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CRITICAL CARE

LETTER

Another explanation for decreased oxygen consumption in lactic acidosis

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See related research by Protti *et al.*, http://ccforum.com/content/14/1/R22

In their recent paper, Protti and colleagues reported depressed oxygen consumption in patients with lactic acidosis due to biguanide intoxication and they suppose that the cause is inhibited mitochondrial respiration [1].

Another explanation for depressed oxygen consumption in these patients is also possible, however. If the blood pH is very low, glucose utilization is decreased [2] because the glycolytic enzyme phosphofructokinase is pH dependent – with decreasing pH, its activity is also decreasing [3]. Glucose utilization is an oxygen-consuming process:

$$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O$$

The consequence of decreased utilization of glucose is thus also decreased oxygen consumption.

The patients reported by Protti and colleagues had on admission very low blood pH of 6.93 ± 0.20 and systemic oxygen consumption of 67 ± 28 ml/min/m^2 [1]. Systemic oxygen consumption 'normalized within the next 48–72 hours' and 'Systemic O_2 consumption was positively associated with arterial pH' (P <0.001). According to Tables 2 and 3 [1], arterial pH reached normal values on days 2 to 3.

Depressed oxygen consumption in patients reported by Protti and colleagues can thus be explained by their very low blood pH.

Authors' response

Alessandro Protti and Luciano Gattinoni

We thank Dr Rosival for his stimulating comment.

Whether acidosis has an impact on oxygen consumption (VO_2) remains unclear. *In vitro*, several studies have demonstrated that tissue VO_2 only starts to diminish when the pH falls below 6 to 6.5 [4,5]. *In vivo*, both animal and clinical studies have reported normal, or even increased, whole-body VO_2 during severe acidosis [6,7]. Accordingly, we have observed no correlation between VO_2 and arterial pH among 762 critically ill patients, at the time of admission to intensive care (R^2 = 0.00, P = 0.88 on linear regression analysis) [8].

In order to directly address the issue raised by Dr Rosival, we equipped two healthy, sedated and mechanically

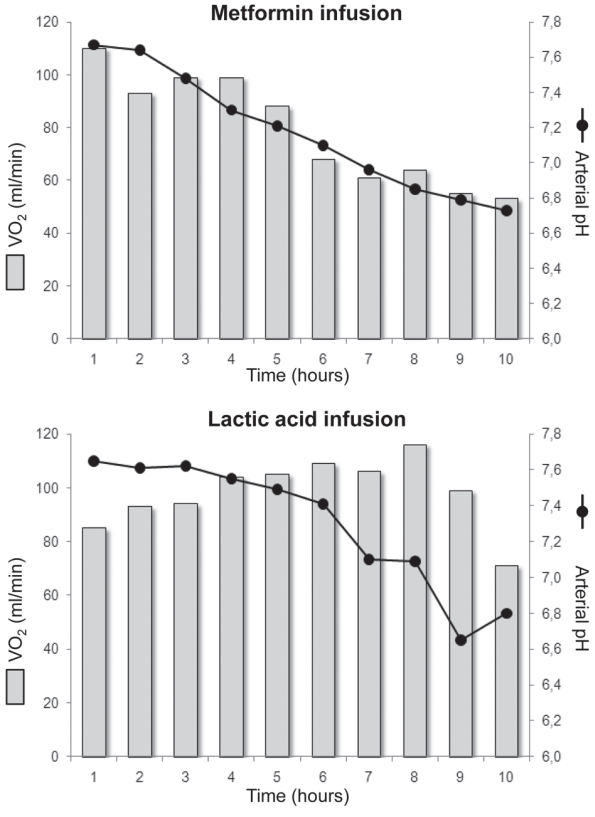

Figure 1. Effect of metformin and lactic acid on arterial pH and oxygen consumption. Upper panel: data recorded from a pig infused with 8 g metformin (final serum drug concentration, 98 µg/ml). Lower panel: data recorded from a pig infused with lactic acid. Lactatemia equally increased from 1 to 25 mmol/l in the two animals. VO_2, oxygen consumption.

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ventilated pigs with a metabolic module (to record VO_2) and a pulmonary artery catheter (to compute the global oxygen delivery). Following baseline recordings, one animal received a continuous intravenous infusion of metformin whereas the other received lactic acid. Arterial pH, VO_2 and oxygen delivery were recorded hourly for 10 hours. As shown in Figure 1, metformin progressively decreased VO_2 but lactic acid did not. Changes in oxygen delivery were always minor.

We are thus tempted to believe that drug toxicity, rather than acidosis, was the major factor responsible for the decrease in VO_2 we observed in patients with biguanide-induced lactic acidosis.

Abbreviations
VO_2, oxygen consumption.

Competing interests
The authors declare that they have no competing interests.

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