Perioperative metformin: Friend or foe

Madam,

Metformin is an oral biguanide hypoglycemic drug used as first line drug in patients with type 2 diabetes mellitus. It acts by non-pancreatic mechanisms without secreting insulin, sensitises insulin, reduces hepatic gluconeogenesis leading to reduced glucose formation, and facilitates peripheral glucose utilization by fat and muscle. When used alone, metformin does not cause hypoglycemia. It prevents endothelial dysfunction, promotes fibrinolysis, lowers lipids and regulates blood pressure.[1] Renal insufficiency, heart and hepatic failure are few contraindications to its use.

Metformin associated lactic acidosis (MALA) is rare with an incidence of 1-15 cases per 100,000.[2] Underlying diabetes mellitus is considered responsible for lactic acidosis in an acute event. Type of surgery (laparotomy, cardiac surgery, trauma), underlying hepatic dysfunction (leading to impaired lactate clearance), renal dysfunction (leading to impaired excretion), surgeries in elderly patients also contributes to lactic acidosis along with situations like sepsis, reduced peripheral oxygen delivery and congestive heart failure. All this could lead to exaggerated effects with metformin co-administration. Serum metformin levels are less than 2 μg/ml when used at therapeutic dose. Metformin levels more than 5 μg/ml is seen in lactic acidosis which could be due to impaired lactate clearance or excretion along with any of the above mentioned reasons in surgical patients. Increased metformin levels due to disturbed homeostatic mechanisms further raises serum lactate. There is an increase in less than 2 mmol/L of plasma lactate in health which gets metabolised by liver and muscles. This lactate rise is due to inhibition of respiratory chain complex 1 in mitochondria which is the mechanism by which hepatic gluconeogenesis is interfered.[3] The randomized controlled trial by Hulst *et al*. also highlighted that peri-operative continuation of metformin in patients with type 2 diabetes did not raise lactate levels to a clinically relevant degree.[4]

AAGBI (Association of Anaesthetists' of Great Britain and Ireland) recommends continuation of metformin on the day of surgery provided it is day care or minor surgery.[5] The subsequent doses for the day could be skipped and regular doses can be restarted once the patient resumes normal diet. In patients with normal renal function (creatinine clearance >60 ml/min), metformin could be continued on the day of surgery which might benefit the patient with its non-diabetic effects.

In elderly patients undergoing major surgeries which could involve blood loss, hypovolemic and pre-renal states, it is recommended to omit metformin. However, Nazer *et al*. felt that perioperative metformin should not be held responsible for lactic acidosis in patients undergoing coronary artery bypass grafting (CABG).

Perioperative metformin offered better glycemic control and overall reduced complications such as organ damage and wound infections.[6]

It is recommended to withhold metformin for up to 48 hrs in patients with renal impairment (creatinine clearance <60 ml/min), who will be receiving intravenous contrast for CT scans, angiograms and interventional radiological procedures. Metformin could be continued in patients with normal renal function.

Presently, the recommendations are not very clear regarding perioperative use of metformin but experts feel that the decision to continue or omit should be individualised depending on the patient and the surgery planned.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Abhijit S. Nair

Department of Anaesthesiology, Basavatarakam Indo-American Cancer Hospital and Research Institute, Hyderabad, Telangana, India

Address for correspondence: Dr. Abhijit S. Nair, Department of Anaesthesiology, Basavatarakam Indo-American Cancer Hospital and Research Institute, Hyderabad - 500 034, Telangana, India.
E-mail: abhijitnair95@gmail.com

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Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/joacp.JOACP_305_17

How to cite this article: Nair AS. Perioperative metformin: Friend or foe. J Anaesthesiol Clin Pharmacol 2020;36:137-8.

Submitted: 27-Oct-2017 **Revised:** 19-Aug-2018 **Accepted:** 31-Aug-2019 **Published:** 18-Feb-2020