MEASUREMENT OF ETHANOL USE IN A CHRONIC PAIN POPULATION USING PHOSPHATIDYLETHANOL

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Introduction

Alcohol (EtOH) use is a significant risk factor for overdose in patients on opioids, and it's recommended they avoid EtOH, often formalized in opioid contracts. Other medications, such as benzodiazepines, also pose risks when combined with opioids. While there is no standard test for EtOH use in chronic pain patients, Phosphatidylethanol (PEth), a lipid byproduct of EtOH, can detect consumption for several weeks and is increasingly used in addiction medicine, liver transplant eligibility, and workplace monitoring.

EtOH use in chronic pain patients is estimated at 25-28%, higher than the general population. Although EtOH may have analgesic effects, it complicates chronic pain treatment and increases the risk of respiratory depression and death when combined with opioids. Many pain medications, including over-the-counter options, also interact poorly with EtOH. Currently, self-reports, like the Alcohol Use Disorders Identification Test (AUDIT), are the most common way to assess EtOH use, though they are often unreliable, particularly in problem drinkers.

This study used the AUDIT questionnaire to assess EtOH use, compared with PEth levels, to evaluate the correlation between self-reported use and PEth in chronic pain patients. It also examined opioid use as a secondary endpoint.

Methods & Materials

This single-center prospective pilot study, approved in May 2020 and closed in April 2024, enrolled 20 patients. Inclusion criteria were adults aged 21 or older with chronic pain (over 3 months) and self-reported EtOH consumption of 2 or more drinks per day, at least 5 days a week. Exclusion criteria included patients under 21, those with less than 3 months of pain, and pregnant or lactating women.

Patients with alcohol use in their social history were contacted before their appointments and asked about their drinking habits. Those meeting the criteria were invited to discuss the study further during their visit. After signing consent, participants completed the AUDIT questionnaire, and blood samples were collected for PEth analysis.

Samples were analyzed using liquid chromatography-tandem mass spectrometry, with alcohol consumption categorized by PEth levels: light (<20 ng/ml), moderate (20-200 ng/ml), and heavy (>200 ng/ml). Patients with PEth levels above 200 ng/ml were offered counseling. AUDIT scores also categorized alcohol use, with different cutoff values for men and women.

Results

Twenty patients were enrolled in the study, of which 17 (85%) were males and 3 (5%) were females. The ages ranged from 46 - 97 years old with an average age of 63 years old. AUDIT scores were 8.1 +/- 1.4 while PEth levels were 178.3 +/- 43.5. 85% of patients had AUDIT scores indicating mild to moderate use of EtOH while 15% had severe use. This result contrasted with PEth levels indicating 70% mild to moderate EtOH use and 30% heavy use. Correlation coefficient r score was 0.2194, N=20, and P-value was insignificant at 0.35268 at a threshold of p<0.05.

Table 1: A Summary of Patient Demographics. This table summarizes the demographic information of the study participants, including age, sex, and race. The first row categorizes patients by age; among the 20 total patients who participated in this study, the ages ranged from 46 to 97 years old, and the average age was 63 years old. The second and third rows show the patients' sex, divided into male versus female. Finally, the remaining rows delineate racial distributions.

Table 1. Patient demographics

Characteristics	Patients (n=20)
Age	63 (46-97)
Sex (male)	17
Sex (female)	3
Race	
White	15
Black	3
Hispanic	2

Results

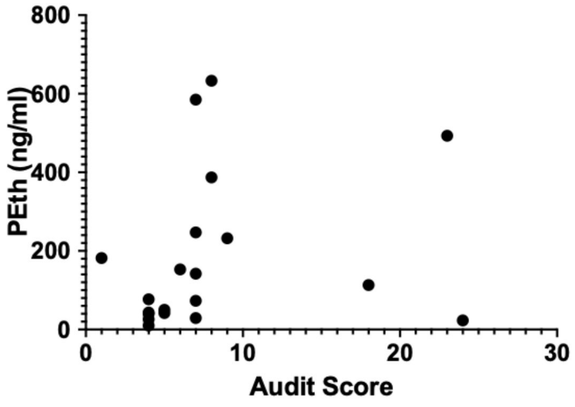


Figure 1: Correlation Graph Between AUDIT Score and PEth Blood Levels. Correlation between AUDIT score (0-40) and PEth level (ng/ml) was done with the Pearson Product-moment correlation coefficient (SPSS). The correlation coefficient (r) was 0.219 (p=0.353). The result is not significant at p<0.05.

Table 2. Comparison Alcohol Use Audit Questionnaire with Peth Blood Values

Alcohol Information	Patients (=20)
Audit score (0-40)	8.1 +/- 1.4
PEth (ng/ml)	178.8 +/- 43.5
Mild to Mod use (Audit)	17 (85%)
Severe Use (Audit)	3 (15%)
Mild to Mod Use (PEth)	14 (70%) 71.6 +/- 14.6
Heavy Use (Peth)	6 (30%) 428.7 +/- 67.9

Values are mean +/- S.E.M.

Audit Mild to Mod Use Female >/5
Male >/ 8
Audit Severe Use Female >/13
Male >/16
Peth Mild to Mod Use 20-200 ng/ml
Peth Heavy Use >200 ng/ml

Table 2: A Summary Comparing EtOH Use with PEth Blood Values. This table shows a comparison of EtOH use as evaluated by the AUDIT questionnaire and PEth blood values. The mean AUDIT score was 8.6 +/- 1.4 with a PEth (ng/ml) value of 178.8 +/- 43.5. 85% of patients had AUDIT scores indicative of mild to moderate use of EtOH while 15% had severe use. This contrasted with PEth levels that indicated 70% mild to moderate EtOH use and 30% heavy use.

Table 3. Alcohol and Opioid Use in Patients

Patients	Characteristic
Patients EtOH and Opioid	5/20, (25%)
PEth (ng/ml) in EtOH and Opioid Patients	273 +/- 101.7

All patients male. N=5
Heavy EtOH use >200 ng/ml
Values are means +/- S.E.M.

Table 3: Summary Showing Relationship Between Concurrent EtOH and Opioid Use. Patients prescribed opioids and using EtOH were 25% (5/20) of the group. The PEth level in patients on opioids and using alcohol was 273 +/- 101.7 ng/ml.

Conclusions

This pilot study explored the use of the AUDIT self-report questionnaire and the PEth biomarker to assess EtOH use in chronic pain patients. Self-reporting has long been considered an inadequate measure of EtOH consumption, and this study confirmed that it is likely also inaccurate for chronic pain patients. While 85% of participants reported mild to moderate EtOH use on AUDIT, PEth data indicated that 30% were engaged in heavy drinking, showing a clear discrepancy between self-reports and objective biomarker data.

The weak correlation ($r = 0.219$, $p < 0.05$) between AUDIT scores and PEth levels suggests that patients significantly underreported their alcohol use. This underreporting occurred even though patients knew they would be tested for EtOH after completing the AUDIT questionnaire. Possible reasons for this discrepancy include fear of judgment, difficulty tracking EtOH consumption, and concern about the consequences, such as being removed from opioid therapy, as EtOH use is prohibited in opioid agreements.

Among the 25% of patients on opioids (all male), PEth levels averaged 273 ng/ml, above the 200 ng/ml threshold for heavy use. This highlights a safety risk, as combining opioids with EtOH increases the likelihood of adverse outcomes. The study also noted the potential utility of PEth in improving patient safety, as traditional urine drug screens primarily detect illicit substances, whereas EtOH is often overlooked, despite its comparable dangers in this population.

Although this small study had limitations, including a sample size of 20 and selection bias, the findings suggest that PEth is a more reliable and clinically relevant tool for detecting EtOH use in chronic pain patients. The ability to provide objective, easy-to-interpret results over a meaningful period makes PEth a valuable alternative to self-reports and other biomarkers, warranting further research in this setting.

References

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(Can contact authors for full list of references if desired.)