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Metformin: An Old Taboo yet a New Friend for Targeted Glucose Control in Critically Ill Patients

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Glucose management in critically ill adults and children has always been controversial. A few recent studies mention that the use of any drug other than insulin for glucose control in intensive care unit is not recommended anymore1.

Increased levels of counter-regulatory hormones and insulin resistance at organ levels contribute immensely to the emergence of hyperglycemia in these patients. Consequently, in some patients higher doses of insulin are required for the maintenance of normoglycemia and in such scenarios incidence of hypoglycemia becomes a real concern. Moreover, insulin therapy might lead to hypokalaemia and hypomagnesaemia which in turns promote insulin resistance and higher blood glucose level (BGL). All these events make insulin administration unavoidable; thereby, beginning a vicious cycle with adverse outcomes. One of therapeutic options in this scenario is using insulin sensitizing agents as an adjunct therapy for glycemic control in critically ill patients. Different studies have shown that metformin, similar to insulin, is of anti-inflammatory and antioxidant properties, improves lipid profile, decreases nursing workload and lowers the incidence of adverse effects related to high-dose insulin therapy without being associated with the increased risk of lactic acidosis or hypoglycemia2-4. Panahi et al., in their study, showed that metformin therapy in hyperglycemic critically ill patients resulted in similar outcomes with insulin thersapy5. Also, there are some studies reporting that metformin limits ischemia reperfusion injury, modulates inflammation; it consequently contributes to the survival benefits probably through increasing adenosine receptor stimulation6-8. In sepsis, there is a biphasic inflammatory response; Systemic Inflammatory Response Syndrome (SIRS), as an initial hyperinflammatory phase, and Counterregulatory anti-inflammatory response syndrome as a later hypoactive phase. Therefore, anti-inflammatory drugs like metformin may be associated with the best results only if added prior to the initial hyperinflammatory response and might have detrimental effects if added during hypoactive phase9,10. Timing of metformin administration may be an important factor contributing to its effect in critically ill patients.

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Finally, in patients with refractoriness to insulin who require high doses of insulin, metformin could be used as a safe adjunct therapy to reach targeted glucose levels. Metformin plus insulin appears to lower the incidence of insulin resistance, insulin requirements while maintaining blood glucose level control, and consequently the incidence of adverse effects related to high-dose insulin therapy, particularly hypoglycaemia. Declined nursing workload is also considered a major benefit. However, two important items should be noted: first, timing of drug administration and second, characteristics of the patients like renal function, hypoperfusion status and monitoring of drug complications.

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