

Arterial blood lactate measurements quickly identified risk for death from paracetamol-induced liver failure

Bernal W, Donaldson N, Wyncoll D, Wendon J. Blood lactate as an early predictor of outcome in paracetamol-induced acute liver failure: a cohort study. *Lancet*. 2002 Feb 16;359:558-63.

QUESTION

In patients with paracetamol (acetaminophen)-induced acute liver failure, can arterial blood lactate measurements identify those likely to die without liver transplantation?

DESIGN

2 cohort studies, 1 for derivation and 1 for validation.

SETTING

Intensive care unit (ICU) of King's College Hospital (KCH), a tertiary-care hospital in London, England, UK.

PATIENTS

All patients met the KCH criteria for transfer of patients with paracetamol-induced hepatotoxicity to the liver ICU: 103 patients (median age 35 y, 50% men) formed the derivation cohort, and 107 patients (median age 36 y, 61% women) formed the validation cohort.

DESCRIPTION OF PREDICTION GUIDE

In the derivation cohort, blood lactate levels were measured early after admission (median 4 h) and after fluid resuscitation (median 12 h). A model using the early blood lactate levels was created, taking into account the effects of demographic, biochemical, and clinical variables. Optimum threshold values for early and postresuscitation lactate levels were applied to the validation cohort.

COMMENTARY

In England, some 70 000 patients overdose on paracetamol (acetaminophen) annually; 400 to 500 of these patients develop severe liver damage and require transfer to a liver unit (1). Once there, sorting those who can be expected to survive with medical management alone (about half) from those who will die without liver transplantation must be done during the narrow window of time in which transplantation is feasible. The KCH criteria (2) have good specificity when predicting the need for transplantation: In this group, only about 15% survive without it. However, sensitivity is a problem, with 20% to 35% of those consigned to medical management dying nevertheless (3). Because roughly one half of the patients listed for transplantation will die before a graft is available (or become ineligible for transplantation because of complications), speedy stratification is imperative (1).

Serum lactate levels increase during the anaerobic metabolism characterizing tissue hypoxia and from impaired hepatic clearance, both of which are typical of severe liver injury. Bernal and colleagues show that lactate levels measured soon after the recognition of severe liver injury can be used to improve early prediction of transplantation candidacy

MAIN OUTCOME MEASURES

Accuracy of blood lactate levels compared with KCH criteria for identifying patients requiring liver transplantation.

MAIN RESULTS

In the derivation cohort, early and postresuscitation lactate levels were higher in patients who died than in those who survived (8.5 vs 1.4 mmol/L, $P < 0.001$ and 5.5 vs 1.3 mmol/L, $P < 0.001$, respectively). Multivariate logistic analysis showed that pH and early and postresuscitation blood lactate levels were predictive of mortality. Receiver-operating characteristic analysis showed an optimum early blood lactate threshold of > 3.5 mmol/L (sensitivity 86% and specificity 92%) and a postresuscitation threshold of > 3.0 mmol/L (sensitivity 82% and specificity 96%) for identifying patients who would not survive. These thresholds were applied to the validation cohort and compared with the KCH criteria (Table). An

Validation of arterial blood lactate levels for identifying liver transplantation candidates*

Indicator	Sensitivity	Specificity	+LR	-LR	Median time (h)†
Early lactate threshold > 3.5 mmol/L	67%	95%	13	0.35	4
Postresuscitation lactate threshold > 3.0 mmol/L	76%	97%	30	0.24	12
KCH criteria	76%	95%	15	0.25	10
Postresuscitation + KCH	91%	94%	14	0.1	12

*KCH = King's College Hospital. Diagnostic terms defined in Glossary.

†Median time from admission to criteria being fulfilled.

early blood lactate threshold > 3.5 mmol/L had lower sensitivity than the KCH criteria, but patients at risk for death were identified sooner. A postresuscitation blood lactate level > 3.0 mmol/L had equivalent sensitivity and higher specificity than KCH criteria, but did not shorten the time to identify these patients. The combination of postresuscitation blood lactate level and KCH criteria was the most accurate approach to identify patients at risk for death but did not identify patients sooner than KCH criteria alone.

CONCLUSION

In patients with paracetamol-induced acute liver failure, arterial blood lactate levels rapidly and accurately identified those likely to die without liver transplantation.

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and that postresuscitation lactate levels in conjunction with KCH criteria can reduce the number of patients wrongly assigned to medical therapy alone. These levels were obtained at a remarkably consistent median of 56 (assessed soon after admission) and 64 (assessed after resuscitation) hours after ingestion, in patients whose alcohol exposure was not reported, and within a medical system admirably efficient in the disposition of this common problem. These issues may confound extrapolation to acetaminophen toxicity in the United States and deserve further study. Meanwhile, serum lactate levels should be included with the KCH criteria in assigning patients with acetaminophen-induced liver failure to medical or surgical treatment.

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References

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