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Critical analysis of mortality in the so-called Metformin-associated lactic acidosis

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There are major pitfalls in many of the epidemiological studies related to 'Metformin-Associated Lactic Acidosis', MALA. In particular, the link between metformin and lactic acidosis is generally analyzed in terms of frequency while the relationship between metformin and lactic acidosis is not a simple one in which accumulation of the drug inevitably leads to this adverse event. This discussion of the relationship between metformin and lactate metabolism is not only of theoretical interest; on the contrary, it impacts the patient's prognosis. It is important to note that the prognosis does not depend on the extent of metformin accumulation. We have previously shown that neither blood lactate concentration nor plasma metformin concentration was of prognostic value with respect to mortality in MALA. However, given that arterial pH and blood lactate concentration may vary widely, a focus on severe MALA is needed in order to try to better understand the paradox whereby metformin provides impressive, beneficial effects but is also associated with life-threatening adverse effects. We studied therefore on the basis of 869 pharmacovigilance reports 56 cases of severe metformin-associated lactic acidosis (mean pH and lactate concentration 6.75 ± 0.17 and 23.07 ± 6.94 mmol/L). Most patients (53%) survived despite a mean pH that is incompatible with favorable outcomes under other circumstances. Such an unexpectedly favorable outcome prompted to form a challenging hypothesis whereby metformin may be protective in severe lactic acidosis that occurs for other reasons in patients taking this drug.

Biography

Jean-Daniel Lalau has completed doctoral studies in Health Sciences and in Philosophy (ethics). He is professor of nutrition and the Head of the Department of Endocrinology-Nutrition in Amiens University Hospital (France). He has published more than 100 papers in indexed journals.

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