Commentary

Recently published papers: Asking the unanswerable – measuring the immeasurable and decontaminating the infected

Hardeep S Benepal[1] and Lui G Forni[2]

[1]Renal and Critical Care Registrar, Department of Critical Care Medicine, Worthing General Hospital, Worthing, West Sussex, UK
[2]Consultant Intensivist, Department of Critical Care Medicine, Worthing General Hospital, Worthing, West Sussex, UK

Correspondence: Lui G Forni, Lui.Forni@wash.nhs.uk

Published online: 6 November 2003
This article is online at http://ccforum.com/content/7/6/402

Critical Care 2003, **7**:402-404 (DOI 10.1186/cc2402)

> "The greater our knowledge increases, the greater our ignorance unfolds."
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> JF Kennedy
> *Address at Vanderbilt University Nashville, Tennessee, May 18 1963*

As 2003 marches on one is left reflecting on yet another year in which the intensive care literature has continued to challenge the accepted tenets, and as always one continues to be surprised by the results. The study conducted by Finney and coworkers [1] illustrates well how our increasing knowledge leads to more questions. Since the study by van den Berghe and coworkers [2] was reported, much attention has been given to rigorous control of blood glucose levels in patients, although as Finney and coworkers [1] pointed out the mechanisms underlying the perceived benefits are unclear. In particular, the observed mortality reduction might have been due to avoidance of hyperglycaemia or to the dose of exogenous insulin, or perhaps a combination of the two.

That observational study of 531 intensive care unit (ICU) patients (523 studied) examined blood glucose levels and quantity of insulin administered; a secondary question was to determine whether there was a threshold glucose concentration associated with increased mortality [1]. Glycaemic control was split into six bands that were determined prospectively. The patients were predominantly male, over 60 years old and overweight. Cardiac surgery was the reason for admission in 85% of individuals, and interestingly only 17 of the patients were judged to be underweight. The relationship between ICU outcomes, glucose control and insulin dose was modelled using multivariable logistic regression. In all cases increased insulin administration was associated with a significantly increased risk for death. Despite the fact that over 16% of patients had diabetes, this was not an independent risk factor. The conclusions drawn were that it is the control of blood glucose levels that account for any observed mortality benefit, rather than intensive insulin therapy. The data also implied that patients whose glucose levels remained predominantly below 10 mmol/l fared better than did those patients whose glucose levels did not, and Finney and coworkers speculated that a blood glucose level of less than 8.0 mmol/l should be the preferred treatment aim.

The authors must be applauded for their honesty in that they accept and demonstrate that glucose levels in the ICU are difficult to control, in which we find some solace. This excellent work joins the increasing body of evidence highlighting the need for glycaemic control, although one is left pondering the potential mechanisms that underlie the observed effects. The study is also a triumph for computerized clinical information systems, although the authors do highlight the limitations of this approach. For those of us who have often bemoaned the lack of high quality data collection, the new millennium appears to have provided an answer. We look forward to interrogating our relatively new system!

From a study that examines a known risk factor for mortality, we turn to one that attempts to predict it. Rocktaeschel and coworkers [3] conducted a retrospective analysis of some 300 critically ill patients to determine whether various acid–base parameters can predict mortality in such a group. The principal thrust of the study was to determine whether base excess, resulting either from unmeasured anions or from anion gap, or both, can predict lactate concentrations. Somewhat unsurprisingly, the overall conclusion was that

ICU = intensive care unit; SDD = selective decontamination of the digestive tract.

these variables are good predictors of hyperlactaemia (defined as >5 mmol/l). The authors conceded that the variables measured should correlate closely, given that they may reflect the same entity.

Rocktaeschel and coworkers should be congratulated in that this is a large study in a general ICU population, the median age being 65.4 years and with a median Acute Physiology and Chronic Health Evaluation II score of 17. As such the results should be widely applicable in ICUs, and will be of particular interest to those physicians who do not have ready access to lactate measurements. The acid–base variables studied, and specifically 'unmeasured anions', were not found to be accurate predictors of in-hospital mortality in this group of patients. The report joins the growing body of publications 'measuring' the unmeasured anions, but it is of interest in that the authors also explained in part the various pitfalls in such calculations and discussed the differences between analytical methodologies. We wonder whether such calculations will be of routine benefit in treating patients. Indeed, Bronsted in 1923 led us away from the concept of ions into the era of acids and bases. Given the difficulties one occasionally experiences in instructing students regarding the intricacies of acid–base balance, the concept of unmeasured anions is often a bridge too far and at worst can be somewhat anachronistic. At present we will stick to the conventional measures of lactate, pH and base excess. If the unmeasured anions are ever discovered (other than those we are already aware of) and are found to be of prognostic significance, then we will certainly think again.

Those involved in the intensive care arena often find themselves making difficult, often end-of-life decisions based on as much information as can be accrued. A recent study attempted to address the decision processes involved in the withdrawal of mechanical ventilation in anticipation of death in ICU patients. Cook and coworkers [4] conducted a prospective study, following adult patients admitted to 15 ICUs in Canada, the USA, Australia and Sweden. They monitored continuous variables such as multiple organ dysfunction score, use of invasive life support (mechanical ventilation, inotropes, vasopressors, haemodialysis), do-not-resuscitate orders, patient's ability to participate in decision making, physician's prediction of survival and projected status 1 month after discharge, as well as patient's preferences regarding use of invasive life support if known. A total of 851 patients who were expected to be on the ICU for at least 72 hours were enrolled, of whom 539 (63.3%) were weaned from the ventilator, 146 (17.2%) died while receiving ventilation and 166 (19.5%) had ventilation withdrawn. Surprisingly, of the 166 patients who had ventilation withdrawn, six survived to the point of discharge from hospital. The main clinical characteristic of those who had ventilation withdrawn was older age (64.4 years versus 60.1 years; $P=0.02$). Those who had ventilation withdrawn were more likely to have do-not-resuscitate orders established while they were in the ICU than were those who died while on ventilation (100% versus 52.1%; $P\leq0.001$). They were also less likely to receive inotropes or vasopressors (69.3% versus 89.7%; $P\leq0.001$) and were more likely to have these treatments withdrawn (62% versus 40.5%; $P\leq0.001$). This group were also more likely to have renal support withdrawn but were no more likely to have renal support than were those who died while receiving ventilation. There was no obvious correlation with admitting diagnosis or organ system failure.

Interestingly, of the four independent factors associated with withdrawal of mechanical ventilation, three were essentially subjective judgements. These were the physician's perception of the patient's preferences regarding use of life support, the physician's predictions of likelihood of survival in the ICU, the physician's predictions of the patient's future cognitive status, and the use of inotropes or vasopressors. Moreover, there was no variation between centres, cities, or countries. This is reassuring because it refutes the traditional perception of withdrawal of life support based on age, severity of illness and worsening organ function. However, it is important to note that, more often than not, these were perceived preferences, and information from family members may be at odds with that from the patient. It is also apparent that the way in which information is disseminated to the family may influence the family's decision. An intuitive view on this article is provided by Drazen [5] and is a thoughtful perspective.

Finally, we turn to a recent report that assessed the effects of selective decontamination of the digestive tract (SDD) on ICU and hospital mortality, as well as the subsequent development, if any, of resistant bacteria [6]. That randomized controlled study was conducted in 934 patients who were expected to have a duration of stay of at least 72 hours. The patients were assigned either to polymyxin E, tobramycin and amphotericin B together with an initial 4-day course of intravenous cefotaxime, or to standard treatment. There were no other significant differences between the groups, and approximately 60% of patients had undergone surgery. The ICU mortality was 15% in the SDD group and 23% in the control individuals. Similarly, in-hospital mortality was 24% in the SDD group and 31% in control individuals, with relative risks of 0.65 and 0.78, respectively. The median ICU duration of stay was also reduced in the treated group. Subsequent follow-up cultures, available in 773 patients, revealed a reduction in resistant organisms in the treated group as well as a reduction in antibiotic usage. Astonishingly, no methicillin-resistant *Staphylococcus aureus* was detected in either group, and one must therefore congratulate the Dutch health service. Also, no differences were observed between medical or surgical patients, despite the fact that medical patients are more likely to be colonized with resistant bacteria before ICU admission. However, whether one adopts the routine use of SDD may well be

influenced by the local rates of resistant organisms. Over 2000 years ago, Hippocrates [7] had an interesting view on therapy, stating that, 'Extreme remedies are very appropriate for extreme diseases.' Who knows, perhaps he too would be a modern day advocate of SDD!

Competing interests

None declared.

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