefold: 1) to educate PCP on the complexities of CP and negative implications of opioid treatment for CLBP while illuminating the benefits of non-opioid management, 2) to review non-opioid treatment methods for CLBP to eliminate opioids, and 3) to construct feasible options for treating CLBP without opioids.

Keywords: chronic lower back pain, opioid use, non-opioid treatment

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Eliminating Opioid Use in Treatment of Chronic Lower Back Pain

Chronic pain (CP) effected over 36 million Americans in 2016. People suffering from CP are often treated with opioids either exclusively or excessively (Kuo, Raji, Chen, Hasan, & Goodwin, 2016). CP is pain persisting longer than the normal recovery time of an acute injury; it is often defined as pain lasting longer than 90 days (Falope & Appel, 2015). CP is often treated with opioids which can cause problems. Between 1999 and 2014 over 160,000 Americans lost their lives related to opioid abuse. In 2013, nearly 2 million Americans were either addicted to or abused opioid prescriptions, and opioid use has been increasing each year. (Dowell, Haegerich, & Chou, 2016). Thus, opioid overuse is an epidemic plaguing the US for several decades.

Originally opioids were intended to treat acute pain. They were never intended to be used chronically. In the last 100 years, clinicians' approach to CP management has changed. Decades ago, CP treatment with opioid was judicious and sparing. However, opioid prescriptions for Medicare part D recipients increased from 4.62% in 2007 to 7.35% in 2012. Data from 2012 show large variance in individual states from a low of 2.84% in New York to a high 10.93% in Utah (Kuo et al., 2016). In addition, opioid/sedative co-prescriptions occurred in over 36% of CP visits to the primary care provider (PCP) (Larochelle, Zhang, Ross-Degnan, & Wharam, 2015). Soporific medications (benzodiazepines, hypnotics, and sleeping aids) prescribed with an opioid increases the risk of opioid-related death. As noted, opioid prescription trends have been moving in the wrong direction. Moving forward, clinicians need to adjust their management of CP by using treatment strategies eliminating opioid medications.

Chronic Lower Back Pain

CP results from a variety of etiologies. Consequently, this paper focuses on chronic low back pain (CLBP) because it is one of the most common causes of CP. It is estimated between 60% to 80% of adults will have lower back pain at some point in their lives, and 30% of those effected will have pain lasting longer than one year (Falope & Appel, 2015; Gordon & Bloxham, 2016). In summation, between 58 and 78 million people in the US suffer from CLBP daily. CLBP is commonly treated with long-term opioid therapy, which can cause increased sensitivity to pain, decreased physical activity, depression, opioid tolerance, and opioid related death.

Proper management of CLBP is imperative to ensure patients experience the best possible quality of life. Non-opioid options in treatment will facilitate a shift in this epidemic. The purpose of this article is threefold: 1) to educate PCP on the complexities of CP and negative implications of opioid treatment for CLBP while illuminating the benefits of non-opioid management, 2) to review non-opioid treatment methods for CLBP to eliminate opioids, and 3) to construct feasible options for treating CLBP without opioids.

Problems Associated with CLBP

CLBP is a complex problem and requires treatment regimens ensuring patients suffering from CLBP have the best possible quality of life. There are many factors making CLBP complex. Common opioid-related problems associated with CLBP include opioid-induced hyperalgesia (OIH), opioid tolerance, side-effects and adverse drug reactions to opioids, and depression; other problems are decreased physical activity, quantifying pain, and type of CLBP.

Opioid Induced Hyperalgesia and Opioid Tolerance

Opioids have two significant side-effects warranting discussion: Opioid-induced hyperalgesia (OIH) and opioid tolerance. The chronic use of opioids can lead to OIH, which is a pain response non-congruent with the stimulus. This occurs because of the body's adaptive

response to opioids. The use of opioids can cause an increase in pain receptors resulting in an increased stimulus or hyperalgesic affect (Bannister, 2015). For example, if a patient has OIH and fractures their ankle, their pain may be much more intense than expected. Opioids, which would normally work, have little effect on their pain perception.

Chronic opioid use leads to tolerance, meaning higher doses of opioids are required to achieve the same effect, contributing to OIH. Tolerance to opioids occurs faster than the body's ability to adjust to the cardio/respiratory depressive side-effects resulting in an increased risk of overdose. Opioid tolerance occurs when mu opioid receptors (the site opioids bind for analgesic properties) become down regulated by receptor endocytosis. This may occur acutely, within minutes of ingestion, and/or chronically over time (Dang & Christie, 2012). This may lead to higher pain ratings and often an increase in the opioid dose.

Negative Implications of Opioids

There are many side-effects of opioids (see table 1). The top three most common and concerning side-effects are respiratory and circulatory depression, chemical dependence, and constipation (Kuo et al., 2016). Patients taking opioids have an increased risk of overdose because of their addictive nature and risk of depression of vital bodily functions, as these are side-effects of the medications. Overdose occurs when too much opioid is taken or by combining with other depressive medications, especially benzodiazepines, resulting in decreased circulatory and respiratory drive depriving the body of oxygen.

Decreased Physical Activity

Adequate treatment of CLBP is paramount because of the decreased quality of life related to inadequate treatment. Under treatment leads to depression and decreased physical activity while overtreatment with opioids leads to detrimental opioid-related adverse effects (Holtzman

& Beggs, 2013). Patients with CLBP attempt to minimize pain by avoiding painful stimulus, which can be exacerbated by physical activity. Thus, patients avoid activity because of the consequential pain. This inactivity causes muscles and bones to weaken and results in increased pain perception in the future. It also leads to a sedentary lifestyle.

Depression

Pain is influenced by perception, body chemistry, emotions, and coping mechanisms (Falope & Appel, 2015; & Mehalick, 2014). CLBP frequently is accompanied and influenced by depression. Tetsunaga, Tetsunaga , Tanaka, & Ozaki (2015) noted greater than 75% of patients with CLBP were classified as depressed, and nearly 40% of CLBP patients with depression had severe depression. Studies have shown opioid use is associated with depression; patients taking opioids were more likely to have depressive symptoms than those not taking opioids with similar pain ratings (Falope & Appel, 2015; Mehalick, 2014; Testunaga et al., 2015). Depression can lead to increase pain perception because of the psychological components of coping mechanisms and emotions (Goesling et al., 2015). A frequent query regarding this subject is, what causes the depression? Is it the opioids or the chronic pain? The answer is both. CP is linked to depression, and depression is listed on the side-effects of opioids. Therefore, depression is commonly seen in people with CLBP treated with opioids.

Quantifying Pain

Another obstacle in properly managing CLBP are the tools used by PCPs to measure pain. There are many pain measurement tools; however, each tool is subjective. Every patient's interpretation, perception, pain, and history are different. This subjectivity varies greatly making it difficult to measure pain. In addition, patients suffering from opioid addiction may inflate

their pain score to obtain fuel for their addiction. Because of subjective pain measurement, PCPs have no choice but to take patients at their word and treat accordingly.

Non-Opioid Treatments Options for CLBP

There are several non-opioid treatment options for CLBP, these may include non-opioid medication, combination medications, physical activity (exercise, yoga, and physical therapy), acupuncture, and spinal cord stimulation.

Pharmacologic Management of CLBP

CLBP is difficult to manage because it can have neuropathic or nociceptive pain or both. Neuropathic is pain caused by disease or lesions affecting a nerve in the peripheral or central nervous system. Nociceptive pain results from stimulation of nociceptors in tissues caused by trauma or disease (Falope & Appel, 2015). Understanding the pathophysiology of CLBP is important when choosing an appropriate treatment regimen for a specific patient.

It is rare to manage CLBP without medications. If CLBP has both neuropathic and nociceptive components, monotherapy is ineffective. There are several non-opioid medications effective for CLBP. These medications include acetaminophen, non-steroidal anti-inflammatory drugs (NSAIDs), muscle relaxants, antidepressants, and anticonvulsants.

A recent study comparing opioid verses non-opioid medications treating chronic back pain and hip or knee osteoarthritis revealed non-opioid treatment is more effective. The study showed better pain rating scores as well as lower adverse drug reactions with non-opioids when compared with opioids (Krebs et al., 2018). This is important because this supports using non-opioid treatments and will help the complications associated with opioid and will result in better patient outcomes.

Acetaminophen. Acetaminophen is a mild analgesic which has antipyretic properties. It decreases the production of prostaglandins, thereby decreasing pain. It has no influence on neuropathic pain and no anti-inflammatory properties, but it does help with nociceptive pain (Falope & Appel, 2015). Acetaminophen is effective in treating mild CLBP. For severe pain, Acetaminophen can be used with other medications and together can effectively treat severe pain. Because acetaminophen works differently than other non-opioid pain medications, the effect of acetaminophen combined other medications is much greater than either medication used separately. In addition, some combinations have a synergistic effect making their combined effect extremely efficacious.

NSAIDs. NSAIDs inhibit either COX-1, COX-2, or both receptors and decrease prostaglandin synthesis. NSAIDs are used as an anti-inflammatory medication. Their anti-inflammatory attributes are valuable for pain relief and have less side-effects than steroids. However, they do have side-effects that merit discussion. COX-1 inhibition prevents the stomach from producing gastroprotective prostaglandins, causes thinning of the stomach lining, and increases stomach acid. COX-2 prevents the synthesis of inflammatory prostaglandins and decreases the ability of platelets to adhere to one another (Falope, & Appel 2015).

NSAIDS place the patient at risk for gastric ulcers and associated bleeding. NSAIDS have anti-inflammatory properties which decrease nociceptive pain, but they do not help with neuropathic pain unless directly related to inflammation. When using NSAIDs long-term, it is best to prescribe a selective COX-2 medication, such as Celebrex, to avoid stomach complications, or use a non-selective medication, such as Ibuprofen, in conjunction with medications with gastro-protective attributes, such as Carafate or Omeprazole.

A recent study compared NSAIDs and tramadol. The study revealed NSAIDs were as effective as tramadol in pain relief and better than tramadol when there was an inflammatory component (Falope & Appel, 2015). NSAIDS are a crucial tool in the treatment of CLBP and combine efficiently with other non-opioid medications. PCPs can treat CLBP with NSAIDs in patients with mild to severe pain especially when inflammation is present. Patients with mild pain may only need an NSAID, but severe pain may need additional medications.

Antidepressants. Antidepressants can be used to decrease neuropathic pain in both the central nervous system and peripheral nervous system independent of its anti-depressive properties. Studies testing antidepressants for the treatment of neuropathic pain have conflicting results. Not all antidepressants aid in decreasing neuropathic pain, but serotonin norepinephrine reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs) have shown to decrease neuropathic pain and are used as a pain adjunct (Falope & Appel, 2015; Williamson, Sagman, Bruins, Boulay, & Schacht, 2014).

Serotonin-norepinephrine reuptake inhibitors (SNRIs). Like TCAs, SNRIs have neuropathic analgesic and anti-depressive qualities. These medications cause an increase in serotonin and norepinephrine at the neuronal junction causing an inhibitory effect resulting in decreased nerve transmission of pain signals (Mehalick, 2014). There have been several studies showing a significant decrease in pain with SNRIs (Falope & Appel, 2015; Skljarevski et al., 2010; Williamson et al., 2013). SNRIs should be used as an adjunct with other medications, such as NSAIDs and Acetaminophen. SNRIs side-effects are tolerated better than TCAs with similar analgesic results. SNRIs should be used first-line anti-depressants for pain adjunct targeting the neuropathic component of CLBP (Falope & Appel, 2015).

Tricyclic antidepressants (TCAs). TCAs decrease neuropathic pain, in addition to their antidepressant effects. TCAs inhibit several different serotonergic areas in the body (McCleane, 2003). Ferjan and Lipnik-Stangelj (2013) isolated mast cells in rats to determine what effects TCAs have on mast cell secretion of serotonin. They determined TCAs inhibit serotonin secretion and reuptake suggesting these medications produce pain relieving effects both peripherally and centrally. Several types of TCAs were tested. The most effective was Clomipramine. TCAs can be used with a NSAID and Acetaminophen, thus targeting both nociceptive and neuropathic pain and successfully treat moderate to severe CLBP. Studies show TCAs are effective for neuropathic pain, but some side-effects are intolerable for some patients. These side-effects include nausea, vomiting, weight gain, decreased libido, sleepiness, vision changes, and confusion.

Anticonvulsants. Anticonvulsants are used as a pain adjunct for neuropathic pain. Anticonvulsants decrease pain by targeting calcium channels on nerves inhibiting painful nerve impulses (Mehalick, 2014). Anticonvulsant drugs vary in mechanism of action and location. For example, Carbamazepine and Phenytoin work on different sodium channels, and Koseride act on strych-nine-sensitive glycine channels (McCleane, 2003). Understanding the mechanism of action is important because it allows PCPs to change medications within the same class but with a different mechanism of action.

Studies have shown anticonvulsants are effective in treating CLBP. Some of their side-effects include somnolence, edema, weight gain, dry mouth, constipation, and vision changes. Anticonvulsants are not used for monotherapy, and Lyrica and Neurontin have the lowest side-effect profile (Falope & Appel, 2015). Anticonvulsants have helped many people suffering with CLBP deal with the pain and experience a better quality of life.

Muscle relaxants. Muscle relaxants can be used as an adjunct for CLBP management. Baclofen has a favorable side-effect profile. It decreases muscle spasms, helps induce sleep, and reduces pain. Muscle relaxants are GABA-s receptors agonists, which inhibit painful neuropathic impulses (McCleane, 2003). The last few medications reviewed (antidepressants, anticonvulsants, and muscle relaxers) all cause somnolence and combining these together can cause respiratory depression similar to opioids. They should not be combined with sleeping aids or alcohol. The soporific effects of combined medications are a critical consideration in treating CLBP and should be monitored closely and prescribed with caution. In addition, they should not be taken with opioids.

Combination medication therapy. Since most medications do not cover both neuropathic and nociceptive pain pathways, it is effective to use combination medication therapy. CLBP stems from many etiologies, and pain and characteristics vary immensely. Each medication has its place and can be used in monotherapy for minor CLBP or in combination for more moderate to severe CLBP. One drug combination is Lyrica and Celebrex. These medications together perform in a synergistic manner and provide significantly better pain control than monotherapy (Falope & Appel, 2015). Another synergistic combination is Acetaminophen, Celebrex, Amitriptyline and Lyrica for severe CLBP pain. Combining Amitriptyline and Lyrica should be used with caution because each can cause dizziness and somnolence side-effects.

Non-Pharmacologic Management of CLBP

Physical activity (PA) including physical therapy (PT), exercise therapy, and yoga is possibly the most important tool PCPs can utilize to improve their patients' quality of life. Patients suffering from CLBP commonly think rest is best for healing. However, PA has positive

implications for patients suffering from CLBP. PA increases circulation, helping nutrients enter the damaged area, facilitates removal of waste, improves healing, decreases pain, promotes muscle growth, and increases strength and flexibility. Increasing strength and flexibility of the trunk helps strengthen the body's core improving musculoskeletal stability. This strength and stability help to prevent future injury, improve disability, and decrease pain (Gordon & Bloxham, 2016). All varieties of PA mentioned in the following sections have similar benefits listed above in addition to improved strength or flexibility.

Physical Therapy

PT has been utilized in healthcare since the 1800s. Studies show PT decreases pain, improves healing, and improves disability. Combining PT with medications helps patients with CLBP tolerate PT, improves performance, and decrease pain (Morris, Pellow, Solomon, Tsele-Tebakang, & Solomon, 2016; Onac, Moldovan, Onac, Igna, & Pop, 2012). PT is well established and is used because it has all the benefits of PA previously listed. PT is a short-term therapy limited by insurance companies. Patients with CLBP should be encouraged to continue a similar active routine after their allotted PT visits are extinguished.

Exercise Therapy and Yoga

Exercise therapy is a great way to get the benefits from PA. PCPs should encourage their patients to start an exercise program incorporating things they enjoy. If patients are unfamiliar with exercise, PCP's can refer to either a personal trainer or physical therapist to help patients establish a simple exercise routine. Exercise therapy is inexpensive, convenient, and shares the benefits of PA previously listed. It allows patients to strengthen weakened areas resulting in increased strength and stability thereby decreasing pain. Gordon & Bloxham (2016) conducted a systematic review of the effects of muscle strengthening exercise, aerobics, and flexibility

exercise and found they resulted in decreased disability and pain in patients suffering from CLBP. Some patients may not like exercise therapy or aerobic type activity. Yoga is another option PCPs can use to promote PA. Studies have shown yoga produces effective results for CLBP by reducing pain and disability and increasing flexibility (Holtzman & Beggs, 2013).

Most Important Intervention

There has been a plethora of research all reaching the same conclusion. PA is one of the most important and efficacious interventions for CLBP. PA enables continual improvement of CLBP. However, PA is underutilized because of lack of knowledge; therefore, it is crucial to educate patients and providers on the importance of PA in treating CLBP. PA is counterintuitive to patients and does not result in immediate pain control. For this reason, patients may be non-compliant with PA. Therefore, education should facilitate breaking down this barrier, and medications can enable patients to tolerate PA in order to further improve their outcome.

Spinal Cord Stimulation

Spinal Cord Stimulation (SCS) is a surgical procedure introduced in the 1960s and can help with severe cases of CLBP that do not respond to treatment. SCS has several benefits, including significant analgesic properties, reduction or elimination of opioid use, long-term decreased health care expenditures, and improved quality of life (Grider et al., 2016).

Some patients with intractable CLBP have achieved 50% reduction in their pain through SCS. Pain reduction can range from 16%-95%, and the surgery has less risks and better long-term outcomes than most back surgeries (Sumner & Lofland, 2014). Recent studies determined SCS works for failed back surgery syndrome, which is significant pain that persists after back surgery and healing. These studies were also reviewed by the National Institute for Health and Care Excellence (NICE) in the United Kingdom. "NICE recommends SCS as a treatment for

patients suffering from refractory chronic neuropathic conditions, including chronic low back pain" (Grider et al., 2016, p. E34).

One study compared traditional SCS to high frequency SCS (HFSCS). The traditional SCS group had 81 participants and showed 55% reduction in pain both short-term (less than 12 months) and long-term (greater than 12 months) compared to the HFSCS group with 90 participants and an 80% reduction in pain both short-term and long-term (Grider et al., 2016). SCS is a valuable tool with potential to transform the worst cases of CLBP from people who are opioid dependent, disabled, and live a sedentary life-style to people who take non-opioids with increased mobility, decreased pain, and better quality of life. SCS allows patients to incorporate PA into their treatment regimen where it may not have been an option prior to the procedure.

Acupuncture

Acupuncture has many positive results and can be used synergistically in combination with other interventions. Acupuncture has existed for over 8000 years; however, it is a topic of controversy in western medicine and frequently a target of skepticism. A recent RCT comparing two groups; one that participated in exercise and auricular acupuncture the other group that participated only in exercise. Both groups showed improvements; however, the combined auricular acupuncture and exercise group had larger statistically significant improvements in mobility, decreased disability, and decreased pain than the exercise group alone. (Hunter et al., 2012).

A meta-analysis was conducted with 17,922 studies involving acupuncture for treatment of many different CP conditions including CLBP, osteoarthritis, migraine and tension headaches, and non-specific musculoskeletal pain (Vickers, Cronin, Maschino, Lewith, & MacPherson, 2012). Vickers et al. (2012) determined acupuncture is more than "sham acupuncture" (p. 7). It

works consistently reducing pain and disability while improving the quality of life for those treated. Another study revealed six benefits of acupuncture: decreased pain, enhanced physical mobility, improved energy levels, relaxation, psychological benefits, and decreased medication use (Hopton, Thomas, & MacPherson, 2013). Acupuncture works synergistically with PA and medications to treat patients with CLBP.

Barriers to acupuncture. Numerous studies have shown acupuncture has merit in treating a variety of afflictions (Hopton et al., 2013; Hunter et al., 2012; Vickers et al., 2012). Hopton et al. (2013) focused on patient perceptions of acupuncture to identify benefits and barriers, which included needle discomfort, temporary increase of pain, financial concerns, and pressure to continue treatment. Without foreknowledge and clear expectations, patients may experience these barriers and stop acupuncture prior to receiving the benefits.

Overcoming barriers. For some, acupuncture took the place of opioid pre-medication prior to PA, and for others, acupuncture resulted in an overall decrease in reliance on and use of opioids. Acupuncture participants first noticed an increased ability to perform physical functions resulting from a decrease in painful stimuli. They could focus more on their abilities rather than their disability. This empowered them to add exercise and active hobbies, enhancing their overall health, quality of life, and pain management (Hopton et al., 2013.) Acupuncture is efficacious and its longevity of existence originating in ancient China thousands of years ago speaks to this. The most effective tool used to break-down barriers was a relationship between the patient and acupuncturist, who educated the patient about expectations and empowered the patient to be proactive in treatment (Hopton et al., 2013).

Implications for Practice

Non-opioid treatment of CLBP begins with clear expectations, honesty, and education. PCPs need to be straightforward with patients, so they can be prepared for the process. Treatment should be centered on the patient's goals; however, if the patient and the PCP's goals are non-congruent, communication and education are the tools needed to get both parties' goals aligned. In addition, targeting the correct pain pathways (neuropathic and nociceptive) for each patient is an important consideration. Patients need to understand there is no cure for CLBP, they will still have some back pain, may not see immediate results, and treatment requires consistent hard work. The foundation for successful non-opioid treatment for CLBP is PA. There are several ways a patient can participate in PA. Since each patient is unique, they should pick an activity they enjoy that suits their situation. PA strengthens their core resulting in a stronger more stable back and decreased disability and pain. Other treatment modalities can enhance and enable patients to participate in their chosen form of PA. Acupuncture is a one way to help decrease CLBP and enable a patient to participate in PA. NSAIDs combined with Acetaminophen and Duloxetine or Lyrica will decrease pain and help patients tolerate PA. If these non-opioid approaches are not tolerated, SCS implantation is an effective way to significantly decrease pain to a level that PA can be tolerated.

Conclusion

CLBP is a monumental problem costing the United States millions of dollars annually. Furthermore, PCPs are treating patients with opioids for CP without giving patients all the information. It takes much less time to prescribe an opioid than spend the time needed educating and motivating a patient on the negative implications of chronic opioid use and the benefits of PA. Studies show long-term treatment with opioids causes tolerance and OIH, and patients who take opioids long term rate their pain scores higher, have addiction issues, decreased PA,

depression, and experience the side-effects of opioids (Bannister, 2015; Dang & Christie, 2012; Falope & Appel, 2015; Goesling et al., 2015; Gordon & Bloxham, 2016). Patients need to be aware that treatment with opioids long-term masks pain initially but results in no long-term benefits. In addition, treatment with opioids does not appear to have better outcomes in any facet of treatment of CLBP. According to Krebs et al. (2018) non-opioid treatment had better pain management at three, nine, and twelve months than when treating with opioids. With the addition of non-pharmacologic treatment, such as acupuncture and PA, patient outcomes would improve more than with pharmacological interventions alone.

Patients need education on the benefits of PA. PA can enable a patient to be free from opioid dependence and opioid related health implications. PCPs need to empower patients with tools that help patients tolerate PA and imbue their patients with knowledge and motivation. PCPs need to teach patients how non-opioid treatment for CLBP can provide them with decreased pain, increased mobility, and better quality of life.

Appendix

Table 1
Side-Effects of Opioids

Common Side-Effects	**Serious Side-Effects**
Dizziness	Respiratory depression
Somnolence	Circulatory depression
Nausea and vomiting	Hypotension
Hyperhidrosis	Increased intra-cranial pressure
Flushing	Seizures
Xerostomia	Bradycardia
Pruritus	Paralytic ileus
Dysphoria/ Euphoria	Biliary spasm
Headache	Hypersensitivity reaction
Constipation	Anaphylaxis
Loss of appetite	Adrenal insufficiency
Rash	Opioid-induced androgen deficiency
Insomnia	Dependency
Anxiety and agitation	Risk for abuse
Muscle spasm	Withdrawal symptoms if stopped abruptly
Depression	Addiction
Abdominal cramping	Dyspnea
Vision changes	Syncope
Fever	Shock
Confusion	Death

Note. Adapted from Epocrates Drug Guide, (Ehrlich, Baldor, & Domino 2018).

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