

Variable rate intravenous insulin infusions in the critical care environment

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Article points

1. Under current evidence-based protocols, the care of people with diabetes in the critical care environment can be sub-optimal.
2. In a pilot audit questionnaire, the authors tested staff knowledge concerning glycaemic control and the understanding of variable rate intravenous insulin infusions (VRIII).
3. The authors identified the need for staff education and the introduction of a new protocol for VRIII, specific to people with diabetes in critical care.

Key words

- Critical care
- Education
- Variable rate intravenous insulin infusion

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As the incidence of diabetes in the UK is increasing, it is important that healthcare professionals are confident in carrying out diabetes care in their clinical area. The care of people with diabetes admitted to hospital can be sub-optimal owing to the limitations of current protocols. In this article, the authors discuss the results of a pilot audit questionnaire testing staff knowledge concerning the use of variable rate intravenous insulin infusions within a critical care environment.

The National Service Framework (NSF) and the NICE Quality Standards for Diabetes in Adults advise that people with diabetes admitted to hospital receive effective care for their condition (Department of Health, 2001; NICE, 2011). The recent National Diabetes Audit highlighted that the risk of death for people with type 1 and type 2 diabetes is 2.6 and 1.6 times higher than that of the general population (NHS Information Centre, 2011).

Recent evidence from the NICE-SUGAR (Normoglycaemia in Intensive Care Evaluation-Survival Using Glucose Algorithm Regulation) study suggested that all critically ill patients within a critical care unit should be treated with a revised, less aggressive variable rate intravenous insulin infusion (VRIII) algorithm (previously known as a sliding scale; NICE-SUGAR Study Investigators et al, 2009).

The rationale behind the use of VRIII in critical care units

In critically ill individuals, stress hyperglycaemia is a common occurrence, irrespective of whether they have been previously diagnosed with diabetes, owing to glucose homeostasis being impaired in the “fight or flight” response (Vanhorebeek et al, 2007; Marik, 2009). While the dangers of hyperglycaemia for people with diabetes are known, those most at risk of hyperglycaemia in critical illness are those not previously known to have diabetes. In one study, this accounted for 12% of all adults admitted to a hospital (Ellahham, 2010). Stress hyperglycaemia used to be considered as an adaptive response to critical illness, with raised blood glucose levels providing a source of fuel for vital organs at a time of increased metabolic demand (Schultz et al, 2006; Marik, 2009). However, in a study by Van den Berghe and colleagues, a reduction in mortality of 32% in critically ill surgical

patients was observed when hyperglycaemia was treated with intensive insulin therapy (IIT), maintaining blood glucose levels at between 4.4 and 6.1 mmol/L (Van den Berghe et al, 2001). Further to this, Dellinger and colleagues in the “Surviving Sepsis Campaign” recommended glucose control for all individuals with severe sepsis, also recommended in their 2008 update (Dellinger et al, 2004; 2008).

A follow-up study conducted in a medical intensive care unit (ICU) by Van den Berghe and colleagues revealed that, in a cohort of patients, IIT significantly reduced the morbidity but not mortality, and for patients treated for 3 or more days, the rates of subsequent death and disease was reduced (Van den Berghe et al, 2006). It is important to note that the nutrition and volume of the intravenous (IV) glucose that was administered varied between the two trials, and the mortality rate in the control arm was higher than that expected in the initial trial in 2001 (Van den Berghe et al, 2001). All of these factors could have had an impact on the positive result for the reduced mortality that was observed with tight glycaemic control in the initial study (Wiener et al, 2008; Marik, 2009). However, following these single-centre studies, protocols and algorithms for insulin infusion rates in intensive insulin therapy, aiming to maintain a tight control of blood glucose levels, were implemented throughout ICUs worldwide and endorsed by national organisations, owing to the perceived reduction in mortality in the treatment group (Ball et al, 2007; Marik, 2009).

Barriers against tight glycaemic control

Blood glucose control is thought to reduce mortality and morbidity in critically ill patients, as hyperglycaemia contributes to systemic inflammation, oxidative stress, poor immune function and endothelial and mitochondrial dysfunction (Van den Berghe et al, 2006; Jones and Fisher, 2007; Kansagara et al, 2011). A strong association with hyperglycaemia has also been observed with prolonged ventilation, infectious morbidity, an increased risk of polyneuropathy in sepsis and the systemic inflammatory response syndrome (Vanhorebeek et al, 2007). Nevertheless, barriers to tight glycaemic control

remain, as VRIIs are infrequently used by some clinicians owing to the increased risk of severe hypoglycaemia, concerns about the validity of some studies and the difficulty in achieving normoglycaemia in critically ill patients (Schultz et al, 2006; NICE-SUGAR Study Investigators et al, 2009). Indeed, Schultz et al (2006) proposed that tight glycaemic control is actually far from standard practice in many ICUs. Wiener et al (2008) also reported that the failure of nursing staff to adhere to tight glycaemic control could be attributed to concerns about the risk of hypoglycaemia and the increased workload arising from the need for regular blood glucose monitoring and changing infusion rates. It has been calculated that a total of 2 hours per day of direct nursing care is required to achieve tight glycaemic control (Aragon, 2006).

Hypoglycaemia detection and management

Hypoglycaemia, which can be defined as when the blood glucose level is <4 mmol/L, is a serious complication and, if left untreated or unrecognised, has the potential to cause neurological damage (Ball et al, 2007; Wiener et al, 2008). The effective implementation of tight glycaemic control requires hourly blood glucose monitoring. However, research has shown that this is considered time consuming and difficult owing to other demands on a nurse's workload (Aragon, 2006; Ball et al, 2007). Notably, many patients in critical care units receive sedative medicines that often mask the clinical signs of hypoglycaemia (Schultz et al, 2006). Hypoglycaemia can also result from the continuation of a VRII when feeds (enteral or parental) or IV fluids have been discontinued (Stanisstreet et al, 2010).

Changes in practice

Two large multicentre controlled trials, the Glucontrol study (Preiser et al, 2009) and the VISEP (Volume Substitution and Insulin Therapy in Severe Sepsis) study (Brunkhorst et al, 2008), designed to assess whether IIT benefits critically ill patients, had to be terminated early due to a nearly four-fold higher rate of severe hypoglycaemia in the treatment groups. Neither trial was able to reproduce the findings from

“Blood glucose control is thought to reduce mortality and morbidity in critically ill patients, as hyperglycaemia contributes to systemic inflammation, oxidative stress, poor immune function and endothelial and mitochondrial dysfunction.”

Page points

1. Over recent years, the confidence in tight glycaemic control for patients in critical care has decreased, owing to the potential for intensive insulin therapy to cause hypoglycaemia.
2. Although the benefits of insulin therapy to control blood glucose levels in critically patients in intensive care units have been documented, there is no current evidence to support the use of insulin therapy for patients in high dependency units.
3. Much of the research concerning the use of variable rate intravenous insulin infusions in critical care does not differentiate between people with and without diabetes.

the study by Van den Berghe et al in 2001 (Van den Berghe et al, 2001; 2009; Ellahham, 2010). Following this, the NICE-SUGAR study revealed that a blood glucose target of 10.0 mmol/L or less resulted in a lower mortality rate than the intensive treatment target range of 4.4–6.1 mmol/L (NICE-SUGAR Study Investigators et al, 2009).

Meta-analyses have been conducted by Wiener et al (2008) and Griesdale et al (2009), the latter of which included the results from the NICE-SUGAR study in 2009. Both concluded that tight glycaemic control in ICU patients is not associated with a significant reduction in mortality, but does present a significant risk of hypoglycaemia, with an incidence of 30–40% in some studies causing them to be terminated early. However, Griesdale et al (2009) does suggest that some surgical patients may benefit from tight glycaemic control therapy.

Prior to these studies, confidence in tight glycaemic control was already waning and suggestions were made that hyperglycaemia in ICUs should be treated with less aggressive insulin therapy, owing to the potential for IIT to cause hypoglycaemia (Watkinson et al, 2006). Following the NICE-SUGAR study, the treatment of hyperglycaemia was still recommended but with new targets for blood glucose levels set at <10.0 mmol/L or 7.8–10.0 mmol/L (Marik, 2009; Ellahham, 2010), aiming to avoid undesirable glucose fluctuations, hypoglycaemia or hypokalaemia (Van den Berghe et al, 2009). Indeed, there is no consistent evidence to demonstrate that IIT improves the outcome for critically ill patients compared with less aggressive insulin therapy, which has a lower risk of causing hypoglycaemia (Kansagara et al, 2011).

Despite the recent research, a telephone survey of all ICUs in the UK found a significant proportion of ICUs had not changed their protocols regarding insulin therapy (Paddle et al, 2011). It was concluded that this could be attributed to barriers in practice, as there have been delays of 5 years noted between the publication of guidelines and widespread integration into clinical practice in the past.

Although the benefits of insulin therapy to control blood glucose levels in critically patients in ICUs have been documented, there is no current evidence proposing the use of insulin therapy for patients in high dependency units (HDUs). In the critical care unit referred to in this article, the policy was changed in accordance with recent guidelines. In addition, the same protocol is currently being used for ICU and HDU patients. The appropriateness of this treatment for HDU patients is not known, and is an area requiring further research.

Should treatment change for people with diabetes in the ICU?

Much of the research concerning the use of VRIII in critical care does not differentiate between those with diabetes and those without, and how their respective needs may vary. Many studies, including those of Graham et al (2010) and Stegenga et al (2010), concur that diabetes is not a risk factor for ICU mortality. Indeed, Siegelaar et al highlight that patients with diabetes in ICUs do not benefit from tight glycaemic control (Siegelaar et al, 2010). In regard to the critical care unit examined in this article, a tight glycaemic control protocol is no longer used and, instead, a revised protocol for less aggressive glycaemic control has been implemented in order to maintain blood glucose levels within the range of 4–10 mmol/L. The ICU VRIII protocol and the hospital's VRIII guidelines have similar values for infusion rates. Thus, for patients with diabetes in the critical care environment, a revised version of the ICU protocol would be appropriate.

Staff knowledge audit

In this pilot audit, a selection of nursing staff ($n=14$) from a critical care unit in an acute hospital were asked a series of questions (see *Box 1*) designed to assess their knowledge on diabetes and the use of VRIII in the ICU and HDU for people with and without diagnosed diabetes. The questions were open to allow for more detailed answers, and to adequately assess the understanding and knowledge of nursing staff. In terms of sampling, the audit was designed to be completed by a selection of staff over a 3-day period. The participants were all registered

Box 1. Pilot audit questions and answers.

- **What is your understanding of type 1 diabetes?**
Answers: Correct=5; Incorrect=3; Basic knowledge=6
- **What is your understanding of type 2 diabetes?**
Answers: Correct=6; Incorrect=3; Basic knowledge=5
- **Does it matter how a variable rate intravenous insulin infusion (VRIII) is stopped for a patient without diabetes? Why?**
Answers: Yes=5; No=7; Not sure=2
- **Does it matter how a VRIII is stopped for a patient with diabetes? Why?**
Answers: Yes=14
- **If a patient without diabetes is eating and drinking, is a VRIII appropriate? Why?**
Answers: Yes=3; No=9; Not sure=2
- **If a patient with diabetes is eating and drinking, is a VRIII appropriate? Why?**
Answers: Yes=5; No=7; Not sure=2
- **How would you define hypoglycaemia?**
Answers: Correct=8; Incorrect=6
- **How would you define hyperglycaemia?**
Answers: Correct=9; Incorrect=3; Not sure=2
- **If a patient with type 1 diabetes has low blood glucose levels and is on a VRIII, should it be discontinued? Why?**
Answers: Yes=3; No=8; Not sure=3
- **If a patient with type 2 diabetes has low blood glucose levels and is on a VRIII, should it be discontinued? Why?**
Answers: Yes=11; Not sure=3
- **Do you feel you have adequate up-to-date knowledge about diabetes?**
Answers: Yes=5; No=5; Not sure=4

nurses with a minimum of 6 months' experience, including 13 qualified staff nurses and one deputy sister. No ethical approval was required for this pilot audit.

It became apparent from the pilot audit that the knowledge concerning the treatment of those with diabetes on VRIII was inconsistent, highlighting the need for a section in the ICU protocol regarding its use for patients with diabetes. The understanding of diabetes was inconsistent with 78.5% ($n=11$) having an accurate or basic understanding of type 1 and 2 diabetes. Despite all the participants being aware that the VRIII cannot simply be discontinued when a patient has diabetes, 7% ($n=1$) knew the correct procedure for stopping the infusion and recommencing normal diabetes medications, as stated in the hospital protocol. Thirty-six per cent ($n=5$) of the participants knew that the patients' normal diabetes treatment needed to be recommenced

but did not know the correct procedure. Owing to this lack of understanding, there have been some incidents reported from the diabetes inpatient specialist nurse (DISN), in which patients have been discharged to the ward without having diabetes medication recommenced following discontinuation of the VRIII. It was concluded that the introduction of information from the general hospital protocol into the ICU protocol regarding how to stop the VRIII correctly would contribute to solving this problem. These findings are also supported by a recent report from NHS Diabetes concerning the understanding of insulin use in hospitals and associated issues of safety (NHS Diabetes, 2011).

When to stop treatment with VRIII

When recommencing normal diabetes medication for a person with diabetes (insulin or oral hypoglycaemic agents), changes to the doses may be required owing to poor appetite,

Page points

1. The decision process for when a variable rate intravenous insulin infusion is no longer appropriate is one that requires further knowledge.
2. Research suggests that once a patient with diabetes in critical care is eating and drinking normally without nausea or emesis, the VRIII should be discontinued.
3. In light of the increasing prevalence of diabetes in the UK, if blood glucose levels remain elevated in a patient without known diabetes once he or she has recovered from their critical illness, staff should consider whether the patient has undiagnosed diabetes.

physiological stress or renal impairment. This can be calculated on the basis of the number of insulin units the person has received over the previous 24 hours (Holt, 2009). A referral to the DISN may be appropriate to aid the ICU or HDU doctors with this process. The decision process for when a VRIII is no longer appropriate for patients either with or without known diabetes is one of which requires further knowledge. Thirty-six per cent of participants ($n=5$) thought that a VRIII was still appropriate if a patient with diabetes was eating and drinking and 14% ($n=2$) were uncertain. Similarly, 21% ($n=3$) thought that a VRIII was still appropriate if a patient without diabetes was eating and drinking and 14% ($n=2$) were unsure. The reasons given were mainly regarding concerns that blood glucose levels may still be elevated.

Research suggests that once a patient with diabetes in critical care is eating and drinking normally without nausea or emesis, the VRIII should be discontinued (Holt, 2009; Hammersley and James, 2010). Continuing a VRIII when a patient is eating and drinking is reactive rather than proactive (Marik, 2009), as protocols do not allow for increasing infusion rates prior to meals and, consequently, blood glucose levels become erratic with raised blood glucose post-meals. Similarly, patients without diabetes who are eating and drinking should not require a VRIII. Once a patient is eating and drinking, they are usually on an HDU and recovering from their critical illness or surgery.

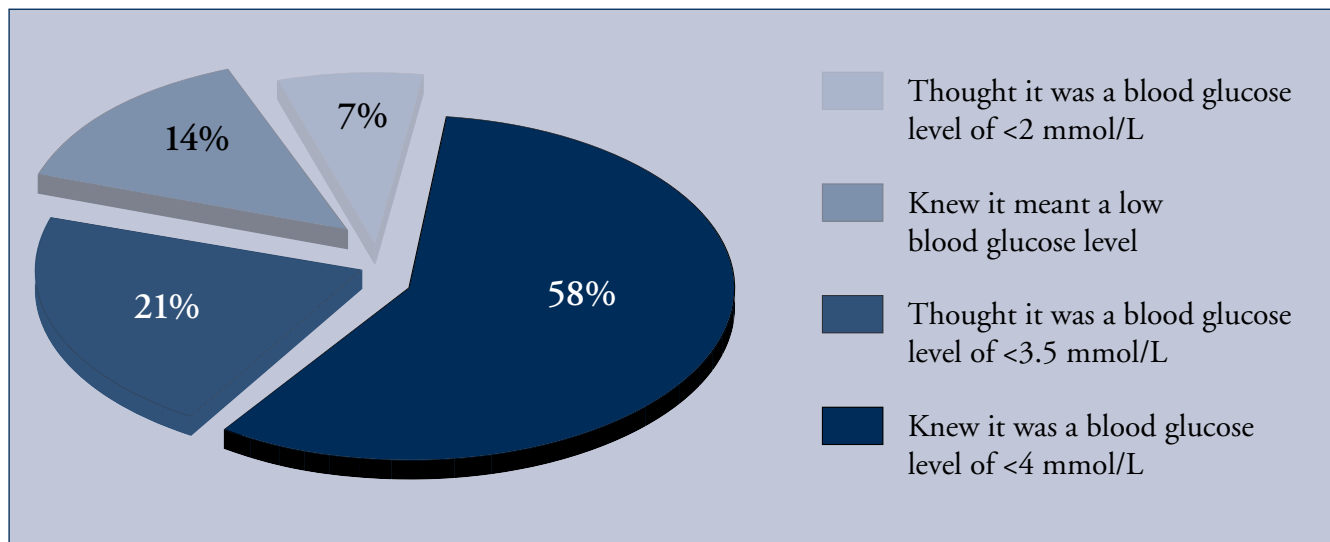
In light of the increasing incidence of diabetes in the UK, if a patient's blood glucose level remains elevated, staff should consider whether the patient has undiagnosed diabetes (Yorkshire and Humber Public Health Observatory, 2010). In such cases, a referral to the DISN would be appropriate. As a patient's condition improves and when he or she is no longer critically ill, regular reviews regarding the need for a VRIII would stop insulin infusions being reviewed and stopped just before a patient is transferred to the ward, allowing blood glucose levels to be controlled prior to transfer to the ward, which would help ward staff and patients by reducing the likelihood of erratic blood glucose levels.

Practice development

The DISN reported that in conjunction with many other hospitals nationwide, a long-acting insulin is administered alongside the VRIII. This is based on the theory that it will reduce the problems with erratic blood glucose levels after the infusion is discontinued, as the patient will have been given long-acting insulin. Thus, insulin deficiency is avoided (particularly with type 1 diabetes) as IV insulin has a short half-life and absorption of subcutaneous insulin is variable (Hammersley and James, 2010).

Currently, the ICU protocol does not state what IV fluids or feeds (enteral or parenteral) should run with the VRIII, whereas the hospital policy specifically recommends IV normal saline or 5% dextrose depending on the patient's blood glucose level. The authors note that, in their experience, there have been no ill effects observed from patients with diabetes having enteral or parental feeds in the ICU, in accordance with the ICU VRIII protocol. However, it needs to be ensured that the enteral feed is adequately absorbed, particularly if used in combination with a VRIII, to reduce the risk of a hypoglycaemic episode. The current ICU protocol recommends that if a feed is stopped, then discontinuation of the VRIII should be considered. Similarly, if a patient is to be transferred, then the VRIII should be discontinued for 4 hours prior to the transfer. However, in the case of a patient with diabetes (particularly type 1 diabetes), they should not be left without insulin treatment. Also, a VRIII should not be discontinued when a patient with diabetes goes to theatre, which is what occurs when patients do not have diabetes. Furthermore, if enteral or parental feeds are not possible, the appropriate IV fluids should be administered alongside the VRIII. The blood glucose levels will remain uncontrolled if this does not occur, putting the patient at risk of developing a diabetes complication (Holt and Kumar, 2003). If the method of providing patients with glucose is changed, their blood glucose levels may require checking more frequently until it is stabilised.

According to the current ICU VRIII protocol, if the blood glucose level lowers to <3.5 mmol/L, the VRIII is stopped. This is where the current hospital protocol differs as the VRIII is not



discontinued; rather, the rate of the infusion is reduced, the episode of hypoglycaemia is reported to the doctor, and treatment with IV glucose commences. Stanisstreet and colleagues suggested that in a period of hypoglycaemia, the VRIII should be discontinued after which the blood glucose levels should be checked every 30 minutes until they are above 3.5 mmol/L and then the VRIII recommenced on a reviewed regimen (Stanisstreet et al, 2010).

The authors suggest that the current ICU protocol needs to be changed in light of the results presented in this article (see *Box 1*). Only 58% of participants in the audit ($n=8$) knew that hypoglycaemia was defined as when the blood glucose level is <4 mmol/L (see *Figure 1*). Furthermore, 21% ($n=3$) thought that in the case of hypoglycaemia, a VRIII should be stopped when a patient has type 1 diabetes and 21% ($n=3$) were unsure. Seventy-nine per cent ($n=14$) would stop a VRIII if a patient with type 2 diabetes was hypoglycaemic, and 21% ($n=3$) were unsure, on the basis that people with type 2 diabetes are able to produce insulin themselves, which may be considered adequate to control blood glucose levels without the need for VRIII; this is also supported by Holt and Kumar (2003). If insulin is no longer administered when a patient has diabetes, yet they continue to have IV fluids or feeds (enteral or parenteral), they are at risk of developing diabetic ketoacidosis or hyperosmolar non-ketotic state (Holt and Kumar, 2003).

Conclusion

In order to comply with the NSF and provide satisfactory care to people with diabetes in critical care, it is evident from the pilot audit that changes need to be made to the current ICU protocol. The authors of this article recognise that the pilot audit only reviewed a relatively small sample of staff. However, the results highlight significant inconsistencies in staff knowledge and practice. It is recommended by NICE and the Department of Health that all healthcare professionals have appropriate training when caring for people with diabetes (Department of Health, 2010; NICE, 2011). Indeed, all the staff who completed the audit, including those who originally claimed they had adequate knowledge, expressed that they would appreciate further education in diabetes and the care of people with diabetes in the critical care environment. The ICU policy is founded from a large source of research. However, further research is required concerning its applicability for HDU patients, and changes are necessary to make it appropriate for use with people with diabetes (see *Box 2*). A suggestion is to use the general hospital VRIII policy for people with diabetes and the revised ICU policy for people without diabetes, as the hospital policy already included the appropriate scale for VRIII. In order to implement changes to the protocol successfully, staff will require education and continued support in practice, to ensure that they understand how to use the

Figure 1. Breakdown of the responses to the question "How would you define hypoglycaemia?"

“All the staff who completed the audit, including those who originally claimed they had adequate knowledge, expressed that they would appreciate further education in diabetes and the care of people with diabetes in the critical care environment.”

protocol and to improve compliance and patient care. Education also needs to be provided to ICU doctors, as they will also be required to understand and comply with the revised protocol. Following a specified period of time, the new protocol should be audited and staff feedback obtained, so that it may be continually updated accordingly. ■

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Box 2. Recommended changes to the intensive care unit protocol.

The authors recommend that the following information is added to the intensive care unit (ICU) protocol:

- How and when to stop a variable rate intravenous insulin infusion (VRIII) for patients with diabetes.
- How to adapt care for patients with diabetes.
- When a referral should be made to the diabetes inpatient specialist nurse
- A prompt to prescribe basal insulin for patients with diabetes.
- When a patient may require more frequent blood glucose checks.
- Alternatively, a section informing staff to use the hospital VRIII for ICU patients with diabetes could be added, rather than making changes to the ICU policy.