

## Extracorporeal removal of metformin

Metformin is the only biguanide antidiabetic agent available in the US. It is available as a single agent, in immediate-release and extended-release formulations, as well as in combination with other medications used in the management of diabetes. Metformin is one of the most prescribed drugs in the US and carries a box warning for metformin-associated lactic acidosis (MALA). Classically described risk factors MALA include renal impairment, age  $\geq 65$  years, receiving iodinated contrast (CT scan), concomitant use of certain medications (ex. topiramate), recent surgical procedures, hypoxia, liver impairment, and excessive alcohol consumption.

Metformin toxicity has a 30% mortality rate and can be difficult to manage. The EXtracorporeal TReatment In Poisoning (EXTRIP) workgroup consisting of international professionals that develop guidelines using currently available evidence and expert opinion published recommendations for the management of metformin toxicity based on published and unpublished data consisting of an observational study, case reports, a descriptive cohort, and pharmacokinetic studies. Extracorporeal treatment (ECTR), preferentially intermittent hemodialysis (HD), is recommended for severe metformin poisoning (Crit Care Med 2015;43(8):1716-30).

Specifically, ECTR is **indicated** if any of the following are present:

- Lactate  $> 20$  mmol/L
- pH  $\leq 7.0$
- Shock
- Failure of standard supportive care measures
- Decreased level of consciousness

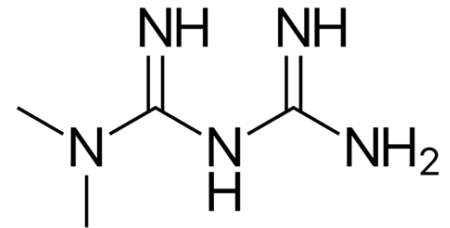
ECTR is **suggested** if:

- Lactate  $> 15-20$  mmol/L
- pH  $\leq 7.1$
- Impaired kidney function
- Liver failure

Continuous renal replacement therapy (CRRT) can be considered if the patient is unable to tolerate hemodialysis or if there is anticipated to be a significant delay initiating HD. ECTR should continue until the lactate is  $< 3$  mmol/L and pH  $> 7.35$  with close monitoring after discontinuation to determine the need for additional ECTR.

A group from Pittsburgh published a case series of 7 patients that underwent hemodialysis for metformin poisoning. All patients were critically ill; mean lactate 23.9 mmol/L, mean pH 6.91, and average mean arterial pressure (MAP) 44 mmHg. All patients were on at least one vasopressor. Vasopressor dose was initially increased in 3/7 patients at the start of HD, though MAP increased by the end of HD (J Emerg Med 2020;58(5):749-55). Six of 7 patients survived.

Call your local poison center at 1-800-222-1222 for patient specific recommendations for management of metformin poisoning.



### Did you know?

**Metformin is sometimes referred to as an anti-hyperglycemic agent instead of a hypoglycemic agent.**

Metformin has a low incidence of hypoglycemia in therapeutic use. The EXTRIP review on metformin highlighted that hypoglycemia occurred in 32% of acute or acute-on-chronic overdoses and 10% with chronic exposures. The hypoglycemia may be due to severity of critical illness as many of these patients develop multisystem organ failure. Treatment for hypoglycemia hinges of administration of supplemental dextrose.

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