Use of microalbuminuria as a predictor of outcome in critically ill patients

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We have investigated the use of microalbuminuria as a predictor of outcome in a pilot study involving 50 critically ill patients in a six-bed hospital intensive care unit (ICU). Urinary microalbumin:creatinine (M:Cr) ratios measured only 6 h after admission to the ICU demonstrated a significant difference (P<0.01) between survivors and non-survivors, allowing rapid identification of patients at increased risk of developing organ failure and at greater risk of death. This work suggests that earlier identification of these patients using a rapid, simple, inexpensive biochemical test is possible; if confirmed in a larger study, it may be that clinical interventions can be targeted at those most likely to benefit.

Br J Anaesth 2000; 84: 239–41

Keywords: complications, microalbuminuria; intensive care, audit; complications, morbidity; complications, mortality

Accepted for publication: September 27, 1999

Multiple system organ failure (MSOF) has been described as the sequential failure of the lungs, liver, kidney and other vital organ systems after a variety of acute pathological conditions, such as sepsis, multiple trauma, haemorrhagic shock or pancreatitis.1 Although the mechanisms involved in the development of this syndrome are not entirely clear, it is proposed that MSOF after trauma or surgery results from a generalized inflammatory reaction with activation of leucocytes and release of free radicals and other mediators, such as cytokines, from these cells.2

The optimal use of intensive care unit (ICU) resources and an accurate method of predicting the outcome of the critically ill has been the aim of many studies over several years.3 Earlier identification of patients most at risk of serious complications and adverse outcomes would mean that they can be targeted more accurately with potentially expensive clinical interventions.

Microalbuminuria has been identified as showing promise as a predictor of outcome,4 but requires application in a mixed population; this has been addressed in our study. Several studies have described a rapid increase in urine albumin (microalbumin) excretion in acute inflammatory conditions, which appears to be related to systemic vascular damage exemplified by capillary leak syndrome.5 6

The aim of our study was to assess the practicability of measurement of microalbuminuria in critically ill patients as a predictor of outcome.

Methods and results

After obtaining approval from the Hospital Ethics Committee and written informed consent from relatives, 50 patients, aged 21–79 yr (median 63 yr), were recruited after ICU admission over a 6-month period. Patients suffering from chronic organ insufficiency before this hospital admission according to APACHE II guidelines, or those with a predicted ICU stay of less than 24 h were excluded. APACHE II scores were determined 24 h after admission to the ICU. To assess the degree of organ dysfunction, a modified daily multiple organ dysfunction score (MODS) was determined.7

Fresh urine samples (approximately 15 ml) were collected at 6 hourly intervals from the urinary catheter and stored at 4°C until analysis of microalbumin by automated immunoturbidimetry on a Beckman Synchron CX-7. Urine creatinine was estimated on a Beckman Synchron CX-7 by a modified Jaffé rate method with alkaline picrate. Results are expressed as the microalbumin (mg):creatinine (mmol) ratio to correct for variations in urine flow rate; for the purpose of this study, a ratio of 3 mg mmol⁻¹ was selected as the cut-off. Inter-assay precision was 7% for a microalbumin:creatinine (M:Cr) ratio of 7.5 mg mmol⁻¹.

Differences in variables between survivors and non-survivors were compared using the non-parametric Mann–Whitney U test with P<0.05 considered to be statistically
In this pilot study, we examined a heterogeneous group of patients with a variety of clinical conditions, which accurately reflected patients admitted to a general ICU in the UK. This was considered advantageous, as any predictive test result must be applicable to all patients with a wide variety of diagnoses, not just small highly selected groups.

Increases in urinary albumin excretion were seen on admission to the ICU in both survivors and non-survivors and appeared to be quantitatively related to the degree of multiple organ failure, with the most microalbuminuria tending to occur in those patients with the highest APACHE II and MODS. Furthermore, the amount of microalbuminuria was significantly associated with outcome as those patients with severe microalbuminuria later died.

The simple measurement of microalbuminuria allowed rapid prediction of outcome in critically ill patients, 6 h after admission to the ICU (Fig. 1) suggests that a correlation between variables. Outcome was assessed according to patient hospital survival; 36 patients survived, while 14 died. Non-survivors were slightly older as a group (median 66 yr) than survivors (median 58 yr; P=0.12); 36% of survivors (13 of 36) were female compared with 43% of non-survivors (six of 14). Survivors had a slightly longer median stay (6 days) in the ICU compared with non-survivors (5 days), but this was not statistically significant (P=0.19).

The onset of microalbuminuria was rapid, with increased urinary albumin excretion observed on admission to the ICU, with marked differences between survivors and non-survivors, even 6 h after admission. Furthermore, the degree of microalbuminuria correlated with the admission APACHE II and day 1 MODS. Spearman correlation coefficients between M:Cr after 6, 12 and 18 h with APACHE II were 0.52, 0.59 and 0.54, respectively (all P<0.001) and with day 1 MODS were 0.43, 0.50 and 0.46 (all P=0.002).

Logistic regression was used to model this situation using the M:Cr ratios at 6 h. The M:Cr ratio at 6 h was significantly different between survivors and non-survivors (chi-square=5.6, df=1, P=0.02) and the relationship between M:Cr score and the predicted probability of mortality is shown in Figure 1. This relationship changed very little for samples collected at 12 or 18 h, and therefore this curve represents the relationship between M:Cr score and the probability of mortality between 6 and 18 h. Sensitivity and specificity for 12 and 18 h were of a similar magnitude as those for 6 h; the same was also true for positive and negative predictive values (typically 50% and 85%, respectively, using a M:Cr cut-off of $\geq$3 mg mmol$^{-1}$).

Comment

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The simple measurement of microalbuminuria allowed rapid prediction of outcome in critically ill patients, 6 h after admission to the ICU; this is much earlier than current clinical scoring systems can be used. A high sensitivity is desirable as this selects those patients who are more likely to die and who may benefit from earlier more intensive treatment.

Calculation of the probability of death for M:Cr ratios obtained in this study (Fig. 1) suggests that a rapid indication of outcome can be obtained within 6 h of ICU admission.

In summary, the speed and magnitude of the renal permeability response to indirect injury and its association with outcome suggest that measurement of microalbuminuria may have a role in the early identification of patients at increased risk of developing MSOF, possibly leading to death. As the number of patients studied was small, further studies in larger numbers of heterogeneous patients are required to confirm this finding, validate the M:Cr cut-off and examine if measurement of microalbuminuria as an indirect measure of capillary leak may be useful as an early predictive indicator; these studies are currently underway. Confirmation of these findings means that measurement of urine microalbumin would provide a rapid, simple, inexpensive test to identify patients who may benefit from appropriate early therapeutic strategies which may prevent further capillary leak and hence the onset of MSOF and death.

Acknowledgement

Financial support for this study was from Aintree Hospitals NHS Trust. We thank the staff of the Department of Clinical Biochemistry and the ICU for their help. We also thank Dr David Wile for helpful comments during the preparation of the manuscript.

References