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Research Article

The Study of Ranitidine Interference With Morphine Detection Test by Thin-Layer Chromatography

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Abstract

Background: Drug abuse is a global and critical problem. One of the most frequent practices done in order to detect the drugs of abuse is Urine Drug Screen. However, for changing the drug test results, adulterants and urine substitutes are being designed. As the referring people's background has shown, ranitidine is one of the interfering drugs in morphine detection test. Therefore, in the present study, the interference of ranitidine in morphine detection test will be studied.

Methods: Ten healthy volunteers who had not used any kind of drug for 72 hours before the test were recruited into the study. First, 2 doses of ranitidine (150 and 300 mg) were administered to the subjects orally and 100-mL urine samples were collected from them before and after taking ranitidine. The second urine sample was collected at 6-8 AM. Ten micrograms morphine was added to both urine samples of each individual. The urine samples were tested using thin-layer chromatography (TLC) technique. The experiment was repeated after 1 week using ranitidine 300 mg.

Results: The TLC test was carried out on 40 urine samples. Twenty samples were tested before and, the rest, after ranitidine consumption. The TLC test results were positive before ranitidine consumption but negative for 18 samples and positive for two samples after taking ranitidine.

Conclusion: Ranitidine may change the urine morphine screening test results via TLC method and induce a false negative result.

Keywords: Addiction, Morphine, Drug Screen, Ranitidine

Background

Drug abuse is a global and critical problem. One of the most frequent practices done in order to detect the drugs of abuse is urine drug screen. There are few occasions and situations in which urine drug screening may be performed such as pre-employment, random testing outlined in employment contract, military service enrollment, legal/criminal cases, marriage, sports participation, postmortem investigation, therapeutic drug monitoring, and suspected drug abuse (1).

Opioids, still among the most commonly used drugs for non-medical purposes, may be the most frequently abused drugs, preceded by stimulants (2). In order to detect drug abuse, prevent family breakdowns and also refer addicts to civil services, precise and exact laboratory tests are routinely and periodically used. For detecting drugs and their metabolites quantitatively, several tests are administered, and routine screening tests such as colorimetric tests and thin-layer chromatography (TLC) are applied. It is worth mentioning that although confirmatory tests such as gas chromatography, high-performance liquid chromatography, immunoassays, and mass spectroscopy require specialized and expensive devices, they are more sensitive and precise (3). Unfortunately, to change drug test results, adulterants and urine substitutes have been designed. The common methods for tampering with a urine specimen are classified into three basic categories: (1) in vivo adulteration; consuming chemical agents before micturition, such as simple dilution via the excess ingestion of water; (2) in vitro adulteration involving adding chemical agents to the urine sample after micturition; and (3) urine substitution where a substance-negative urine specimen is deliberately replaced with a substance-positive urine specimen throughout the sampling (4).

Given the accuracy and importance of the results of narcotic material detection tests, the attempt of the individuals to change laboratory results in order to obtain unreal answers, and also the observations and experiments in diagnostic laboratories, it seems that the confounding effects of some drugs with urine samples collected from

patients, have caused unreal laboratory results. As observing and studying the background of people referring for drug abuse tests has shown, ranitidine is one of the interfering drugs in morphine detection test by TLC. Ranitidine is a histamine H_2 receptor antagonist whose serum's half-life ranges from 1.1 hours to 4 hours; however, its duration of action depends on the administered dose. H_2 antagonists are cleared by a combination of hepatic metabolism, glomerular filtration, and renal tubular secretion (5). Therefore, in this study, the interaction between ranitidine and morphine will be investigated.

Methods

In this interventional research in which 10 healthy adult volunteers who did not consume any kind of drug during the 72 hours before the exam were recruited. The individuals consumed 2 doses of ranitidine, 150 and 300 mg (5), orally within 1-week interval. Urine samples of 100 mL were collected from the individuals at 10-11 PM and then ranitidine 150 mg was orally administered. The second urine sample was collected between 6 to 8 AM. Ten micrograms morphine (3) was added to both urine samples of each individual. The urine samples were tested using TLC (6). After 1 week, the experiment was repeated using ranitidine 300 mg. In these experiments, each of individuals was the control for himself so the need for matching the control group and treatment group for age and sex was eliminated.

It is worth mentioning that TLC method is less expensive than HPLC and GC-MS in terms of fundamental equipment and other initial set-up costs. Therefore, to achieve functional outcome, in the current study, TLC method was used for detection of interactions. All of the samples were transferred to a laboratory where urine morphine test by TLC is routinely conducted.

Thin-Layer Chromatography Method

The kit (Rima Optic, Zist Abzar Pajohan Company) used in this study has several main components: resin column, activator buffer, extraction solution, and silica gel plate.

The resin column was placed on a vacuum chamber at pressure of 0.1, and 3 mL of commercial activation buffer is added. After discharging, the buffer was added to 10 mL centrifuged (at 2000 rpm for 2 minutes) urine sample column and allowed to be discharged slowly. Then, 3 mL distilled water was added to the column to remove the waste material from the column and after discharging, the negative pressure of the vacuum chamber was decreased to -0.3, so that the resin was completely dried and powdered. Next, a commercial extraction solution or methanol was added to the column, and using a clamp it was placed on a 110°C heater. The solution extracted from the column was collected in a 5-mL beaker and kept on the 110°C heater to conduct concentration. When less than 0.5 mL of the solution remained, it was stained on an activated silica gel plate (20 minutes at 110°C) using a pipette or optic tube.

Tank Solution

The tank solution, as the moving phase, moves the stained material on silica gel (which is the constant phase) and the materials will move based on their physical and chemical properties. In this study, according to the kit instructions, the chloroform, methanol and ammonia solutions were mixed at the ratios of 12, 1.6 and 0.5, respectively, and 20 minutes after the solution was poured in the chromatography tank, the tank space was saturated.

Reagent Hexachloroplatinate

This color, which is a combination of two solutions hexachloroplatinate and potassium iodide, is effective to detect opiates and is used as a spray.

Ethical Considerations

The present study was approved by the Medical Research Ethics Committee of Hamadan University of Medical Sciences.

Results

In this interventional study, the morphine urine test by TLC was carried out in the presence and absence of ranitidine. The TLC test was carried out on 40 urine samples. Twenty urine samples were tested before ranitidine consumption, and the rest after ranitidine consumption (Table 1).

Table 1. Comparison of Morphine Screen Test Results Via Thin-Layer Chromatography Before and After Ranitidine Consumption (150-300 mg)

Sample	Detection of Morphine (Before Using Drug)	Detection of Ranitidine (After Using Drug)	Detection of Morphine (In the Presence of Ranitidine 150 mg)	Detection of Morphine (In the Presence of Ranitidine 300 mg)
1	+	Unknown	+	_
2	+	+	_	_
3	+	+	_	_
4	+	+	_	_
5	+	+	_	_
6	+	+	_	_
7	+	+	_	_
8	+	+	_	_
9	+	+	_	_
10	+	+	+	_

Discussion

Increased drug abuse has been witnessed in most parts of the world, and therefore different serious social, psychological, and physical problems associated with it are likely (7,8). However, unfortunately, readily available methods such as adulterant and urine substitutes are used to change the drug test result.

Morphine detection tests on the urine samples of the individuals who took ranitidine showed false negative results. Morphine detection tests were positive in these individuals before taking ranitidine. In these experiments individuals were the control for themselves, so the negative result of the morphine detection test is due to the ranitidine presence in the urine.The positive result due to the150 mg Ranitidine in 2 cases may be related to the variation of drug responses between different individuals. In a study, Hajhashemi et al evaluated the interaction between oral contraceptive and urine morphine test. They concluded that there is no interaction between HD contraceptives and urine morphine diagnostic tests both in vitro and in vivo (9). In another study, the effect of carbon copy paper, nitrogen-based chemical fertilizers, lemon juice, and diluted urine sample on urine morphine screening test was evaluated. Interestingly, it was found that adding some lemon juice or even fertilizer at concentrations lower than those of morphine can somehow affect the morphine detection test results (3).

Ranitidine excretion pathway is kidney and after 2-3 half life, a comparably greater amount of drug is secreted in the urine (5). In this study, each individual also served as the control for himself. Morphine detection test before ranitidine usage was positive, but after ranitidine the test response was negative. This may be related to ranitidine present in the urine.

In Iran, one of the common approved procedures for detecting narcotic materials in urine is column chromatography-TLC. The reliability of the data obtained from morphine ELISA kit versus an available, inexpensive confirmatory analytical method, namely, TLC has been evaluated in different studies. In these studies, it was also concluded that although TLC is more specific, it is more time-consuming and less-sensitive, in comparison to ELISA. It is worth mentioning that although TLC is an old method, it is much more reliable than ELISA (10).

Conclusion

Ranitidine may change the urine morphine screening results by TLC method and induce false negative result. This study should be also replicated in addict individuals to investigate ranitidine-morphine interaction in the body and how urine morphine test result can be changed.

Authors' Contributions

AM and AK carried out sampling. FN helped in writing the manuscript. FZ acted as the supervisor.

Conflict of Interest Disclosures

None declared.

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