Focused Review

Monitoring Opioid Adherence in Chronic Pain Patients: Assessment of Risk of Substance Misuse

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Disclaimer: There was no external funding in preparation of this manuscript.
Conflict of Interest: None

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Manuscript received: 11/01/2010
Revised manuscript received: 12/17/2010
Accepted for publication: 01/12/2011

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Background: Use of opioids for chronic non-cancer pain (CNCP) has increased in recent years because this pain had been undertreated. There was also a simultaneous increase in misuse and abuse of opioids. Deaths due to such abuse and misuse also have risen as seen in the many reports published every day in local papers as well as in the medical literature. So, it is imperative that patients who are prescribed these medications be monitored for adherence so misuse and abuse can be curtailed and opioids are available to those who genuinely need them for chronic pain control. There are various screening tools available to monitor such adherence, and there is an abundance of literature about it in addiction and psychiatric medicine. There is, though, a paucity of such literature as applied to pain medicine.

Objectives: Our objectives for this review were twofold. We wanted to identify which screening tools are available to monitor opioid adherence and we wanted to see if there were prospective comparative studies of these tools to identify a single best tool that can be applied to all chronic non-cancer pain patients managed with opioids.

Study Design: We did a review of the current literature about monitoring of opioid adherence. We also looked at their use, validity, and comparative studies.

Methods: We performed a literature search using PubMed, EMBASE, and the Cochrane library. The search was conducted using the terms opioids, non-cancer pain, monitoring, and adherence. The databases from 1996 to November 2010 were reviewed. The search included prospective and retrospective studies, review articles, and FDA records. Bibliographies and cross references were reviewed when deemed appropriate.

Conclusion: We found 52 publications, of which 22 met the criteria to be included in this manuscript. We found only one study that was prospective, and compared the various screening tools that are available to monitor opioid adherence. In the majority of the studies the number treated was small. There was not a single screening tool that can be applied universally to all patients who are on opioid therapy for chronic non-cancer pain.

Key words: Opioids, chronic pain, chronic non-cancer pain, opioid adherence, monitoring of opioid adherence, controlled substances, prescription monitoring programs, screening tools

Pain Physician 2011; 14:E119-E131

Eighty million Americans suffer from chronic pain. It affects various aspects of their life and utilizes tremendous resources. Twenty-one percent of emergency room visits and 25% of missed work days are related to chronic pain. This translates into an annual cost of $100 billion. (1-3). Chronic pain is defined by the International Association for the Study of Pain as "pain that persists beyond normal tissue

healing time, which is about 3 months." Chronic pain that is not associated with acute pain, post-surgical pain, cancer pain, and pain at the end of life is termed chronic non-cancer pain (CNCP). The American Society of Interventional Pain Physicians (ASIPP) defines CNCP, using a combination of definitions, as, "pain that persists 6 months after an injury and beyond the usual course of an acute disease or a reasonable time for a comparable injury to heal, that is associated with chronic pathologic processes that cause continuous or intermittent pain for months or years that may continue in the presence or absence of demonstrable pathology; may not be amenable to routine pain control methods; and healing may never occur" (4,5).

CNCP is a leading cause of disability (6,7). Opioids are one of the most prescribed medications to treat pain. Opioids are accepted for the treatment of acute pain, post-surgical pain, and cancer pain, but their use for CNCP is open to debate (8-14). Opioids are effective in short-term trials to treat neuropathic pain (11). There is limited evidence of their effectiveness in long-term management of CNCP (9-16).

The decade of pain management was the 1990s. The Joint Commission on Accreditation of Health Care Organizations (JCAHO) mandated new pain management standards for inpatients and outpatients (12). State medical boards liberalized their guidelines governing the prescribing of opioid medications for treatment of CNCP (17). These changes in the regulations and consensus of professional societies about pain being undertreated led to an increase in opioid prescriptions (18-20). Now the pendulum has swung too far in the other direction in the United States (21).

In the process of advocacy and politics, we as pain physicians have forgotten that traditionally chronic pain was not treated with opioids. It seems that behavioral and physical approaches, including interventional techniques, to pain management, have assumed historical importance rather than a place in clinical practice. Even so, the increase of surgical interventions and interventional techniques also has been escalating, escalating at a more rapid pace for opioids than others (22-30). Further, patients undergoing surgery, after surgery, and patients receiving interventional techniques also continue to receive opioids (20,21). Opioids, despite their misuse, overuse, abuse, and deaths, avert various adverse consequences and deaths (31-56). In addition, it has also been illustrated that interventional techniques are an effective modality for managing at least chronic spinal pain, thus reducing opioid dosages and also avoiding adverse consequences (57-85). However, to achieve this effect the evidence must be synthesized appropriately, utilizing the proper principles of evidence-based medicine and comparative effectiveness research (86-93). Consequently, the liberal prescription of opioids has brought the responsibilities of the pain physician into the limelight, as this is also associated with significant hazards, including death (8-21,94-97).

Americans constitute only 4.6% of the world's population, yet they consume 80% of the world's opioid supply, and 99% of the world's hydrocodone supply. They also use two-thirds of the world's illicit drugs. (20,21,98,99). Retail sales of morphine, hydrocodone, hydromorphone, and fentanyl base have skyrocketed. This has resulted in increased emergency room visits and unintended deaths. Unintentional death from prescription opioids overdose has surpassed those from cocaine or heroin overdose (Fig 1). In Reader's Digest of December 2010, Jetter (100) wrote: "Prescription drugs are more popular with teens than cocaine, heroin and methamphetamine combined and the scariest part is you probably have these pain killers in your medicine cabinet right now." Nora Volkow ,MD, director of The National Institute of Drug Abuse (NIDA) stated that one 40 mg methadone pill, washed down with 2 gin and tonics, can be fatal (101).

This is an epidemic, and as responsible pain management physicians we must help tackle this public safety issue. If opioids are to have a place in our pain practice armamentarium, and a place in the management of CNCP, then there has to be a balance between safe and appropriate prescribing of these drugs as well as prevention of misuse, abuse, and diversion of the same. Those who abuse or misuse these drugs obtain them from pill brokers or dealers, doctor shoppers, the open air drug market, the Internet, family and friends, and "script doctors" who prescribe opioids for a fee without a physical examination, in addition to nurses.

Misuse, abuse, and diversion should be addressed on 3 fronts.

1. Prescription drug monitoring programs (supply)
2. Screening tools to monitor opioid adherence (demand)
3. Development of Abuse Deterrent Formulations (ADF) of opioids (drugs).

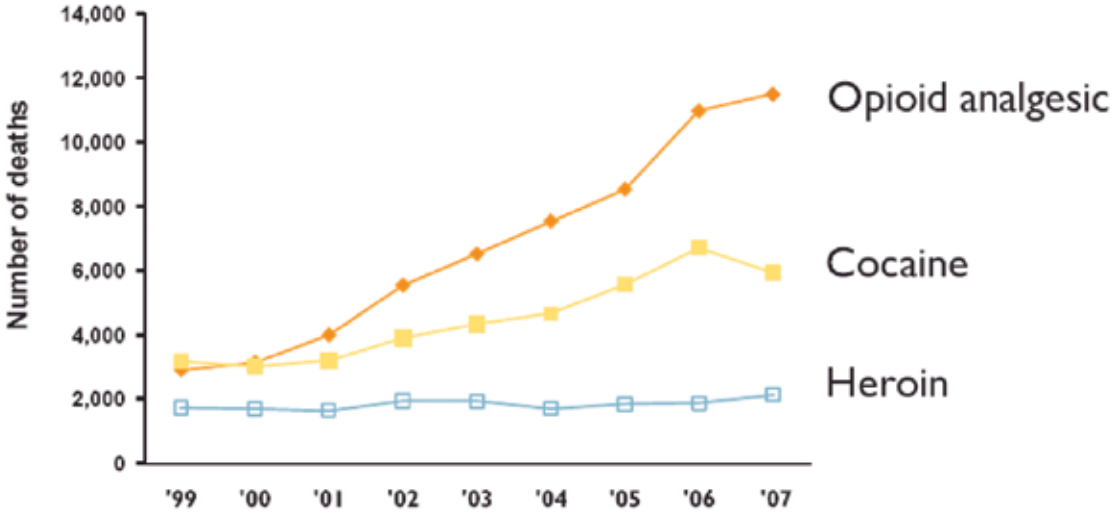

Fig. 1. *Unintentional drug overdose deaths by major type of drug, United States, 1999-2007.*
Source: National Vital Statistics System

1.0 Methods

This comprehensive review is undertaken to evaluate various instruments available in the assessment of the risk of substance misuse specifically in chronic non-cancer patients.

The methodology utilized here follows a systematic review process derived from evidence-based systematic review and meta-analysis of randomized trials and observational trials (86-93,102-104), Consolidated Standards of Reporting Trials (CONSORT) guidelines for the conduct of randomized trials (105,106), STROBE guidelines (107), Cochrane guidelines (10), and Chou and Huffman (11,108) guidelines.

A comprehensive search of the literature was conducted for the period 1996 through June 2010. Databases for the search included PubMed, EMBASE, Cochrane reviews, and clinicaltrials.gov. The search also included cross-referencing bibliographies from notable primary and review articles, and abstracts from scientific meetings, and peer-reviewed non-indexed journals. The search emphasized opioid therapy in managing non-cancer-related pain. Due to the paucity of the literature and also the diagnostic nature of these studies, methodologic quality assessment was not performed.

2.0 Results

Multiple manuscripts were identified for all aspects of monitoring, including prescription monitoring programs (PMP), screening tools to monitor opioid adherence, and development of ADFs of opioids.

2.1 Prescription Monitoring Programs

PMPs collect state-wide data about prescription drugs and track their flow (97,109). There are 3 components of these programs. First is data collection for prescriptions that shows the physicians who wrote them and the pharmacies that dispensed them. Pharmacies are required to report the data by law. Physicians are encouraged to report but are not mandated to do so. Second, there should be a central repository for this data, and lastly there should be a protocol in place describing how this data from the central repository can be made available to appropriate authorities and agencies. To date, 38 states have PMPs, but there is a significant difference in the manner and frequency with which the data is collected.

President George W. Bush signed into law the National All Schedule Prescription Electronic Reporting Act (NASPER) in 2005 which was created by ASIPP and enacted by Congress (110). This law requires states to

collect prescription information for Schedule II, III, and IV medications. It also requires states to have the capability to share this information with each other. This can decrease cross-border narcotic trafficking. It is heartening to know that this program is now funded by the federal government.

At one point, only 3 states allowed physician's access with physician-friendly programs to monitor drug utilization. These included Kentucky, Utah, and Idaho. Now, with enactment of NASPER and/or other funding from the Harold Rogers Prescription Monitoring Program, multiple states are operating physician-friendly programs where pain physicians can identify the risk of overuse and abuse (97,109-112).

2.2 Screening Tools to Monitor Opioid Adherence

There are a number of screening tools that have been developed to monitor possible abuse and misuse of opioids. All of them have their applicability and limitations. Various screening tools are listed below. Each one could show effectiveness in some pain management scenarios. Various authors have reviewed these screening tests to identify patterns of abuse or addiction.

1. Alturi: 6-point screening (113)
2. Cut Down, Annoyed, Guilty, Eye-Opener (CAGE) and CAGE-AID (114)
3. Chabal: 5-point prescription opiate abuse checklist (115)
4. Current Opioid Misuse Measure (COMM) (116)
5. Drug Abuse Screening Test (DAST) (117)
6. Opioid Risk Tool (ORT) (118)
7. Prescription Drug Use Questionnaire (PDUQ) (119)
8. Pain Medication Questionnaire (PMQ) (120)
9. Screening Instrument for Substance Abuse Potential (SISAP) (121)
10. Short Michigan Alcoholism Screening Test/Adapted to Include Drugs (SMAST- AID) (114)
11. Screener and Opioid Assessment for Patients with Pain (SOAPP) (122)
12. Screening Tool for Addiction Risk (STAR) (123).

There is not a single instrument that is available that can be uniformly accepted and broadly applied to the current practice of pain management.

Chou and his colleagues (124) evaluated 9 studies (N=1,530) for accuracy of screening tools for identification of aberrant drug-related behavior in patients who were on long-term opioid therapy for CNCP. They found that none of the investigators were blinded to the results of the screening instruments. There was a significant variation in the aberrant drug-related behavior across the studies. Only 2 studies out of 9 made evaluations using the Pain Medication Questionnaire. Out of the 8 instruments studied, 2 were self-administered, 4 were interviewer-administered, and in the remaining 2 studies the methodology was not described. Pain scores were recorded in only one study, and none of the studies documented the doses of the opioids used. In one higher quality study, self-administered COMM was used to determine the diagnostic test characteristics of this instrument (116). It showed a sensitivity of 0.75 (95% CI, 0.63-0.84) and specificity of 0.73 (95% CI, 0.65-0.80). In another lower quality study, the interviewer-administered Addiction Behavior Checklist (ABC), showed a sensitivity of 0.88 and specificity of 0.86 (125). Screening instruments in 4 studies showed poor diagnostic accuracy.

SOAPP contains 24 items. Each can be answered on a 5-point scale. It was administered to 175 patients with CNCP and repeated after 6 months in 95 patients. It was concluded that a score of 7 or higher might be a cutoff for SOAPP (116). Akbik et al (126) put the SOAPP validity and reliability to test to determine the risk of abuse in patients taking opioids. They found 5 factors that could predict abuse. These were:

1. History of substance abuse
2. Legal problems
3. Medication craving
4. Heavy smoking
5. Mood swings.

But the results have not been reproduced.

COMM was developed and validated by Butler (116). It consists of 40 items, of which 17 showed reliability and consistency to predict aberrant drug behavior. This is a measure that can be used to assess adherence in patients already on opioids. But its long-term reliability has not been confirmed. It has also not been tested in diverse patient populations and in varied clinical scenarios.

Adam et al (120) developed the PMQ. This was designed to test the inappropriate use of opioid medication. It consists of 26 items; the responses are evaluated on a 5-point scale. The subjects can be classified as the lowest, middle, or the highest third, depending on the PMQ scores. Despite its effectiveness, the questionnaire is lengthy and takes time to complete, so its clinical applicability might be limited. Further research is needed before it can be applied as a broad-based tool. This tool is most useful in judging the progress of pain patients who are already taking opioids.

Miotto et al (119) developed PDUQ. It is physician administered. It contains 42 items that have yes and no answers and takes 20 minutes to complete. The validity of this instrument was tested in patients with CNCP being treated at a university-based pain center (127). It was a pilot assessment tool. Results show that they were able to identify certain drug-seeking behaviors like multiple prescription providers, increasing the dose or the frequency of the opioid, and getting prescriptions from the emergency room. They also found that 3 screening criteria were firm predictors of addictive behavior, but these have not been validated.

Friedman developed the STAR (123). It consists of 14 yes and no questions and was developed to assess addiction risk. It has been validated in chronic pain patients with and without addiction. Despite these results, larger studies are needed to determine its ability to predict aberrant drug-taking behavior.

ORT was formulated by Webster and Webster (118). It is a 5-item self-reporting tool with yes or no answers. It is designed to predict the probability of the patient to display aberrant drug behavior when opioids are prescribed. They tested this tool in 185 new patients and found that 94.4% of patients were in the low risk category (score of 0-3) and did not display aberrant drug behavior; whereas 90.9% in the high risk group (score of 8 or higher), and 28.5% in the moderate risk (score of 4-7) group did. This tool has tremendous clinical appeal because of its brevity and ease of scoring. But it is susceptible to deception. So, the clinician needs to decide whether to administer longer and more cumbersome instruments to guard against such deception. It is sensitive and specific in determining which individuals will be at risk for opioid abuse, but its universal application has not been demonstrated.

SISAP was developed and validated by Coambs et al (121). It is administered by the physician. It is designed to identify patients with CNCP who might be at risk of abusing opioids if they are prescribed. It showed an accuracy of 80%, sensitivity of 91%, and specificity of 78%. Such a tool can stratify chronic pain patients in a primary care setting, so those who need opioids can be identified and given a prescription. This tool was developed from the largest database of pain patients, approximately 5,000 patients. So, it is amazing to note that it is not validated by prospective trials to determine this tool's ability to predict aberrant drug-taking behavior.

A clinician-administered instrument to identify inappropriate drug use in chronic pain patients was published by Wu et al (125). It is brief and includes behaviors both during the clinic visit and between clinic visits. The tool was validated in 136 veterans. The conclusion was that psychometric findings can help the physician determine appropriate versus inappropriate use of opioids.

There are multiple standardized addiction screening tools that are sensitive enough to identify addiction disorders. Three of them are appropriate for screening in clinical practice: CAGE-AID Screen, Cyr-Wartman Screen, and Skinner Trauma Screen (128). The questionnaires are listed in Table 1.

Table 1. *Addiction screening: questionnaires for 3 commonly used screens.*

CAGE-AID	Have you felt you ought to cut down on your drinking or drug use? Have people annoyed you by criticizing your drinking and drug use? Have you felt bad or guilty about your drinking and drug use? Have you ever had a drink or used drugs first thing in the morning to steady your nerves or to get rid of a hangover (eye-opener)?	Two positive answers constitutes a positive screen.
Cyr-Wartman Screen	Have you ever had a problem with alcohol (or drugs)? When was your last drink (or drugs)?	A positive screen that roughly correlates with the CAGE in terms of specificity and sensitivity is "yes" and within 24 hours of the medical appointment.
Skinner Trauma History	Since your 18th birthday, have you: Had any fractures of dislocations to your bones or joints? Been injured in a road traffic accident? Injured your head? Been injured in an assault or fight (excluding injuries during sports)? Been injured after drinking?	Two positive answers from 5 questions constitute a positive response.

Adapted from: Savage SR. Assessment for addiction in pain-treatment settings. *Clin J Pain* 2002; 18:S28-S38 (128).

CAGE-AID was developed for screening for alcohol use and was then adapted to assess misuse of other drugs (129). With 2 positive answers the sensitivity was 70% and specificity was 85%. This improved to a sensitivity of 79% and specificity of 77% when a criterion of one positive answer was used. The CAGE-AID has been validated in pain patients. Many clinicians are familiar with it. It is brief to administer. These aspects make it a reasonable choice to use for initial screening and then use another instrument to predict aberrant drug behavior. The Cyr-Wartman Screen was also developed to assess alcohol misuse, but including all drugs makes it more useful to indicate general substance abuse (130). The Skinner Trauma Screen is also used to identify alcohol abuse, but has been clinically adapted to identify drug abuse problems (131). It is important to note that none of these tools are diagnostic nor are they specific for drug misuse, abuse, or addiction.

Chabal et al (115) developed a physician-administered checklist to evaluate prescription opioid abuse in patients with CNCP. It evaluates a series of behaviors rather than relying on the answers. They were able to show that if the patient met 3 or more of the following criteria, that patient can be classified as an opioid abuser. The criteria were as follows:

1. Overwhelming focus on opiate issues
2. Three or more early refills or escalating drug use without changes in the medical condition
3. Multiple phone calls or visits requesting additional opiates or early refills
4. Reports of lost or stolen medication
5. Getting opiates from multiple providers, emergency rooms, or illegal sources.

This was validated in a single population of veterans. A broader population sample needs to be studied to better evaluate the utility of these criteria. It is a useful tool to gauge adherence once a patient is on opioid therapy. It can also help in making changes in treatment and level of monitoring. It can also provide valuable information to the referring physician about the degree of non-adherence by the patient.

Atluri and Sudarshan (113) developed a tool to detect the risk of inappropriate use of prescription opioids in chronic pain patients. They developed this tool to be used in the interventional pain management setting. They identified 6 clinical criteria that could predict opioid misuse:

1. Focus on opioids
2. Opioid overuse
3. Other substance abuse
4. Low functional status
5. Unclear etiology of pain
6. Exaggeration of pain.

This screening tool is based on the number of positive criteria from 0 to 6. Patients who misused opioids scored above the cutoff of 3. Patients with scores higher than 3 had an odds ratio of 16.6 (95% CI: 8.3-33 and $P < 0.001$) for opioid abuse. The drawback of this study is that it is retrospective and is limited to patients with CNCP who were being treated with opioids. Manchikanti et al (132) used these criteria prospectively to test 500 patients in an interventional pain setting. Out of these 500 patients, 100 had a history of drug abuse. They concluded that this was a cost-effective screening tool for drug abuse potential in an interventional pain setting. It was also reliable. They also used this screening tool to see if it could predict illicit drug use (133). It accurately predicted substance abuse but did not identify illicit drug use.

In Table 2, behaviors suggestive of addiction are listed. This was described by Savage (128). Patients using opioids could manifest one or more of these behaviors as shown in Table 2. This requires further studies

Table 2. *Patterns suggestive of addiction in pain patients*

Adverse Consequences/Harm Due to Use
Intoxicated/somnolent/sedated
Declining activity
Irritable/anxious/labile mood
Increasing sleep disturbance
Increasing pain complaints
Increasing relationship dysfunction
Impaired Control Over Use/Compulsive Use
Reports lost or stolen prescriptions or medications
Frequent early renewal requests
Urgent calls or unscheduled visits
Abusing other drugs or alcohol
Cannot produce medications on request
Withdrawal noted at clinic visits
Observers report overuse or sporadic use
Preoccupation with Use Due to Craving
Frequently misses appointment unless opioid renewal expected
Does not try nonopioid treatments
Cannot tolerate most medications
Requests medications with high reward
No relief with anything except opioids
Any of these behaviors could occur from time to time in patients using opioids appropriately for pain relief or when pain is inadequately relieved. A pattern of these behaviors in the context of titrated pain therapy suggests the need for further evaluation.

Adapted from: Savage SR. Assessment for addiction in pain-treatment settings. *Clin J Pain* 2002; 18:S28-S38 (128).

to determine if they could predict inappropriate drug use.

The best approach to identify potential drug abuse or misuse is to use multiple instruments in a coordinated manner because of the lack of a single instrument that can be used for this purpose (134,135).

Moore et al (136) compared commonly used and preliminarily validated screening tools like SOAPP, ORT, and Diagnosis, Intractability, Risk, and Efficacy (DIRE) inventory to see how they compare in predicting aberrant drug behavior. Those in the study also participated in a 45-minute interview with a clinical psychologist. Each tool had a cut-off point. Participants who scored greater than 6 on the SOAPP, and less than 14 on the DIRE, were considered "high risk." For ORT, those who scored from 4 to 7 were "medium risk" and those above 7 were "high risk." Highest sensitivity was for the clinical interview (0.77). SOAPP achieved a high sensitivity value of (0.73), ORT had a sensitivity value of (0.45), and for DIRE the sensitivity value was (0.17). When the clinical interview was combined with the SOAPP, the sensitivity increased to 0.9. The limitation of the study is that the sample size was small and there was no comparison group. Their conclusion was that SOAPP performed best out of these 3 screening tools. They also stated that an interview with a trained psychologist was the best predictor of future drug-related aberrant behavior.

There are external and internal factors that can affect pain, psychopathology, and substance abuse and these should be taken into consideration to predict controlled substance abuse. Factors like pain due to traumatic accidents, pain at multiple sites, and a history of illicit drug use might predispose a patient to controlled substance abuse. Socio-economic factors can also play a role. Manchikanti et al (137,138), showed that there is an increased incidence of prescription drug misuse and illicit drug use in the Medicaid population. They were also able to demonstrate that it decreased by 50% when adherence monitoring was instituted (139).

There are numerous screening tools available to evaluate pain, psychopathology, and drug misuse and abuse. So far there is no ideal instrument that is available that can screen for all these and reliably predict the potential for substance misuse or abuse. Even if such an instrument were available, it might be difficult for the patient to accurately fill it out and complete it. It is recommended that it might be better to use multiple instruments and use a coordinated approach to identify and predict the patients who are likely to misuse or abuse prescribed opioids (134,135). This template is useful and effective, but is not likely to provide needed information in all patients and in all clinical settings.

It is important to note that there are no studies that have looked at the effectiveness of risk assessment and monitoring for improving clinical outcomes or reducing the risk of aberrant drug behavior.

2.3 Development of Abuse Deterrent Formulations of Opioids

The pharmaceutical industry is under growing pressure to develop ADFs of opioids (140). This potentially can curtail abuse but still have opioids readily available for pain management for those who need them. It is imperative that ADFs be developed because opioids are attractive for abuse. The potential for abuse depends on the formulation, route of administration, and rapid rise of plasma concentration resulting in drug liking and reinforcement. Various types of ADFs are being developed, but these do not necessarily decrease abuse in those who will consume the drug intact. Some ADFs employ physical barriers that resist common methods of tampering like crushing the pill and subjecting the pill to various chemical manipulations to extract active ingredients so that they can be snorted or chewed. A combination of opioid agonists and opioid antagonists have been tried. One such example is Talwin, but it also decreases its efficacy to treat moderate pain. Another ADF is a prodrug that needs to be metabolized to an active form after ingestion to produce an analgesic action. It incorporates aversive stimulants like niacin or capsaicin. If the drug is tampered with before ingestion, the aversive stimulants are released, producing an uncomfortable physical sensation. Manufacture of ADFs also can increase the manufacturing cost of the opioids. In the long run though, it might be economical if the ADFs can change the pattern of behavior associated with abuse of prescription opioids, thereby decreasing the consequences and associated medical costs as well as death. ADFs can also make the active ingredient less accessible and less attractive for those who would like to use the drug by an alternate route.

3.0 Discussion

Without question, there is a "drug problem"; but it is not a simple problem, and therefore cannot be mitigated by simple solutions (10-13,17-22,31-47,141-144). The nature of the problem is multi-fold: While it may be that opioids are inappropriately used and prescribed, it is important to identify the reasons for this misuse and mis-prescription. Obviously, pain physicians

recognize the axiomatic obligation to safely and effectively treat patients' pain. Yet, given the subjective nature of pain, and the increasingly complex picture of pain as affected by (and correlated to) other neural and psychiatric conditions, including potential for substance abuse, the economic and temporal restrictions placed upon the practice of pain medicine could hamper physicians' abilities to spend sufficient time with each and every patient to allow insight into this complexity. Thus, physicians could feel compromised in their ability to exercise expert knowledge and capacity, and could be abreactive to patients' explicit requests (if not demands) for specific (opioid) drugs in light of fears of malpractice litigation, DEA prosecution, and professional sanction.

Long-term opioid therapy for chronic pain, while common, indicated and necessary, is associated with risks of adverse side effects as well as potential for misuse, abuse, illicit drug use, and diversion. It is incumbent upon the pain physician to be aware of those effects and to discuss the risks and benefits of the use of controlled substances with patients or surrogate(s). As well, it is the physician's responsibility to recognize the potential for and occurrence of substance misuse, abuse, and addiction, and in light of this, the necessity of the means of predictive assessment, determination, and treatment.

Adherence monitoring is essential in this regard, and mandates a prudent combination of initial evaluation(s) and periodic review and monitoring utilizing initial screening, testing, and evaluation throughout the course of treatment, using various screening tests, urine drug testing, prescription monitoring programs, and controlled substance agreements.

Consequently, the evidence shows that no single evaluation, either prescription monitoring programs, screening tools to monitor opioid adherence, development of ADFs of opioids, or urine drug testing alone, are dependable to assess the risk of substance misuse. Among the screening tools to monitor opioid adherence, of the 12 identified tools (113-123), none were reliable in identifying misuse.

4.0 Conclusion

There are a number of screening tools that have been developed to monitor possible abuse and misuse of opioids. All of them have certain applicability and limitations. Similarly, drug monitoring programs, urine drug testing, and abuse resistant formulations also might be helpful, but none are diagnostic.

Acknowledgments

The authors wish to thank Bert Fellows, MA, and Tom Prigge, MA, for manuscript review, and Tonie M. Hatton and Diane E. Neihoff, transcriptionists, for their assistance in preparation of this manuscript. We would like to thank the editorial board of *Pain Physician* for review and criticism in improving the manuscript.

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