

Behind the glucose protocol

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In 2001, Belgian professor Greet Van den Berghe, PhD, and her colleagues at the Leuven University Hospital began a small revolution with the publication of the 2001 study *"Intensive insulin therapy in critically ill patients"*.

According to the study, tighter glucose control based on insulin therapy lowered rates of morbidity and mortality at the ICU. While some welcomed the study, others feared that the lower concentration of glucose recommended would lead to hypoglycemia.

acute^{care}testing.org recently spoke with Greet Van der Berghe about the study, its implications and the important role nurses play in the successful implementation of the protocol.

acute^{care}testing.org: How did you get the idea for the study?

Greet Van den Berghe: I have had a focus on

endocrine research for many years. We were looking for a marker of morbidity and mortality and we found that the lack of insulin effect in the liver was related to risk of death.

This made us think of hyperglycemia as a possible marker or mediator. Suddenly it all fell into place, but it was not until we had all the data that we saw the big picture.

acute^{care}testing.org: How long time did it take from having the idea for the study to publishing its findings?

Greet Van den Berghe: Actually, it was a very fast process. We discussed the idea for a couple months and began the study on February 2, 2000. My boss told me this would be a good day to start, as it is the annual celebration day of our university. The study ended in January 2001 and was published at the end of that year.

acutecaretesting.org: How did you choose the glucose-insulin algorithm used in the study?

Greet Van den Berghe: The algorithm developed itself during the preparation of the study by trying out the procedure with the nurses. They just wrote down what they were doing and we have not changed it substantially since.

acutecaretesting.org: There are different protocols found in literature. Which one should one follow?

Greet Van den Berghe: It all boils down to how much responsibility the nurses take or are willing to take. In my view, this controls the algorithm. Many have asked for my protocol, but those that have implemented it have probably changed it to fit the needs of their specific department.

I have heard of places where it does not work that well, and I believe this has to do with the motivation level. There are hospitals where tight glucose control is considered a task for the physician.

However, in my view nurses have to take ownership of the protocol for it to become a success.

acutecaretesting.org: Has anyone calculated how much money hospitals actually save by implementing the tight glucose control protocol?

Greet Van den Berghe: Yes, we have just finished a calculation, which will be published soon. We came up with savings of at least up to USD 3000 per treated patient, and I presume this will be an underestimation. These numbers are based on US costs.

acutecaretesting.org: Does the more frequent glucose measurements impose a risk of infections and blood loss?

Greet van den Berhge: We did not change anything in our blood sampling procedure, except the number of measurements during the first 12 hours. We

do the glucose measurement on the blood gas analyzer while we measure blood gases. Most of the patients have an arterial line, i.e. no extra sticks are needed.

acutecaretesting.org: What are your recommendations for sampling sites and glucose measuring systems?

Greet Van den Berghe: Choosing which sample type to use is a big issue. We always use arterial samples, but venous samples are probably just as good. And it is not only a question of sampling site, but also of sampling technique.

We need studies that can tell us more. With respect to the measuring system, my best recommendation is to watch out. We have tested several devices that did not provide the performance needed for the protocol. Watch out for the lower range.

Users do not question this enough, and this is something that should be thoroughly investigated. One thing is certain: The sample must be measured at the point of care due to the need for fast results.

acutecaretesting.org: What are the criteria for the analytical performance for glucose?

Greet Van den Berghe: We chose to do the study with a blood gas analyzer that provided high-quality glucose measurements, as described in my article from 2001.

As for analytical performance, the bias should be constant and small. Minus 3 to plus 8 % is probably an acceptable range as long as it is constant and preferably corrected. CV must absolutely be below 5 %. We used the Bland-Altman plot for comparison studies.

acutecaretesting.org: How many hospitals have implemented tight glucose control?

Greet Van den Berghe: That is difficult to say. I get a lot of requests on how to do it, but many still fear hypoglycemia.

acutecaretesting.org: Is hypoglycemia a real threat?

Greet van den Bergh: For decades, we have accepted hyperglycemia and feared hypoglycemia. This has given the wrong idea of what is normal and what it is not when it comes to glucose concentration levels.

It is for example OK to have a glucose concentration of 60 mg/dL, which is a concentration many healthy subjects have just before a meal. To prove that point to nurses who were concerned about hypoglycemia, I know of a group who actually measured the nurses' blood glucose levels.

Their glucose levels were normal, as expected, and by realizing how "low" these normal values are, this reassured them that the set target for blood glucose of 80-110 mg/dL is perfect. Furthermore, the impact of brief hypoglycemia is not critical within the timeframe we monitor glucose in the ICU.

It has to do with the duration of hypoglycemia. The threat is real for people with diabetes outside the ICU with for example an overnight hypoglycemia, but with the tools and personnel we have available in the modern ICU, severe side effects will not occur. Our data showed that we have never had a clinically important problem with hypoglycemia.

Evidently, alertness and motivation are again crucial.

acutecaretesting.org: Do you have any good advice for hospitals wanting to implement the protocol in their ICUs?

Greet Van den Berghe: The protocol does not work if someone from the outside comes and tells you to implement it. Nurses themselves must be motivated by the ICU physicians in charge. It is also important to take a multidisciplinary approach when implementing the protocol.

Communication with the nurses is very important. The more I speak about the protocol with my group, the more they feel motivated.

acutecaretesting.org: The protocol has really stirred things up for many hospitals. How does it feel to be in the center of this "revolution"?

Greet Van den Berghe: It feels good. I feel a great obligation to share my findings with others, because it can save people's lives. However, I would feel even better if we had confirmation studies.

So far only ours and some smaller studies have been conducted. More evidence-based studies would add credibility to our initial findings. Our own repeat study in medical ICU patients is about to be finalized soon.

acutecaretesting.org: How has the publication of the protocol affected your life?

Greet Van den Berghe: Dramatically - both privately and professionally. My working days are long, and there is so much interest in the studies we have conducted that I could easily spend all my time traveling and giving presentations on the protocol. I will probably feel close to the area around tight glucose control for the rest of my life and follow other studies in this field.

Currently, my research group has expanded to eight people doing basic research on avoiding hyperglycemia. We are learning so much that I am convinced we will come up with new findings in the future.

acutecaretesting.org: Are there still any challenges for you in this area?

Greet Van den Berghe: We have to unravel the mechanisms of avoiding hyperglycemia and, like I said, there is still a lot to learn. Another major challenge is to teach nurses how to implement and maintain tight glucose control.

It would be great, if we found a smarter way to do this. Besides that, we need studies that prove the protocol can be used outside intensive care, i.e. in medical wards, pediatric ICU, departments for stroke patients, etc. We also need to investigate the hypothesis we started out with, namely the impact of optimizing insulin effect in the liver.

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