Diabetic ketoacidosis: principles of management

Sir,

The article 'Diabetic ketoacidosis: principles of management' by Sharma and Hadebe (vol 68(3), 2007, p. 184) contains several discrepancies.

The authors write 'The basic mechanism for the development of [diabetic ketoacidosis] DKA is a reduction in the effective insulin concentration and increased counter-regulatory hormones ...'. Schade et al (1981) refer to 12 papers reporting sufficient amounts of insulin in plasma of patients with DKA. Sharma and Hadebe also write 'Euglycaemic DKA has been reported in up to 18% of cases' – euglycaemia is identical to euinsulinaemia. Where are the published reports on the lack of insulin in patients with DKA? According to Waldhäusl et al (1979), 'increased counter-regulatory hormones' are the consequence of DKA, not its cause... .

The authors then write: 'Bicarbonate replacement has no documented benefit in DKA ...'. According to Edge et al (2006), very low blood pH is the immediate cause of coma in DKA: the activity of the glycolytic enzyme phosphofructokinase decreases with decreasing pH, and thus use of glucose is impaired. This is detrimental, especially for brain cells, thus the clinical consequences of decreasing blood pH are drowsiness, stupor, coma then death in coma (in 'up to 14%'). Administration of sodium bicarbonate (or other alkalizing solutions) is important to increase blood pH, not for 'bicarbonate replacement'. In contrast to the 14% mortality of DKA reported by Sharma and Hadebe, several authors have achieved zero mortality of comatose patients with DKA (Kitabchi et al, 1976; Viallou et al 1999; Yordam et al, 2005) by use of alkalizing solutions. Where are the published reports on zero mortality in comatose patients with DKA without alkalizing solutions?

It would be useful if the authors could explain these discrepancies to readers.

Viktor Rosival
Clinical Biochemist
SYNLAB Department of Laboratory Medicine
Dérer's Hospital
SK-.833 05 Bratislava
Slovakia

Edge JA, Roy Y, Bergomi A, Murphy NP, Ford-Adams ME, Ong KK, Dunger DB (2006) Conscious level in children with diabetic ketoacidosis is related to severity of acidosis and not to blood glucose concentration. *Pediatr Diabetes* **7**(1): 11–15
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Sir,

We thank Dr Rosival for the interest in our article. The pathophysiology of DKA is complex, and needs a detailed description and further references which are beyond the scope of this letter or the previous article. A list of references which the readers may find beneficial is available from the authors (drvvs@rediffmail.com).

In response to the second query, euglycaemia is not identical to euinsulinaemia. Euglycaemic ketoacidosis was originally described whereby the initial blood glucose was <16.7 mmol/litre and plasma bicarbonate ≤10 mmol/litre. The cause of preserved euglycaemia could be greater urinary loss of glucose triggered by counter-regulatory hormones or decreased rate of hepatic glucose production (De and Child, 2001). The rate of development of ketosis is rapid during periods of insulin deficiency after a fast. A fast of moderate duration, such as might be expected to occur during the development of DKA, predisposes patients with type 1 diabetes to euglycaemic ketoacidosis during periods of insulin deficiency. Furthermore, decreased rates of hepatic glucose production are responsible for lower plasma glucose values seen during a fast. This accelerated development of ketosis may be attributable to the effects of elevated levels of glucagon and/or catecholamines on lipolysis (Burge et al, 1993).

The debate over bicarbonate administration is never-ending, with most current reviews discouraging the use of bicarbonate in DKA since DKA corrects with insulin therapy (Kitabchi et al, 2001). In response to the comment about the effect of acidosis on brain cells, a prospective randomized study examined the effect of bicarbonate *vs* no bicarbonate in two groups of patients in DKA, and found that bicarbonate and pH levels were higher in the CSF than in the plasma in patients with DKA. This study also showed that ketones and glucose were higher in plasma than in CSF with the osmolality being similar in both compartments, and concluded that the blood–brain barrier provides greater protection against acidosis for the brain. They felt that administration of bicarbonate to patients with pH 6.9–7.14 provided no biochemical or clinical advantage (Morris et al, 1986; Barnes et al, 1990). We believe that bicarbonate can be administered as we indicated.

The mortality figure of up to 14% was obtained from the Intensive Care National Audit and Research Centre, whose database is linked to intensive therapy units across the country. In the authors' opinion these are the most accurate national data which can be obtained. The average mortality rate for ketoacidosis in developed countries is estimated at 5–10%, although reported rates vary (Schade et al, 1981). Differences in the definition of ketoacidosis and in patient selection partly explain the variation, but mortality is generally higher in less specialized centres and in groups such as the elderly (Gale et al, 1981).

V Sharma/N Hadebe
Trust Registrar in Anaesthesia/Senior House Officer in Anaesthesia
Morriston Hospital
Swansea SA6 6NL

Barnes HV, Cohen RD, Kitabchi AE, Murphy MB (1990) When is bicarbonate appropriate in treating metabolic acidosis including diabetic ketoacidosis? In: Gitnick G, Barnes HV, Duffy TP, et al, eds. *Debates in Medicine.* Yearbook, Chicago: 172
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