ARTICLE

Measuring the glycaemic index – consensus and issues of debate

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South Africa is in the process of legislating food labelling for the glycaemic index (GI). This paves the way for inclusion of specific health messages regarding the GI on product labels. However except for the Food and Agriculture Organization (FAO) guidelines there is currently no internationally approved, detailed and standardised method for determination of the GI. The South African Department of Health therefore convened a working group consisting of scientists and delegates from the industry in order to formulate a scientifically sound and standardised method of GI determination. The purpose of this process is to enable comparison of GI between foods and to provide health professionals with a scientifically sound dietary tool. Consensus has been reached on most issues pertaining to this standardised method although some issues of debate still remain, owing *inter alia* to lack of convincing scientific evidence. This article focuses on the proposed methodology used for determination of the GI for labelling, the consensus that has been reached, and in particular some of the issues of debate. We also make recommendations on how to handle these issues.

In order for labelling regulations governing use of the glycaemic index (GI) on foods to be truthful, not misleading, and to play an educative role, a standardised methodology for GI measurement needs to be followed. As with all areas of science, lack of data promotes controversy. Without new data, it will be difficult to establish a scientifically sound concept of the GI.[1] The usefulness of the GI concept as a public health strategy and in particular standardisation of the GI methodology is a subject currently receiving worldwide attention. The potential role of the GI in educating diabetic consumers on healthier carbohydrate-containing food choices is invaluable. Until at least a method for GI measurement has been standardised, the GI will not find universal acceptance as a dietary tool and will be criticised continuously. A South African Department of Health (DOH) working group has therefore been convened to develop a standardised method for use in South Africa paving the way for GI labelling and subsequent consumer education.

Definition of the GI

The GI is defined as the *incremental area* under the blood glucose response curve of a *50 g carbohydrate portion* of a test food expressed as a percentage of the response to the same amount of carbohydrate from a *standard food* taken by the same subject.[2] The italicised items are discussed below because different interpretations of these concepts may profoundly affect the GI obtained.

Incremental area under the curve

There are several possible ways of calculating the area under the blood glucose response curve. One is to calculate the total physiological response to a carbohydrate load,[3] starting from the lowest glucose concentration in the response curve (including hypoglycaemic values, lower than the fasting value). Another option is to calculate the area under the curve (AUC) starting from the fasting value as baseline and therefore excluding any part of the curve that drops below the fasting value. The latter method was chosen by the DOH working group as the method of choice because it is used most often internationally and is also recommended by the FAO/World Health Organization (FAO/WHO) Expert Consultation Group on Carbohydrates in Human Nutrition.[2]

50 g carbohydrate portion

Not all carbohydrates ingested contribute to the blood glucose response. Free sugars and starch are the main contributors to blood glucose while resistant starch and non-starch polysaccharides move through to the colon where they are either fermented into short-chain fatty acids (mainly resistant starch and soluble fibre) or excreted (mainly lignin and cellulose). Fructose and galactose are not immediately available as glucose after absorption. They are mainly converted to glucose only once they pass through the liver, and therefore play a smaller part in the immediate glucose response. Not all ingested carbohydrate should therefore be included in the 50 g portion.

Other terms that cause confusion are the terms

'*glycaemic*' and '*available*' carbohydrates. These two terms are not synonymous. Available carbohydrates also include resistant starch and soluble fibre, because they are available to the body, although not as glucose but as short-chain fatty acids. Glycaemic carbohydrates, on the other hand, include only carbohydrates that provide carbohydrate for metabolism.[2] We therefore support the proposal that in the determination of the 50 g portion only '*glycaemic carbohydrate*' should be used, since this is the carbohydrate fraction that elicits the blood glucose response.[2,4] This glycaemic carbohydrate fraction should be analysed for each product. The calculated '*carbohydrate by difference*' value, which is indicated in the South African Food Composition Tables, should not be used as this was not directly measured. The method of Englyst *et al*.[5] is an example of an analytical technique that can be used to determine different starch fractions in a product, e.g. free sugar glucose, rapidly available starch, slowly available starch and resistant starch.

Standard food

Either glucose or white bread can be used as the standard food.[2] The DOH working group decided to use glucose as the standard food for labelling purposes since it was the chosen food used in an international inter-laboratory study.[6] The aim of the latter study was to evaluate the method recommended by the FAO/WHO in order to determine the magnitude and sources of variation in the GI values obtained by experienced investigators in different international centres. Glucose is easily standardised whereas differences in locally produced white breads might add to analytical variation. However, the abovementioned study found that the variation in GI of locally produced white bread (one of the test foods) did not differ from the variation in GI of other centrally produced test foods (instant mashed potato, white spaghetti and pot barley) and might therefore still be a viable option in the selection of a standard food.

Before labelling can be legislated a standardised

Methodology

method of GI determination has to be agreed upon. Guidelines for such a methodology have been published by the FAO,[2] and another more detailed and standardised method has been proposed in the draft regulations governing the labelling and advertising of foodstuffs.[7] The full proposed methodology will therefore not be discussed in this article. Only some of the most important outstanding issues will be highlighted.

Analytical principles

Good laboratory practice guidelines must be followed at all times, which means that all data can be traced back to source at any point in time. The ethical principles as outlined in the Declaration of Helsinki and science-based practices should also be applied throughout the process. Since GI measurement is in essence an experimental procedure a human ethical committee must approve all measurements in humans and signed informed consent must be obtained from all volunteers.

Pre-test meal

All subjects should consume a standardised pre-test meal no later than 22h00 on the evening before testing. Examples of such meals have been included in the proposed standardised methodology. The rationale behind this standardised pre-test meal is to prevent components of the evening meal (before the testing) from influencing the glycaemic response of the test meals ('second meal effect').[8] However, Campbell *et al*.[9] recently showed that there was no difference in the mean incremental area under the blood glucose curve of 13 subjects following either a standardised pre-evening meal or a non-standardised, normal pre-evening meal. This gives some indication that a standardised pre-evening meal may not be essential, but some doubt exists since the study needs to be verified and also seems to be somewhat underpowered.

Consumption of meals

Each subject should consume both the standard and the test meals on different occasions. However, the standard meal should be consumed three times and the average of the three tests should be used for calculation of the GI. When consuming standard test meals under standardised conditions the glycaemic responses of the same subject will vary from day to day – this is called the within-subject variation. According to Wolever *et al*.[10] the mean within-subject variation of the glycaemic response after consumption of either glucose or white bread is 15% in type 2 diabetics, 23 - 25% in non-diabetic subjects and 30% in type 1 diabetics. Since the GI is the individual's glucose response to a test food versus to a standard food, it is crucial that the glucose response of the standard food be measured accurately. Because of the high within-subject variation of the glucose response, the three measurements of the standard food are essential for the accurate calculation of the GI.

The draft regulations governing the labelling and advertising of foodstuffs[7] suggest that when the same subjects are used on a regular basis, the reference food need only be tested every 6 months. This presents some challenges. Since the GI is expressed as the individual's glycaemic response to a test food compared with a standard food it is essential that there be no change in glucose homeostasis from the time the standard food is consumed until the test food is consumed. This is, after all, the principle on which the GI is based. However, over a 6-month period several factors might influence glucose homeostasis and these should be strictly controlled for if the standard food is to be consumed only every 6 months. Some of these factors include change in exercise pattern,[11] weight

change,[12,13] presence of infections,[14,15] change in alcohol consumption patterns,[16] change in stress levels,[17] seasonal variation in glucose and insulin levels,[18] use of certain medications, e.g. corticosteroids (Meticorten), oestrogens (Premarin), diuretics (Dyazide), nicotinic acid, beta-blockers (Inderal or Tenormin) and even aspirin.

Another basic scientific prerequisite is that all subjects should receive all treatments but in random order. The current proposal is that the standard food is only tested once every 6 months, which means that there will be no randomisation of subjects to intervention since subjects will consume only the test food at a given time. This might further lead to introduction of analytical bias since the standard and test food GI analysis will not take place on the same day. It is therefore proposed that facilities that measure GI should test foods in batches with the appropriate measurement of standards to ensure randomisation to treatment. More than one group of volunteers could be used to increase analytical throughput as long as the appropriate randomisation is done.

Blood sampling

Consensus has been reached on the use of capillary blood for glucose determinations, provided that the capillary blood sample is obtained in a standardised manner. It was found that capillary blood samples had a lower coefficient of variation (CV) than venous samples and were on average higher than in venous plasma.[6,19]

Type of subjects in experimental groups

Consensus has not been reached on the issue of whether subjects for GI determination may include both normal and diabetic individuals. There is some indication in the literature that the GI of specific foods is similar between normal and diabetic individuals. According to Jenkins *et al*.[20] there was a significant relationship between the GI of 15 foods in normal and diabetic volunteers ($r = 0.756$, $p < 0.01$). However, the mean area under the 3-hour blood glucose curve for the 15 foods tested in the diabetic subjects was 681 ± 54 mmol/l/min which was almost 5 times that of the same foods tested over 2 hours in normal subjects (119 ± 11 mmol/l/min). It is also worth while mentioning that this comparison was not done in one study with mixed subjects but in two different studies each containing a homogeneous group of subjects (either diabetics or normal). In a study comparing GIs of food in type 1 and 2 diabetics, Jenkins *et al*.[21] found that GIs for type 1 and type 2 diabetics were similar ($r = 0.9$, $p < 0.01$) and also did not differ significantly from each other. However, this conclusion is based on a subanalysis of between 4 and 7 subjects per group. The analysis is therefore underpowered, and it is not possible to conclude that the lack of a difference is real since there is a high likelihood of a type II error (not seeing a difference when in actual fact there is one). In another study, Wolever *et al*.[22] concluded that the mean GI values for foods correlated significantly ($r = 0.927$, $p < 0.001$) in type 1 and 2 diabetics. However, the study also found that the difference in GI between type 1 and 2 diabetics was statistically significant for 19 of the 20 individual test meals. Therefore, although correlations exist between the GI of normal individuals, type 1 and type 2 diabetics, the absolute values may differ significantly and for that reason the three types of subjects should not be combined into one test group for GI determination.

Another reason for not combining diabetics and healthy individuals is the fact that the calculation of the AUC for diabetics is done over a period of 3 hours while for normal individuals it is done over only 2 hours. After a thorough literature search on Pubmed, no studies could be found in which diabetics and normal individuals were combined in one group. Therefore, because of a lack of scientifically sound, evidence-based research it is suggested that diabetics and normal individuals be divided into two separate groups for GI determination.

Number of subjects

To determine the number of subjects required to do a scientific study a power calculation should be done.[23] If enough subjects are not included in the experimental groups it is not possible to know if the GIs of two foods are different from one another because real differences may be obscured owing to a too-small sample size. The idea behind a power calculation is to give results a certain amount of power. Studies can have different degrees of power, but a normal/acceptable power for a study is usually 80% power at a 5% level of significance. The 80% power means that, assuming the means really are different, the experiment has an 80% chance of finding a significant difference at $p < 0.05$, and therefore an 80% chance of detecting the difference. The 5% significance means there is a 95% chance that the means really are different or a 5% chance or less that the means are the same.

The formula for the power calculation to have 80% power with 5% significance for paired samples with normal distribution is: $n = ([0.842+1.96]^2 \times SD^2)/CD^2$ where n is the number of subjects. The critical difference (CD) is the difference that should exist between the GIs of two foods in order for them to be considered clinically different from one another. The SD is the standard deviation of the variable, in this case the GI. There is currently no standardised, agreed upon critical difference value for the GI. In the absence of a known critical difference two rules of thumb are often applied. The one assumes 10% to be a significant difference and the other considers 1 SD to be a clinically important difference. Both these approaches are widely used, especially in cases where the real clinically relevant difference is not known. The SD for GI values of healthy individuals, measured using

capillary blood, is ± 20%.[6] In his review Leeds[24] showed that if the GI of the whole diet was reduced from 70% to less than 60%, there were clinically significant improvements in insulin-stimulated glucose uptake and in some markers of risk of vascular disease. It must be kept in mind that this figure is not the result of changing a few individual items but reflects the total diet as a whole. Miller[25] found similar results and indicated that measurable clinical gains were found in diabetics when the GI of their whole diet was reduced by more than 11% by substituting approximately 50% of their carbohydrates from the high-GI category with low-GI foods. Unfortunately it is not yet clear whether this difference of ~10% will result in improved clinical outcome when two individual products are compared.

As an example, to calculate the number of subjects necessary to do a GI determination, a CD of 10% will be used. If $n = ([0.842+1.96]^2 x SD^2)/CD^2$, a CD of 10% will result in 32 subjects per group. If a CD of 20% is chosen, 8 subjects should be included in a group. The sample sizes therefore depend on the size of the difference in GI that will result in a clinically significant difference, a factor that is as yet undefined.

Another way of looking at this issue is to determine how precise measurement of the GI should be. This is done by reporting the 95% confidence interval (CI) of the reported mean; this CI is, *inter alia* dependent on the number of subjects. CIs give the estimated range of values which is likely to include the true mean. A 95% CI is often used and it means one can be 95% certain that the true mean of the population will lie within that interval, e.g. 56 (52 - 60). Should more than 30 subjects be used for the determination of the GI, e.g. 32 as indicated with the power calculation, then the 95% CI is determined as follows: mean ± 1.96 x $SD/\sqrt{n}$. If for example a GI of 50 is used, then the 95% CI with 32 subjects would be 43.1 - 56.9. If less than 30 subjects are used the equation is as follows: mean ± C x $SD/\sqrt{n}$, where C is the critical value of 2-tailed t for df of n-1. If 10 subjects are used, the CI for the mean GI of 50 will be 35.7 - 64.3, a much larger interval than that obtained with 32 subjects. Therefore the interval within which you can say with 95% confidence that the true mean will be, increases significantly as the number of subjects decreases. It is therefore much more difficult to determine if the GI of two products differs when the sample size is small because of the relative uncertainty (larger interval) of the true mean GI of the two samples. This is in agreement with the relatively large sample size needed, as determined by the power calculation, and also stresses the importance of a large enough sample size in order to make labelling of GI practical.

The number of subjects used to determine the GI becomes even more important when considering the large variation in GI measured in different subjects. The results presented by Venter and co-workers[19] in this issue of the *Journal* show the variation in GI for a particular food between subjects. From these results it is clear that a particular food (mean GI of 78) may have a high GI in some individuals (6 out of 19) and a low GI in others (8 out of 19). Even though the mean GI was categorised as 'high', the food was measured as having a low GI in more subjects than measured a high GI. These data cast serious doubt on the notion that foods with a low GI will usually cause a low glycaemic response in most individuals and vice versa. Although their study was not designed to investigate this phenomenon, it is worth while investigating this issue in more depth to find the most important sources of variation, enabling health professionals to utilise the GI accurately as a dietary tool.

GI categories or continuum?

Labelling

It is scientifically misleading to present only means without giving CIs, the estimated range of values likely to include the mean. Fig. 1 presents results of an experiment undertaken in our laboratory comparing the GIs of two oats products.

The horizontal lines indicate the different GI categories

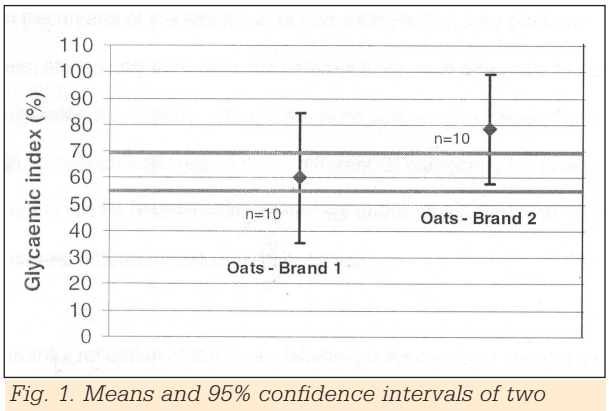

Fig. 1. Means and 95% confidence intervals of two different oats products.

(0 - 55 = low, 56 - 69 = intermediate, 70 - 100 = high) as suggested by the draft regulations governing the labelling and advertising of foodstuffs.[7] A very important aspect to take into consideration is the fact that the CIs sometimes fall across two or even all three of the suggested categories. The mean of brand 1 was 60, while the mean of brand 2 was 78.5. These two means clearly fall in two different categories, viz. intermediate and high. But if one considers the 95% CIs of these two means, the oats with a mean of 60 has a 95% CI ranging from 35 to 85. It can therefore be stated with 95% confidence that the true mean of the population falls somewhere between 35 (low GI) and 85 (high GI). The 95% CI of the oats with a mean of 78.5 ranges from 58 to 99 indicating that the true mean can range from 58 (intermediate GI) to 99 (high GI). In conclusion, although the means of the two types of oats indicate that they are in two different categories, statistically they were not different from each other owing to their large CIs, indicating that there is no difference between these two products. This

complicates use of these different GI categories for labelling. These two oats products will be labelled intermediate and high GI respectively, while in effect there is no real difference between their GI values!

A more truthful reflection of the GI for labelling purposes is to present the GI values on a continuum and not categorised with fixed cut-off values. Fig. 2 is an example of such a continuum.

The GI value is then presented as a mean (dot) with

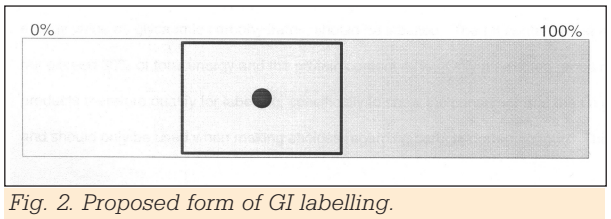

Fig. 2. Proposed form of GI labelling.

95% CI (square). When labelling packaging, neutral colours should be used. The colour red should not be used to signify a high GI, as red commonly indicates danger, and customers might interpret such products as unhealthy. That is an important misconception, which has the potential to be misused in the marketing of foods. This is in agreement with the philosophy that there are no good or bad foods, only good or bad diets. By presenting the GI as a continuum, two products can still be compared without specifically categorising them as high or low GI. Products can be evaluated by comparing the position of the GI value on the continuum. In this way consumers can still make an informed decision about which of two products has a higher or lower GI.

Role of GI labelling in food choices

It is essential that consumers understand the role of GI in food choices. The GI should not be used as the only tool when making food choices – it is most definitely not there to contradict or replace the Food Based Dietary Guidelines. The GI can only be used to make choices regarding carbohydrate-rich foods. For that reason the DOH working group has advised that only foods containing 40% or more of the total energy value as glycaemic carbohydrates, should be labelled. The fat content must also not exceed 30% of total energy and the protein content 42%. Only a selected group of products therefore qualify for labelling, specifically to show the consumer that the GI can and should only be used when making choices regarding carbohydrate-rich food. This will also prohibit misuse of GI labelling, for instance producers of products with a low carbohydrate, high fat content will not be able to label them 'low-GI' foods.

Substitution of one high-GI food with one low-GI food will probably not result in any clinical gains, but if the GI of the whole diet can be decreased then improvement in clinical symptoms can be expected, as has been proved in several studies.[20-25] This must be kept in mind when discussing the labelling of products for GI. The aim is not solely the comparison of two individual products, but rather the use of the label for continuous healthy food choices in order to improve the quality of the diet as a whole.

Despite the variations in methodology for GI determination and many of the valid objections to its use in clinical practice it is quite clear that the GI has a role to play in the management of diabetes and impaired glucose tolerance. In addition to this, Opperman and co-workers[26] have shown that application of the GI may also have health implications in terms of dyslipidaemia. Correct GI determination forms the basis of correct application. It is essential to determine GI in a scientifically valid way in order for us to know the real public health impact of its application in both diabetic and other populations.

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