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Reasonability of urine toxicology screening for methamphetamine and cocaine in young acute myocardial infarction

Genç akut miyokard infarktüslerinde metamfetamin ve kokain için idrar toksikoloji taramasının uygulanabilirliği

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Abstract

Aim: Prior cocaine and methamphetamine use influence treatment strategies in subjects with acute myocardial infarction. Often patients may not self-report illicit drug use on admission but urine analysis may reveal etiology. This study aimed to investigate if routine screening of cocaine and methamphetamine use by urine analysis is reasonable in young myocardial infarction.

Material and Methods: This study enrolled 50 consecutive young patients (≤ 50 years old) with acute myocardial infarction. Mean age was 41.3 ± 7.8 (21-50) and 80% of patients were male. Patients were queried about the use of any illicit drug use on admission. Urine samples for cocaine and methamphetamine analysis were done using immunoassay tests within the first day of admission. Cocaine use was considered as positive if the level of benzoylecgonine was above 300 ng/mL. Methamphetamine use was considered as positive if the level was above 1000 ng/mL. All the patients underwent coronary angiography and percutaneous coronary revascularization if they had significant coronary artery stenosis.

Results: ST elevated acute myocardial infarction was diagnosed in 38 patients (76%) and non-ST elevated acute myocardial infarction was diagnosed in 12 patients (24%). No patient self-reported cocaine or methamphetamine use. Urine analyses for cocaine were negative in all 50 patients. In urine analyses methamphetamine were found to be positive in 5 patients (10%). Classical risk factors for atherosclerosis were similar between the groups.

Conclusion: As we found 10% incidence of methamphetamine use, it may be reasonable to screen methamphetamine use but not cocaine use by urine analysis in younger myocardial infarction patients.

Keywords: methamphetamine; urine toxicology; acute myocardial infarction

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Öz

Amaç: Öyküsünde kokain ve metamfetamin kullanımı olan, akut miyokart enfarktüsü geçiren hastalarda tedavi stratejisi değişmektedir. Hastalar genellikle hastaneye kabulde yasa dışı uyuşturucu kullanımını kendi kendine bildirmeyebilirler ancak idrar analizi etyolojiyi ortaya çıkarabilir. Bu çalışma, genç yaşta akut miyokart enfarktüsü geçirenlerde kokain ve metamfetamin kullanımının idrar analizi ile rutin olarak taranmasının makul olup olmadığını araştırmayı amaçlamaktadır.

Gereç ve Yöntemler: Çalışmaya akut miyokart enfarktüsü geçiren ardışık 50 genç hasta (≤ 50 yaşında) alındı. Hastaların yaş ortalaması 41.3 ± 7.8 (21-50) di ve hastaların %80'i erkekti. Hastalar hastaneye kabul sırasında herhangi bir yasa dışı uyuşturucu kullanımının olup olmadığı hakkında sorgulandı. Kokain ve metamfetamin analizi için idrar örnekleri, yatışın ilk günü içinde immünolojik testler kullanılarak yapıldı. Benzoylcegonine seviyesi 300 ng / mL'nin üzerindeyse kokain kullanımı pozitif olarak kabul edildi. Eğer seviye 1000 ng / mL'nin üzerindeyse, metamfetamin kullanımı pozitif olarak kabul edildi. Tüm hastalara koroner anjiyografi yapıldı ve ciddi koroner lezyonu olanlara perkütan koroner revaskülarizasyon uygulandı.

Bulgular: 38 hastada (%76) ST yükselmeli akut miyokart enfarktüsü, 12 hastada (% 24) ST yükselmez akut miyokart enfarktüsü saptandı. Hiçbir hasta kendiliğinden kokain ve metamfetamine kullandığını belirtmedi. 50 hastanın hiçbirinde idrar analizinde kokain saptanmadı. 5 hastada (%10) idrar metamfetamine düzeyi pozitif saptandı. Ateroskleroz için klasik risk faktörleri gruplar arasında benzerdi.

Sonuç: Metamfetamin kullanımını %10 bulduğumuz için, daha genç miyokart infarktüsü geçiren hastalarda idrar analiziyle metamfetamin kullanımının taranması makul olabilir.

Anahtar kelimeler: Metamfetamin; idrar toksikolojisi; akut miyokard enfarktüsü

Introduction

Illicit drugs use is increasing considerably in recent decades worldwide and imposes a significant socioeconomic and health burden. Among these drugs cocaine and metamphetamine can cause acute myocardial infarction by inducing coronary vasospasm and thrombosis.[1-4] Knowing the association of illicit drug use with acute myocardial infarction especially in young adults without coronary risk factors is important because the treatment strategies differ from the treatment of acute coronary syndrome unrelated to illicit drug use. However these patients often may not self-report illicit drug use on admission but urine analysis may reveal etiology. It is debatable to specifically recommend the routine screening of certain subgroups of patients for illicit drug use. In this study our aim was to investigate if routine screening of cocaine and methamphetamine use by urine analysis is reasonable in young patients with acute myocardial infarction.

Material and Methods

This study enrolled 50 consecutive young patients (≤ 50 years old) presenting with ST elevated or non-ST elevated acute myocardial infarction. Mean age was 41.3 ± 7.8 (21-50) and 80% of patients were male. ST elevated acute myocardial infarction was diagnosed based on the universal definition of the acute myocardial infarction. [5] Patients were diagnosed as non-ST elevated acute myocardial infarction if symptoms of unstable coronary artery disease were associated with objective signs of myocardial ischemia and elevated biochemical markers of myocardial

necrosis according to European Society of Cardiology guideline. [6] Clinical characteristics of the patients are demonstrated in Table 1. Patients were queried about the use of any illicit drug use on admission. Urine samples for cocaine and metamphetamine analysis were withdrawn within the first day of admission. Urine analysis for cocaine were done using qualitative immunoassay detection of benzoylcegonine which is a cocaine metabolite in the urine. Cocaine use was considered as positive if the level of benzoylcegonine was above 300 ng/mL. Benzoylcegonine has a urinary half-life of 6 to 8 hours and it can be detected in the urine for about 24 to 48 hours after cocaine usage. Urine analysis for methamphetamine were studied using enzymatic immunoassay test and its presence in urine was confirmed using a hyphenated mass spectrometry chromatographic method. Methamphetamine use was considered as positive if the level was above 1000 ng/mL. It can be found out in the urine one hour after use and up to 72 hours after use. Possible sources of methamphetamine other than illicit drug use such as drugs for obesity, parkinsonism, attention deficit hyperactivity disorder and decongestants were excluded by querying medical history in addition to clinical findings.

Statistical analysis

We used SPSS 22.0 statistical package program (SPSS Inc. Chicago, IL, USA) perform statistical analyses. Distribution pattern was analysed by KolmogorovSmirnov test. Continuous data were displayed as median and interquartile range or mean \pm standard deviation. Categorical variables were presented as frequencies and percentages. To analyse the differences

between the two groups, t-test or Mann-Whitney U test was used to compare continuous variables. Pearson's chi-square or Fisher's exact tests were used to compare categorical variables. A p value of <0.05 was deemed statistically significant. The research was conducted in accordance with the Second Helsinki Declaration. The Local Ethics Committee approved the study (E.Kurul E-16-949, June 1, 2016).

Results

ST elevated acute myocardial infarction was diagnosed in 38 patients (76%) and non- ST elevated acute myocardial infarction was diagnosed in 12 patients (24%). We performed coronary angiography in all patients and percutaneous coronary revascularization was carried out if they had significant coronary artery stenosis. Coronary angiographic findings of patients are shown in Table 1.

Table 1. Baseline clinical, laboratory, and angiographic characteristics of the study patients

Variable	Methamphetamine Positive (n=45)	Methamphetamine Negative (n=5)	p Value
Age(years)	41±6	42±4	0.961
Sex, Male (n/%)	35(77)	5(100)	0.333
Hypertension,(n/%)	10(24)	0(0)	0.228
DiabetesMellitus, (n/%)	3(6)	0(0)	0.547
Hyperlipidemia,(n/%)	1(2)	0(0)	0.734
Smoking,(n/%)	9(20)	1(20)	0.741
FamilyHistory,(n/%)	1(2)	0(0)	0.874
Creatinine, (mg/dl)	0.91±0.14	0.89±0.15	0.933
Total Cholesterol, (mg/dl)	186±57	200±63	0.716
LDL Cholesterol, (mg/dl)	116±49	115±42	0.979
HDL Cholesterol, (mg/dl)	35±7	36±8	0.801
Triglyceride, (mg/dl)	179±133	251±276	0.305
Troponin I, (ng/ml)	31±36	46±48	0.414
Urine Methamphetamine Levels, (ng/ml)	141.8±243.4	2677.4±1751.3	<0.001
STEMI/NSTEMI, (n)	34/11	4/1	0.950
Culprit Vessel, (n)			
LAD	24	1	
Cx	11	0	0.980
RCA	9	3	
NCA	1	1	

LDL: low density lipoprotein, HDL: high density lipoprotein, STEMI: ST segment elevation myocardial infarction, NSTEMI: non-ST segment elevation myocardial infarction, LAD: left anterior descending coronary artery, Cx: circumflex coronary artery, RCA: right coronary artery, NCA: normal coronary artery

In general medical treatment consisted statin, beta blocker, aspirin, clopidogrel and angiotensin converting enzyme inhibitor or angiotensin receptor blocker. No patient self-reported cocaine or methamphetamine use. Urine analysis for cocaine were negative in all 50 patients. Urine analyses for methamphetamine were found to be positive in 5 patients (10%). Clinical and laboratory findings of the patients with positive urine methamphetamine were not found to be significantly different from the subjects with negative urine methamphetamine (Table 1). Well-known risk factors for atherosclerosis such as diabetes mellitus, smoking, hypertension, and hyperlipidemia and family history were found to be more prevalent in patients with positive urine methamphetamine compared to others but the difference did not reach statistical importance. All of the patients with positive urine methamphetamine analysis were male patients. Four patients admitted with acute ST elevated myocardial infarction and 1 patient admitted with non-ST elevated acute myocardial infarction. Right coronary artery in 3 patients and left anterior descending coronary artery in 1 patient were culprit vessels. Focal thrombotic lesions in these vessels were treated by deploying bare metal or drug eluting coronary stents. Coronary angiography was found to be normal in 1 patient. Beta blockers were not given to these 5 patients and intravenous benzodiazepines were administered. After discharge they were proceeded to attend addiction treatment and rehabilitation program.

Discussion

In the present study including 50 young adults with acute myocardial infarction we could not find cocaine use in any patients but we were able to find methamphetamine use in 5 patients (10%) by screening urine analysis in addition to history taking. In these 5 patients with acute myocardial infarction related to methamphetamine use beta blockers were not given and benzodiazepines were administered. Percutaneous coronary revascularization using bare metal stents were performed in 4 patients with positive urine methamphetamine. None of these 5 patients self-reported illicit drug use on admission. A potential significant drawback is that patients may underreport illicit drug use history on admission because of their fears and lack of self-confidence or they are unable to communicate. Treatment strategies of acute myocardial infarction related to the cocaine and methamphetamine use have different aspects. In these patients main etiopathologic mechanism is sympathetic overactivity and beta blocker treatment is contraindicated unlike the usual treatment of myocardial ischemia due to atherosclerosis.[7]



While beta blockers inhibit beta receptors, over activation of unopposed alpha receptors worsen clinical course by inducing coronary artery vasoconstriction and increased blood pressure. Intravenous benzodiazepines as early management should be routinely administered in patients with acute myocardial infarction related to cocaine and amphetamine use unlike traditional treatment of myocardial infarction.[8,9] Benzodiazepines lower the central stimulatory effects of these drugs and impact cardiac hemodynamics and neuropsychiatric manifestations. Percutaneous coronary revascularization should be preferred over fibrinolytics because case reports document higher rate of intracranial hemorrhage after lytic treatment. [10-12] In these patients bare metal stents may be preferable because they have not good compliance with the long-term dual antiplatelet regime which is needed for drug eluting stents. After dischargement, cessation of illicit drug use which is the primary goal can be achievable with psychosocial interventions. [13]

Negative finding for cocaine in this study may be due to lower incidence of cocaine use in Turkey compared to other countries. In general the illicit drugs use frequency in Turkey is less than the European Union countries. According to European Drug Report, it has been estimated that more than 80 million adults in the European Union have used illicit drugs at least one time in their lives. Among the illicit drugs cannabis is the most frequently used drug (78.9 million). Cocaine, Methylenedioxymethamphetamine (commonly known as ecstasy), and amphetamines use for the lifetime were estimated to be 15.6 million, 12.3 million and 12.0 million respectively. There are considerable differences between countries for frequency of lifetime illicit drugs. Approximately one-third of adults in France, Denmark and the United Kingdom whereas less than 10% of the adults in Turkey, Romania and Bulgaria are estimated to have tried illicit drugs in their lives.[14] According to the Turkish drug report life-time drug use level is estimated to be 2.7% in Turkey and significantly increased drug use was reported in the 15-24 age group, in males compared to females, in adults having a lower income and using tobacco. Cannabis and derivatives are the most commonly used drugs (84.1%), followed by volatiles (32.9%) and stimulants (22.7%). [15] To our knowledge 7 cases of acute myocardial infarction related to illicit drug use (4 cannabis, 2 Bonzai and 1 marijuana) have been reported from Turkey so far. [16-22]

Cocaine and methamphetamine act as powerful sympathomimetic agents and can cause acute myocardial infarction by inducing tachycardia, hypertension and

thrombosis. [3,4] These agents appear to be fundamental trigger for acute myocardial infarction in young men who also smoke cigarettes.[23] Previous studies have reported that among the patients admitted with chest pain after cocaine use, the incidence of cocaine-associated acute myocardial infarction ranges from 0.7% to 6%. In a study of 130 adults with cocaine related acute myocardial infarction, the mean age was just 38 years.[24] Therefore we conducted this study in young acute myocardial infarction patients who often smoke cigarettes. Previous studies have defined "young" patients with acute myocardial infarction as the patients younger than 40 to 50 years old. We used 50 years for young age definition.

As we found 10% incidence of methamphetamine use and zero incidence of cocaine use in this study, it may be reasonable to screen methamphetamine use but not cocaine use by blood or urine analysis especially in younger acute myocardial infarction patients with or especially without classical coronary risk factors. Our findings support this suggestion at least for Turkey and for countries in which incidence of methamphetamine use is higher than Turkey. Based on results of this study we can not even suggest to screen cocaine use in other countries. Our study has several limitations. It is a single center trial which enrolled limited number of patients. These findings can not be generalized to other countries.

Conclusion

We suggest that routine screening for methamphetamine use but not cocaine use in all young patients with acute myocardial infarction is reasonable at least in Turkey. In young patients presenting with acute myocardial infarction without a history of illicit drug use or unable to communicate, doing urine analysis for methamphetamine may be prudent and may impact treatment strategies.

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Conflict of Interest: None

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