“Correlation of Several Formulas to Evaluate Insulin Sensitivity With the Predicted M Index (PREDIM) in Healthy Individuals”

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1. INTRODUCTION

The term insulin sensitivity-insensitivity is referred to for the first time in 1936 by Himsworth, who took a background from redactions dating back to 100-200 BC. of C. Insulin sensitivity is defined as its effectiveness in lowering blood glucose by promoting glucose uptake by muscle and adipose tissue cells, increasing hepatic glycogen production, and reducing hepatic glucose production. [2,3] Therefore, insulin resistance is a pathophysiological phenomenon in which, for a given concentration of this hormone, an adequate reduction in blood glucose levels is not achieved, which is results in the event for which the individual is able to maintain a normal tolerance to glucose over finite periods and comes intolerance carbohydrates and at consecuence, the occurrence of various diseases as diabetes mellitus, the arterial hypertension and central obesity.[4,5]

Early diagnosis of insulin resistance along with timely intervention can prevent the onset of these conditions. He currently has several methods for measuring sensitivity, within which the most accurate and precise, considered the "gold standard" is the clamp to hyperglucemic-hyperinsulinemic. However, they are expensive and time-consuming and personnel-intensive, so they are limited for use in specialized experimental clinical research centers and not as a diagnostic means. This has led to the search and development of indices that allow to quantify insulin sensitivity/resistance, classified according to the data used for the calculation in:[7]

1. Indices calculated using fasting plasma concentrations of insulin, glucose and triglycerides: HOMA-IR (Homeostatic Evaluation Model), Quantitative verification of insulin sensitivity (QUICKI), insulin sensitivity (ISI), Raynaud's, fasting insulin resistance (FIRI), Bennett, triglycerides and glucose (TyG).
2. Indices calculated using plasma insulin and glucose concentrations obtained over 120 min of a standard (75 g glucose) PTOG: Hyperglycemic-hyperinsulinemic clamp (CLAMP), McAuley, Belfiore, Cederholm, Avignon, Stumvoll, Gutt, Matsuda.

Recently, an index based on the oral glucose insulin sensitivity index (OGIS) in combination with anthropometric variables, called PREDIcted M (PREDIM), has been proposed; however, there is no evidence of its validation with respect to the various indices for the evaluation of insulin sensitivity, so the objective of this protocol is compare them with the afore mentioned indices.[8]

2. MATERIALS AND METHODS

2.1 Study desing

An analytical cross-sectional study will be carried out.

2.2 Universe of work

Healthy male and female population, 30 to 60 years old, residents of the Guadalajara metropolitan zone.

2.3 Sample size

The sample size was calculated with the formula for simple correlation in a group [9]:

$$n = 3 + \frac{K}{C^2}$$

	PREDIcted M (PREDIM)
	Insulin sensitivity
Confidence level	95 %
Statistical power	80 %
K ($Z\alpha + Z\beta$)	13.0[9]
R	0.692[8]
C= $0.5 \ln \frac{1+r}{1-r}$	0.8517
N	20.92
n with 20 % losses	**25**

2.4 Selection criteria

2.4.1 Inclusion criteria

- Both genders
- Age 30 to 60 years
- BMI <25 kg/m^2
- Patients who are not sedentary or who participate in heavy physical activities
- Stable weight in the last 3 months

2.4.2 Exclusion criteria

- Blood pressure >120/80 mmHg
- Glucose >100 mg/dL
- Glucose postprandial >140 mg/dL
- Cholesterol >200 mg/dL
- Triglycerides >150 mg/dL
- Smoking
- Women with polycystic ovary syndrome
- History of metabolic, cardiovascular, thyroid, renal, pancreatic and/or arterial hypertension disease
- Use of medications that modify insulin sensitivity (corticosteroids)
- Previous surgery or infection
- Symptoms of vomiting and/or excessive nausea

2.4.3 Elimination criteria

- Nausea and/or vomiting
- Feeling faint or faint
- Intolerance to oral anhydrous glucose load
- Withdrawal of consent under information

2.5 Variables

2.5.1 Independent variable

- PREDIcted M (PREDIM)

2.5.2 Dependent variables

- Insulin sensitivity
- McAuley index
- Belfiore index
- Cederholm index
- Avignon index
- Matsuda index
- Gutt index
- Stumvoll index
- HOMA-IR index
- ISI index
- Raynaud index
- QUICKI index
- FIRI index
- Bennett index
- TyG index

2.5.3 Intervening variables

- Follicular phase of a woman's menstrual cycle.

2.6 Study groups and administration of the intervention

- 25 healthy patients will be tested for oral glucose tolerance **test**.

2.7 Measurement and evaluation procedures

2.7.1 Clinical determinations

Age:

Patients from 30 to 60 years old will be included volunteers who agree to participate and sign informed consent, residents of the metropolitan area of Guadalajara.

Gender:

It will be registered as M (Male) and F (Female).

BMI:

It will be obtained from the division between the weight in kilograms and the height in square meters (kg/m^2).

Waist circumference:

It will be measured with a tape measure of flexible material graduated in centimeters (cm), with the subject in a standing position, for which, the tape will be placed in a plane parallel to the horizontal and without clothing at the level of the measurement. The tape will be placed at the level of the middle zone between the costal border and the iliac crests at the end of a normal expiration

Weight:

Measurements will be recorded in kilograms (kg) using a stationary TANITA® electrical bioimpedance scale. It will be measured with the participant in a standing position and wearing light clothing, without footwear and with the bladder evacuated before the measurement.

Blood pressure:

Measurements will be recorded in millimeters of mercury (mmHg) using the OMRON HEM 907 XL digital sphygmomanometer. For this, the subject will be placed in a sedative position and after 15 min of rest, a bracelet will be adjusted 3 cm above the fold of the elbow of the left arm. 3 intakes and an average blood pressure will be taken.

2.7.2 Laboratory determinations

For serum glucose measurements (fasting and PTOG at 3 h), secretion and sensitivity to insulin, total cholesterol, triglycerides, creatinine and uric acid, a catheter will be placed for the venous blood sample, the measurements will be made by simple enzymatic-colorimetric techniques with an automated clinical chemistry analysis equipment XL-100Erba® brand, which will be routinely calibrated according to the general laboratory log and will be operated by a single certified chemist assigned to this study.

2.7.3 Calculations

Insulin sensitivity:

it will be calculated with the indices:

Index	Formula
PREDICted M (PREDIM)	$A + B \times log_e(OGIS) + C \times log_e(IMC) + D \times log_e(2hGlu) + log_e(INSf)$
Matsuda	$\frac{10000}{\sqrt{(G_0 I_0)(G_{mean} I_{mean})}}$
McAuley	$e[2.63 - 0.28\ In(I_0) - 0.31\ In\ (TG_0)]$
Belfiore	$\frac{2}{ISI_{Belfiore}} = \frac{G_s}{G_N} \times \frac{I_s}{I_N} + 1$
Cederholm	$\frac{75000 + (G_0 - G_{120}) \text{ x } 1.15 \text{ x } 180 \text{ x } 0.19 \text{ x } body\ weight}{120 \text{ x } Glu_{mean} \text{ x } log(Ins_{mean})}$
Avignon	$Sib = \frac{10^8}{I_0\left(\frac{\mu U}{l}\right) \times G_0\left(\frac{mmol}{l}\right) \times VD}$ $Si2h = \frac{10^8}{I_{120}(\mu U/l) \times G_{120}(mmol/l) \times VD}$ $SiM = \frac{(0.137 \text{ x } Sib) + Si2h}{2}$
Stumvoll	$0.156 - 0.0000459 \text{ x } I_{120}[pmol/l] - 0.000321 \text{ x } I_0[pmol/l] - 0.00541 \text{ x } G_{120}(mmol/l)]$
Gutt	$\frac{75000 + (G_0 - G_{120})(mg/dl) \times 0.10 \times PC}{120 \times G_{mean}(mmol/l) \times \log [I_{mean}](\mu U/l)}$
HOMA-IR	$\frac{(Fasting\ insulin)(\mu IU/ml) \text{ x } (Fasting\ glucose)(mmol/l)}{22.5}$
ISI	$\frac{10000}{(fasting\ insulin) \text{ x } (fasting\ glucose)}$
Raynaud	$\frac{40}{fasting\ insulin}$
QUICKI	$\frac{1}{log(fasting\ insulin)(\mu IU/ml) + log(fasting\ glucose)(mg/dl)}$

FIRI	$\frac{(fasting\ insulin)\ \mathrm{x}\ (fasting\ glucose)}{25}$
Bennett	$\frac{1}{log(fasting\ insulin)\ \mathrm{x}\ log(fasting\ glucose)}$
TyG	$\frac{Ln(fasting\ triglycerides)(mg/dl)\ \mathrm{x}\ (fasting\ glucose)(mg/dl)}{2}$

2.7.4 Description of the study

Scrutiny visit

All patients will be scheduled at 8:00 AM with a minimum of 8 hours of fasting. The candidate volunteers will be provided with the information regarding the study, and the benefits to their health, the possible adverse effects, the objectives and the methodology that will be implemented will be indicated, with the purpose of submitting to the patient's consideration the signature of the consent under information to accept to participate. Once signed, the screening tests will be carried out according to the inclusion criteria, as well as capturing the clinical history and the complete physical examination. A venous blood sample will be taken for evaluation of clinical biochemical selection criteria, which include serum concentrations of: fasting glucose, lipid profile, creatinine and uric acid.

All participants who satisfactorily meet the selection criteria will be included in the intervention phase..

Baseline visit (Day 1)

The patient will be scheduled at 8:00 AM with a minimum of 8 hours of fasting. Weight, height, waist circumference and blood pressure will be taken. Subsequently, a catheter will be placed for the venous blood sample; an oral glucose tolerance and insulin sensitivity test will be performed, for which a 75 g dose of glucose dissolved in water will be administered orally. After the ingestion of the glucose solution, the venous blood will be taken at times 0, 30, 60, 90, 120, 150 and 180 minutes.

3. STATISTIC ANALYSIS

Statistical analyses will be performed using SPSS statistical software (version 25). Values will be presented as measures of central tendency and dispersion, mean ± standard deviation. Nominal variables in numbers and percentages. The Kolmogorov-Smirnov test will be performed to determine if the variables follow a normal distribution. Spearman correlation coefficients will be used to analyze the univariate relationship between index Predicted M (PREDIM) technique with various indices (McAuley, Belfiore, Cederholm, Avignon, Matsuda, Gutt, Stumvoll, HOMA-IR, ISI, Raynaud, QUICKI, FIRI, Bennett and TyG). A *P* value less than 0.05 will be considered significant.

4. FINANCING

The financing will be by own resources of the University of Guadalajara.

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