Good renal and vital prognosis of metformin induced lactic acidosis

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INTRODUCTION

Metformin is the only representative of the class of biguanides used in first line treatment of type 2 diabetes since the recall of phenformin because of a high frequency of lactic acidosis (MALA). Accumulation of lactate after taking metformin is plural. Metformin leads to an increase lactate production and inhibition of their degradation by inhibition of gluconeogenesis from various substrates including lactate and glycolytic production of lactate in the guts. Overproduction of lactic acidosis could be also secondary to shock, liver failure, hypoxemia. These situations are worsened by metformin. The renal prognosis and mortality are poor in the literature but many reports does not distinguish these two entities (metformin and other situations), which explains the high mortality rate almost 50% and poor renal prognosis.

METHODS	INCLUSION AND EXCLUSION CRITERIA
We conducted a retrospective observational study of type 2 diabetic patients admitted to intensive care unit (ICU) for MALA between January 2010 and July 2015 in tertiary hospital. From the list of patient admitted with acidosis we identified 17 patients who fulfilled inclusion criteria. The information was assessed by the patients electronic records with ICD 10 Code for Acidosis E87.2	Lactic acidosis was defined by a Ph less than 7.35 and an elevation of lactate higher to 5 mmol/L. Use of metformin.

| PATIENTS	AT ADMISSION	MANAGEMENT
Nine men, mean age of 60 years (extreme 39 to 80) . 87% from emergency department, 3 patients from surgery (trans ureteral prostatic resection), and medicine (one for kidney insufficiency and one for abdominal pain and diarrhea) departments. Ten % of patients were followed by a diabetes specialist. The duration of diabetes : 1 to 35 years (n=6). Two (10%) non-francophone patients, 2 with cognitive disorders. Six patients (35%) had only metformin as antidiabetic treatment, 11 had combined antidiabetic therapies (DDP4 inhibitors, sulphonylurea, insulin). Retrospectively, 6 patients (35%) could have a contra indications to metformin use: 4 had a serum creatinine clearances <45ml/min (mean = 36ml/min); 2 patients had alcohol abuse, 1 had cirrhosis, and 1 patient had chronic respiratory failure.	**Associated condition** Kidney insufficiency in 7/17 (dehydration); and 13 patients (76%) had acute renal failure Sepsis in 7/17 Voluntary metformin intoxication in 3/17 **Characteristics of MALA at presentation** pH 7.05 (6.58 to 7.35), Lactate concentration: 10.33 mM (5.12 to 15.2) Creatinine: 551 µM (56-1338) Blood sugar: 162 mg/dL (29 to 450). Plasma metformin level 4.8 to 27.9 mg/L (N=6/17)	A duration of ICU stay was 10.2 days (1-26 days) A duration in post ICU department (medicine) for 12 patients was 12.4 days (6-30 days). Renal epuration in 11/17, 1 to 4 dialysis session (average 1.3), during a 1 or 2 days period

KIDNEY AND VITAL PROGNOSIS
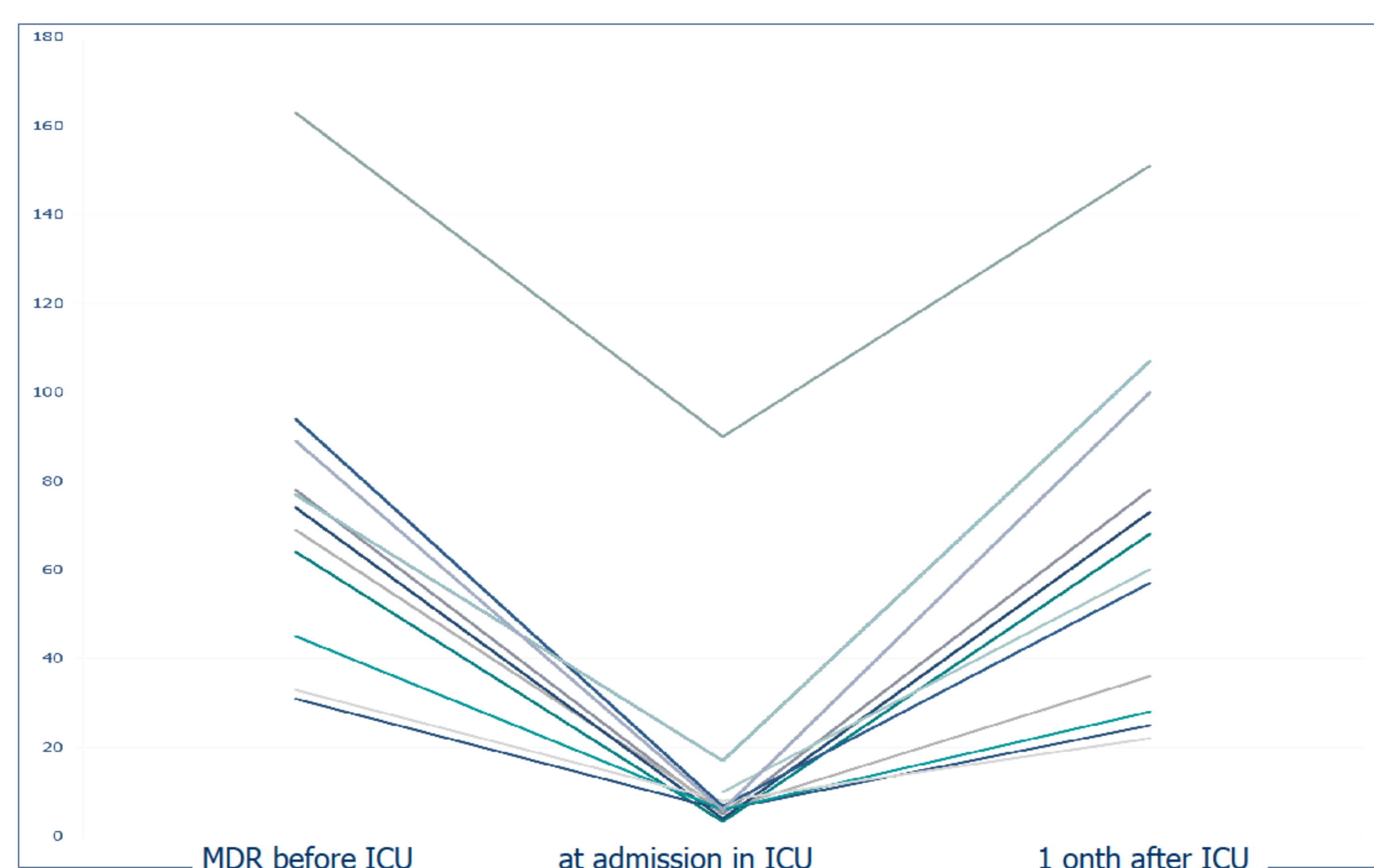
The initial creatinine levels were known for 15/17 patients: mean = 92.8µmol/L (extreme 42 to 176) =>mean GFR (MDRD) = 79 ml/min (extreme 31 to 163). Mean GFR were 31 ml/min in ICU (n=17) and 71 ml/min one month after ICU (n=11) respectively.

8/10 with initial GFR > 60 ml/min return to GFR > 60 ml/min one month after MALA.

For these 8 patients with pre and one month post ICU GFR, there was a loss of 8.6 ml/min of clairance

Two patients (10%) died of septic shock (1 ischemic colitis and 1 psoas abscess)

CONCLUSIONS

Thus at the opposite of Lactic Acidosis due to others causes, MALA represents a situation with good vital prognosis and rapid renal improvement by dialysis.