

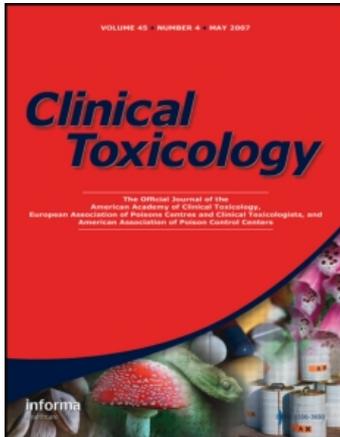
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Publisher Informa Healthcare

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Clinical Toxicology

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597279>

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Online Publication Date: 01 March 2008

To cite this Article Glintborg, Bente, Olsen, Lenette, Poulsen, Henrik, Linnet, Kristian and Dalhoff, Kim(2008)'Reliability of self-reported use of amphetamine, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, and opiates among acutely hospitalized elderly medical patients',*Clinical Toxicology*,46:3,239 — 242

To link to this Article: DOI: 10.1080/15563650701586397

URL: <http://dx.doi.org/10.1080/15563650701586397>

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ARTICLE

Reliability of self-reported use of amphetamine, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, and opiates among acutely hospitalized elderly medical patients

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Background. Undisclosed use of illicit drugs and prescription controlled substances is frequent in some settings. The aim of the present study was to estimate the reliability of self-reported use of amphetamine, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, and opiates among acutely hospitalized medical patients. **Methods.** Patients admitted to an acute medical department were interviewed about their drug use. Patients provided blood and urine samples for drug analysis. Results of a toxicology screen were compared to self-reported drug use. Toxicology screens positive for drugs not reported during the interview were only considered truly positive after verification by a substance specific analysis. **Results.** Five hundred patients were included. The median age was 72 years and 298 (60%) were female. In total, 103 patients (21%) reported use of opiates and 65 patients (13%) used benzodiazepines. Only 8 patients reported use of illicit drugs (cannabinoids, 2%). Toxicology analyses were performed in a randomly selected sub-sample of 100 patients. Among 27 patients (27%), the analyses indicated use of one or more drugs, mainly benzodiazepines (15 patients), morphine (12 patients) or cannabinoids (5 patients). Another 6 patients had screenings unexpectedly positive for opiates, but the verification analysis indicated use of codeine-containing drugs. The overall sensitivity of self-reports in detecting drug use was 66%. The negative predictive value of a patient not reporting use of a drug was over 90% for all 7 drug-types screened. **Conclusion.** Among 100 randomly selected mainly elderly medical patients, undeclared use of illicit drugs was rare. However, some patients underreported use of benzodiazepines and cannabinoids.

Keywords Drug history; Medical patients; Reliability; Self-report; Toxicology screen

Introduction

The use of illicit drugs and misuse of prescription controlled substances is frequent in the general population (1–3). Upon hospitalizations, knowledge of any drug use is important in order to interpret symptoms correctly (4). Furthermore, a complete medication list is a prerequisite for the safe prescribing of drugs. A major cause of prescription errors and adverse drug effects is lack of knowledge of the medications the patient is already taking (5,6). Clinicians often rely on patient's self-reports when constructing the list of used drugs. However, self-reported drug use is not always reliable depending on setting and drug type (4). Undisclosed use of prescription controlled substances and illicit drugs occurs

frequently among, e.g., arrestees and subjects involved in crime (7). On the other hand, subjects report with high reliability upon inclusion into substance dependency treatment (8). Little is known about the frequency of substance use and the reliability of self-reports among acutely hospitalized medical patients (9).

The aim of the present study was to describe the use of amphetamine, barbiturates, benzodiazepines, cannabinoids, cocaine, methadone, and opiates among patients admitted to an acute medical department. Drug use was estimated by 1) patient's self-report and 2) drug analysis. The two measures were compared in order to test the reliability of self-reported drug use.

Materials and methods

The study was conducted from February to September 2005 in an acute medical emergency ward at a University hospital in Copenhagen. The ward accepted patients with infectious,

Received 17 April 2007; accepted 20 July 2007.

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gastrointestinal, pulmonary, endocrine, and cardiac medical diseases. Patients were eligible in the study if admitted on weekdays between 8:00 and 15:00. Patients unable to communicate sufficiently were excluded. All included patients gave written informed consent. The Regional Ethics Committee and the Danish Registry Board approved the study.

A predefined number of 500 patients were included in the study on the day of their admission. The physician that performed all the interviews was employed at another hospital. It was explained to the patients upon study inclusion that all data were handled confidentially. This was in order to make the patient as comfortable as possible. Patients were questioned about their use of prescribed and over-the-counter drugs in the preceding week by a semi-structured interview technique. Furthermore, they were asked if they ever used illicit drugs and when the drugs were most recently used. The patients were specifically prompted to mention any use of amphetamine, cannabinoids and cocaine. The patients were asked to provide a urine sample immediately after the interview.

Among the 246 patients able to provide the requested urine sample, 100 samples were selected at random according to a computer-generated list. Drug screenings were only performed in this subset of samples to limit resource demands. Furthermore, a power calculation showed that a sample size of 100 would imply acceptably narrow 95% confidence intervals also at low prevalence rates. For example, with a sample size of 100, using frequencies above 5% would involve 95% confidence intervals (CI) with lower bounds excluding zero. Thus, even if we detected a low prevalence of use, we would be able to preclude zero drug use with high certainty. The screening was done by standard enzyme-immunoassays (SYVA ETS Plus with Emit d.a.u. assays, Dade Behring). The screening was considered positive if the concentrations were over the following cut-off limits: amphetamine and derivatives: 300 ng/ml, barbiturates: 200 ng/ml, benzodiazepines (including alprazolam, bromazepam, chlorthalidoxepoxide, clobazam, clonazepam, demoxepam, diazepam, flunitrazepam, lorazepam, lormetazepam, midazolam, nitrazepam, oxazepam, triazolam): 200 ng/ml, cannabinoids: 50 ng/ml, cocaine metabolite: 300 ng/ml, methadone: 300 ng/ml, and opiates (including apomorphine, codeine, dextrorphan, dihydrocodeine, hydrocodone, hydromorphone, levorphanol, meperidine, monoacetylmorphine, morphine, morphine-3-glucuronide, normeperidine, normorphine, oxycodone, oxycodone, morphine): 300 ng/ml. In individual patients, a screening positive for a drug not reported during the interview was only considered truly positive after verification by a substance specific analysis. Thus, a positive screening consistent with the patient's self-reported use was considered a true positive without further verification.

A screening unexpectedly positive for amphetamines, cannabinoids, or cocaine was verified by a GC-MS-method (gas chromatography with mass-spectrometry detection) at Department of Clinical Pharmacology, Rigshospitalet. We used urine samples for verification analysis of these illicit

drugs in order to get a large time window for detection of drug use (10).

In urine screenings unexpectedly positive for barbiturates, benzodiazepines, methadone or opiates, verification analysis was performed on blood samples drawn immediately after admission. We chose blood for the verification analysis of these prescription controlled substances, as high plasma levels might be indicative of misuse. Analyses were performed at the Department of Forensic Chemistry using liquid chromatography with mass-spectrometry detection (LC-MS/MS).

The patient's self-reported use of individual drugs was compared to the results of the drug analyses in order to describe 1) the ability of structured questioning to correctly identify drug users (the sensitivity of self-reports) and 2) the reliability of self-reported non-drug use (the negative predictive value, NPV). The gold standard of drug use was presence of the drug in urine/blood according to the toxicologic analysis.

Results

Among 710 patients screened, 500 patients were included in the study. Reasons for exclusion were inability to give informed consent (severe dementia, confusion or aphasia: 118 patients) or immediate referral to other departments (82 patients). Another 10 patients did not wish to participate. The 500 patients included in the study were admitted for a variety of endocrine, cardiac, pulmonary, urinary, and gastrointestinal medical diseases. The median age of the patients was 72 years (range 17–97 years, mean 68 years, mode 79 years) and 298 patients were female (60%). Age and sex distribution was similar among included and excluded patients ($p > 0.05$). Included patients remained in the acute medical ward or in a stationary medical department in the hospital for a median of 3 days (range 0–121 days).

According to self-reports, the total number of patients using prescription controlled substances was as follows: barbiturates (ATC code N03AA)(11): 4 patients (1%), benzodiazepines (N05BA): 65 patients (13%), methadone (N07BC): 8 patients (2%) and opiates (N02A): 103 patients (21%). The self-reported illicit drug use was amphetamine: 0 patients (0%), cannabinoids: 8 patients (2%) and cocaine: 0 patients (0%).

The median age of the 100 patients selected for drug screening was 71 years (range 22–97 years, mean 65 years) and 61 (61%) were women. The self-reported drug use is compared to drug analysis in Table 1. In total, 5 patients had a positive analysis for cannabinoids despite not reporting any use. Similarly, 7 patients had analysis indicating undeclared use of benzodiazepines; one of these patients had a benzodiazepine-concentration higher than therapeutic range and the remaining 6 patients had concentrations within or below the therapeutic range (12).

In 6 patients, the screening was unexpectedly positive for morphine contents. However, all these patients had verification analysis showing morphine present in concentrations below therapeutic range or present concomitantly with

Table 1. Self-reported drug use compared to the results of the toxicology screening (n = 100 patients, 7 drug analysis on each patient)

Drug	Positive screening analysis, n	Self-reported use		Negative screening analysis, n	Self-reported use		Sensitivity, % (95% CI) TP/(TP+FN)	Negative predictive value, % (95% CI) TN/(TN+FN)
		Use	No use		Use	No use		
		TP	FN		FP	TN		
Amphetamine	0	0	0	100	0	100	–	–
Barbiturates	2	2	0	98	0	98	100	100
Benzodiazepines	15	8	7	85	4	81	53 (43–63)	92 (87–97)
Cannabinoids	5	0	5	95	0	95	0	95 (91–99)
Cocaine	0	0	0	100	0	100	–	–
Methadone	1	1	0	99	1	98	100	100
Opiates	12	12	0	88	8	80	100	100

TP: True positive; FP: False positive; FN: False negative; TN: True negative.

codeine. Thus, recent use of codeine containing analgesics possibly explained the morphine contents and we concluded that the analysis was non-compatible with un-disclosed morphine use (12).

As shown in Table 1, the overall number of positive screening results was 35 (27 patients). Compared to the patient's self-reported drug use, 12 of the drugs were not reported whereas 23 of the drugs were correctly reported during the interview. Thus, the self-reports identified drug use with an overall sensitivity of 66% (23/(12+23), 95% CI 48–81%). The 12 patients not reporting use of a drug otherwise detected by drug analysis had similar age and sex distribution compared to all screened patients ($p > 0.05$). According to drug interviews and toxicology screens no patients had used amphetamine or cocaine. The negative predictive value (NPV) of a patient not reporting use of benzodiazepines or cannabinoids was below 100% due to underreporting (false negative results).

Discussion

In the present study including mainly elderly, one fourth of the patients had a positive toxicology screen result. The used drugs were mainly prescription controlled substances and more rarely illicit drugs. Patient's self-reports had low sensitivity in identifying use of benzodiazepines and cannabinoids. We found all NPVs over 90% indicating high reliability when a patient stated non-use of a drug.

The self-reported use of prescription controlled substances among included patients was similar to the use in the general population. In 2006, 16% of Danes aged 60+ purchased at least one prescription for opiates and 12% purchased benzodiazepines. For both drugs, the use increased with increasing age (13). The reliability of self-reported opiate use was difficult to establish due to the uncertainty when interpreting the drug verification analysis. Presence of codeine and morphine concomitantly or presence of morphine in sub-therapeutic concentrations is compatible with use of a codeine-containing

drug although use of morphine or heroin cannot be completely excluded. Codeine containing drugs are available on prescription or over-the-counter (13). Some degree of underreporting is likely as the patients were questioned about their over-all drug use and none of them reported use of codeine containing drugs. Similar underreporting of over-the-counter analgesics has previously been shown (14).

In total, 2% of included patients reported use of cannabinoids. For comparison, the use in the general population is approximately 4–6% (1,3). Some underreporting seemed likely as additionally 5 patients had a positive cannabinoid screening result. Positive cannabinoid screenings must be interpreted with caution and does not necessarily represent recent use: tetrahydrocannabinol and its metabolites are highly soluble in lipids and may be present in the body and the urine more than a month after heavy use. The result must preferably be discussed with the patient in order to clarify the clinical relevance (15). Amphetamine and cocaine are mainly used by adolescents (3). This might explain the infrequent use in our study, as we included many elderly.

Several patients stated use of drugs that could not be detected in their blood/urine (false positive). This especially happened for legal drugs (benzodiazepines, methadone and opiates) and may be explained by either exaggerated reporting (16,17) or more likely by pharmacokinetic circumstances due to fast elimination half lives of used drugs, diluted urine, etc. (10,15). As we primarily aimed at describing under- and not over-reporting, we presented no calculations of specificity and positive predictive values.

It was beyond the scope of our study to estimate the clinical impact of false negative self-reports, and individual patients and treating physicians were not informed about the screening results. However, for both diagnostic and treatment purposes a complete medication history is important upon hospitalisations (18–20). Use of illicit drugs may cause unfortunate drug-drug interactions (21) or may impair adherence to prescribed regimens (22). Inappropriate drug use might cause hospitalisation (10) or provokes changes in mental status among the elderly (23).

Our study-results are not immediately comparable to results stemming from high-risk populations where drug use is much more prevalent (7). Only few studies have previously described the use of toxicology screenings in hospital settings. In a Finish study, 16% of acutely hospitalised patients had a positive benzodiazepine screening whereof 33% admitted use (NPV=89%) (9). Patients presenting in emergency departments are considerably younger of age but have also been found to report substance use with intermediate sensitivity (4,15,17).

Undeclared drug use must be expected even more frequently outside a research setting where patients are not structurally interviewed or motivated by drug analysis (17). The diagnostic benefits of toxicologic screens must be held against the extra costs, workload and waiting time connected to additional analysis. Furthermore, any positive screening result must be interpreted with caution and in the right clinical context. Not all positive screenings are of clinical relevance (15). Due to the apparent low prevalent use of individual drugs among acutely hospitalised medical patients, a general toxicology screening does not seem beneficial. A toxicology screening must however be considered in individual cases for diagnostic purposes when symptoms are unexplained.

Our study was mainly powered to describe overall drug use and not to make subgroup analysis; this may explain why we found no factors discriminating patients with undisclosed substance use. Furthermore, we made no efforts in trying to distinguish between prescribed drug use and recreational use. Patients not reporting use of prescription controlled substances may differ from patients using illicit drugs. Embarrassment, unawareness or memory failure might be reasons for underreporting (4). The 100 samples randomly selected for screening must be assumed representative of all urine samples available. However, the patients not able to provide a urine sample might have introduced bias if they had distinctive characteristics (15). For instance, patients with undisclosed drug use might be unwilling to provide a sample for analysis. If this was case, our estimation of undisclosed drug use represents a best-case scenario. The screening procedure did not necessarily identify all the patients with recent drug use as some users might have had drug concentrations below the detection limit during screening. This would again lead to an underestimation of undisclosed drug use. Our exclusion of patients unable to give informed consent might have excluded the patients having most difficulties explaining their drug use or we might inadvertently have excluded patients with altered mental status caused by drug use. Our inclusion of study participants during daytime on weekdays only potentially introduced bias by omitting the more severely ill patients often hospitalised evening and nights.

In conclusion, the clinicians must be aware that some patients underreport their use of cannabinoids or benzodiazepines. The patient's self-reported drug use must be called in question if symptoms remain unexplained and a toxicology screening might be relevant in doubtful cases. The majority of patients are however reliable if stating non-use.

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