Letters

DOI:10.1111/j.1464-5491.2011.03398.x

Insulin dose requirement in diabetic ketoacidosis

Diabet. Med. 29, 153 (2012)

There is much to commend in the recently published guidelines on the management of diabetic ketoacidosis [1]. However, the suggested bedside calculation of insulin dose is unnecessary and potentially hazardous.

A calculation of insulin dose based on estimated body weight will, in practice, inevitably introduce dosage calculation errors and particularly order-of-magnitude errors. Guidelines must be safe for all situations, including when read for the first time by junior staff working without supervision in pressured emergency units. These first-line staff often will have had little experience of intravenous insulin dose ranges. This risk is present even in well-staffed units, as exemplified by a recent urgent phone enquiry from the intensive care unit in another hospital after a 'calculated' intravenous bolus of 200 units of Actrapid was given. Calculations in the acute situation will inevitably throw up occasional errors. We have learned this dosage calculation lesson time and time again.

Fortunately, there is no need for the calculation of insulin administration rate on a per kg/h basis, as suggested in the new guidelines. The introduction of fixed low-dose insulin treatment for diabetic ketoacidosis [2] was followed by a series of studies trying to establish the lowest fixed dose for the safe treatment of severe diabetic ketoacidosis. The lowest answer demonstrated was 1 unit per hour (114 patients with severe diabetic ketoacidosis, rapid recovery and zero mortality) [3]. The reason why this extremely low dose is effective is simply that both ketogenesis and hepatic glucose production are suppressed at markedly lower plasma insulin levels than those required for glucose disposal. The well-established standard insulin infusion rate of 6 units/h is thus sixfold greater than the minimum demonstrated to be safe. It achieves plasma insulin levels of approximately 100 mU/l, several times greater than required for the specific metabolic task (approximately 20 mU/l). In diabetic ketoacidosis, insulin resistance to glucose disposal in muscle does not affect the overall response to insulin, as muscle glucose uptake is likely to play only a minor part in the fall of blood glucose. Early work established that insulin resistance, even as a result of severe infection, was not relevant. Blood glucose falls mainly because of suppression of hepatic glucose production and dilution. The supposition that the increasing weight of the population indicates the need for higher insulin infusion rate is not supported by the available information.

All guidelines require to take into account the rare individual with diabetic ketoacidosis who genuinely requires very high plasma insulin levels to achieve control. Need for very high insulin levels in an individual does not reliably scale with body weight and is both rare and unpredictable. The new guidelines very usefully specify a rate of fall of blood glucose of < 3 mmol/l per h as requiring change in insulin administration. A stipulation of twofold increases in insulin infusion rate, repeated if necessary, would usefully be included in the guidelines to cover this unusual circumstance.

Keep it simple; especially for emergency medical unit personnel. In a later era, Hippocrates might have extended his most famous aphorism: At least do no harm—and minimize calculations at the bedside.

Competing interests

Nothing to declare

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DOI:10.1111/j.1464-5491.2011.03395.x

Response to Taylor. Insulin dose requirement in diabetic ketoacidosis

Diabet. Med. 29, 153–154 (2012)

We thank Taylor for his considered comments on our recommendations for the use of a fixed-rate, weight-based continuous intravenous insulin infusion for the initial management in diabetic ketoacidosis [1]. This issue was hotly debated by the writing group and, for reasons of necessary brevity, was not included in the 'controversial areas' in the paper published in *Diabetic Medicine*. It is important to note that the recommendations do not amount to 'high dose' insulin infusion as, in a typical adult with Type 1 diabetes weighing 70 kg, the insulin dose will be 7 units/h; the recommendation is there to

ensure enough insulin is delivered. Whilst the majority of patients will respond to low-dose insulin, as quoted by Taylor from Wagner *et al*. [2], we have all encountered patients whose blood ketone levels fail to fall and who remain acidotic, even when the insulin infusion rate is the standard 'low dose' of 6 units/h. The use of variable insulin infusion rates ('sliding scales') would appear to be even more dangerous. It has been a common—albeit anecdotal—experience amongst the writing group that they have had to intervene to administer weight-related insulin infusions in individuals where the blood ketones remain high despite having relatively normal blood glucose levels. These normal glucose levels lull the unwary junior doctor to revert to the use of the variable-rate intravenous insulin infusion leading to inappropriately low levels of insulin being given. In our experience, such cases are not rare and it is probably their commonality that leads to them not being reported in the medical literature.

The study demonstrating safe use of low-dose insulin [2] was driven by the need to lower blood glucose and was performed before the availability of ketone meters. This area is therefore still bedevilled by suboptimal data and we hope that the introduction of ketone meters will allow high-quality research to be performed to clarify the issues raised by Taylor, as we are now able to easily measure the metabolite responsible for the acidosis.

The approach we advocated has been successfully used in the USA and by paediatricians around the world for many years [3–5] and, as far as we are aware, no published data of dosing errors have been reported. Junior doctors routinely use weight-based dosages and we have found no difficulties in this regard. Moreover, the guidelines explicitly recommend the involvement of the specialist diabetes team at the very earliest opportunity, and also that any Integrated Care Pathway used in hospitals be used by healthcare professionals specifically trained in its use.

Taylor suggests that the insulin resistance of infection is irrelevant in this situation. We would dispute this assumption, with the elevation in counter-regulatory hormones associated with the stress of diabetic ketoacidosis, the rise in free fatty acids and ketone bodies, together with the electrolyte deficiencies, all conspiring to exaggerate the insulin resistant state [6]. The guideline is also aimed to help address the increasingly common issue of ketosis-prone Type 2 diabetes, which also has a degree of insulin resistance [7]. With this in mind, there are data to show that lower insulin doses may not be able to fully suppress hepatic gluconeogenesis [8].

Competing interests

MWS has received honoraria from Medical Societies for talking on Diabetes Ketoacidosis. The other authors have nothing to declare.

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DOI:10.1111/j.1464-5491.2011.03424.x

Clark *et al*. Nurse-led interventions used to improve control of high blood pressure in people with diabetes: a systematic review and meta analysis

Diabet. Med. 29, 154–155 (2012)

We are writing with respect to the above article. Clark *et al*. seem confused about the term 'nurse prescribing'. These authors recently published a systematic review of nurse-led interventions for improved control of hypertension [1] and this paper, a subgroup analysis of the review, presents findings for nurse-led interventions to control blood pressure in people with diabetes mellitus.

Clark *et al*. claim that five of the 11 studies reviewed included nurse prescribing in the intervention. However, at no stage do the authors in these studies mention or use the term 'nurse