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Intraoperative vasopressor use during emergency surgery on injured meth users

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ABSTRACT

Background Methamphetamine is a growing drug of abuse in America. Patients with recent methamphetamine use pose potential complications to general anesthesia due to changes in hemodynamics and arrhythmias. Limited data exists on the incidence of intraoperative complications on methamphetamine-intoxicated patients requiring urgent or emergent trauma surgery. This study aims to describe intraoperative complications observed in methamphetamine and amphetamine-intoxicated patients requiring emergent surgery.

Methods Using the Trauma Registry at our ACS-verified level I trauma center, we completed a single-center, descriptive, retrospective cohort review between July 1, 2012 and June 30, 2016, of adult patients requiring emergent surgery with a positive urine-drug screen for methamphetamines or amphetamines. The objective was to evaluate vasopressor utilization during surgical operation.

Results A total of 92 patients were identified with a positive UDS for amphetamine and/or methamphetamine who went to the operating room within 24 hours of admission. Thirty-two (34%) patients received one or more (≥1) doses of vasopressor, while 60 patients (66%) received no vasopressor. Changes in mean arterial pressure (MAP) were noted in 64%, while only 3% experienced an EKG change. A binomial logistic regression showed age, base deficit and change in MAP to be predictive of vasopressor use ($p<0.002$). No intraoperative cardiac events or anesthetic complications were seen.

Discussion Hemodynamic instability in the amphetamine and methamphetamine-intoxicated population may be more directly related to degree of resuscitation required, than the presence of a positive UDS.

Level of evidence IV

INTRODUCTION

Methamphetamine is one of the fastest rising drugs of abuse, with 4.7 million Americans having reported intake at some time in their lives.[1] The acute and chronic use of recreational stimulants has the potential to complicate the intraoperative care of surgical patients. Methamphetamines are non-catecholamine, sympathetic amines with central nervous stimulation activity, that promote the release of monoamine neurotransmitters including norepinephrine, serotonin and dopamine.[2] Chronic amphetamine exposure and stimulation of adrenergic receptors may cause depletion of catecholamine receptor storage. In the presence of general anesthesia, this relative deficiency may lead to intraoperative hypotension, requiring treatment with either fluid boluses or direct-acting vasopressors such as epinephrine and phenylephrine.[2]

In addition to the potential for hemodynamic changes, patients with methamphetamine intoxication are at risk for cardiac dysthymias. Corrected QT Interval (QTc) prolongation has been reported in up to 30% of active methamphetamine users. Often the extent of this prolongation is reversible and dose dependent.[2] Prolonged QTc has the potential to lead to cardiac arrhythmias including ventricular tachyarrythmias such as Torsade de pointes.[3] The use of general anesthesia is an independent risk factor for cardiac arrhythmias and may increase the incidence in a high at-risk population.[4]

At this time, a limited number of studies are available regarding the effects of general anesthetics on patients using illicit or prescribed methamphetamines. One study[2] evaluated eight patients taking oral amphetamines that required general anesthesia. The authors found no postoperative hemodynamic instability or adverse events during the hospitalization. While this helps to provide guidance in the oral-prescribed amphetamine population, it does not capture or describe the illicit drug population that uses methamphetamine quantities far above prescribed doses.

There has been an overall increase in positive methamphetamine screens in the trauma population.[5 6] Previous studies have found that this population can be particularly resource intensive with increased need for emergency surgery and ICU admission.[6 7]

This study hopes to illustrate potential complications during anesthesia in patients requiring emergent surgery after trauma who have positive urine drug screen (UDS) concentrations of amphetamines/methamphetamines by evaluating vasopressor administration and EKG changes during the operation. A waiver of authorization was approved by University of Kentucky Office of Research Integrity for this study protocol, IRB # 17-0101-P2H.

METHODS

We completed a single-center, descriptive, retrospective cohort study of patients requiring emergent surgery with a positive UDS for amphetamines or methamphetamines. The trauma registry at our ACS-verified level I trauma center was used to identify patients for this study. All trauma patients requiring a trauma team activation at our institution undergo drug and alcohol screening on admission. We included all adult (>17 years) patients admitted between 1 July 2012 and 30 June 2016 who had a UDS positive for amphetamines or methamphetamines obtained on admission and who underwent emergent or urgent surgery within 24 hours of

presentation. Amphetamine and methamphetamine users were identified by quantitative urinalysis using liquid chromatography and mass spectrometry. The range of detection provided by the laboratory was 25–1000 ng/mL for amphetamine and 25–2500 ng/mL for methamphetamine. Levels above the upper range limit were displayed as >1000 ng/mL and >2500 ng/mL for amphetamine and methamphetamine, respectively.

Patient variables extracted included age, gender, race, mechanism of injury (MOI), operative procedures, laboratory values, American Society of Anesthesiologists (ASA) physical status, admission vitals, Injury Severity Score (ISS), ICU length of stay, mortality, insurance and disposition location. The intraoperative variables extracted included vital signs, ECG results, doses of vasopressors/vasodilators, transfusion requirements, estimated blood loss (EBL) and postoperative vitals. Patients who died prior to reaching the operating room were excluded.

The objective of this study was to evaluate vasopressor utilization, defined as receiving ≥1 dose of vasopressors during the operation in patients operated on emergently while on methamphetamines. The primary outcome of one or more vasopressor doses was analyzed by χ^2 test, and p value<0.05 was significant.

Variables were analyzed via descriptive statistics for frequency. Statistical analysis conducted using SPSS V.23.0 included descriptive data, independent t-test, Mann-Whitney U test, χ^2 test and Fisher's exact test where appropriate. Non-parametric analysis was reported as medians with IQRs, and parametric data were reported as mean±SD. A p value <0.05 was significant. Following the univariate analysis, a binomial regression was performed to ascertain the effects of significant variables.

RESULTS

During the study period of 1 July 2012–30 June 2016, 92 patients were identified with positive UDS for amphetamines or methamphetamines who also went to the operating room within 24 hours of admission. The majority of these patients were white (97.8%), young (median age 32±19) and male (77%). The most common MOI was blunt (60%). The median ISS was 14 (±12), and there were two mortalities in the cohort. Most patients had no known comorbidities; hypertension was the most commonly noted comorbidity followed by hepatitis C. Quantitative drug screen levels for amphetamines were above the upper limit of detection in 49 (53%) of the patients, while methamphetamine levels were above the upper limit of detection in 48 (52%). Eighty-five (92%) patients tested positive for both amphetamines and methamphetamines.

Thirty-two patients received at least one dose (≥1) of a vasopressor (34%) and 60 received no vasopressor. Seven patients received a vasopressin infusion, and two patients required an epinephrine infusion. Only two patients received doses of nitroglycerin for vasodilator therapy.

Patients who received vasopressors were older, experienced more penetrating trauma as the MOI and had a worse ASA class prior to the operation (table 1). However, there was no association of ISS and the reception of vasopressors. There were no differences between the groups in intubation prior to the operating room or immediacy of operation (table 1). Polysubstance use was frequent with 85% of patients identified having another substance positive on urine drug screening, and this was not associated with more intraoperative vasopressor use (table 1). Opioids were the most frequently identified concurrent substance (57%), followed by marijuana (50%), benzodiazepines (40%), buprenorphine (15%) and cocaine (11%).

Table 1 Characteristics of patients who received no vasopressors compared with those who received any vasopressors during operation

Factor	No vasopressor (n=60)	1 or more vasopressor doses (n=32)	P value
Age	31 (±18)	37 (±17)	0.045
Male gender, n (%)	45 (75)	26 (81)	0.496
White race, n (%)	58 (96)	32 (100)	0.580
Polysubstance on UDS, n (%)	51 (85)	28 (87)	0.743
Mechanism of injury, penetrating, n (%)	21 (35)	19 (59)	0.025
ISS (continuous)	12 (±13)	13.5 (±12)	0.708
ISS categories and scores: (n, % within group)			0.305
Mild (<9)	10 (16)	8 (19)	
Moderate (9–15)	26 (43)	9 (28)	
Severe (16–25)	15 (25)	12 (44)	
Profound (>25)	9 (15)	3 (9)	
OR duration	2.5 (±9)	2.75 (±7.5)	0.760
ASA class, n (% within group)			<0.01
1	2 (3.3)	0 (0)	
2	30 (50)	7 (21)	
3	12 (20)	17 (53)	
4	7 (11)	5 (15)	
5	9 (15)	3 (9)	
Emergent OR, n (%)	36 (60)	24 (75)	0.150
Intubation prior to OR, n (%)	20 (33)	11 (34)	0.920

ASA, American Society of Anesthesiologists; ISS, Injury Severity Score; OR, Operating Room ; UDS, urine drug screen.

Vasopressor use was not associated with OR duration or ISS (table 1). Preoperative MAP was not associated with intraoperative vasopressor doses. However, base deficit on arrival was significantly associated with increased vasopressor doses (table 2).

A 20% change in MAP was noted in 64% of the patients. Not surprisingly, the change in MAP was associated with one or more doses of vasopressor (table 2). Three patients had EKG changes requiring treatment, all were in the one or more vasopressor group (table 2). Patients who received one or more doses of vasopressor did not have an increased estimated blood loss or transfusion requirement as compared with those who did not receive any vasopressors (table 2). When evaluating vasopressor doses between patients with a detectable (<2500 ng/mL for methamphetamine and <1000 ng/mL amphetamine concentration) versus patients above the upper limit of detection, there was no difference in requiring one or more vasopressors,

Table 2 Hemodynamic variables of patients who received vasopressors in the operating room compared with those who did not

Factor	No vasopressor (n=60)	1 or more vasopressor doses (n=32)	P value
Preoperative MAP	85 (±19)	85 (±127)	0.718
Base deficit on initial VBG/ABG	**−0.3 (IQR 5)**	**−3 (IQR 22)**	**0.02**
Transfused, n (%)	12 (20)	8 (40)	0.580
Transfusion, number of units of product	0 (±24)	0 (±15)	0.605
EBL	100 (±325)	200 (±249)	0.230
EKG changes requiring treatment	**0**	**3 (9.4)**	**0.016**
20% change in MAP	**33 (55)**	**26 (81)**	**0.012**
MAP change requiring treatment, n (%)	14 (23)	23 (71)	<0.001

ABG, arterial blood gas; EBL, estimated blood loss; EKG, electrocardiogram; MAP, mean arterial pressure; VBG, venous blood gas.

Table 3 OR for one or more vasopressor doses

Factor	B	SE	Wald	df	P value	OR (95% CI for OR)
Age	0.067	0.026	6.70	1	0.010	1.06 (1.01 to 1.12)
MOI	0.948	0.523	3.280	1	0.070	2.58 (0.93 to 7.19)
ASA class	−0.165	0.287	0.331	1	0.565	0.848 (0.48 to 1.48)
Base deficit	−0.140	0.059	5.56	1	0.018	0.87 (0.77 to 0.97)
Change in MAP by 20%	1.77	0.685	6.69	1	0.010	5.8 (1.5 to 22.4)

ASA, American Society of Anesthesiologists; MAP, Mean Arterial Pressure; MOI, mechanism of injury.

44.4% vs 39.2%, respectively (p=0.22). This does not support the theory that higher UDS concentrations of amphetamine or methamphetamine are more likely to require vasopressors doses.

A binomial logistic regression was performed to ascertain the effects of age, ASA class, base deficit on arrival, percentage change in MAP and penetrating MOI on the likelihood of vasopressor use (table 3). The logistic regression model was statistically significant, χ^2 (5)=19.3, p<0.002. The model explained 30% (Nagelkerke R^2) of the variance in one or more vasopressor doses and correctly classified 72% of cases. Of the five predictive variables, only age, shock panel base deficit and 20% change in MAP during operation remained significant. Increasing age was associated with increased likelihood of one or more vasopressor doses, but a base excess was protective. Patients with a 20% change in MAP during operation were 5.88 times more likely to require one or more vasopressor doses (table 3).

DISCUSSION

We noted no intraoperative cardiac events or anesthetic complications in our population. There were no intraoperative deaths. The majority of patients did not require one or more vasopressor doses.

In the univariate analysis, age, ASA class, MOI, base deficit and 20% change in MAP were associated with one or more doses of vasopressor. However, in the binomial regression, only age, base deficit on arrival and 20% change in MAP remained significant. Time in the operating room was not associated with vasopressor use. The concern regarding hemodynamic instability in this population may more directly relate to degree of resuscitation required (base deficit) as opposed to methamphetamine use alone. Time in the operating room or time exposed to anesthetic was not a risk factor for one or more vasopressor doses. Lastly, timing of operation, immediate versus delayed within a 24-hour time frame was not associated with one or more vasopressor doses. The risk of anesthesia in this population is difficult to assess as anesthetic complications are relatively rare. However, we present a high-risk population of traumatically injured patients receiving emergency surgery, and thus, complications may be more common in this population.

Methamphetamine use is increasing and is one of the most commonly produced illicit substances in the USA. Previous research has described injury pattern and severity in methamphetamine users; however, no intraoperative data had been examined. Similar to previously published work, we note that methamphetamine users tended to be young, white and male. We noted a high percentage of penetrating trauma (40%) in this study, which was consistent with our inclusion criteria of operation within 24 hours of admission.

The strengths of this study include the study population and the patient-level hemodynamic assessment. Our patients were moderately to severely injured, as evidenced by the median ISS, and about a third of them required intubation prior to transfer to the operating room. The need to operate early on trauma patients is not uncommon and if not indicated emergently is often urgently. Our population included patients who underwent urgent orthopedic procedures, within 24 hours of admission, not just patients immediately being operated on for penetrating torso trauma. This is an important inclusion since these patients are clinically complicated as there is need for urgent operation and yet concern regarding anesthetic complications related to methamphetamine levels. The weaknesses of our study include small numbers and no control cohort. We were unable to reliably quantify total fluid during the first 24 hours, due to lapsed documentation in a number of patients across the continuum of care from emergency department, to operating room, to ICU. Additionally, these patient toxicology samples were based on UDS, not plasma drug screen. An assumption of physiologic effect is extrapolated but cannot be confirmed.

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Competing interests None declared.

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