

Original Research Article

Clinical and Therapeutic Features of Metformin-Associated Lactic Acidosis in Intensive Care at the Intercommunal Hospital Centre (CHI) of Evreux, France

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Abstract: *Introduction:* Metformin intoxication, although uncommon, represents a significant cause of admission to intensive care units. This study aims to assess the clinical and therapeutic characteristics of patients admitted to the ICU at CHI Evreux for metformin intoxication. *Objectives:* To describe the clinical presentation and therapeutic management of patients with metformin intoxication. *Patients and Methods:* This retrospective study was conducted over a three-year period and included 20 patients admitted to the ICU for metformin intoxication. Clinical data and management parameters were collected and analyzed. The findings were compared with previously published studies. *Results:* The hospital frequency of metformin intoxication was 1.56%. Patients were predominantly elderly males, with a median age of 69.5 years. The main presenting symptoms were abdominal pain, anorexia, and nausea/vomiting. All patients exhibited acute kidney injury and severe metabolic acidosis. Management required aggressive fluid resuscitation, vasopressor support, and renal replacement therapy in many cases. The mortality rate was 11.11%. *Conclusion:* Metformin intoxication is a severe condition requiring intensive management. The results of this study are consistent with existing literature, although some variations were observed.

Keywords: Metformin intoxication; acute kidney injury; renal replacement therapy; vasopressors.

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INTRODUCTION

Type 2 diabetes has been increasing worldwide for several years, largely due to population ageing and rising obesity rates. Biguanides, owing to their mechanism of action, remain key pharmacological agents in diabetes management [1]. Metformin, introduced in Europe in 1957 and in the United States in 1995, has been maintained in therapeutic guidelines due to extensive research highlighting its benefits and its central role in glycemic control [2]. Today, it is prescribed to more than 120 million individuals worldwide [3].

However, its most serious, albeit rare complication, is metformin-associated lactic acidosis (MALA). Although its incidence is low, MALA carries a high mortality rate [1]. This complication arises in various clinical contexts and may require renal replacement therapy [4]. Preventing MALA in at-risk patients relies on strict adherence to metformin

contraindications. A thorough understanding of the clinical and therapeutic aspects of metformin intoxication is essential to improving ICU management.

Objective

To investigate the clinical and therapeutic characteristics of patients admitted to the intensive care unit of the Eure-Seine Hospital Centre in Evreux for metformin intoxication.

PATIENTS AND METHODS

This study was conducted in the ICU of the Intercommunal Hospital Centre of Eure-Seine, France. It was a retrospective, cross-sectional, descriptive study covering a three-year period (December 2021 to December 2024). The target population consisted of all ICU admissions during the study period in whom metformin intoxication was diagnosed.

An exhaustive recruitment strategy was used, including all patients with suspected voluntary or accidental metformin intoxication and an admission metformin level > 4 mg/L. Inclusion criteria were: ICU admission during the study period, suspicion of metabolic acidosis secondary to metformin intoxication, and initial metformin level > 4 mg/L. Exclusion criteria were: alternative final diagnosis unrelated to metformin overdose, or medical records with excessive missing data.

Data were collected using a standardized form from electronic medical records (AXIGATE software), nursing charts, and therapeutic sheets. The dependent variable was metformin intoxication; independent variables included age, sex, BMI, metformin level, medical history, type of intoxication, clinical presentation, and therapeutic interventions. Data were analyzed using Epi Info software.

RESULTS

Hospital Frequency

A total of 1,274 patients were admitted to the ICU during the study period, of whom 20 met inclusion criteria, representing a frequency of 1.56%.

Sociodemographic Characteristics

Sex and Age:

Male patients were predominant (sex ratio 1.22). The median age was 69.5 years (range: 58–89 years).

Type of Intoxication

Two groups were identified: voluntary intoxication and accidental overdose. Accidental overdose accounted for 90% of cases.

Clinical Characteristics

Comorbidities

Obesity was present in 50% of patients, hypertension in 85%, cardiopathies in 40%, coronary artery disease in 20%, and chronic kidney disease in 30%.

Presenting Symptoms

The most common symptoms were abdominal pain (45%), nausea/vomiting (35%), and anorexia (30%). Dyspnea (30%) and confusion (20%) indicated more severe systemic involvement. Hypothermia was present in 44.44% of patients. Notably, 20% of patients had no functional symptoms at presentation.

Clinical Assessment at Admission

More than half of the patients (55%) exhibited hemodynamic instability. Seventy per cent presented with respiratory distress requiring immediate support. Altered consciousness was present in 50%, with a Glasgow Coma Scale ≤ 8 in 83.33% of these cases. All patients had acute kidney injury.

Blood Glucose

All voluntary intoxication cases had normal capillary glucose. Among accidental overdoses, 50% had normal glucose, 5.56% hypoglycemia, and 44.44% hyperglycemia.

Arterial Blood Gas Analysis

Mean pH was 7.1. Among accidental overdoses, 50% had pH < 7.1. All voluntary intoxications had pH > 7.1. Mean lactate level was 8.9 mmol/L, higher in voluntary intoxications (11.4 mmol/L) than accidental overdoses (8.6 mmol/L). Most patients (61.11%) had lactate > 5 mmol/L, indicating severe lactic acidosis.

PaCO₂ was low in 77.78% of accidental intoxications and 100% of voluntary intoxications. All patients had low bicarbonate levels.

Biochemistry and Ionogram

Hyperkalemia was present in 72.22% of accidental overdoses and 50% of voluntary intoxications. Mean potassium level was 5.7 mmol/L.

Creatinine levels were significantly higher in accidental overdoses (mean 655.7 μ mol/L) compared with voluntary intoxications (132.5 μ mol/L). Most accidental overdoses had severely reduced glomerular filtration rates.

Urea levels were elevated in most accidental overdoses. Prothrombin time was abnormal in 55% of accidental overdoses, but normal in all voluntary intoxications.

Septic shock was the main associated diagnosis (8 patients).

Clinical and Therapeutic Management Hemodynamics

Most patients received initial fluid resuscitation (94.44% accidental, 100% voluntary). Vasopressors were required in 65% of cases, mostly at doses < 1 μ g/kg/min. Five patients (38.46%) required noradrenaline > 1 μ g/kg/min.

Respiratory Support

Most patients received oxygen via nasal cannula. Intubation and mechanical ventilation were required in 27.78% of accidental overdoses and 50% of voluntary intoxications. Non-invasive ventilation was used in one patient.

Renal Management

Diuretics were used in 20% of cases. Most patients received alkalization therapy.

All voluntary intoxications required renal replacement therapy (one HDI, one CVVHDF). A significant proportion of accidental overdoses required renal replacement therapy, mainly CVVHDF. Half of the

patients received renal replacement therapy upon admission.

Mean duration of intermittent hemodialysis was 9 hours. Mean duration of CVVHDF was 2.89 days.

Complications and Outcomes

Persistent acute kidney injury was common (83.33% accidental, 100% voluntary). Multiorgan failure occurred in a minority of patients. No nosocomial infections or DIC were reported.

Hepatocellular insufficiency occurred in 33.33% of accidental overdoses and 50% of voluntary intoxications.

Mortality was 10% (two deaths in accidental overdoses). No deaths occurred in voluntary intoxications.

DISCUSSION

The hospital frequency of metformin intoxication at CHI Evreux was 1.56%, slightly higher than the 1% reported by Peters *et al.*, Differences may relate to sample size and study duration. Literature generally reports a low incidence (3–10 per 100,000 patient-years).

Median age (69.5 years) aligns with Peters *et al.*, and Kuan *et al.*, The predominance of males is consistent with epidemiological data from the French diabetic population.

Accidental overdoses were far more common than voluntary intoxications, consistent with findings from Zitouni *et al.*,

Digestive symptoms were the most frequent presenting signs, as widely described in the literature. Dyspnea, often linked to metabolic acidosis, was also common. Hypothermia was present in 44.44% of cases, lower than the >60% typically reported, possibly due to early pre-hospital warming.

Hyperglycemia was more common than hypoglycemia, consistent with the pharmacodynamics of metformin.

Biological parameters indicated severe metabolic acidosis, elevated lactate levels, and significant renal impairment, consistent with published studies.

Hemodynamic instability and vasopressor use were frequent and comparable to other studies. Respiratory distress and altered consciousness were also common.

Renal replacement therapy was widely used and remains a cornerstone of management in severe metformin intoxication.

Mortality (11.11%) was lower than some published rates (up to 50%), but higher than in Zitouni's study, possibly reflecting differences in early recognition and management.

CONCLUSION

Metformin intoxication, although rare, is a serious cause of ICU admission. Affected patients are typically elderly males with multiple comorbidities. High rates of acute kidney injury, severe metabolic acidosis, and multiorgan dysfunction highlight the need for rapid and intensive management. Standardized treatment protocols and further research are essential to optimize outcomes in this potentially life-threatening condition.

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