Commentary

Blood glucose increments as a measure of body physiology

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Abstract

The initial distribution volume of glucose (IDVG) can be calculated from the arterial plasma glucose level between 3 and 7 min after a bolus intravenous infusion of 5 g glucose. Ishihara and colleagues have investigated the value of IDVG over the past decade. Although IDVG is simple and cheap to measure, there have been several very different proposals regarding what it should be used for. The most interesting and logical correlate is that between IDVG and cardiac output. A recent study showed that it does not matter much whether the calculation of IDVG is based on blood or plasma samples.

In this issue of *Critical Care* the Japanese research group headed by Ishihara [1] highlight the issues involved in measuring blood glucose. Their approach does not involve attempting to reduce mortality by controlling the glucose level; rather, they use its response to a glucose bolus as an index of physiological parameters such as plasma volume and cardiac output. Their work is admirable, and more effort should be given to simplifying the measurement of parameters that are useful in intensive care. We should not overlook the potential utility of glucose measurement, as pioneered by Ishihara over the past decade.

Ishihara and coworkers introduced the concept of the initial distribution volume of glucose (IDVG), which is determined by measuring the arterial blood glucose level just before and repeatedly for about 10 min after a bolus infusion of 5 g glucose is administered. The data are analyzed by computer according to a one-compartment kinetic model, in which the concentration–time profile is represented as a function of glucose clearance and the volume of distribution of administered glucose. It is crucial that measurements are taken from an arterial line because glucose is rapidly distributed over 65% of the total extracellular fluid volume as soon as the blood passes through the capillary bed [2]. When measured in this manner the glucose concentration extrapolated to time zero is diluted in proportion to cardiac output. This principle is identical to that of thermodilution. The glucose clearance then becomes a hybrid of the distribution of exogenous glucose between plasma and the interstitial fluid and the glucose uptake into cells.

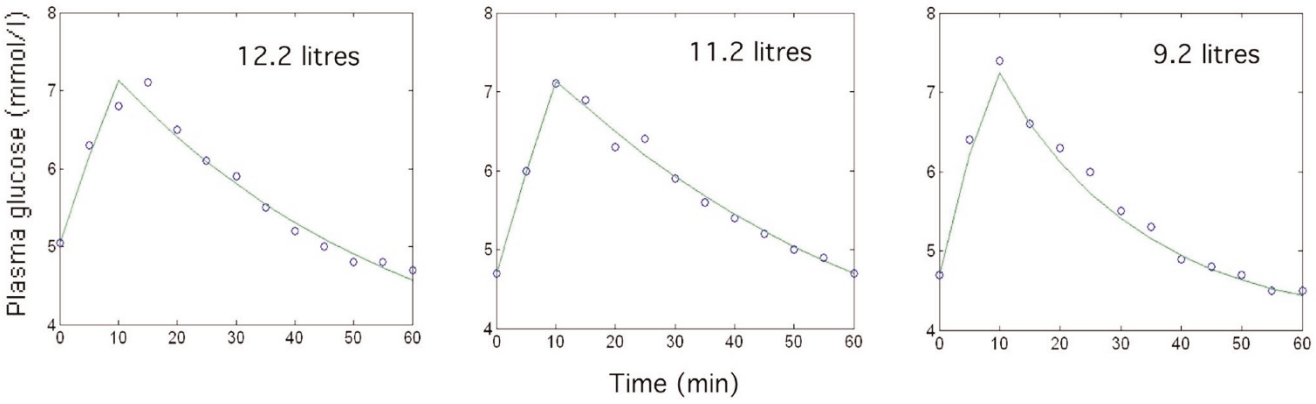
This approach was first reported in 1993, and Ishihara and coworkers [3,4] concluded that only two samples are needed to estimate IDVG: one before the bolus infusion and another 3 min later. Such a simplification is justified because variations in glucose clearance and endogenous glucose production are of little importance over short time increments, at least when it is applied in a fairly coherent group of patients. In subsequent studies, however, sampling was usually extended to 7 min.

There have been several additional proposals concerning what IDVG represents. IDVG correlates reasonably well with plasma volume in bled dogs [5] and with the incidence of hypovolaemic hypotension after surgery for oesophageal cancer [6], although these findings may merely reflect the effect of hypovolaemia on cardiac output. In later studies, Ishihara and coworkers [7,8] suggested that IDVG is a measure of the 'central' extracellular fluid volume as well as of cardiac preload.

Their views became more complex when indocyanine green was introduced as a direct measure of plasma volume. A deviation in the ratio of indocyanine green to IDVG is said to indicate capillary leakage of proteins after cardiac surgery, because this marker binds to proteins [9]. As for glucose clearance, however, <10 min is a very short period for ongoing capillary leakage to make a difference. Furthermore, any such leakage would cancel out if a concentration–time curve of dye is extrapolated back to time zero. Alternative explanations should not be overlooked because control methods designed to measure capillary leak (such as use of radioactive albumin) were not applied, and a similar increase

IDVG = initial distribution volume of glucose.

Figure 1



Relative stability of the volume of distribution of glucose when 5 g glucose is given by intravenous infusion over 10 min on three occasions immediately following each other in one healthy volunteer. Plasma glucose was measured in venous blood. Ishihara and coworkers infuse glucose even faster and use the arterial plasma glucose level measured between 3 and 7 min to calculate the volume of distribution. Figure used with courtesy of Dr Zule Sicardi.

in the indocyanine/IDVG ratio also occurs early after induction of intravenous anaesthesia [10] and after administration of histamine [11].

All of these ideas about the physiological meaning of IDVG may be difficult to differentiate for the intensivist. Although IDVG perhaps most directly reflects a fraction of the extracellular fluid volume, several of Ishihara and coworkers' later studies actually strongly support their first interpretation, namely that IDVG indicates cardiac output. This correlation between IDVG and cardiac output is logical and renders IDVG highly useful because it both predicts a key parameter in body physiology and can be measured quickly and with little effort and cost. Unfortunately, this view is somewhat countered by the fact that IDVG is said to be undisturbed by vasoactive drugs, although most of these agents actually change cardiac output [12].

What the limits are and the errors that may be hidden in the determination of IDVG are the most recent issues. IDVG is apparently accurate if it is repeated after 30 min in clinical patients [13], although the study presented in this issue [1] holds that blood glucose remains elevated for another 30 min, which is also the case in healthy individuals (Fig. 1).

In study presented in this issue, Ishihara and coworkers [1], in addition to repeating their previous finding that a 3-min postinfusion sample is sufficient to predict IDVG [3,4], also compare calculations of IDVG based on plasma glucose and blood glucose. The difference is quite small and, logically, should be accounted for by displacement of glucose from the parts of the red blood cells that consist of haemoglobin. The authors found no correlation between the plasma–blood difference in IDVG and the haematocrit, but I believe that haemoglobin would be a more reasonable comparitor because haemoglobin reflects differences in the water content of blood [14]. Nevertheless, the authors conclude that measurements can be based on both plasma and blood samples, although these are not interchangeable. Once chosen, use of either body fluid should probably be consistent.

It appears that the IDVG will be ready for limited implementation once it has been tested by additional independent groups. The method is safe and easy to apply, but intensivists must reach a consensus about its place in the clinic and what it really shows. I foresee that IDVG may serve as a screening test to separate patients with a hyperkinetic circulation from those with a hypokinetic one.

Competing interests

The author(s) declare that they have no competing interests.

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