TOXICOLOGY SCREENING TESTING IN PATIENTS UNDERGOING ELECTIVE SURGERIES: ZAGAZIG UNIVERSITY HOSPITAL

BY

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ABSTRACT

Background: when patients with chronic back pain seek general surgery, it's typical to see them abusing opioids and other non-steroidal anti-inflammatory drugs, Paracetamol, muscle relaxant drugs, and gabapentin. There have been reports of substance abuse and misuse among these patients as a result of the excruciating pain. Patients who have abused opioids and other previous medications over an extended period of time have begun to experience painful postoperative adverse effects. Planning for appropriate preoperative optimization and perioperative management is aided by toxicology screening tests (TST). **Aim of the study** to determine whether TST by immunoassay followed by gas chromatography is feasible and whether it could deliver information that is more trustworthy than self-reporting. **Subjects and Methods:** we created a cross section research to track the accuracy of these patients' self-reports and TST tested all abused substances. **Results:** The data suggests that the relationship between pre-operative drug use confirmed by toxicology screening rather than self-report and intra-operative use of propofol as well as post-operative pain as outcome parameter. There was a statistical significant strong positive correlation between number of drugs detected in TST and induction dose of propofol (Spearman correlation r=0.78), suggesting that the dose of propofol should be raised when the number of drugs used was increased, pain score in the last week (r=0.84), as well as length of hospital stay (r=0.71) with p value <0.001. **Conclusion:** TST is a valuable test to identify substances taken by patients when they are scheduled for elective surgery because self-report is frequently unreliable.

Key Words: *Elective surgery, Peri-operative Optimization, Propofol, Toxicology Screening Testing.*

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INTRODUCTION

Globally, chronic pain is a significant social and economic issue. Those who suffer from unbearable chronic pain are commonly given opioid medications. These individuals may have demonstrated opioid dependency and drug tolerance, which are symptoms of mental illnesses such anxiety, affective disorders, and substance addiction ***(Fishbain, 2015)***.

Chronic opioid usage, Defined as 90 days of continuous opioid use or 120 days of non-continuous use ***(Inacio, et al., 2016)***, has negative side effects on surgical patients, such as worse postoperative pain, longer pain duration despite higher drug dosages, increased dosage of anethetics agent as propofol, increased risk of complications, and subpar outcomes ***(Chapman et al., 2019; Lawrence et al., 2018)***.

Moreover, stronger anesthetic doses are needed when using marijuana and alcohol more frequently. This has been observed in patients who use alcohol and marijuana regularly. As a result, it is extremely difficult for patients who are scheduled for surgery to have their usage of opioids, non-steroidal anti-inflammatory drugs, Paracetamol, muscle relaxant drugs, and gabapentin, and recreational drugs appropriately checked and assessed ***(Flisberg et al., 2019)***.

A patient's medical history should ask about any drug and alcohol abuse. The inquiry should allow the surgeon and anesthesiologist to accurately care for the patient and should not be utilized for criminal matters ***(Khalili, et al., 2021; Rockett et al., 2016)***.

The three types of problematic use were defined as follows in the ***Vowles et al. (2015)*** review: (1) misuse, which is the use of

opioids against the prescription drug maker's instructions; (2) abuse, which is the use of opioids for non-medical purposes (such as euphoria or altered consciousness); and (3) addiction, which is the continued use of opioids despite impaired control, compulsive use, craving, or proven or potential harms. Between 1% to 81% of studies overall reported problematic usage across 38 studies, with rates of misuse, abuse, and addiction falling between 21% and 29% and 8%, respectively ***(Vowles et al., 2015)***.

Drug misuse screening in regular testing has received extensive research. Results of toxic urine screening are provided within 30 minutes of sample collection and receipt. The most often examined screening panels include tests for marijuana, amphetamines/ methamphetamines, phencyclidine (PCP), cocaine, opioids, barbiturates, and benzodiazepines ***(Sirri et al., 2017)***.

Tachycardia, tremors, an odor of alcohol, and poor dental health are physical examination indicators that may lead a doctor to believe a patient is abusing drugs. The surgical interference should be postponed if acute intoxication on top of chronic abuse is verified by a history, physical examination, or laboratory tests. Referral to a treatment facility should be urged if use is chronic. Acute intoxication and chronic substance abuse can have a negative impact on all areas of perioperative treatment, including the insertion of intravenous lines, maintaining airway security, intraoperative procedures, and postoperative pain control. Patients who have been drinking before surgery run the risk of hemodynamic compromise, poor wound healing, altered consciousness, and trouble controlling their pain ***(Kudsi et al., 2013)***.

To our knowledge, only a few prior researches looked into how well patients undergoing elective surgery responded to toxicological screening tests (TST).

AIM OF THE WORK

The purpose of this study was to determine whether the toxicology screening testing is feasible and whether it could deliver information that is more trustworthy than self-reporting.

SUBJECTS AND METHODS

Study population

This cross-sectional study was done on people who were admitted to General Surgery Department at Zagazig University hospitals before having surgery between 15th February 2023 and 15th May 2023. Patients between the ages of 25 and 60 who are classified as American Society of Anaesthesiology (ASA) 1 or 2 patients ***(De Cassai et al., 2019)***.

Knuf et al. (2020) and Horvath et al. (2021), declared that American Society of Anaesthesiology was developed to provide perioperative clinicians with a straightforward classification of a patient's physiological status that can aid in surgical risk prediction.

ASA 1: A patient in typical health.

ASA 2: A patient with a minor systemic illness.

ASA 3: A patient with a major systemic illness that is not life-threatening.

ASA 4: A patient with a major systemic illness that is a constant threat to life.

ASA 5: A patient who is terminally ill and unlikely to survive without surgery. Without surgery, the patient is not anticipated to live past the next day.

ASA 6: A Organs are being extracted from a brain-dead patient with the goal of transplanting them into another person.

We enrolled patients in our trial who had a history of chronic back pain lasting more than 12 weeks and who were planned for elective surgery (cholecystectomy, herniotomy, or thyroidectomy) within the next three months. Those who underwent urgent surgery, those with abnormal consciousness levels, people with a history of psychological disease, and those who refused to consent were eliminated. Just 75 patients were chosen for this study based on these exclusion criteria.

Ethical approval:

A letter of approval was acquired from the Faculty of Medicine's Ethics Committee for Research Institutional Review Board (IRB), Zagazig University (ZU-IRB # 10397/13-2-2023). Before collecting the sample, a written informed permission describing the study's purpose and the participant's right to withdraw at any time without affecting the health services offered was obtained.

Patient anonymity is protected through the gathering of anonymous data, and the data will only be utilized for research. This study was conducted in conformity with the Declaration of Helsinki, which is the World Medical Association's code of ethics for human subjects' studies.

Methods:

Questionnaire includes:

Sociodemographic information on age, gender, education, occupation, income, smoking status, medical history of chronic diseases, drug usage and duration, surgical history, and kind (cause) of surgery were all included in this questionnaire.

Pain intensity:

A numerical rating scale ***(Treede et al., 2019)***, was used to quantify pain intensity. The patient was asked to rate their average pain level over the previous week on a 10-point numerical rating scale (NRS), with 0 being the least pain and 10 being the most pain. With 1-3 minor, 4-6 medium, and 7–10 major pains.

Preoperative laboratory investigation:

Preoperative laboratory testing included hepatitis B and C, HIV, complete blood count, liver, and kidney function tests.

Self-reporting of any type of drug abuse.

Toxicology Screening Test:

Via urine drug testing, toxicology screening Urine drug testing (UDT) is frequently referred to as the "gold standard" monitoring strategy since it is the most accurate way to detect opioid usage in individuals with chronic pain ***(Turk et al., 2008; Eilender et al., 2016)***.

Consequently, a 5-mL urine sample will be taken prior to surgery on the day of the clinic visit (sample 1), and a second sample will be taken prior to surgery on the day of the procedure but prior to the patient receiving any preoperative drugs (sample 2). *The following methods will be used to analyze two samples:*

a- Dip steak with a multi-drug screen panel. Chromatography immunoassay called ABONtm (Abon Biopharm (Hangzhou) CO., Ltd): It enabled the qualitative identification of numerous substances in one location. The ability of this kit to identify the drugs that are most frequently misused in Egypt, such as amphetamine, cocaine, opioids, benzodiazepines, barbiturates, hashish, and tramadol, led to its selection. . For any of the medications described earlier, a single colored line at region C indicated a favorable result, whereas two colored lines at regions C and T indicated a negative outcome. The particular kit was eliminated since the lack of colored lines indicated that it was invalid.

b-Gas-chromatography assay: Then the positive results of the two samples were confirmed using a gas chromatography assay in Almokhtabar-Lab. It is confirming the structure of positive results in a single run**.** A positive result in any sample confirmed the substance use.

STATISTICAL ANALYSIS:

The data was collected in excel sheet, cleaned and coded then exported and analyzed by to statistical package of social science program version 25 (SPSS 25). The data was tested for homogeneity using Kolmogorov-Smirnov test. Qualitative data was presented as number and percent, chi square and Fisher exact tests were used as applicable. Quantitative data was presented as mean, standard deviation (SD) and range and analyzed using t test if data was normally distributed, additionally median and interquartile range were used for skewed data and Mann-Whitney U Test was used for its analysis. Spearman correlation was used to detect the association between number of drugs detected in TST and induction dose of propofol, pain score in the last week as well as length of hospital stay. P value < 0.05 considered significant and p value < 0.01 considered highly significant on both sides.

RESULTS

Seventy-five patients included and completed the study. **Table (1)** shows sociodemographic and clinical characteristics of participants. Their mean age was 46.16±9.6 years old (range, 26–60 years), more than half were males (52%), with elementary level of education (42.7%) and had insufficient income (50.7%). Close to one third of them were professionals (30.7%). Regarding the clinical history, 44% were currently smokers with17.3% of them were currently marijuana smokers. Nearly one fourth of them had hypertension and Diabetes Mellitus (29.3%

and 24%) respectively. More than half complained mild pain intensity (57.3%) and median pain score was 1 (IQR, 1-7). Median length of hospital stay was 4 days (IQR, 4-7 DAYS), with 12% were admitted to ICU. The average induction doses of propofol was 154.3 ±45.3 mg.

Self-reported drug abuse was only 17.3% for Tetrahydrocannabinol. However, toxicology urine screening test was positive in 29.3% (22/75), with 12% of participants were screened positive for single or two drugs.

The prevalence of screened positive drugs was Tetrahydrocannabinol (22.7%), tramadol (17.3%), morphine (9.3%), and the least prevalent one was amphetamine (2.7%). History of self-reported other medical drugs commonly used by patients were NSAIDs, paracetamol, muscle relaxant and gabapentin (69.3%, 34.7%, 22.7% and 16%) respectively with 42.7% of them used multiple drugs**. (Table 2).**

Table (1): Socio-demographic and clinical characteristics of the study participants.

Sociodemographic and clinical characteristics	Frequency= 75	%
Age group (years): Mean ± SD (Range)	46.16±9.6 (26 – 60)	
Gender:		
- Males	39	52.0
- Females	36	48.0
Educational Level:		
- Elementary level	32	42.7
- Intermediate	27	36.0
- University	16	21.3
Occupation:		
- Not working/house wife	16	21.3
- Un skilled worker	22	29.3
- Skilled worker	14	18.7
- Professional	23	30.7
Income:		
- Insufficient	38	50.7
- Sufficient	30	40.0
- Sufficient and more	7	9.3
Smoking status:		
- No	42	56.0
- Yes	33	44.0
Current marijuana smoking:		
- No	62	82.7
- Yes	13	17.3
Chronic disease history: ‡		
- No	45	60.0
- Hypertension	22	29.3
- Diabetes Mellitus	18	24.0
- Cardiac diseases	2	2.7
Types of indicated surgical operations: §		
- Hereniotomy	39	52.7
- Cholecystectomy	21	28.4
- Thyroidectomy	14	18.9
Pain intensity in the last week using numeric rating score: Median (IQR)	1 (1-7)	
ICU admission:		
- No	66	88.0
- Yes	9	12.0
Length of hospital stay (days): - Median (IQR)	4 (4 - 7)	
Induction doses of propofol (mg) Mean ± SD (Range)	154.3 ±45.3 (120 – 300)	

‡ Total more than 100% due to multiple choices. ***§*** *Missed data of one case* ***IQR:*** *Interquartile range*

Table (2): Toxicology urine screening test and the used medical drugs of the studied Patients.

Parameters	N.= 75	%
Self-reporting of drug abuse:		
- No drug abuse	62	82.7
- Yes (Tetrahydrocannabinol)	13	17.3
Number of positive drugs in Toxicology screening testing:		
- No	53	70.7
- Single drug	9	12.0
- Two drugs	9	12.0
- Three drugs	4	5.3
Types of drugs discovered in toxicology screening testing:		
- Tetrahydrocannabinol (THC)	17	22.7
- Tramadol	13	17.3
- Morphine	7	9.3
- Amphetamines	2	2.7
Other medical drugs used by patients: ‡		
- Non-steroidal anti-inflammatory drugs (NSAIDs)	52	69.3
- Paracetamol	26	34.7
- Muscle relaxant drugs	17	22.7
- Gabapentin	12	16.0
Number of other medical drugs used by patients:		
- Single drug	43	57.3
- Multiple drugs	32	42.7

‡ Total more than 100% due to multiple choices.

Table (3) shows the disagreement between self-report usage and toxicology urine screening test results of individual drugs among participants. The highest noted discrepancy was for tramadol (17.3%), morphine (9.3%), tetrahydrocannabinol (5.3%) and the least one was for amphetamine (2.7%). There was statistical significant strong positive correlation between number of drugs detected in TST and induction dose of propofol (Spearman correlation r=0.78), pain score in the last week (r=0.84), as well as length of hospital stay (r=0.71) with p value <0.001. **Figure 1 (A, B, C)** respectively.

Table (4) demonstrates that there was statistical significant association between sociodemographic and clinical characteristics of participants with the TST results.

The positive results of TST were significantly higher among males than females (86.4% vs 13.6%, p<0.001), skilled workers (mainly drivers) compared to other occupations (p=0.006), who are currently smokers and marijuana smokers (77.3% and 59.1%) versus their counter parts (22.7% and 40.9%) respectively with p value <0.001. In addition, positive TST results were significantly higher among diabetic patients, those administered multi-relaxant drugs, and those who admitted to ICU compared to their counter parts. The median length of hospital stay and median pain score were higher among those had TST positive results (8 vs 4 days, p<0.001) and (7 vs 1, p<0.001) respectively as well as higher mean induction dose of propofol (208.64±34.27 vs 131.7±26.07 mg, p<0.001).

Table (3): Agreement/Disagreement between self-report usage and toxicology urine screening test results of individual drugs among participants.

Substance	Negative history/ Negative TST	Negative history/ Positive TST	Positive histor Negative TST	Positive histor Positive TST	Disagreement
Tetrahydrocannabinol (THC)	58	4	0	13	5.3%
Tramadol	62	13	0	0	17.3%
Morphine	68	7	0	0	9.3%
Amphetamines	73	2	0	0	2.7%

History: self-reported drug history, TST: toxicology urine screen test.

For each substance, a participant could fall into one of 4 categories: 2 categories indicated agreement (negative history/negative TST and positive history/positive TST), whereas 2 categories indicated inconsistency between self-reporting and the TST; namely, either the study participants reported no use of a substance that appeared in the TST (negative history/positive TST) or they reported use of a substance that did not appear in the screen (positive history/negative TST).

Table (4): The relationship between toxicology urine screening test results with sociodemographic and clinical characteristics of participants.

Sociodemographic and clinical characteristics	Negative TST N.=53 (%)	Positive TST N. = 22 (%)	P value
Age group (years): Mean ± SD	44.96±9.93	49.05±8.42	¥ 0.09
Gender:			
- Males	20 (37.7%)	19 (86.4)	<0.001**
- Females	33 (62.3)	3 (13.6)	
Educational Level:			
- Elementary level	22 (41.5)	10 (45.5)	
- Intermediate	21 (39.6)	6 (27.3)	0.54
- University	10 (18.9)	6 (27.3)	
Occupation:			
- Not working/house wife	15 (28.3)	1 (4.4)	
- Un skilled worker	16 (30.2)	6 (27.3)	0.006**
- Skilled worker	5 (9.4)	9 (40.9)	
- Professional	17 (32.1)	6 (27.3)	
Income:			
- Insufficient	31 (58.5)	7 (31.8)	
- Sufficient	19 (35.8)	11 (50.0)	0.062
- Sufficient and more	3 (5.7)	4 (18.2)	
Smoking status:			
- No	37 (69.8)	5 (22.7)	<0.001**
- Yes	16 (30.2)	17 (77.3)	
Current marijuana smoking:			§
- No	53 (100.0)	9 (40.9)	<0.001**
- Yes	0 (0.0)	13 (59.1)	
Chronic disease history: ‡			
- No	35 (66.0)	10 (45.5)	0.097
- Hypertension	15 (28.3)	7 (31.8)	0.76
- Diabetes Mellitus	9 (17.0)	9 (40.9)	0.027*
- Cardiac diseases	1 (1.9)	1 (4.5)	0.52
Other medical drugs used by patients: ‡			
- Non-steroidal anti-inflammatory drugs (NSAIDs)	37 (69.8)	15 (68.2)	0.89
- Paracetamol	22 (41.5)	4 (18.2)	0.053
- Muscle relaxant drugs	8 (15.1)	9 (40.9)	0.015*
- Gabapentin	6 (11.3)	6 (27.3)	0.086
Pain intensity in the last week using numeric rating score: Median (IQR)	1 (1-1)	7 (7 – 8)	¶ <0.001**
ICU admission:			§
- No	52 (98.1)	14 (63.6)	<0.001**
- Yes	1 (1.9)	8 (36.4)	
Length of hospital stay (days):			¶
- Median (IQR)	4 (3 – 4)	8 (6.75 – 10)	<0.001**
Induction doses of propofol (mg):			¥
- Mean ± SD	131.7±26.07	208.64±34.27	<0.001**
- Range			

‡: Total more than 100% due to multiple choices T-test. Chi square Test was used §: Fisher exact test
*¥: t test ¶: Mann-Whitney U Test * significant level p< 0.05 ** highly significant level p< 0.01*

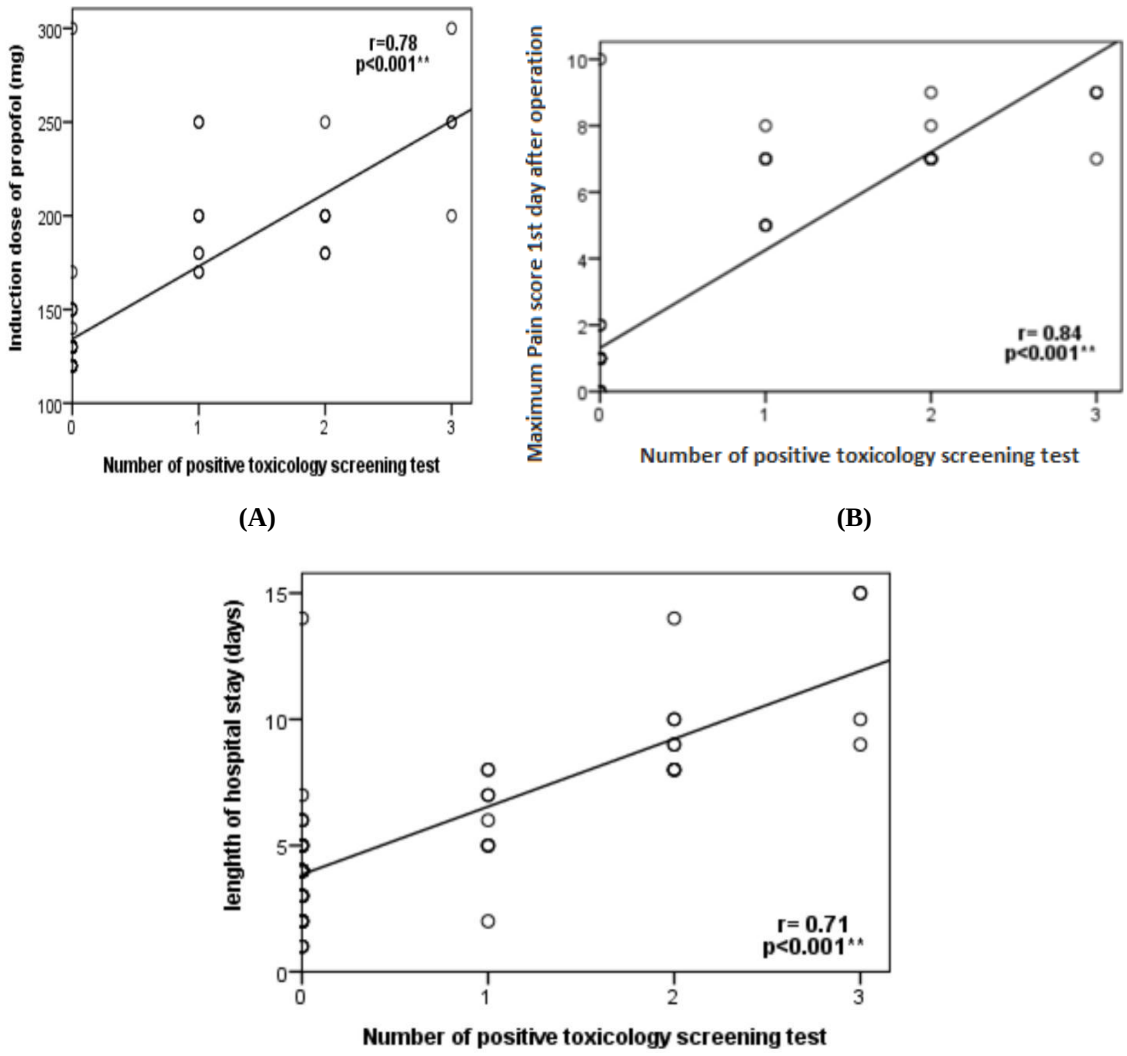

Figure (1): Spearman correlation between number of drugs detected in toxicology urine screening test (TST) with induction dose of propofol in mg (A), pain score in the last week (B), and length of hospital stay in days (C).

DISCUSSION

Drug abuse affects many people in the society, including those who need anaesthetic for surgery. Those who could be acutely intoxicated or persistent abusers can benefit from a history and toxic screening. The doctor needs to be aware of any potentially dangerous situations that may arise during anaesthesia or postoperative treatment. ***(Afshar et al., 2014)***.

Seventy-five patients were included in and finished our study. Their mean age was 46.16±9.6 years old (range, 26–60 years), more than half were men (52%), with elementary level of education (42.7%) and had insufficient income (50.7%).

These findings closely resemble those of ***Claudia et al. (2021)***, who discovered that the median age of patients was 59 years (ranging from 33 to 76 years).

We discovered discrepancies in self-report usage and toxicological urine screening test results of specific substances among participants, as some patients reported no use of a substance that was subsequently detected in the TST, whilst others supported the use of a compound that was not detected. Tramadol (17.3%), morphine (9.3%), tetrahydrocannabinol (5.3%), and the least significant differences were identified for these drugs.

Only 17.3% of participants in a study by ***Chapman et al. (2019)***, acknowledged

abusing tetrahydrocannabinol. However, 29.3% (22/75) of participants in the toxicological urine screening test were found to be positive, and 12% of participants were found to be positive for one or more substances. Tetrahydrocannabinol (22.7%), tramadol (17.3%), morphine (9.3%), and amphetamine (2.7%) had the highest prevalence of substances that tested positive. NSAIDs, paracetamol, muscle relaxants, and gabapentin were the most frequently reported other medicinal substances used by patients in their past (69.3%, 34.7%, 22.7%, and 16%), with 42.7% of them using several medications.

Inconsistencies between self-reporting and TST were discovered in 24 of the 27 study participants (88%) by ***Claudia et al. (2021):*** Acetaminophen, opioids, benzodiazepines, and other groups had such variances. muscle relaxants, antidepressants, NSAIDs, antiepileptics, antihistamines, lidocaine, and hypnotics are some examples of prescribed medications. NSAIDs (44%), benzodiazepines (33%), and opioids (25.9%) had the biggest differences.

In a preoperative toxicology screening of 1057 patients undergoing bariatric surgery, **Grace et al. (2023)** observed that 134 patients (12.7%) had positive toxicology testing. Of these, 21 (16%) and 37 (28%) tested positive for cotinine and opiates, respectively.

Our findings showed a statistically significant strong positive association (Spearman correlation r=0.78) between the number of medications found in the TST and the induction dose of propofol, the pain score from the previous week (r=0.84), and the length of hospital stay (r=0.71) with p value <0.001.

However, ***Claudia et al. (2021)*** revoked The Spearman correlation between polypharmacy (number of medicines found in the TST) and the propofol induction dose was 0.509, indicating that propofol use may have increased as the number of substances found rose. The pain score tended to rise (Spearman correlation: 0.340). The pain score tended to rise (Spearman correlation: 0.340).

Additionally, those who misused more medicines experienced more postoperative pain. These results support past studies done by ***Gressler et al. (2018); Armaghani et al. (2016)***. Marijuana's impact on anesthetic dosages has been seen in a study done by ***Flisberg et al. (2019)***.

Our study's results offer the first evidence that utilizing a TST to assess for drug use is preferable to depending just on self-reporting. Additionally, performing a TST the day before surgery is easy and fast. Our results suggest that the treatment and safety of perioperative patients depend on multidisciplinary planned strategies that are developed using high-quality, reliable quantitative data regarding the drugs that patients are currently abusing at the time of surgery. Additionally, the data collected might be used for In patients who are at risk, treat and prevent withdrawal syndrome. The TST can be used to guarantee patient safety before operations of all kinds, including surgery.

Limitations of the study:

The current findings support beginning a larger prospective, randomized investigation to establish the clinical basis for routine preoperative TST and to put recommendations into practice in this patient population. The current study is a cross-sectional study. Thus, the sample size has a built-in constraint. Moreover, consent was necessary because this was a prospective study. This might have caused some patients who were denied drug testing to self-select against enrolment.

CONCLUSION

Toxicology Screening Testing (TST) is a valuable test to identify substances taken by patients when they are scheduled for elective surgery because self-report is frequently unreliable. The creation of postoperative pain management techniques that could shorten hospital stays and improve postoperative withdrawal syndrome care.

RECOMMENDATIONS

Larger prospective, randomized investigation to establish the clinical basis for routine preoperative TST and to put recommendations into practice in chronic back pain patient undergoing elective surgeries.

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