

FORENSIC PAIN MEDICINE

Medico-legal Rounds: Medico-legal Issues and Alleged Breaches of “Standards of Medical Care” in Opioid Rotation to Methadone: A Case Report

David A. Fishbain, MD, FAPA,^{a-f} R.B. Cutler, PhD,^{a,d-f} Brandly Cole, PsyD,^{e,f} John Lewis, PhD,^{a,d} R. Steele Rosomoff, BSN, MBA,^{b-f} and H.L. Rosomoff, MD, DMedSc, FAAPM^{b-f}

Departments of ^aPsychiatry, ^bNeurological Surgery, and ^cAnesthesiology, University of Miami ^dSchool of Medicine; University of Miami ^eComprehensive Pain & Rehabilitation Center at ^fSouth Shore Hospital

ABSTRACT

Objectives. The objectives of this medico-legal case report were the following: 1) To present an example of a medico-legal problem that developed as a result of a decision to rotate a chronic pain patient (CPP) to methadone in order to taper the CPP from oxycodone; 2) To present both the plaintiff's and defendant's expert witnesses' opinions as to if and where the care of that patient fell below the “standard of medical care;” and 3) Based on these opinions, to develop some recommendations on how, in the future, pain medicine physicians and other physicians should proceed, in order to avoid allegations of breach of “standards of care” when using methadone.

Methods. This is a case report of a CPP treated at a regional hospital pain clinic. Methadone rotation was used in order to taper the CPP from oxycodone because of addictive disease.

Results. During the rotation process, the CPP expired. This had medico-legal consequences. Expert witnesses differed as to whether methadone caused the death.

Conclusion. Pain physicians should proceed with caution in using methadone for opioid rotation.

Key Words. Methadone; Chronic Pain; Addiction; Opioid Rotation; Opioid Detoxification; Medico-legal; Standards of Medical Care; Expert Witness; Drug Toxicology Screens

Introduction

Methadone is a synthetic opioid of the diphenylpropylamine class [1,2]. It has excellent oral bioavailability, low cost, extensive liver metabolism, no active metabolites, and is excreted mainly by the fecal route, therefore, it does not accumulate significantly in patients with renal impairment [2,3]. Because of the above, and its long-half life that enables extended dosing intervals (daily or 2–3 times per day), it has been uti-

lized as a maintenance drug for heroin addicts [1–5] and chronic pain patients [1,5]. Methadone has also been used as a detoxification agent in detoxification protocols from other opioids [6,7].

However, methadone has a number of negative aspects, which have made its use difficult. First, there are large interindividual variations in the pharmacokinetics of methadone. It is characterized by a rapid distribution phase (half-life 2–3 hours) that is followed by a slow elimination phase. This elimination phase has been noted to vary from 4.2 to 130 hours in some patients. Thus, variations in the elimination phase could lead to accumulation toxicity in some patients [1–3]. In addition, methadone may interact with other drugs. These are drugs that can affect (inhibit or

Reprint requests to: David A. Fishbain, MD, FAPA, University of Miami Comprehensive Pain Center, 600 Alton Road, Miami Beach, FL 33139. Tel: (305)-532-7246; Fax: (305)-534-3974; E-mail: d.fishbain@miami.edu.

induce) the cytochrome P450 system, specifically the CYP3A4 isoenzyme system. Thus, inhibitors of 3A4, such as some selective serotonin reuptake inhibitors, have the potential to increase levels of methadone [3]. Methadone may also partially inhibit the CYP2D6 isoenzyme system, thus affecting levels of such drugs as dextromethorphan, codeine, hydrocodone, secondary tricyclics, haloperidol, phenothiazine, and beta-blockers [3]. These properties of methadone decreased the popularity of the drug in the 1980s and early 1990s [1,4].

Recently, however, the popularity of methadone for pain treatment has increased due to a number of converging scientific discoveries about methadone. In addition to opioid agonist activity, methadone has been noted to demonstrate a relatively potent N-methyl-D-aspartate (NMDA) receptor antagonism [3,4]. Thus, methadone has been touted as having a potential role in opioid resistance and neuropathic pain [3]. For these types of problems and where uncontrollable side effects to other opioids occur, rotation to methadone from the current opioid has been advised [3]. A number of studies [8,9] have demonstrated that rotation to methadone does indeed result in significant reduction in pain and/or reduction of side effects.

The case described below was that of a chronic pain patient rotated from controlled-release (CR) oxycodone to methadone for detoxification purposes. The rotation appeared to result in dire medical consequences, which then resulted in a medico-legal suit. Because this case highlights a number of issues with respect to methadone use and issues in detoxification, it is described below.

Case Report

Mr. X was a 35-year-old Caucasian male who arrived at a detoxification facility with the chief complaint of opioid addiction. His alleged medication use (per Mr. X) was as follows: oxycodone CR, 800 mg per day; oxycodone 5 mg/acetaminophen 500 mg, 70 tablets per day; hydrocodone 7.5 mg/acetaminophen 325 mg, 70 tablets per day; and alprazolam 2 mg, up to 12 tablets per day. Mr. X would take one of the three above opioids daily. Mr. X claimed that he was taking these doses for chronic low back pain that resulted from a motor vehicle accident 3 years previously. He was getting these medications from two physicians and claimed that he had last used medications approximately 48 hours previously. He was complaining

of restlessness, shakiness, nausea, and abdominal cramping. His vital signs were stable, and his sensorium was clear at admission. He had been last detoxified 3 months previously, using methadone. There was a history of illicit drug use (crack cocaine and cannabinoids since adolescence and recently). On admission, he was placed on oxycodone CR 60 mg per day, oxycodone 5 mg/acetaminophen 500 mg every 6 hours as needed, and alprazolam 2 mg three times a day by the on-call psychiatrist. These doses were chosen according to telephone information transmitted by the nursing staff.

Mr. X was evaluated the day of his admission by the family medicine doctor, who noted that he demonstrated withdrawal symptoms (diarrhea, cramps, gooseflesh, sweats) and assigned a diagnosis of opioid withdrawal. Approximately 24 hours after admission, Mr. X was evaluated by the psychiatrist who diagnosed opiate dependence. The psychiatrist then discontinued the oxycodone CR and placed Mr. X on a 5-day alprazolam and methadone taper. In addition, he ordered clonidine 0.1 mg twice a day and zolpidem 10 mg as needed, at bedtime. The first step of the methadone taper was 35 mg twice a day.

That day, Mr. X received 70 mg of methadone and 0.2 mg of clonidine in addition to 20 mg of oxycodone CR and 10 mg of zolpidem (Figure 1). However, that night, at midnight, Mr. X was noted to be fully awake, not somnolent, and in no distress. Unfortunately, 2 hours later, Mr. X was found in the bathroom expired, lying in vomit. For a detailed timeline, please refer to Figure 1.

Coroner autopsy results fixed the cause of death as asphyxia secondary to aspiration of gastric contents. Postexpiration laboratory results yielded the following information. Admission drug screen was positive for benzodiazepines and cocaine. Twenty-hour postadmission drug screen was positive for benzodiazepines, cocaine, and opioids. Post-mortem body fluid analysis yielded a methadone blood level of 0.81 mg/L (toxic levels are 2 mg/L and therapeutic levels are 0.1–0.4 mg/L) [10].

Very soon after the death, a medical malpractice suit was filed against the addiction facility and the psychiatrist. We are only concerned with the medical malpractice aspects of this case. The plaintiff's expert witness noted a number of medical areas that she felt fell "below the standard." These are presented in Table 1. The defendant's expert witness responded to these allegations as shown in the second column of Table 1. The third column of the table outlines

Time	Event
-2,160	Previous detoxification with methadone
-24	Last claimed opioid use
0	Arrival at hospital
+1	Given oxycodone 5 mg/acetaminophen 500 mg
+3	Evaluated by family medicine physician—withdrawal symptoms: diarrhea, cramps, gooseflesh, sweats, vital signs stable; diagnosis: opioid withdrawal
+5	Given oxycodone CR 20 mg
+8	Given oxycodone CR 20 mg
+17	Given oxycodone 5 mg/acetaminophen 500 mg
+20	Given oxycodone CR 20 mg
+22	Given oxycodone 5 mg/acetaminophen 500 mg
+24.30	Evaluated by psychiatrist—diagnosis: opioid dependence; placed on methadone and alprazolam taper over 5 days and clonidine
+25	Given methadone 35 mg, clonidine 0.1 mg
+27.30	Given methadone 35 mg, clonidine 0.1 mg
+31.30	Given zolpidem 10 mg
+34.00	At midnight, patient noted to be in hallway requesting cotton balls for his ears as roommate snoring; patient in no distress, not somnolent
+36.00	Found dead in bathroom lying in vomit—resuscitation unsuccessful

Figure 1 Time line of events in hours beginning at Mr. X's arrival at the hospital

what might be construed to be the current “standard of care” in reference to each allegation.

The plaintiff's expert witness essentially alleged that Mr. X had expired from going into respiratory depression from a methadone overdose. The defendant's expert witness believed that Mr. X had died from aspiration secondary to vomiting. Vomiting could have been caused by the opioid itself (methadone, oxycodone), from opioid withdrawal, or from other reasons such as cocaine intoxication [11]. The most likely possibility, however, was opioid withdrawal. In a later deposition, the coroner indicated that, in her opinion, Mr. X did not die from a methadone overdose. The case was, therefore, settled for substantially less than policy limits.

Discussion

The nature of Mr. X's case and the subsequent comments of the expert witnesses bring to light

a number of issues recently presented in the pain literature. These issues are now becoming important to patient care. In addition, Mr. X's case also highlights or illuminates other older issues, which have also been important to good patient care for many years. These issues are the following.

First, as pointed out by the plaintiff's expert witness, there is an expectation that physicians will see/evaluate patients before prescribing and that this will be done in a timely manner (allegation #1). As pointed out by the defendant's expert, in certain circumstances, such as prevention of withdrawal, this expectation is waived. This allegation is closely related to allegations #2 and #3.

Second, the plaintiff's expert raises a complex medico-legal clinical issue, that of whether drug-dependent/intoxicated/abusing/addicted patients should be believed about their current drug use and whether clinical decisions should be based on

Table 1 Plaintiff’s and defendant’s expert witnesses’ opinions as to alleged breach of standards in Mr. X’s medical care and the medical/legal practice importance of these allegations to pain medicine

Plaintiff’s Expert Witness’s Allegation of Medical Care Area “Below the Standard”	Defendant’s Expert Witness’s Response to Allegation of Medical Area “Below the Standard”	Medical/Legal and Practice Importance of Allegation to Pain Medicine and Current Standard of Care
1. Psychiatrist should have examined patient (within 24 hours) before prescribing oxycodone (controlled substance); 24 hours is the standard of care.	There is no such rule. In detoxification facilities, drugs are often prescribed before patients are fully evaluated based on the history given to the professional staff in order to keep patients from going into withdrawal. Psychiatrist did not fall below standard of care here.	In general, physicians should attempt to see newly admitted patients within 24 hours to avoid this accusation.
2. Psychiatrist should not have relied on nursing and other physician reports before prescribing and should have looked for symptoms of opioid withdrawal himself.	Psychiatrist did not fall below standard of care here as this is standard detoxification procedure at other facilities.	Pain physicians should remember that if they rely on other professionals for information and make decisions based on faulty information, the fact that they received faulty information will not be held as an adequate defense.
3. Psychiatrist allowed the nurses to dispense medications without properly reported withdrawal symptoms.	Psychiatrist did not fall below the standard here. None of the orders were tied to presence/ absence of symptoms of withdrawal but were written in order to prevent withdrawal.	Same as #2 above.
4. Psychiatrist should not have believed patient about doses of medication that he was taking, as on those doses he should have been intoxicated or in respiratory distress or having severe withdrawal symptoms.	Psychiatrist did not fall below the standard here. It is standard procedure to believe patients about what/how they are taking their drugs in order to properly prevent withdrawal. It is incorrect to conclude that at the patient-reported doses Mr. X should have been intoxicated or in respiratory depression, as Mr. X could have built up significant tolerance to opioids. In addition, it is incorrect to conclude that Mr. X should have been having severe withdrawal symptoms at these doses, as before presentation Mr. X could have taken his drugs (as outlined in the history) and withdrawal may have only partially started.	Pain physicians in this situation may wish to obtain collateral information from drug stores, physicians, significant others, and pharmacy bottles on quantities of drugs utilized. However, this is not yet the “standard.”
5. Urine toxicology results should have been utilized before prescribing opioids for potential withdrawal and done in a stat manner, and if not available at the hospital, patient should have been sent to an emergency room for toxicology before detoxification.	Psychiatrist did not fall below the standard here. It is not standard procedure in detoxification facilities to obtain urine toxicology on a stat basis and withhold treatment until this is available as in most cases these tests are not available on a stat basis. Treatment to prevent withdrawal should not be withheld until urine toxicology results are available. In addition, urine toxicology results are not reliable, especially in the case of short-acting opioids [12].	Urine toxicology results are useful in checking on the patient’s history and checking for illicit drugs. However, limitations of urine toxicology should be kept in mind. Clinical decisions should be made by utilizing a combination of clinical variables, which may/may not include urine toxicology results.
6. There was insufficient evidence for Mr. X being in withdrawal in order to start opioids.	Psychiatrist did not fall below the standard here. It is standard in the community to prevent withdrawal and not let patients go into withdrawal and then treat the withdrawal. In addition, the observations of the family medicine physician support the fact that Mr. X was in withdrawal at time +3 hours.	Although opioid withdrawal is not considered to be dangerous, it is the duty of the physician to try to prevent discomfort associated with this syndrome.
7. Psychiatrist had given enough oxycodone CR and oxycodone to relieve withdrawal symptoms and, therefore, should not have given methadone.	Psychiatrist did not fall below the standard here. He chose to rotate Mr. X to methadone in order to detoxify Mr. X, using methadone. This is a well-recognized detoxification protocol [6,7].	Pain physicians doing opioid detoxification have the choice of which agent they will use in their detoxification protocol. For example, Mr. X could have been detoxified with oxycodone CR [6,7].
8. Patient received too much methadone, too fast. Starting dose should be no more than 35 mg with buildup to 70 mg in 3 weeks (practice guidelines of the American Society of Addiction medicine, J Am Psychiatric Association)	Psychiatrist may not have fallen below the standard here. If one accepts the history given by Mr. X and uses published equivalency tables, Mr. X should have been able to tolerate 1050, 600, or 233 mg/day methadone, which are equivalencies for the amounts of hydrocodone, oxycodone CR, and oxycodone, respectively, allegedly taken before admission. From the case report, it is also clear that Mr. X was at least able to tolerate an equivalency of	The issue of methadone equivalencies is a major point of controversy and is discussed further in the Discussion.

Table 1 *Continued*

Plaintiff's Expert Witness's Allegation of Medical Care Area "Below the Standard"	Defendant's Expert Witness's Response to Allegation of Medical Area "Below the Standard"	Medical/Legal and Practice Importance of Allegation to Pain Medicine and Current Standard of Care
<p>9. Methadone was given within too short a period of time after stopping oxycodone CR; opiates should have been discontinued for at least 8 hours before starting methadone.</p>	<p>60 mg/day of methadone when he was placed on oxycodone CR and oxycodone as needed on the first day. As he did not demonstrate any opioid toxicity, it can be assumed that he could tolerate at least that dose of methadone. Mr. X received 70 mg of methadone the next day. As such, it is unlikely (according to standard published equivalencies) that he should have developed opioid toxicity.</p> <p>Psychiatrist did not fall below the standard here.</p> <p>This expert witness is not aware of any specific guidelines that direct physicians to have an 8-hour interim of time before stopping one controlled-release opioid and starting a long-acting one.</p>	<p>Physicians will need to use their medical judgment if performing this type of rotation in terms of when one opioid is stopped and the next started.</p>
<p>10. Psychiatrist should have started with 35 mg methadone per day and not escalated until patient showed significant signs of withdrawal.</p>	<p>Psychiatrist did not fall below the standard here.</p> <p>Orders for methadone were written as an equivalency in order to begin a taper procedure.</p>	<p>As per #6 above.</p>
<p>11. Psychiatrist did not demonstrate that patient was physically dependent before placement on methadone.</p>	<p>Psychiatrist did not fall below the standard here.</p> <p>Mr. X demonstrated tolerance to opioids by tolerating significant oxycodone CR doses on admission without signs of opioid toxicity and some signs of withdrawal.</p>	<p>NA</p>
<p>12. Cause of death was respiratory depression secondary to methadone overdose caused by the overprescribing of methadone.</p>	<p>Psychiatrist did not fall below the standard here.</p> <p>There is no evidence that Mr. X went into respiratory depression. Mr. X was seen to be awake and nonsomnolent 2 hours before death. In addition, Mr. X was not found in bed, which would be expected if he became somnolent and then went into respiratory depression. Methadone level, although above therapeutic levels, was not within toxic range. Finally, the coroner did not identify the cause of death as related to methadone overdose.</p>	<p>NA</p>
<p>13. Psychiatrist should have switched patient to a long-acting benzodiazepine for detoxification from alprazolam.</p>	<p>Psychiatrist did not fall below the standard here.</p> <p>There is no evidence in the chart that Mr. X went into a sedative withdrawal. Although current literature recommends that patients undergoing sedative detoxification should be transferred to a long-acting benzodiazepine, this is not considered mandatory [6,7].</p>	<p>Sedative withdrawal is potentially dangerous [6,7]. As such, patients with potential sedative withdrawal should not be undermedicated.</p>
<p>14. Vomiting was caused by the methadone and is implicated in patient's death.</p>	<p>Psychiatrist did not fall below the standard here.</p> <p>Vomiting is associated with cocaine intoxication [11]. In addition, vomiting is associated with opioid withdrawal and there is significant evidence that Mr. X was in opioid withdrawal at admission and on his first day. Opioid toxicologies support this opinion also (negative on admission and positive on second day). The opioid toxicologies are consistent with the history given by the patient. As Mr. X was tolerant to a significant amount of opioid, it is unlikely that he would develop vomiting secondary to the methadone, as patients tolerant to an opioid are tolerant to the emetic effects of the drug.</p>	<p>NA</p>

the history that they provide. There is good study evidence [12] and important previous studies reviewed by Fishbain et al. [12] that indicate that a high percentage of these patients do not provide a correct drug history or a history that can be relied upon to make clinical decisions. This is aptly demonstrated by Mr. X's case, where, according to the history given and the calculated equivalencies, Mr. X could have been taking 1050 mg, 600 mg, or 233 mg of methadone per day. As such, the plaintiff's expert advocated discounting any presented history, allowing the patient to go into withdrawal, and basing treatment on urine toxicology results (allegations #4, #5, #6, #10, and #11). The defendant's expert disagreed with this position and advocated a preventative prompt approach to withdrawal treatment, which may have been based on information that may have been incomplete or unreliable. Even though opioid withdrawal is not considered to be dangerous, the literature advocates a preventative approach [6,7]. This supported the position of the defendant's expert. As opioid withdrawal is not considered to be dangerous at first glance, there may be less medico-legal risk in the plaintiff's expert's approach. However, opioid withdrawal can produce nausea and, as such, could lead to aspiration, as in Mr. X's case. Thus, the senior author advocates the following approach when encountering the problem situation demonstrated by Mr. X. Treatment should not be withheld, and a preventative approach to withdrawal should be undertaken. However, before this is initiated, the pain physician should utilize all possible information sources before deciding on the prescription. These sources should be the following: The history presented by the patient; information from the pharmacy bottle(s); information from prescribing physicians; collateral information from significant others; and calculated equivalencies data. An *attempt* to tap these sources can be considered to be the current standard of care for this problem. Urine toxicologies, *if* available within a short period of time (hours), can be used as additional sources of information and can serve as a check on the patient's history. However, urine toxicologies are often unreliable [12] and, thus, may confuse the situation. The urine toxicology results should then be interpreted with caution in developing the detoxification protocol. At the present time, urine toxicology results are not the standard of care in developing a detoxification protocol and in preventing withdrawal. Overall, therefore, the defen-

dant's expert's approach more closely follows what is the current "standard of care."

Third, as indicated in Table 1, the defendant's expert disagreed with all 14 falling below the standard of care allegations except perhaps allegations #8, #12, and #14. Although it is unlikely, as presented, that Mr. X died from methadone overdose, these allegations have some literature support. In calculating the equivalencies of methadone that Mr. X could tolerate, a ratio of 3:2 of morphine to methadone was used. This is a standard ratio found in textbooks. However, recent literature indicates that this ratio is incorrect and should be larger. It has been suggested that the calculated equianalgesic dose of methadone in methadone rotation should be reduced by 75–90% [13]. This relates to the greater-than-expected potency of methadone, potential accumulation of methadone [2,13–15], and the possible predisposition of patients previously exposed to high doses of opioids to methadone toxicity [3]. Keeping these difficulties in mind, a number of protocols for rotation to methadone have been developed [2–4,14]. The literature indicates that clinicians rotating patients to methadone from another opioid should use a much lower equianalgesic ratio or one of the suggested rotation protocols. This could now be considered to be the "standard of care." It is to be noted that one of those protocols [3] stops the original opioid and immediately rotates to methadone. Thus, allegation #9 of the plaintiff's expert is not viable as, according to that study, the psychiatrist did not "fall below the standard of care" here.

The final point relates to allegation #7. Here, the plaintiff's expert questioned why the patient was rotated to methadone from oxycodone CR if his withdrawal symptoms were relatively well controlled. As indicated by the defendant's expert, rotation to methadone was done in order to detoxify Mr. X. As this is an acceptable detoxification strategy [6,7], this allegation is also not viable. As such, the defendant did not fall below the standard of care here either. However, there are other detoxification strategies [6,7], such as detoxifying with the opioid of abuse (oxycodone CR), which could have been chosen. In light of what was presented above for potential difficulties with methadone, perhaps an alternate detoxification protocol should have been chosen, decreasing the possibility of problems.

A final issue relates to whether the psychiatrist made his clinical decision based on medical system administrative pressures. It is to be noted that

detoxification facilities are now at increased pressure from health insurers and HMOs to detoxify patients in the shortest period of time possible. Presently, some HMOs allow only 3 days to complete opioid detoxification, while others allow 5 days. Alcohol/sedative detoxification is now usually limited to less than 1 week. In this case, the psychiatrist placed Mr. X on a 5-day methadone and alprazolam taper. As such, this choice may have been dictated by the administrative pressure described above. It is to be noted that withdrawal is generally thought to be preventable if the daily decrease in medication does not exceed 50% of the previous day's dosage [16]. However, in the first author's experience, such daily decreases invariably lead to the development of significant withdrawal symptoms, with patients experiencing substantial difficulties. In addition, it is difficult to complete detoxification in 5 days even using the 50% decrease per day guideline *if* the patient begins detoxification from a large daily dose of opioid. Thus, these artificial administrative guidelines for length of detoxification treatment limit physicians' options with patients taking large doses of drugs. In addition, such administrative guidelines force physicians working in this area to proceed with detoxification at a rate that could lead to significant withdrawal in these patients and, thus, increased risk of liability. As a result of this pressure, rapid and ultrarapid (operative) [16] detoxification protocols have been developed. Chronic pain patients who are dependent/addicted to opioids or other drugs present the dual problem of chronic pain and drug dependence/addiction. According to the senior author's experience and the current literature [17], these patients are generally difficult to detoxify successfully unless concomitant pain treatment is provided. As such, it is difficult to detoxify these patients in addiction facilities where pain treatment is not provided. Ideally the patient should be detoxified, if necessary, in pain facilities. Knowledge of the above issues can help physicians make decisions about detoxification that are not influenced by administrative pressure.

Conclusion

Pain physicians should proceed with caution in rotating to methadone. Such rotation should either proceed very slowly or utilize an accepted/published rotation protocol.

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