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Concurrent Use of Alcohol and Sedatives among Persons Prescribed Chronic Opioid Therapy: Prevalence and Risk Factors

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Abstract

Taking opioids with other central nervous system (CNS) depressants can increase risk of oversedation and respiratory depression. We used telephone survey and electronic health care data to assess the prevalence of, and risk factors for, concurrent use of alcohol and/or sedatives among 1848 integrated care plan members who were prescribed chronic opioid therapy (COT) for chronic non-cancer pain. Concurrent sedative use was defined by receiving sedatives for 45+ days of the 90 days preceding the interview; concurrent alcohol use was defined by consuming 2+ drinks within 2 hours of taking an opioid in the prior 2 weeks. Some analyses were stratified by substance use disorder (SUD) history (alcohol or drug). Among subjects with no SUD history, 29% concurrently used sedatives vs. 39% of those with a SUD history. Rates of concurrent alcohol use were similar (12 to 13%) in the two substance use disorder strata. Predictors of concurrent sedative use included SUD history, female gender, depression, and taking opioids at higher doses and for more than one pain condition. Male gender was the only predictor of concurrent alcohol use. Concurrent use of CNS depressants was common among this sample of COT users regardless of substance use disorder status.

Keywords

Chronic opioid therapy; alcohol; sedatives; concurrent; substance use disorder

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The increase in prescribing chronic opioid therapy (COT) in recent years^{14, 39} has been accompanied by a rise in adverse events and a greater focus on the safety of these medications^{1, 31, 38, 56}. Opioids are known to produce respiratory depression and sedation, and these effects have been implicated in serious adverse events including overdose^{4, 16, 26, 41, 42, 59} and falls/fractures^{11, 20, 46}. Concurrent use of other types of central nervous system (CNS) depressants such as sedatives and alcohol can exacerbate respiratory depression and sedation and their associated risks¹⁵. A study of opioid-related mortality reported that most deaths involving prescription opioids identified other drugs in the blood stream on autopsy, including alcohol, sedatives and/or illicit drugs²⁸.

Some studies have assessed the prevalence of concurrent use of other CNS depressants among patients receiving COT. For example, Fleming et al. reported that 36% of daily opioid users drank alcohol in the last 30 days, while 40% had taken sedatives during the same time period²³. However, little is known about factors associated with concurrent use of sedatives and alcohol among persons prescribed COT. One study among COT patients reported higher rates of benzodiazepine prescription among patients who demonstrated addictive behaviors and/or pain dysfunction compared to “typical” chronic pain patients³. While these results are suggestive, the study's main focus was not on factors associated with concurrent use of CNS depressants among patients prescribed COT and how such factors compare to other characteristics that have been shown to increase a person's risk for opioid related problems such as abuse/dependence, misuse, and overdose.

A substance use disorder (SUD) history is the most well-documented factor associated with increased risks of problems with prescription opioids.^{15, 19, 29, 36, 43, 54} Focus on this risk factor has led some to conclude that COT patients with no history of SUD are at relatively low risk for opioid abuse/dependence or misuse. For example, Fishbain's²¹ meta analysis reported that the risk of opioid abuse/addiction and aberrant drug-related behaviors fell dramatically if patients were screened for a history of abuse/addiction. Based on observations from autopsy studies of overdoses involving prescription opioids, it has been inferred that prescription opioid overdose is predominately a problem among persons with a SUD. For example, Hall et al. reported that a minority (44%) of persons dying from an opioid-related overdose had obtained their medications from a physician²⁸.

Yet there is growing evidence of significant risks associated with COT among patients with no SUD history. Although a recent study found that a SUD history was related to overdose among patients receiving COT, the large majority of overdoses did not have information suggesting substance abuse documented in the medical record¹⁶. In a study by Fleming et al.²⁴, clinically significant patterns of opioid misuse, such as increasing opioid dose without prescription, were not uncommon among COT patients without a recent SUD. Regarding concurrent use of other CNS depressants, one study reported that 28% of COT users without an SUD diagnosis had used sedative medications on at least 180 days in the prior year⁶¹. Such high rates of concurrent sedative use among what some would regard as a population at low risk for opioid-related misuse is concerning given that sedative use among COT users has been shown to be independently associated with the presence of opioid abuse/dependence^{5, 18}, opioid-related overdose¹⁶, ED visits⁷ and alcohol and drug-related medical encounters (withdrawal, overdose or toxicity)⁷.

Our objective is to assess the prevalence and predictors of concurrent use of sedatives and alcohol among persons receiving COT for non-cancer pain. We examine these relationships among patients with and without a substance use disorder history.

MATERIALS AND METHODS

Setting and Participants

The CONSORT study (CONsortium to Study Opioid Risks and Trends) was designed to study chronic opioid therapy for non-cancer pain among adults in Group Health Cooperative (GHC), located in Washington state, and Kaiser Permanente of Northern California (KPNC)⁵⁸. Together, these health plans include about four million patients--over one-percent of the US population. CONSORT research plans were reviewed and approved by the Institutional Review Boards of both health plans and all participants in the survey described in this report gave informed consent. Patients in these analyses were receiving chronic opioid therapy and completed a telephone interview about pain, mental health and opioid use.

Electronic pharmacy and medical encounter data

Both health plans maintain electronic pharmacy and medical encounter data for all covered services. Pharmacy files contain generic drug name, strength, directions for use, date dispensed, quantity dispensed, days supply, prescriber identification number, and National Drug Code. Surveys at both health plans have consistently found that more than 90% of patients obtain almost all of their prescription medications through health plan pharmacies^{45,48}. Automated files also include visit date and diagnoses for all covered medical encounters.

Eligibility

Health plan enrollees age 21-80 years were eligible if they had filled an opioid prescription within 30 days of the sample selection date, and had filled at least 10 opioid prescriptions and/or received at least 120 days supply in a one-year period prior to the sample selection date, with at least 90 days between the first and last opioid dispensing in that year. These criteria for chronic opioid therapy have been shown to predict a high probability of sustained opioid use one year later⁵⁸. Additional eligibility criteria included continuous enrollment in the health plan for at least one year prior to sampling. We excluded patients who had received a cancer diagnosis (except for non-melanoma skin cancer) in local cancer registries or who had two or more cancer diagnoses in automated visit records in the year prior to sampling.

Sampling

Because a large proportion of all milligrams of opioids are prescribed for a relatively small number of higher dose patients^{17,58}, we selected an equal number of eligible patients within three daily dosage ranges in the 90 days before the sample selection date (1-49 milligrams, 50-99 milligrams, and 100+ milligrams, morphine equivalent). This approach oversamples patients receiving higher dosage levels because most patients receive relatively low dosage levels within these health plans⁶. Analyses weighted observations by the inverse of the probability of selection to obtain estimates that were representative of the population of long-term opioid users from which the sample was selected.

Telephone survey

Interviews began in June 2008 and ended in November 2008 at GHC and began in January 2009 and ended in October 2009 at KPNC. Potentially eligible patients were mailed a letter explaining the study and containing a pre-incentive (a \$2 bill at GHC and a \$5 gift card at KPNC). Experienced non-clinician survey interviewers at each health plan research center called potential patients. Interviews were conducted using Computer-Assisted Telephone Interview technology which has been recognized as the industry standard for the last

decade²⁵. Patients were asked to participate in a 25-30 minute telephone interview and to allow the study to access their electronic health care data from the time they enrolled in the health plan until three years after the date of the interview. Patients who completed the interview were mailed a \$20 cash reimbursement at GHC and a \$50 gift card at KPNC. The differential in incentive payments was based on prior experience in the two populations suggesting the level of incentive payments needed to achieve an acceptable response rate.

Measures

Opioid type and dose variables-- Based on electronic pharmacy data, characteristics of opioid prescription were estimated using methods described elsewhere⁵⁸. Average daily dose was estimated by the total morphine equivalent dose (MED) during the 90 days prior to the interview date of each subject, divided by 90. Opioids were classified into two types: long-acting opioids and short-acting opioids. Long-acting opioids included methadone, transdermal fentanyl, levorphanol tartrate, and sustained release formulations of oxycodone, morphine, hydromorphone, and oxymorphone. Subjects were classified as predominate users of either short- or long-acting opioids depending on which type had the larger total days supply in the 90 days prior to their interview date. In case of ties, the opioid type with the larger MED was chosen.

Concurrent sedative use—Concurrent sedative use was defined as receiving sedatives for 45+ days of the 90 days preceding the interview according to electronic pharmacy data maintained by the health plans. A limitation of this definition of concurrent sedative use is that it is based on what was prescribed, which may not always correspond with how patients actually take the medications. Given the time constraints of the telephone interview and its primary focus on opioid use, the survey did not include questions about sedative use. However, prior research has shown high levels of concordance between filling multiple prescriptions for psychoactive medications and self-reported use of such medications⁴⁷. Sedatives included benzodiazepines, barbiturates, muscle relaxants (e.g. methocarbamol, carisoprodol), and miscellaneous anxiolytics, hypnotics, and sedatives (e.g. zolpidem, meprobamate). All of these medications are CNS depressants and respiratory depressants.

Concurrent alcohol Use—Concurrent alcohol use was based on self-report. Subjects were classified as concurrent users of alcohol if they reported that they had had two or more drinks within two hours before or after taking opiates within the past two weeks.

Substance Use Disorder history—Substance use disorder history was assessed through a combination of self-report and electronic data. A person was classified as having a SUD history if s/he: 1) received a diagnosis of drug or alcohol abuse or dependence according to electronic data in the 3 years prior to the survey date; or 2) endorsed the survey question “have you ever had an alcohol or drug problem?”; or 3) received a score of 7 or greater on the AUDIT-C alcohol screen⁴⁴. The AUDIT-C is a self-report measure of alcohol consumption designed to identify risky drinking as well as alcohol use disorders (AUD); since our purpose was to identify substance abuse/dependence, we used a higher cut-off than is typically used to identify risky drinkers^{9,12} (see below). Alcohol consumption has been shown to increase markedly with AUDIT-C scores of 7 and above with little gender interaction (personal communication with Kathy Bradley).

Risky Drinking—We compared our measure of concurrent alcohol use with a classification of risky drinking derived from the AUDIT-C^{9,12}. Scores for the AUDIT-C range from 0-12. For women, risky drinking was defined by scores of 3-6; for men the scores for risky drinking ranged from 4-6¹⁰. Men or women with scores of 7 or greater were classified as having an AUD (see above)⁴⁴.

Depression—Depression was assessed through a combination of self-report and automated data. The self-report measure obtained in the telephone interview was the 8 item version of the *Patient Health Questionnaire*, a validated and widely used self-report measure of depressive symptoms^{33,34}. This version of the PHQ has a cut off score of 10 indicating likely major depression. We also used electronic data to determine whether the subject had received a diagnosis of depression in the 3 years prior to the survey date. A person was classified as depressed if his or her PHQ score was 10 or greater or s/he had been diagnosed with depression according to electronic data.

Other measures—Age and gender were obtained from electronic data files and confirmed prior to the telephone interview. Educational attainment, smoking status, and number of pain days in the last 6 months were obtained through patient self-report. Pain intensity in the 3 months prior to the survey was measured using a 0-10 average pain intensity rating scale from the Graded Chronic Pain Scale^{55,57}. Body mass index (BMI) was calculated from self-reported weight and height. Subjects were asked to list the pain conditions for which they took opioids in the last 3 months. Subjects were also asked to rate how helpful opioids were in the last month in relieving their pain using a 1-5 scale anchored by “not at all helpful” and “extremely helpful.”

Analyses

We limited analyses to patients who reported taking opioids everyday in the last 2 weeks to establish simultaneous use with sedatives. The question about alcohol use established simultaneous use of alcohol and prescription opioids. Some analyses were stratified to provide estimates of prevalence rates and predictors of concurrent use of opioids and other CNS depressants among persons with and without a history of SUD. Analyses used SAS PROC SURVEYMEANS, PROC SURVEYFREQ or PROC SURVEYLOGISTIC to account for the stratified random sampling design, providing unbiased estimates (proportions and means) for the population surveyed. These analyses weight respondents based on their probability of selection within strata. Between group differences in proportions were tested using chi-square statistics. We examined the association between concurrent sedative use and concurrent alcohol use (in 2 separate models) with our hypothesized predictors using PROC SURVEYLOGISTIC. The predictors were the same in the 2 models and were included based on their significance in univariate analyses. The predictors included: SUD history, health plan, age (21-44 (reference); 45-64; 65+), gender, depression status; average daily opioid dose (1- < 20 mg. MED (reference); 20-< 50 mg. MED; 50- < 120 mg. MED; >= 120 mg. MED); number of pains for which opioids were taken in the last 3 months (1 vs. 2+); and average pain intensity (continuous).

RESULTS

Survey Response

Overall, 3790 patients were approached (2185 at GHC and 1605 at KPNC), 185 were ineligible (76 at GHC and 109 at KPNC), and interviews were completed for 2163 (1191 at GHC and 972 at KPNC), for an overall response rate of 60% (57% at GHC and 65% at KPNC). Response rates were higher in both health plans for patients over the age of 65 (65% at GHC and 68% at KPNC), but gender differences were small. Response rates increased with higher average daily dose at KPNC (58% for <50 mg. MED; 66% for 50 to <100 mg. MED; and 71% for 100+ mg. MED), but this was not seen at GHC (58% for <50 mg. MED; 57% for 50 to <100 mg. MED; and 55% for 100+ mg. MED), possibly due to lower incentive payments at GHC. Among the 2163 survey respondents, 1883 (87%) patients reported using opioid medication every day for the last two weeks. Of these, we included the 1848 (98%) subjects who could be classified as to SUD status.

Substance Use Disorder history

Overall, 31% (n=685) of subjects were found to have a history of SUD (Table 1a). Table 1a also shows the breakdown of sources of the SUD classification. For example, 16.4% of the overall sample received a diagnosis of drug or alcohol abuse or dependence in the prior 3 years according to electronic health plan data; 22.1% reported ever having a drug or alcohol problem. Agreement between the self-report measure and the electronic health care data diagnosis of a drug or alcohol disorder was modest ($\kappa=0.28$). Agreement was lower ($\kappa=0.16$) between having an AUD according to the AUDIT-C (score of 7+) and receiving a diagnosis of an alcohol disorder in the electronic medical record (data not shown). Table 1a displays the SUD history classification data by concurrent alcohol use status. Not surprisingly, concurrent alcohol users were significantly more likely to be classified as having an AUD according to the AUDIT-C. Otherwise there were no differences in the SUD history identification variables according to concurrent alcohol use status. In contrast, patients concurrently using sedatives were significantly more likely to be classified as having a SUD history than were their counterparts, primarily due to higher rates of electronic diagnoses of drug disorders (Table 1b).

Prevalence and predictors of concurrent use of CNS depressants

In the entire sample of daily opioid users, 12.4% concurrently used alcohol (Table 1a), 31.9% simultaneously took sedatives (Table 1b) and 3.1% used all three substances concurrently (data not shown). Table 1a describes the characteristics of the sample, both overall and stratified by concurrent alcohol use status. Overall, the sample was about two-thirds female, middle aged (mean age 55.7 years) and highly educated. About 60% were classified as depressed and roughly one-quarter were current smokers. Average daily opioid doses were fairly high (81 mg. MED), with about one-third of the sample predominantly using long-acting opioids in the prior 90 days. The subjects were experiencing high average levels of pain (average pain intensity of 5.8). The 12% of subjects with concurrent alcohol use-- two or more drinks within two hours of taking an opioid--were more likely to be male, took lower daily opioid doses, had lower average pain levels and tended toward being less depressed than those not using both substances at the same time. They were also much more likely to be classified as risky drinkers according to the AUDIT-C (64.7% vs. 7.1%). Table 1b presents the same data by concurrent sedative status. Concurrent sedative users were significantly younger, more likely to be female, were prescribed higher average daily opioid doses, were more likely to be depressed, and tended to take opioids for more than one pain condition. Rates of risky drinking did not differ among patients according to concurrent sedative use status. BMI, educational attainment, number of pain days in the last 6 months, opioid type (short-acting or long-acting), smoking status, and ratings of opioid helpfulness were not related to either concurrent sedative or alcohol use status.

We examined prevalence rates of concurrent alcohol and sedative use stratified by SUD status. Table 2 shows that rates of concurrent alcohol use were similar among subjects with a history of SUD (13.2%) and those with no such history (12.0%). In contrast, rates of concurrent sedative use were higher among subjects with a SUD history vs. those without—38.9% vs. 28.7%. Rates of taking all three substances simultaneously were similar across SUD strata—about 3% (data not shown). Table 2 also report rates of concurrent alcohol and sedative use by variables that showed differences in Tables 1a and 1b. For example, among subjects with no SUD history 34.9% of patients classified as depressed concurrently used sedatives compared to 20.8% of patients who were not depressed ($p=.0002$, see Table 2). Opioid daily dose was also strongly related ($p=.0004$) to concurrent sedative use among those with no SUD history, with rates of simultaneous use among patients taking the highest daily doses about two times higher than among those using the lowest daily opioid doses. Among subjects with no SUD history, females, younger subjects and persons taking opioids

for more than one pain condition were also more likely to use sedatives concurrently (Table 2). We observed similar patterns of concurrent sedative use among patients with a SUD history, with the magnitude of the differences generally being somewhat greater (Table 2). In contrast, rates of concurrent alcohol use among those with no SUD history were lower among depressed patients and those using higher daily opioid doses (Table 2). These differences were not observed among those with a SUD history. Rather, subjects with lower average pain intensity ratings were significantly more likely to concurrently use alcohol. Male gender was strongly associated with concurrent alcohol use in both SUD strata.

After controlling for variables found to be significantly associated with either concurrent alcohol or sedative use in univariate analyses, as well as health plan site and SUD history, only male sex emerged as a significant predictor of concurrent use of alcohol and opioids. ($p = <.0001$, Table 3a). SUD history, depression, daily opioid dose, number of pains for which opioids were taken, female sex, and health plan site were all significantly related to concurrent sedative use (Table 3b). Even after controlling for SUD history, patients with average daily doses of 50+ mg. MED were more than twice as likely to concurrently use sedatives than those using the lowest daily opioid dosages. Depressed patients and patients taking opioids for more than one pain condition were about 50% more likely to simultaneously use opioids and sedatives.

DISCUSSION

Guidelines advise that clinicians counsel COT patients about the risks of simultaneous use of CNS depressants¹⁵. Despite this, concurrent sedative use was quite common in this sample—about 32% overall. Although concurrent alcohol use was less common, we still found that one in 8 patients had two or more drinks within two hours of taking an opioid, regardless of SUD history. Risk factors for concurrent sedative use were consistent across SUD strata—female gender, younger age, depression, higher daily opioid doses, and taking opioids for more than one pain condition. Male gender was the only risk factor related to concurrent alcohol abuse across SUD strata. Among persons with no SUD history, higher daily opioid doses and depression were associated with lower rates of concurrent alcohol use. In addition to these risk factors, SUD history (among 31% overall) was significantly related to sedative use ($p = .05$) in multivariate analyses. However, SUD history was not a significant predictor of concurrent alcohol use in multivariate analyses.

Evidence of the dangers of simultaneous use of CNS depressants continues to build. Concurrent use of sedatives among long-term opioid users has been reported to independently increase the risk of emergency department visits⁷, visits for alcohol and drug-related medical encounters⁷, overdose¹⁶, and opioid and non-opioid abuse/dependence¹⁸. Studies have reported that the majority of fatal opioid overdoses involve other drugs, including alcohol²⁸. In a case-control study of opioid-related mortality, 85% of decedents were prescribed benzodiazepines in the prior 6 months²⁶. Among 160 pharmaceutical opioid-involved drug overdoses in the Seattle area in 2009, 83% involved other psychoactive drugs, most commonly benzodiazepines (33%), alcohol (18%), cocaine (16%), heroin/opiate (11%), and muscle relaxants (4%)². Dunn et al found that concurrent sedative use was a significant predictor of fatal and non-fatal overdose after controlling for other factors, including opioid dose¹⁶.

Overall, about 12% of opioid users in our study reported having 2 or more drinks within 2 hours of taking an opiate in the last two weeks. This is a strict definition of concurrent alcohol use—three-quarters of persons meeting this definition met criteria for risky drinking or an AUD based on the AUDIT-C. Using a looser criterion, Fleming et al. found that about one-third of daily opioid users drank alcohol in the last 30 days²³. Overall, about one-third

of the COT users in this study were concurrently prescribed sedatives. Similarly high rates of sedative use among COT patients have been reported by Boudreau (28%)⁶, Fleming et al (40%)²³, and Braden et al (43%)⁷. Even among those with no known SUD history, 29% were prescribed sedatives on more than 45 days in the last 90—a finding that agrees with that a previous report⁶¹. These rates of concurrent use far exceed rates of co-occurring substance use disorders^{23,35,51}. For example, Fleming et al. reported that less than 1% of daily opioid users had a DSM-IV diagnosis of sedative abuse or dependence²³. Although Banta-Green et al reported higher rates (~11%) of sedative-related problems per the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)³, the levels were still far lower than the rates of concurrent sedative use observed in our study. Risks associated with concurrent use of CNS depressants are not restricted to opioid users who abuse those substances. And, the increased risk of concurrently using CNS depressants is not restricted to opioid users with a SUD history.

Our results suggest that the younger, depressed, female patient receiving higher dose COT for multiple pain problems is at highest risk for sedative use. This profile presents a potent combination of risk factors since younger age¹⁸, higher daily opioid doses^{4,16, 26,46} and depression^{40,52}, have all been shown to be independently associated with worse opioid-related outcomes and, in the case of depression, higher rates of long-term COT use^{8, 53}. The wide-spread practice of concurrent prescribing of opioids and sedatives, particularly among patients receiving COT at high opioid dosages, deserves increased scrutiny.

Our finding that concurrent sedative use was concentrated among females while concurrent alcohol use was much more common in males is another example of gender differences pertaining to opioid-related prescribing and complications. Studies have shown that women use prescribed opioids at higher rates than men^{13,49}. On the other hand, men are more likely to exhibit substance abuse behaviors than women^{32,60}. A recent study³⁰ found that men and women differed in risk factors for aberrant prescription use, with women's misuse problems more likely caused by emotional issues and affective distress while men's problems tended to be related to legal and problem behavior issues. The authors suggest that women with significant affective distress could be educated about avoiding the use of opioids for dealing with anxiety and sleep disturbances. Our findings strengthen and extend this recommendation. Clinicians should not just be cognizant of the increased risk of opioid misuse among depressed females who are prescribed opioids; but also of the increased risk of their using a potentially dangerous combination of opioid and sedative medications.

The findings of this study must be viewed within the context of the patients' pain experience. Mean average pain intensity ratings over the 3 months prior to the interview were about 6 on a 10-point scale; worst pain in the same period was about 8.8 (data not shown). These high pain ratings occurred in spite of the majority of patients (60%) reporting that opioids were very or extremely helpful in managing their pain. Two-thirds of patients reported taking opioids for more than one pain condition. Chronic pain of such magnitude is often associated with comorbid sleep⁵⁰ and anxiety²⁷ disorders. The fact that the sedatives analyzed in this study are primarily used to treat anxiety and sleep disorders likely explains their high rates of use among this sample of COT patients. Regarding concurrent alcohol use, the close proximity in time in which patients drank two or more alcoholic drinks and took opioids suggests that alcohol may be viewed by some as an additional means of pain control.

This study has important limitations. The SUD history of some patients was likely misclassified because self-report and administrative data can be inaccurate^{22,54} and we only examined electronic health records for the prior 3 years. The response rate for this study was about 60%. It is possible that responders and non-responders to the survey differed as to the

variables in this report. The definition of “concurrent” was not parallel across measures. Opioid users were those using opioids regularly over a one-year period and daily during the 2 weeks prior to the telephone survey; sedative users were those who, according to automated data, were prescribed opioids for at least 45 of the 90 days immediately preceding the surveys. While the automated pharmacy data provide accurate information of what was prescribed, we do not know how patients actually took the medications. Further, this paper did not evaluate adverse events that may have been related to the patients’ concurrent use of opioids and other CNS depressants.

Concurrent sedative and alcohol use was common in this sample of patients receiving COT, even among those with no known SUD history. Risk factor profiles for concurrent sedative and alcohol use differed greatly, including by gender. Given the high rates of concurrent use of CNS depressants, even among patients at “low risk” for misuse, and the risks associated with concurrent use of other CNS depressants, the absence of a SUD history alone does not adequately define a low risk COT patient population.

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Perspective

Risks associated with concurrent use of CNS depressants are not restricted to COT users who abuse those substances. And, the increased risk of concurrently using CNS depressants is not restricted to opioid users with a prior SUD history. COT requires close monitoring, regardless of substance use disorder history.

Table 1a

Persons using chronic opioid therapy for non-cancer pain: sample characteristics by concurrent alcohol use and overall. Limited to persons taking opioids everyday out of the last 2 weeks.

Variables	Concurrent Alcohol Use		p-value	Total Sample
	No	Yes		
Number of patients	1661 (87.6%)	187 (12.4%)	-	1848
Female (%)	65.1	42.5	0.0001	62.3
Mean age	55.8	54.8	0.48	55.7
Mean BMI	31.0	30.2	0.29	30.9
Some college education (%)	60.4	63.9	0.52	60.9
Current Smoker (%)	24.1	29.2	0.29	24.7
Risky Drinker per AUDIT-C (%)	7.1	64.7	< .0001	14.2
Depressed (%)	62.0	51.4	0.07	60.7
Average pain intensity last 3 months (0-10)	5.9	5.5	0.045	5.8
Mean days with pain in prior 6 months	167.6	170.2	0.36	167.9
Using opioids for more than one pain condition (%)	63.5	64.2	0.91	63.6
Mean daily opioid dose (mg. MED) prior 3 months	82.5	69.4	0.22	80.9
Daily opioid dose $\geq$ 120 mg. MED (%)	16.8	10.0	0.006	15.9
Opioids very/extremely helpful (%)	59.1	59.5	0.94	59.1
Predominate use of long-acting opioids in the prior 3 months (%)	32.7	26.5	0.19	31.9
SUD Identification				
Any SUD Diagnosis from electronic data-drug or alcohol (%)	16.7	14.2	0.43	16.4
Diagnosis from electronic data—alcohol (%)	6.3	9.9	0.19	6.7
Diagnosis from electronic data—drug (%)	13.8	10.9	0.33	13.4
Self-report drug or alcohol problem (%)	22.0	22.8	0.85	22.1
Alcohol Use Disorder per AUDIT-C (%)	0.7	10.9	0.0003	2.0
Any of the Above (%)	31.0	33.5	0.60	31.3

Abbreviations: BMI, body mass index; AUDIT, Alcohol Use Disorders Identification Test; MED, morphine equivalent dose; SUD, substance use disorder

NOTES: Unweighted N's and weighted percents Risky Drinking does not include AUDIT-C scores of 7 or greater

Table 1b

Persons using chronic opioid therapy for non-cancer pain: sample characteristics by concurrent sedative use. Limited to people taking opioids everyday out of the last 2 weeks.

Variables	Concurrent Sedative Use		p-value
	No	Yes	
Number of patients	1153 (68.1%)	695 (31.9%)	-
Female (%)	58.2	71.1	0.0001
Mean age	56.6	53.8	0.0006
Mean BMI	31.2	30.3	0.12
Some college education (%)	59.8	63.1	0.34
Current Smoker (%)	23.1	28.3	0.08
Risky Drinker per AUDIT-C (%)	14.6	13.4	0.65
Depressed (%)	55.1	72.7	<.0001
Average pain intensity last 3 months (0-10)	58	6.0	0.16
Mean days with pain in prior 6 months	168.5	166.6	0.48
Using opioids for more than one pain condition (%)	60.0	71.4	0.0005
Mean daily opioid dose (mg. MED) prior 3 months	68.1	108.2	<.0001
Daily opioid dose $\geq$ 120 mg. MED (%)	13.0	22.2	<.0001
Opioids very/extremely helpful (%)	59.1	59.2	0.99
Predominate use of long-acting opioids in the prior 3 months (%)	31.4	33.1	0.56
SUD Identification			
Any SUD Diagnosis from electronic data-drug or alcohol (%)	13.0	23.8	<.0001
Diagnosis from electronic data—alcohol (%)	6.1	8.1	0.27
Diagnosis from electronic data—drug (%)	9.9	21.0	<.0001
Self-report drug or alcohol problem (%)	21.2	24.1	0.32
Alcohol Use Disorder per AUDIT-C (%)	2.5	0.9	0.03
Any of the above	28.1	38.1	0.002

Abbreviations: BMI, body mass index; AUDIT, Alcohol Use Disorders Identification Test; MED, morphine equivalent dose; SUD, substance use disorder

NOTES: Unweighted N's and weighted percents Risky Drinking does not include AUDIT-C scores of 7 or greater

Table 2

Prevalence (%) of concurrent alcohol and sedative use by categories of demographic, clinical and opioid-related variables—stratified by history of substance use disorder (SUD).

Variables	Concurrent Alcohol Use (%)		Concurrent Sedative Use (%)	
	No SUD	SUD	No SUD	SUD
Overall	12.0	13.2	28.7	38.9
Age				
21-44	14.3	17.6	35.0	50.3 *
45-64	11.3	13.2	28.8	40.2
65+	12.1	9.4	24.3	24.6 *
Sex				
Female	9.3 *	5.9 ***	32.4 **	48.4 **
Male	17.8	20.3	20.8	29.6
Depression				
No	16.1 *	12.8	20.8 **	26.4 **
Yes	8.8	13.4	34.9	44.3
Average daily opioid dose				
1- < 20 mg. MED	15.4	10.6	20.9 **	17.3 **
20- < 50 mg. MED	12.4	15.4	26.5	41.1
50- < 120 mg. MED	10.2	14.7	36.0	40.8
120+ mg. MED	5.5	10.3	41.6	47.9
# of pain conditions for which opioids are taken				
One	11.1	14.9	21.7 **	33.5
Two or more	12.5	12.4	33.0	41.5
Average pain intensity in last 3 months (0-10)				
0-4	10.5	22.8 *	25.5	33.4
5-6	12.2	13.0	28.1	40.9
7+	11.5	7.6	31.8	40.6

Abbreviations: MED, morphine equivalent dose NOTE: Significance tests compare categories of variables within a column, not across columns.

* Significant at P = .05

** Significant at P = .01

*** Significant at P < .0001

Table 3a

Multivariate Logistic Regression Results for Concurrent Alcohol Use

Variables	OR (95% C.I.)	Overall p-value
Gender		< .0001
Female	0.36 (0.22, 0.58)	
Male (reference)	1.0	
Age		0.21
65+	0.63 (0.31, 1.3)	
45-64	0.63 (0.37, 1.06)	
21-44 (reference)	1.0	
SUD history		0.75
Yes	1.07 (0.71, 1.62)	
No (reference)	1.0	
Depression		0.60
Yes	0.88 (0.55, 1.42)	
No (reference)	1.0	
Daily Opioid Dose		0.06
120+ mg. MED	0.43 (0.22-0.84)	
50- < 120 mg. MED	0.77 (0.43-1.39)	
20- < 50 mg. MED	0.75 (0.39-1.43)	
1- < 20 mg. MED (reference)		
Number of Pain Conditions for which opioids taken		0.28
Two or more	1.31 (0.81, 2.1)	
One (reference)	1.0	
Average pain intensity	0.95 (0.85, 1.05)	0.32
Health plan site		0.69
Group Health	0.91 (0.58, 1.43)	
KPNC (reference)	1.0	

Abbreviations: OR, odds ratio; C.I., confidence interval; MED, morphine equivalent dose; KPNC, Kaiser Permanente Northern California

Table 3b

Multivariate Logistic Regression Results for Concurrent Sedative Use

Variables	OR (95% C.I.)	Overall p-value
Gender		0.0005
Female	1.77 (1.28, 2.44)	
Male (reference)	1.0	
Age		0.14
65+	0.61 (0.37, 1.01)	
45-64	0.83 (0.56, 1.23)	
21-44 (reference)	1.0	
SUD history		0.0502
Yes	1.35 (1.00, 1.82)	
No (reference)	1.0	
Depression		0.03
Yes	1.47 (1.04, 2.1)	
No (reference)	1.0	
Daily Opioid Dose		0.004
120+ mg. MED	2.36 (1.46, 3.80)	
50- < 120 mg. MED	2.12 (1.32, 3.41)	
20- < 50 mg. MED	1.73 (1.05, 2.8)	
1- < 20 mg. MED (reference)	1.0	
Number of Pain Conditions for which opioids taken		0.03
Two or more	1.41 (1.04, 1.92)	
One (reference)	1.0	
Average pain intensity	1.01 (0.94, 1.1)	0.75
Health plan site		0.003
Group Health	0.63 (0.47, 0.85)	
KPNC (reference)	1.0	

Abbreviations: OR, odds ratio; C.I., confidence interval; MED, morphine equivalent dose; KPNC, Kaiser Permanente Northern California