SCIENTIFIC LETTER

Analysis of the value of lactic acid as a predictive factor associated with poor outcome in acute intoxication by drugs of abuse

Análisis del valor del ácido láctico como factor predictivo asociado a mala evolución en intoxicaciones agudas por drogas de abuso

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Acute intoxications due to drugs of abuse (DA) are a common reason for consultation in emergency departments (ED).[1] Most cases evolve favorably. However, a small percentage require hospital admission (hospitalization unit, HU), including admission to intensive care units (ICU).[1-4] Lactic acid is a predictive factor of severity in scenarios such as sepsis.[5] Moreover, it is elevated in intoxications caused by certain drugs, and this possibility should be considered in cases of hyperlactatemia of unknown origin.[6,7] Tissue hypoxia produces hyperlactatemia or lactic acidosis (hyperlactatemia with pH < 7.35) type A, due to decreased oxygen supply to the cell, and this must be distinguished from drug-induced causes (type B). Recent studies in patients with acute intoxications suggest that hyperlactatemia could be a predictor of poor outcomes,[8,9] but its role as a predictor of poor progression in intoxications due to DA has not been specifically evaluated. The objective of this study is to determine whether there is a lactic acid concentration associated with poor outcomes, defined as the need for admission to HU, ICU, or death during the episode, in patients intoxicated by DA.

Therefore, we conducted a prospective observational study including all cases of DA intoxications treated in an ED between March and November 2024 in a university hospital. The diagnosis of intoxication was established through medical history, clinical presentation, and determination of DA in urine by immunoassay when indicated.[10] Data collected included demographic variables, type of drug consumed, clinical and laboratory data, administered treatment, and discharge destination from the ED. Statistical analysis was performed using SPSS v.23. Student t test or Mann–Whitney U test was applied for comparison of quantitative variables, and the chi-square test with Fisher or Pearson correction when necessary for comparison of proportions. To determine whether lactic acid is an independent factor of poor outcome, a multivariate analysis was performed, including sociodemographic variables (age and sex) and those showing a trend ($P < .1$) or statistical significance in the bivariate analysis. A value of $P < .05$ was considered statistically significant. The study was approved by *Hospital del Mar de Barcelona* Ethics Committee (2024/11561).

During the study period, a total of 328 patients were treated for DA intoxication. In 116 cases, lactic acid determination was not performed; therefore, 212 patients were finally included. Of these, 17 met criteria for poor outcome. Patients with poor outcomes had a higher mean age [36 years (SD, 7.7) vs 30 years (SD,

Table 1. Baseline characteristics of the population

	Favorable progression N = 195 n (%)	Poor evolution N = 17 n (%)	*P*
Age [mean (SD)]	30 (10.4)	36 (7.7)	.120
Sex, male	160 (82.1)	13 (76.5)	.524
Geographic origin			
Spain	53 (27.2)	4 (23.5)	1.000
Maghreb	59 (30.3)	4 (23.5)	1.000
Western Europe	28 (14.4)	2 (11.8)	1.000
Latin America	19 (9.7)	1 (5.9)	1.000
Eastern Europe	9 (4.6)	2 (11.8)	.184
Asia	8 (4.1)	1 (5.9)	.500
Sub-Saharan Africa	2 (1.0)	0 (0.0)	1.000
North America	1 (0.5)	0 (0.0)	1.000
Unknown	16 (8.2)	3 (17.6)	–
Disposition			
Discharge < 12 hours	95 (48.7)	0 (0.0)	**< .001**
Discharge > 12 hours	60 (30.8)	0 (0.0)	**.004**
Escape	26 (13.3)	0 (0.0)	.237
Voluntary discharge	9 (4.6)	0 (0.0)	1.000
ICU	–	11 (64.7)	Not applicable
Hospitalization	–	5 (29.4)	Not applicable
Death	–	1 (5.9)	Not applicable
Intentionality			
Recreational	183 (93.8)	16 (94.1)	1.000
Suicidal	6 (3.1)	1 (5.9)	.448
Accidental	3 (1.5)	0 (0.0)	1.000
Criminal	3 (1.5)	0 (0.0)	.286
Treatment			
Fluid therapy	141 (72.3)	11 (64.7)	.576
Sedation	38 (19.5)	8 (47.1)	**.014**
Antidote			
Flumazenil	29 (14.9)	5 (29.4)	.159
Naloxone	23 (11.8)	9 (52.9)	**< .001**
Others	0 (0.0)	0 (0.0)	–
Orotracheal intubation	–	9 (52.9)	Not applicable
DAO performed			
Yes	149 (76.4)	16 (94.1)	.128

N: number; SD: standard deviation; ICU: intensive care unit; DAO: determination of drugs of abuse in urine.
Bold values indicate statistical significance ($P < .05$).

Table 2. Characteristics of acute intoxications treated

	Favorable progression N = 195 n (%)	Poor progression N = 17 n (%)	*P*
Alcohol	83 (42.6)	4 (23.5)	.126
Drugs of abuse			
Cocaine	106 (54.4)	9 (52.9)	.910
THC	84 (43.1)	5 (29.4)	.274
Benzodiazepines	56 (28.7)	7 (41.2)	.281
Methamphetamine	47 (24.1)	8 (47.1)	**.047**
MDMA	42 (21.5)	5 (29.4)	.542
Amphetamine	37 (19.0)	6 (35.3)	.120
GHB	20 (10.3)	4 (23.5)	.109
Pregabalin	16 (8.2)	0 (0.0)	.374
Methadone	16 (8.2)	3 (17.6)	.185
Other drugs	14 (7.2)	6 (35.3)	**.002**
Ketamine	7 (3.6)	0 (0.0)	1.000
Nitrites (poppers)	3 (1.5)	0 (0.0)	1.000
LSD	2 (1.0)	0 (0.0)	1.000
PCP	0 (0.0)	0 (0.0)	–
Glue	0 (0.0)	0 (0.0)	–
New designer drugs / Unidentified	0 (0.0)	0 (0.0)	–
Polysubstance intoxication*	84 (43.1)	7 (41.2)	.879
Symptoms			
Agitation	49 (25.1)	7 (41.2)	.159
Anxiety	22 (11.3)	2 (11.8)	1.000
Vomiting	18 (9.2)	3 (17.6)	.229
Headache	15 (7.7)	0 (0.0)	.616
Cerebellar symptoms	11 (5.6)	1 (5.9)	1.000
Hallucinations	10 (5.1)	3 (17.6)	.074
Seizures	9 (4.6)	2 (11.8)	.217
Arrhythmias	8 (4.1)	1 (5.9)	.536
Chest pain	7 (3.6)	0 (0.0)	1.000
Palpitations	4 (2.1)	0 (0.0)	1.000
Psychosis	3 (1.5)	2 (11.8)	.053
Vital signs			
Heart rate > 90 bpm	75 (38.5)	6 (35.3)	.838
Heart rate 60–89 bpm	80 (41.0)	7 (41.2)	.940
Heart rate 0–59 bpm	32 (16.4)	3 (17.6)	.868
Glasgow Coma Scale (points)	13 (9-15)	5 (3-9)	**.000**
GCS ≤ 12 points	79 (43.4)	14 (82.4)	**.002**
GCS ≤ 10 points	61 (33.5)	14 (82.4)	**< .001**
GCS ≤ 8 points	32 (17.6)	10 (58.8)	**< .001**
Laboratory			
Hypoglycemia (≤ 60 mg/dL)	1 (0.5)	0 (0.0)	.759
Hyperglycemia (≥ 120 mg/dL)	43 (22.1)	2 (11.8)	.204
Hyperlactatemia (mmol/L)			
≥ 2,2	76 (39.2)	7 (41.2)	.871
≥ 5	15 (7.7)	4 (23.5)	.053
≥ 6	10 (5.2)	3 (17.6)	.075
≥ 7	6 (3.1)	3 (17.6)	**.027**
≥ 8	4 (2.1)	2 (11.8)	.076
Anion gap (mEq/L) [median (IQR)]	13.7 (11.5-16.6)	17.3 (12.9-21.2)	**.040**
pH [median (IQR)]	7.34 (7.30-7.38)	7.28 (7.18-7.37)	**.006**
Bicarbonate (mEq/L) [median (IQR)]	23.9 (21.6-26.0)	20.9 (16.9-25.5)	.055

N: number; THC: delta-9-tetrahydrocannabinol; MDMA: 3,4-methylenedioxymethamphetamine; GHB: gamma-hydroxybutyric acid; LSD: lysergic acid diethylamide; PCP: phencyclidine; IQR: interquartile range; bpm: beats per minute; GCS: Glasgow Coma Scale.
Defined as consumption ≥ 2 drugs.
Bold values indicate statistical significance (*P* < .05).

10.4)], and most were men (76.5% vs 82.1%). A total of 48.7% of patients with favorable progression were discharged within 12 hours of admission. Recreational intent was the most frequent in both groups, with percentages close to 94%. Among cases with poor outcomes, 11 patients (64.7%) required ICU admission and 5 (29.4%) were admitted to HU. Only 1 death was reported due to arrhythmia secondary to intoxication. All these results are shown in Table 1.

The most frequently consumed substances were cocaine (54.4% in patients with favorable progression vs 52.9% in those with poor outcomes) and cannabis (43.1% vs 29.4%). Alcohol consumption was associated in 42.6% and 23.5% of cases, respectively (Table 2). Polysubstance intoxication (≥ 2 drugs) showed a similar distribution in both groups (43.1% vs 41.2%).

Drug-induced psychotic symptoms were more prevalent in the group with poor outcomes (11.8% vs 1.5%, *P* = .053). Differences were found in the Glasgow Coma Scale (GCS) score, both in mean values and in different cutoffs (Table 2). Sedation was required in 47.1% of cases with poor outcomes vs 19.5% in those with favorable progression (*P* = .014). Flumazenil was administered in 29.4% vs 14.9% (*P* = .159), and naloxone in 52.9% vs 11.8% (*P* < .001), respectively. Finally, 52.9% of patients with poor outcomes required orotracheal intubation.

Regarding laboratory parameters, differences were observed in the anion gap (17.3 mEq/L in the poor outcome group vs 13.7 mEq/L in patients with favorable progression; *P* = .04), pH (7.28 vs 7.34; *P* = .006), and bicarbonate (20.9 mEq/L vs 23.9 mEq/L; *P* = .05) (Table 2). Only a lactic acid concentration ≥ 7 mmol/L was associated with poor outcomes. These levels were reached in 6 cases (3.1%) among patients with favorable progression and in 3 (17.6%) among those with poor outcomes (*P* = .027). Multivariate analysis showed that the only factors independently associated with poor outcomes were a GCS score ≤ 10 and pH ≤ 7.20, with lactic acid losing statistical significance [OR, 8.5 (95% CI, 0.9–76.8); *P* = .056] (Table 3).

Intoxications due to DA occur predominantly in young adults and males, probably due to the recreational nature of their use. This study found a percentage of recreational intent higher than that observed in studies analyzing all intoxications, not only those due to DA.[6,9]

The higher incidence rate in young patients reinforces the need for awareness campaigns regarding drug use. Cocaine, alcohol, cannabis, and benzodiazepines were the most frequently detected substances. Notably, there was a high frequency

Table 3. Multivariate logistic regression analysis of factors associated with poor outcome

	OR (IC 95%)	*P*
Lactic acid ≥ 7 mmol/L	8.5 (0.9-76.8)	.056
pH ≤ 7.20	15.7 (2.9-83.4)	**.001**
GCS ≤ 10 points	12.1 (2.4-60.9)	**.002**

GCS: Glasgow Coma Scale; OR: odds ratio; 95% CI: confidence interval.
Bold values indicate statistical significance ($P < .05$).

of polysubstance use, close to 40%, in line with data from the National Drug Plan.[11] The use of methamphetamines and non-classical substances was significantly associated with poor outcomes, probably due to their potency and adulterated composition.[12]

Regarding prognostic factors, the value of different laboratory parameters (anion gap, bicarbonate, or pH) should be highlighted. Although some reached statistical significance in the bivariate analysis, only a pH ≤ 7.20 was independently associated with poor outcomes. Focusing on lactic acid, various studies have demonstrated its usefulness in acute intoxications,[9] as well as in cases of overdose due to drugs and illicit substances.[13] In these studies, lactate thresholds associated with poor outcomes were lower than those found in the present study (2.2 and 5 mmol/L[9,13]). This difference could be explained by a larger sample size in those studies and the inclusion of other types of toxic substances. The present study found that a lactic acid concentration ≥ 7 mmol/L is associated with poor outcomes in patients with DA intoxication. However, after adjustment for other variables, statistical significance was lost, although it remained very close to it.

This may be due to the number of patients included in the study, so its role as a predictive factor for poor outcomes in these patients cannot be definitively ruled out.

This study has several limitations. First, its observational and single-center design may generate limitations. The sample size also reduces statistical power and could explain the loss of significance in patients with lactate ≥ 8 mmol/L. This loss of statistical significance in the multivariate analysis does not allow a categorical confirmation of this association. Finally, the absence of confirmatory analytical techniques prevents definitive toxicological characterization.

Although multicenter studies with a larger number of patients are needed, it could be inferred that lactic acid values ≥ 7 mmol/L and pH ≤ 7.20 may be associated with unfavorable outcomes in cases of DA intoxication.

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