

EDITORIAL

Does it matter where we sample blood for blood glucose control?

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In this issue of the *Netherlands Journal of Critical Care*, Bhurayanontachai describes the results of a study comparing arterial blood glucose test results with venous blood glucose test results.^[1] Arterial samples were tested with a point-of-care device, while venous samples were tested in a central laboratory. It was also determined whether arterial blood glucose test results would have resulted in different clinical decisions using a local algorithm for insulin titrations compared with venous blood glucose test results. The main finding was that the two strategies did not differ too much. Also, only two out of the 45 analysed paired samples would have led to a different clinical decision for insulin titration in this setting.

Glucose control in critically ill patients has received extensive scientific interest over recent decades. Single-centre randomised controlled trials showed benefit from a strategy aiming for normal blood glucose levels in adult patients^[2,3] and age-adjusted normal blood glucose levels in paediatric patients.^[4] Even though these findings could not be reproduced in successive multicentre trials of so-called 'strict glucose control', the 'intensive care world' has changed since the pivotal single-centre trials: hyperglycaemia is no longer accepted, and many if not all critically ill patients receive insulin intravenously for shorter or longer periods during their stay in an intensive care unit (ICU).^[5,6] The focus of blood glucose control, however, has changed over recent years, from 'strict' to 'safer' blood glucose control strategies.

Increased risks for hypoglycaemia^[7,8] caused the ICU team to obtain blood glucose tests more frequently, preferably at the bedside, and also demands more accurate ways of testing blood glucose. Not surprisingly medical companies jumped on these issues, trying to develop 'continuous glucose monitors', with varying success.^[9] Moreover, there has been more emphasis on building 'better' algorithms for insulin titration in critically ill patients, not only focusing on the blood glucose level per se, but also on several factors that could influence the blood glucose level other than the dose of insulin infused.^[9]

One major question is whether we should rely on arterial blood glucose testing or whether venous blood glucose testing is also acceptable when applying blood glucose control with insulin. Arterial blood glucose testing has been recommended by consensus for some reasons.^[10] First, arterial blood glucose levels are usually higher than venous blood glucose levels. Second, venous blood glucose levels from different sites, i.e., peripheral or central catheters, could be quite different. Of note, even though Bhurayanontachai directly compared arterial with venous blood glucose levels, it should be noted that the blood glucose levels were measured with different devices, a point-of-care device in the unit and a device in the central laboratory, which makes comparing the test results with regard to known differences in blood glucose levels in arterial and venous blood a bit risky.

One challenge almost all device accuracy studies in critically ill patients are facing is that the paired blood glucose measurements are mostly, if not exclusively, within a relatively narrow blood glucose range, i.e., hypoglycaemic and hyperglycaemic levels are seldom if ever seen. The devices, however, should be accurate in all ranges of the blood glucose levels, not in the last place because both hypoglycaemia and hyperglycaemia are associated with mortality.^[11,12] The study by Bhurayanontachai faces the same problem. Why might this have happened? First, the target of the algorithm for blood glucose control was high, higher compared with targets in earlier trials of blood glucose control. Second, it could be that nurses have become much better in preventing hypoglycaemia. Furthermore, during any study on blood glucose control, or accuracy of blood glucose monitors, there is the risk that participating nurses are aware of that study, causing them to be more aware of the importance of safe and proper blood glucose control. Finally, when blood glucose levels are measured frequently, as often is the case in accuracy studies, nurses could respond to trends in the blood glucose level, maybe allowing them to prevent hypoglycaemic or hyperglycaemic episodes. How can we tackle this specific problem, how to have

more values tested outside the normoglycaemic range? Maybe this is where 'big data' analysis could help, using approaches such as 'data mining'.^[13] Through 'data mining' of electronic medical records, coincident testing of the blood glucose level by means of a point-of-care device and in a central laboratory can be identified. These 'paired' samples can be used for accuracy testing of the point-of-care device.^[13]

One other thing Bhurayanontachai showed is that 'inaccuracies' in blood glucose measurements would not have affected insulin dosing according to their local guideline. Here we need to be a bit careful. This may very well depend on the characteristics of the algorithm for insulin titration in use. For example, in a setting where a 'strict' algorithm is used, strict meaning targeting strict normal blood glucose levels, a small inaccuracy in the blood glucose measurement may result in importantly different advice regarding insulin titrations. For instance, with an algorithm targeting blood glucose levels between 80 and 110 mg/dl, an inaccuracy of 20 mg/dl could already lead to erroneous insulin titrations, compared with one that targets much higher blood glucose levels. Note that the algorithm in use in the study by Bhurayanontachai targeted blood glucose levels between 100 and 180 mg/dl. Extrapolation of the results of Bhurayanontachai, thus, could be difficult. How could we overcome this problem? Could 'simulation studies' be of help here? Simulation studies such as 'Monte Carlo simulations' have been used to model the effect of the blood glucose measurement errors^[14] and blood glucose measurement frequencies on blood glucose control before.^[15]

So, does it matter where we sample blood for blood glucose control in critically ill patients? Maybe not, in the setting of Bhurayanontachai; maybe it does, in settings that use different algorithms – we need more studies like the one published in this issue of our journal together with data mining and simulation studies.

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