Opioid and the usage in chronic non-cancer pain

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Abstract

The use of opioid in various guidelines for chronic non-cancer pain is controversial because evidence of their long-term benefits is weak. The potential for serious adverse effects and local regulations warrant caution in both prescribers and users. However, opioids have a role in the management of chronic non-cancer pain in carefully selected patients with regular monitoring and as a part of multimodal therapy. Common adverse effects should be treated promptly to improve patient compliance. We believe that opioid therapy at low doses is beneficial in some patients. It should not be denied but carefully considered on a case-by-case basis.

Keywords: chronic non-cancer pain, multimodal therapy, opioid

Introduction

Opioids are the most potent and effective analgesics available, and have become accepted as appropriate treatments for acute and cancer pain. However, there is concern regarding their use in chronic non-cancer pain because of fear that they are ineffective in the long term, that their use will lead to a deterioration in the patient's condition, and that the medical prescription of opioids will lead to an increase in their non-medical use within society. In certain countries, physicians may also fear triggering scrutiny and sanctions by regulatory agencies when prescribing long-term opioids for chronic pain of non-malignant origin.[1–3] However, relief of pain is a humanitarian issue and it has been said that `to leave a person in avoidable pain and suffering should be regarded as a serious breach of fundamental human rights.[4]

The use of opioids for chronic non-cancer pain (CNCP) has been a fast-rising treatment phenomenon in the last two decades. Although opioids are advocated in various chronic pain management guidelines, their use in chronic non-cancer pain remains controversial, as evidence for this approach is still weak. This paper highlights the potential adverse effects associated with opioid use in pain management, including an increase in tolerance, dependence, and addiction outcomes. Nonetheless, opioids are important in contemporary CNCP management of selected patients. However, pain management must involve regular monitoring and multimodal strategies.. Therefore, patient selection and outcome assessment are essential, and long-term use should be preceded by a trial in which the goals of the treatment agree with the patient.

Opioid Pharmacology

Opioids were classified by their strength (Table 1), duration of action (Table 2), or source (natural, semi-synthetic, or synthetic). Opioids exert their effects through endogenous opioid receptors. These receptors are widespread throughout the central and peripheral nervous systems. Several endogenous opioid receptors have been described, including the mu opioid receptor (MOR), delta opioid receptor b(DOR), and kappa opioid receptor (KOR). The binding characteristics and overall effects of opioids vary; however, to date, the most important factor is mu receptor binding. The significance of this variation in cli

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nical practice for treating persistent chronic pain is unknown. However, this variation in binding characteristics may be helpful in managing opioid tolerance and side effects. Very recently, some evidence has been published where delta opioid receptor function is enhanced in chronic pain, and an agonist at DOR[5,6] may help persistent pain. How-

Table 1. Common weak and strong opioids[7]	
Weak opioid	Strong opioid
Codeine	Morphine
Hydrocodone	Hydromorphone
Dihydrocodeine	Fentanyl
Tramadol (depends on the dose and has been classified as strong in BNF*)	Diamorphine
	Buprenorphine
	Methadone
	Oxycodone

ever this aspect requires further investigation. There is little evidence to support the recommendation of one opioid over another in terms of the quality of analgesia. Some medications augment their overall effects via receptors other than opioid receptors (tramadol and methadone). They may be more effective in conditions (e.g., such as tramadol in fibromyalgia) where pure opioid agonists may be ineffective. The potency of the common opioids is shown in Table 3.

Table 2. Some common long and short acting opioids[7]			
Analgesic	Dose per 24 h	Equivalent to oral morphine per 24 h	Conversion rations drug: Morphine
Codeine phosphate	240 mg oral	24 mg	10:1
Dihydrocodeine	240 mg oral	24 mg	10:1
Diamorphine	3 mg subcutaneous	10 mg	1:3
Oxycodone	100 mg oral	150-200 mg	1:1.5-2.0
Hydromorhone	1 mg oral	5-10 mg	1:5-10
Tramadol	400 mg oral	40 mg	10:1
Buprenorphine patch	10 mcg hourly release	15 mg	1:60
Fentanyl patch	25 mcg	90 mg	1:150
Methadone*	10 mg	10-15 mg	1:1-1.5

The analgesic effect of codeine phosphate requires its conversion to morphine in the liver. Nine percent of Caucasians[8] lack the enzymes required for this conversion. Morphine is metabolized in the liver by glucuronidation to morphine 3 glucuronide (inactive) and morphine 6 glucuronide (pro-analgesic effects). These metabolites are renally excreted, and M6G may accumulate during renal impairment.

Hydromorphone, a semi-synthetic derivative of morphine and 5 times more potent, differs structurally from morphine, with a keto group replacing the hydroxyl group at position 6 of the benzyl ring. This results in glucuronidation at position 3, only into a non-active metabolite. Therefore, hydromorphone may be preferred in patients with renal impairment[9] and needs further validation.

Table 3. Conversion table for commonly prescribed opioid medications[7]			
Analgesic	Short acting version/immmeddiate relase	Long acting version (slow or modified relase)	Route of administration
Morphine	Yes	Yes (12 h, 24 h preparations)	Oral, parentral, rectal, intrathecal, epidural)
Oxycodone	Yes	Yes (12 h preparation)	Oral, parentral, rectal
Dihydrocodeine	Yes	Yes (modified relasee 12 hourly preparation)	Oral, parental,
Hydromorphone	Yes	Yes (slow release 12 h preparation)	Oral, can be sprinkled over soft food.
Tramadol	Yes	Yes (slow relase 12/24 hourly preparations)	Oral, parentral
Codeine	Yes	No	Oral, parentral
Methadone	No	Yes	Oral, parentral

Methadone[10], an opioid, an N-methyl-D-aspartate receptor antagonist, and a serotonin reuptake inhibitor have an unusually variable elimination half-life (4.5-130 h), which can lead to accumulation. Methadone has been associated with prolonged QTc interval[11] (in moderate doses), torsade de pointes[12] (high doses), sleep apnea, and sudden death.[13] Methadone has been used for analgesia, opioid dependence, tolerance, and as a part of opioid rotation (described later). Its advantages include long duration of action, low cost, no dose adjustment required for renal and hepatic insufficiency, and no active metabolites. Tramadol is a weak MOR agonist that releases serotonin and prevents the reuptake of noradrenaline.

Opioids can be administered via intranasal, buccal, sublingual, oral, transdermal, rectal, parentral, epidural, and intrathecal routes. There is little evidence to suggest the superiority of one route over another

in chronic non-cancer pain.[14] However, a change in route may improve analgesia, adverse effects, and patient compliance. We do not recommend the use of parenteral preparations to assess opioid responsiveness. Regular long-acting preparations have been recommended over repeated short-acting (immediate-release) preparations. This may improve pain control, reduce adverse effects, and decrease the risk of addiction. However, patients may have more opioid-related concerns while taking the drugs regularly rather than on an as-needed basis.[14,15] Furthermore, there is little evidence to support the use of sustained release preparations as opposed to immediate release medications.

Adverse Effects

Opioid medications are associated with substantial adverse effects[16], commonly as drowsiness, constipation, nausea, vomiting, itching, sweating, and mood changes. Eighty percent of individuals on opioids experience at least one side effect.[7] These contributes to a high rate of discontinuation of medication. Respiratory depression, addiction, and drug misuse lead to caution and apprehension regarding opioid use. Other adverse effects included hyperalgesia and endocrinological suppression.

Opioid induced constipation

Opioids reduce gut motility and secretions, leading to gastrointestinal (GI) fluid absorption.[17–19] This is mediated principally through GI opioid receptors in the gut submucosa and to a lesser extent through central mechanisms. In general, no tolerance was observed for constipation on continued use. Treatment strategies include adequate hydration, a high-fiber-content diet, and encouraging physical activity. Laxatives (oral and rectal) and bulk-forming agents have been used extensively. Opioid switch[20] (e.g.,codeine to tramadol) and changes in the route of administration (morphine to transdermal buprenorphine patches) can help some patients. To improve the results, opioid antagonists have been used successfully without reducing analgesic effects. These included naloxone[21] (used in combination with oxycodone), methylnaltrexone, and alvimopan. Two percent of naloxone is absorbed systemically and has an extensive first-pass metabolism. However, there are some case reports where high-dose combination of oxycodone and naloxone resulted in reduced pain relief. The costs preclude the routine use of these drug combinations; however, they can be considered in certain circumstances, especially in the elderly.

Nausea, vomiting and sedation

These are common adverse effects of initiation or dose escalation, but tolerance develops in most patients after a few days, and persistent effects are infrequent. Antiemetics in the trial phase, slow titration, and patient education are important considerations. Opioids are known to cause dizziness, drowsiness, lack of concentration, and confusion, and can affect an individual's ability to drive or work; higher doses increase the risk of falls (and fractures) in the elderly. Previous research suggests that there is no evidence of deterioration of psychomotor and cognitive skills once the patient is in a stable dose.[22,23] Recently, some questions have been raised regarding the above interpretation, and some authors have added some prerequisites.[24] However, caution should be exercised in the initiation of therapy and dose titration.

Opioid induced hyperalgesia

Opioid-induced hyperalgesia (OIH) is defined as a state of nociceptive sensitization caused by exposure to opioids.[25] It results in a worsening pain state, especially with certain pain stimuli (mechanical allodynia and cold perception) and is frequently seen in patients' long-term opioids for surgical postoperative pain. Various mechanisms have been proposed including NMDA activation, descending facilitation, and spinal dynorphins. It probably uses pathways similar to neuropathic pain.[26] Therefore, patients with neuropathic pain might be more susceptible to this phenomenon. Clinically, it is difficult to diagnose OIH as the cause of deteriorating pain perception, but it should be suspected if the pain has a different quality, site, and distribution compared to pre-existing pain. Pain may worsen with escalation of opioids. If suspected, the best treatment would be to reduce opioids in consultation with the patient.

Endocrine effects

The most prevalent endocrine disorder associated with opioids is deficiency of gonadotrophins, leading to a reduction in sex hormones, particularly testosterone.[27–29] This may occur with any route of administration and is more likely with doses above 100 mg daily morphine equivalent.[30] It may occur within a few weeks of opioid use and is reversible if opioids are withdrawn. Diagnosis is made by the presence of symptoms (e.g., reduced libido, sexual dysfunction, fatigue, mood change) and signs (e.g., infertility, reduced hair growth, testicular atrophy, menstrual disorder), and the presence of reduced hormone levels. However, the symptoms and signs are not exclusive to androgen deficiency, and the minimum levels of testosterone are not clearly defined. Replacement therapy is available and will correct the abnormality but is not without risks. Therefore, our practice was to refer patients with suspected androgen deficiency to a specialist endocrine unit for evaluation, treatment, and long-term follow-up.

Addiction/death

Opioids are associated with the risk of addiction and unintentional death.[31] a pattern that is seen in North America, where there was a 3-fold increase in opioid-related deaths during 1999-2007 and a twofold increase in deaths from methadone and codeine in the United Kingdom. According to a report by the International Narcotics Control Board, 6.2 million American and 1.4-1.9 million Germans are addicted to pharmaceutical medication.[32] According to this report, young adults are the most vulnerable group. Therefore, it is important to have robust patient selection criteria and clear outcome measures. Tolerance and physical dependence are the normal physiological features that occur during regular drug use. They are often seen in patients who are addicted to or abuse drugs. These should not be confused with addiction.[33]

Chronic Non-Cancer Pain

The International Association for the Study of Pain (IASP) defines "chronic pain aspain that persists beyond normal tissue healing time, which is assumed to be three months".[34] It can be nociceptive (e.g., inflammatory, traumatic, or degenerative in nature) or neuropathic (e.g., a lesion or disease affecting the somatosensory system) in nature. Chronic non-malignant pain, chronic pain of non-malignant origin, and chronic benign pain are other terms used to describe the same condition. Common CNCP conditions include musculoskeletal pain, neck and lower back pain, fibromyalgia, headache, post-herpetic neuralgia, diabetic peripheral neuropathic pain, pelvic pain, and ischemic pain.

Chronic non-cancer pain (CNCP) can be typically described as moderate or severe pain that lasts for six or more months and is attributed to conditions such as neuropathic pain, rheumatoid arthritis, lower back pain, osteoarthritis, fibromyalgia, and several other conditions.[35] People with CNCP rarely enjoy their lives, as they find it hard to sleep, often feel fatigued and depressed, and struggle to form meaningful social relationships with family and friends. In the United States, 26 percent of adults have at least one chronic condition, such as arthritis, diabetes, and hypertension. Most of the time, these patients experience persistent and recurrent pain that worsens their condition. Therefore, CNCP is one of the main causes of morbidity and interference with a person's ability to perform daily activities. Chronic conditions not only affect the patient but also their families, communities, and health systems, as they are stakeholders in the struggle to control the disease and its complications. These continuous and endless struggles contribute to frustration and depression in these patients. Frustration between these patients is linked to the complexity and unpredictability of pain. As a result, patients have been found to stop their self-care activities and essential prescriptions. In other cases, the suffering person may lose interest in living and would prefer to die rather than continue with the present living situation.[36] In this regard, opioids are used to relax patients and relieve some of their pain.

The goal of CNCP treatment is similar to that of all other patients with chronic pain, which is to improve pain outcomes and maintain functionality. Some of the targeted milestones in successful pain management strategies include positive coping skills, stress minimization, and the establishment of better social support systems. The effective management of comorbid neuropsychiatric complications also maximizes functionality.[37]

Multidisciplinary Approach to Chronic Non-Cancer Pain

Chronic non-cancer pain affects the quality of life and socioeconomic activities of millions of Americans. These pains also lead to expenditures of billions of dollars annually and a loss of productivity in the economy. Although there is no definitive cure for chronic non-cancer pain, many studies suggest a multidisciplinary pain program that emphasizes ensuring that a person's independence is restored and their quality of life improved.[38] Multidisciplinary pain management approaches are usually developed along with a biopsychosocial model of chronic non-cancer pain. Multidisciplinary care is essentially transformative care, as it incorporates comprehensive, patient-centered self-management strategies with evidence-based treatments as routine care for various chronic pain conditions and ensures that consequences are effectively prevented and managed. This kind of transformative care significantly improves long-term outcomes and reduces the dependence of the patient on the healthcare system, thereby leading to improvements in both the patient's life and healthcare system. For this reason, health leaders should always strive to integrate self-management strategies into clinical practice that aims to engage, educate, and empower people to prevent chronic pain and addiction.[39] In this regard, transformative care assists in improving the experience of the patient, improving patient health, and controlling healthcare costs.

The integration of training and treatment is another important component of multidisciplinary pain management. Training health professionals can help minimize some of the barriers that may reduce the effectiveness of various strategies. Some of the challenges that can be solved through training include care coordination and fragmentation, poor communication, and conflicting treatment. McCrorie et al. indicated that this approach is relatively effective in the treatment of chronic back pain and has been highly recommended for the treatment of low back pain.[40] Some common features of this model include standardized group sizes, treatment strategies, and high-intensity treatment. In relation to treatment strategy, the approach consists of interventional injection techniques, such as epidural, periradicular and facet joint injections, which are done frequently. These injections are augmented with other treatment approaches, including modification of analgesic medication, transcutaneous electrical nerve stimulation, aquatraining, massage therapy, and back education, among others.[39]

A multidisciplinary approach also encompasses behavioral management. Physiotherapists perform behavioral therapy at least twice a week based on the severity of CNCP as well as other psychological cofactors. According to studies based on the Numeric Rating Scale (NRS) and the Oswestry Disability Index (ODI), behavioral management strategies were found to improve pain outcomes and functionality in patients. The study indicated that the integration of multiple strategies with different components in pain management led to better results than when a single intervention was applied.[39] The efficacy of multidisciplinary programs was found to be better than that of standard medical treatment and other non-multidisciplinary treatments. Moreover, multidisciplinary programs for patients with chronic pain allow them access to specialized treatments. Nonetheless, as with any other intervention, multidisciplinary approaches are affected by both methodological and conceptual limitations, which make them relatively difficult to implement.

Stepwise approach to prescribing opioids for chronic non-cancer pain

A stepwise approach is important for selecting the appropriate patients for opioid therapy (Table 4). There must be a plan for discontinuing opioids when treatment fails to meet predetermined goals for significant pain relief and an enhanced quality of life. The aim should be improved function without the expectation of complete alleviation of pain

Initial evaluation and referral

Opioids are a valuable alternative when patients do not respond to other analgesics or treatment regimens. One of the primary issues when prescribing opioids is balancing the benefits of pain relief with the risk of opioid abuse. Risk stratification is a key step in determining whether a patient is suitable for opioid therapy. Clinicians must be cognisant of potential risk factors when assessing whether a patient with CNCP is an appropriate candidate for opioid therapy.[41] A complete history and physical examination,

including assessment of psychosocial factors and family history is part of the initial assessment for patient risk stratification.[42]

Table 4. Stepwise approach for prescribing opioid therapy in non-cancer pain[43]

Initial Evaluation	• Detailed medical history and physical examination to include: nature and intensity of pain, current and previous pain treatment, effect of pain on physical and psychosocial function, history of sub tance abuse. • Assess risk of subtance abuse, misuse and addiction with apporapriate screening tools e.g.SOAPP-R, ORT, DIRE.
Referral	• Pattiens with a personal or family history of alcohol or drug abuse are at risk of aberrant drug-related behaviour and should be referred to a specialist with expertise in addiction medicine or pain management for assessment.
Informed consenst	• Obtain informed consent before starting opioid theraphy. • Establish an opioid agreement wit the patient. • Discuss goals, expectations, risks, benefits and alternatives to chronic opioid therapy.
Initiation	• Choice of opioid, initial dose, and tiration should be individualised and based on patient's medical condition. • A short-team trial of opioid lasting from 4 to 8 weeks is recommended. • Descision to proceed with long-term theraphy should be based on the outcome of the trial e.g.efficacy, side, effects, meeting goals, ect.
Monitoring	• Regular monitoring is recommended for all patients on chronic opioid theraphy. • In patients at low risk for adverse outcomes and stable doses of opioids, monitoring at leats once every 3 to 6 months may be suffcient. • More frequent monitoring is suggested after initation of theraphy or changes in opioid doses and in patients at higher risk for aberrant drug related begaviours, those in an occupation demanding mental acuity, and in older adults or patients with comorbid medical conditions. • For patients at high risk for adverse outcomes, monitoring on a weekly (or more frequent) basis may be required. • Monitoring of the following is recommended: pain severity, functional ability, progress towards achieving theraputic goals, presence of adverse effects and presence of aberrant drug related behaviours. • Pill counts, family member or caregiver interviews, and use of prescription monitoring programme date can be useful supplements. • Periodic urine drug screening is recommended in all high-risk patients.
Discontinuation	• Patients should be tapered or weaned off chronic theraphy when they engage in serious or repeated aberrant drug realated behaviours or diversion, experience intolerable adverse effects, or make no progredd towards meeting therpeutic goals. • When patients is taking more than 200 mg morphine or its equivalent per day without any significant pain relief, discontinuation of opioid therapy should be considered. • Tapering can often be achieved in the oytpatient setting in patient without severe medical or psychistric comorbidities • Weekly reduction in dose by 10% is generally well tolerated without severe medical symptoms od opioid withdrawal. • In more complex cases, detoxificatioin in a rehabilitation setting can be helpfull, especially for patients unable to reduce their opioid dose in a less structured setting. • If the aberrant behaviours are related to addiction, addcition treatment resources should be made available.

An ongoing, past, and family history of addiction must be evaluated.[44] This is because a personal or family history of alcohol or drug abuse is highly predictive of opioid abuse, misuse, or other aberrant drug-related behaviours.[45] Younger age and the presence of psychiatric comorbidities may also be predictive of opioid abuse. Therefore, at-risk patients should be referred to a specialist trained in addiction or pain medicine for further evaluation.

Validated screening tools are useful adjuncts for risk stratification in major pain centers worldwide. The Revised Screener and Opioid Assessment for Patients with Pain (SOAPP-R)[46], Opioid Risk Tool (ORT)[47] and Diagnosis, Intractability, Risk, Efficacy (DIRE) Instrument[48] may be useful in some patients but are not commonly employed. However, a detailed individualized assessment remains key in selecting patients for opioid therapy.

Informed consent

If the patient is deemed suitable for a trial of opioid therapy, informed consent should be obtained prior to initiation of therapy, preferably in the form of an opioid treatment agreement with the patient.[49]

Goals of therapy, expectations, risks and benefits as well discontinuation of opioid therapy if there are no improvements in pain or function should be discussed.

Initiation of opioid

The initial opioid therapy must be based on identifying the minimal effective dose at which pain is controlled and balanced with minimal adverse effects in an individually tailored pharmacological program. While opioids are associated with a variety of adverse effects these can often be minimised with careful drug titration and maintenance.[50] Commonly encountered side effects include constipation, sedation, nausea and vomiting. Oral opioids are preferred over injectable opioids owing to their ease of administration. Sustained-release formulations are preferred over immediate-release formulations because steady plasma drug concentrations can be achieved. Pethidine was administered intravenously or intramuscularly. However, it has no unique clinical advantages over other opioids such as morphine. Accumulation of its active metabolite, norpethidine, can potentially cause neurotoxicity. Pethidine also possesses a higher potential for abuse than other opioids, as it produces more intense euphoria after drug injection.[51] The general consensus from various working groups is that pethidine has no role in the management of CNCP.[52] A short-term trial of opioid therapy over 4 to 8 weeks is generally recommended. During the trial, physicians should see the patient more frequently to make dose adjustments based on pain intensity, side effects, and functional improvements. The task force recommends a trial duration of 8 weeks and an upper titration dose limit of 200 mg of oral morphine or its equivalent dose per day[53], beyond which the harm may outweigh the benefits of opioid therapy in non-cancer pain.[54] The decision to proceed with long-term opioid therapy should be based on the trial outcomes. These outcomes may also be discussed with patients at the initiation of the trial to foster a better understanding of the trial and treatment objectives. Opioids can be continued if there is a satisfactory response to the initial therapeutic trial, with acceptable side effects.

Dose titration and monitoring

Dose titration is necessary to establish the optimal and minimal effective doses while minimizing the likelihood of adverse effects. In most controlled studies, the opioid dose was ≤180 mg of morphine or equivalent per day.[55] A recent cohort study reported an 8.9-fold increase in overdose risk for patients receiving ≥100 mg/day for CNCP, indicating that there is a direct link between dosage and the risk of overdose.[56]

Therefore, regular monitoring is recommended for patients undergoing chronic opioid therapy. The risk of polypharmacy and drug interactions must always be taken into consideration.[50] The patient's medication history, including additions or replacements with new medications for other medical conditions, should be reviewed at every visit.

In the first five years after the onset of a chronic pain problem, patients are at an increased risk of developing problems and disorders associated with new drug use. The risk appears to be highest among those with a history of drug use disorder or psychiatric comorbidity.[57] Not infrequently, a history of substance abuse emerges only after the current misuse of medications has been identifi ed, thus requiring physicians to monitor treatment closely.

It is estimated that the incidence of aberrant medication taking behaviour ranges from 5% to 24%, and the prevalence of current substance use disorders may be as high as 50%.[58,59] Even higher rates are reported in patients with a history of substance abuse.[58] The prescribing physician must be vigilant in detecting signs of opioid abuse or diversion.

Patients at low risk of drug abuse or on stable doses of opioids can be reviewed once every 2–3 months. More frequent monitoring is recommended for patients at high risk of aberrant drug-related behaviors or when there are changes in opioid doses. Assessment and documentation of four domains (4 As), namely, analgesia, activities of daily living, adverse effects and aberrant drug-taking behaviour, should be included in every visit.[60]

Adherence monitoring is crucial to ensure appropriate opioid use and avoid abuse. Risk reduction measures may include urine drug screening, pill counts, and regular offi ce visits.[48,61]

Discontinuation of opioid therapy

Controversy surrounds the long-term use of opioid for chronic nonmalignant pain.[62] Studies generally last less than 18 months and are complicated by high rates of discontinuation because of adverse events or insufficient pain relief. Opioids should be slowly tapered to avoid withdrawal and completely discontinued if the risks (side effects, toxicities, and aberrant drug-related behavior) outweigh the objective benefits (analgesia and functional improvements).

Opioid therapy should be tapered off when a patient exhibits aberrant drug-related behavior or diversion or experiences intolerable adverse effects (Table 5). When predetermined therapeutic goals, namely pain reduction and functional improvement, are not achieved[52], despite escalating the opioid dose to more than 200 mg morphine or its equivalent per day, discontinuation of therapy should be considered. A gradual reduction in dose which is well tolerated will prevent symptoms of opioid withdrawal.[63]

Patients should be referred to an appropriate specialist for further evaluation when other forms of therapy, including surgery, interventional procedures, or psychological therapy, are available.

Table 5. Types of aberrant drug behavior

Doctor shopping
Forging prescriptions
Stealing or borrowing drugs
Multiple episodes of loss or theft of prescription drugs
Not following prescribed dose and shedule
Multiple unauthorised dose increases
Pushing for higher dose of opioids
Repeatedly seeking drugs from other provioders or emergency departments
Noncompliance with non-pharmmacological compenents of pain treatment (e.g. physiotherapy, psyicological therapy)
Showing up only for medication appointments (e.g. misses, camcels, or no-shows at other appointments)
Concurrent use of illiicit drugs (e.g. heroin, cocaine, methamphetamine, marijuana, others)
Concurrent use of alcohol
Tobacco use
Past history pf abuse of prescription medications or illicit drugs
Requests for spesific drugs, especially a preference for immediate-relase over sustained-relase preparations
Positive urine drug test for illicit drugs or unauthorized drugs
Appearing intoxicated
Deteriatation of function at work, in the family or socially

Conclusion

Opioids play an important role in the management of chronic non-cancer pain. Opioids should not be the drug of choice for chronic pain, and should only be used when necessary. The goal of CNCP treatment is similar to the treatment of all other chronic pain patients and that is to improve pain outcomes and maintain functionality. Multidisciplinary pain management approaches have been developed along with a biopsychosocial model of chronic non-cancer pain. This study indicated that the integration of multiple strategies with different components in pain management led to better results than when a single intervention was applied. The efficacy of the multidisciplinary programs was found to be better than the standard medical treatment and other non-multidisciplinary treatments.

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