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DIABETIC Medicine

LETTER

Re: Managing hyperglycaemia during antenatal steroid administration, labour and birth in pregnant women with diabetes – An updated guideline from the Joint British Diabetes Society for Inpatient Care

Letter to the Editor,

We commend Dashora and colleagues on the recently published Position Statement of the JBDS on the important management issue of glycaemic control following antenatal corticosteroids (ACS) in women with diabetes in pregnancy, particularly with respect to minimising neonatal hypoglycaemia.

We agree that intensive treatments to maintain at-target maternal glucose may be more important following ACS than in labour, as there is evidence that ACS presents a unique heightened risk of neonatal hypoglycaemia,[1] which may be mitigated by at-target glycaemic control.[2]

We note a key concern of this updated guidance is that use of variable rate intravenous insulin (VRII) may increase the risk of maternal hypoglycaemia following ACS (Section 2). However, we are concerned that this view is not supported by available data. At the outset, it should be noted that published VRII protocols are not identical or comparable. Our studies have shown that VRII protocols that are not inherently customised for pregnancy may be more risky and less effective.[2,3] The marked variations in published VRII protocols may explain the heterogeneity of outcomes reported.[2-6] We urge caution that analysis (and implementation) of VRII studies must consider the specific VRII protocol when assessing outcomes.

Secondly, we note that the arguments presented against the use of VRII in Table 2 mostly highlight the potential for implementation errors (or theoretical risks that have not been seen in published studies), rather than an inherent criticism of VRII methodology. Insulin treatment is universally acknowledged as a high-risk medication, and hospitalisation represents a unique risk period for all insulin-treated patients. Therefore, meticulous staff training, quality assurance, and audit is an essential practice on all insulin-using wards, irrespective of whether this be with multiple daily subcutaneous injection, continuous subcutaneous infusion (CSII, pump), or VRII. The use of patient-controlled CSII presents an equivalent serious risk, as hospital staff unfamiliar with insulin pump use are equally at risk of systemic error resulting in patient harm. Therefore, we urge vigilance in all settings, but do not view the "Potentials" in Table 2 as a compelling reason to avoid properly implemented VRII. However, irrespective of insulin delivery method, the focus on partnering with the patient to achieve glycaemic outcomes and recognising the benefits of patient autonomy, is a valuable emphasis of the updated JBDS guidance.

Thirdly, we disagree with the evidence presented that VRII is associated with increased maternal hypoglycaemic risk. To specifically address the VRII studies cited, Kline et al[7] (cited in Table 1), found that use of a VRII in labour was associated with a numerically lower risk of hypoglycaemia than the use of subcutaneous insulin. Further, we disagree that the NICE-SUGAR study, testing intensive glucose control in critically ill non-pregnant adults,[8] is appropriate evidence that the strategy of maintaining pregnancy-specific ambulatory glucose targets in hospitalised women should be dismissed.

Therefore, to establish the baseline (ambulatory) rate of hypoglycaemia in women with Type 1 diabetes, we reference ambulatory CGM data at 34 weeks' gestation from the CONCEPTT trial.[9] For these women, time with glucose <3.5 mmol/l was median 3% (interquartile range 1–6%). Women wearing blinded CGM had ambulatory time with hypoglycaemia of 4% (IQR 2–8%). 11–12% of ambulatory women with Type 1 diabetes at 34 weeks gestation had an episode of severe hypoglycaemia requiring third party assistance. By contrast in a real-world study of 44 women with Type 1 diabetes managed with the VRII Pregnancy-IVI following betamethasone, the on-infusion time with maternal glucose <3.8 mmol/l was 2% (interquartile range 2–3%),[3] which is a lower rate of hypoglycaemia than in a

comparable ambulatory population.[9] Furthermore, duration of maternal hypoglycaemia following betamethasone using the Pregnancy-IVI are lower in women with Type 2 diabetes (2%, IQR 1–2%),[3] and extremely rare in gestational diabetes (98% of women have glucose >3.8 mmol/l for entirety of VRII).[2] We further highlight that the studies of this VRII, the Pregnancy-IVI, were conducted in real-world ward-based care settings, and therefore are generalisable to standard practice.[2]

Finally, the Position Statement advocates a glucose management strategy following ACS of empiric increase in subcutaneous insulin, or the woman's self-management using CSII/CGM. However, we are concerned that the efficacy and safety of these approaches remain largely untested. A large retrospective study of maternal and neonatal outcomes following betamethasone in diabetes in pregnancy using a subcutaneous insulin algorithm reported numerically higher rates of maternal hypoglycaemia following the subcutaneous protocol than in the baseline period,[10] suggesting that a subcutaneous insulin approach is not inherently safer.

In conclusion, we strongly support the initiation of randomised trials with clinically meaningful endpoints to inform clinical practice in this area. Although such data are awaited, we emphasize that when used following ACS in a ward-setting the Pregnancy-IVI VRII has a comparable hypoglycaemic risk to ambulatory women and has efficacy data in all types of diabetes in pregnancy.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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