Research Article

Proposal for a new oral disposition index with OGIS as a marker of insulin action

Abstract

Aim: The euglycemic clamp is the gold standard for measuring insulin action, but has a disadvantage that makes it impractical. There surrogates as OGIS, based on a mathematical model derived from kinetic studies of plasma glucose humane methods. It has better performance over other options (Matsuda, HOMA, Quicki). Searching an integrated manner the compensation capacity of the beta cell to different states of insulin sensitivity, disposition index, which serves as a predictor developed of incident diabetes. Can be calculated using surrogates indexes both secretion and action insulin. Present study proposes using OGIS as a marker of insulin action and a new disposition index.

Materials and methods: All OGTT of 3 to 5hours made in 2007 to 2013 at INNSZ were included. The secretion index and action of insulin were calculated too. The oral disposition index (IDO) was estimated as the product of (Delta 0-30insulin/delta 0-30glucose x (1/basal insulin). OGIS was used as a marker of insulin action and HOMA-B as a secretion marker. Their correlation and concordance were evaluated.

Results: Data from 2097 patients were collected, only 1619 with complete information were included in the analysis. Its main features were: 73%(1177) women and 27%(442)men; 816(50%) BMI>30, 500(31%) were overweight; 1039(64%) were categorized as normal glucose tolerance, 175(11%) with IFG, 194(12%) with IGT, 139(9%) with IGT+IFG and finally 72(4%) with DM2. There were significant differences in the value of IDO by comparing status of glucose tolerance (normal:0.21, IFG:0.11, IGT:0.10, DM2:0.08, p<0.001). When OGIS was including showed increasing the magnitude of the difference between status of glucose tolerance (normal: 777, IFG: 438, IGT: 382, DM2: 349, p<0.001). The opposite phenomenon occurred when using HOMA-B as an indicator of beta cell function. The correlation between IDO and the new index based on OGIS was 0.773 (p<0.001). Considering as abnormal condition to the lowest quartile of both indicators showed agreement was moderate (kappa 0.518).

Conclusion: We showed an alternative index of disposition based on OGIS as surrogate insulin action. Has the advantage of a greater discrimination capability status of tolerance glucose compared to the original method.

Keywords: euglycemic clamp, oral glucose tolerance test, insulin action, ODI

Aguirre Karina, Mehta Roopa, Gulías Alfonso, Aguilar Carlos

Department of Endocrinology and Metabolism, Instituto Nacional de Nutrición Salvador Zubirán, Mexico

Correspondence: Aguirre Karina, Department of Endocrinology and Metabolism, Instituto Nacional de Nutrición Salvador Zubirán, Mexico, Email kaguirre1981@gmail.com

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Introduction

The deficiencies in the secretion of β-cell and insulin resistance are the two major pathophysiological mechanisms of diabetes. Both can be demonstrated in individuals at high risk of developing long before hyperglycemia.[1] Evaluation of insulin secretion in humans under physiological conditions has been a challenge due to the complex interplay between insulin action and hepatic extraction of it.[2]

The euglycemic clamp is the validated technique for measuring the action of insulin in vivo. It provides information about the amount of glucose metabolized by peripheral tissues during insulin stimulation. The clamp methodology has been developed and widely used by De Fronzo since 1979.[3] Is considered the gold standard to measure the action of insulin, however, has some disadvantages which do not allow applying to large populations.

In the last two decades, several research groups have proposed alternative methods that attempt to evaluate simultaneously both the function of beta cell as the action of insulin on the basis of protocols both intravenous and oral.

The insulin secretion pattern allowing evaluation of the beta cells after a bolus intravenous injection of glucose, for example, during a test of intravenous glucose tolerance (IVGTT) or after ingestion glucose, for example, an oral glucose tolerance test (OGTT) or a mixed meal.

Oral tests are certainly more physiological that intravenous because incretin effect in OGTT and food because of the presence of nutrients, ie: proteins and fats.

Minimal model allows evaluating an index of insulin sensitivity by means of the intravenous glucose tolerance test. When the value of AIR is multiplied by disposal rate the result is called DISPOSITION INDEX and determines whether insulin secretion is appropriate to the level of action of the same.

The DISPOSITION INDEX shows the failure of the beta cell to compensate for insulin resistance in subjects at high risk for developing type 2diabetes and impaired fasting glucose.

Prospective studies have shown that DISPOSICION INDEX is greatly reduced before the presence of hyperglycemia. Therefore, a

low rate of DISPOSITION INDEX is an early marker of inadequate compensation of beta cells.[4].

Using the minimal model intravenous, an oral minimal model was developed based on the oral glucose tolerance test (OGTT). It is less accurate but simpler to implement and it's often used in epidemiological or intervention studies. Also it assesses different aspects of beta cell function.

Some surrogate measures of insulin secretion and insulin sensitivity have been developed from the OGTT as are the HOMA (homeostasis model assessment).[5] both HOMA B and HOMA IR index; QUICKI (quantitative insulin sensitivity check index).[5] and Matsuda insulin sensitivity index (ISI).[6–11]

In 2001, OGIS was proposed as an index of insulin action derived of OGTT, based on a physiological model of glucose and insulin. This index is comparable to the calculation of glucose clearance obtained in the clamp. It was validated in thin and obese subjects with impaired fasting glucose and type 2diabetes.

This method use the values obtained from OGTT, was compared to the clamp being able to obtain a good correlation (r=0.77, p=0.0001). Moreover this method has been tested independently showing that the performance of the other methods (Matsuda, HOMA, Quicki) is lower.[7,12]

Utzschneider et al.[9] showed on the basis of the hyperbolic relationship of the components of the following formula between (delta 0-30 insulin/delta glucose 0-30x1/fasting insulin), that their product known as ORAL disposition index = ODI, is an actual measurement of the beta cell function and decreases progressively from individuals with oral normal glucose tolerance, glucose intolerance and diabetes (p<0.001 for all comparisons). Similar results were obtained when calculated using HOMA-S in place of 1/fasting insulin.[9]

Indeed, the ODI has emerged as a valuable tool in clinical research by providing an integrated system of measuring the offset of the beta cell, while insulin secretion is appropriately evaluated against sensitivity to predominant insulin. A lower ODI is clearly present in subjects with pre-diabetes. THE ODI has approx. 70% heritability and can be a useful feature to identify genetic predisposition to DM. Increased ODI was associated with a lower risk of DM at 10years. OR 0.40.95% CI 0.25- 0.66, p<0.001) after adjusting for age, sex, BMI, fasting glucose and glucose 2h.[9]

This study proposed a new index of oral disposition on the basis of the values obtained from the OGTT using OGIS as an index of insulin action because of its demonstrated better correlation with clam versus other surrogate indices.

Methodology

A retrospective cross-sectional observational comparative study. Values of glucose and insulin curves for three to five hours made in the past five years at National Institute of Medical Sciences and Nutrition Salvador Zubirán were collected.

Review of relevant records was conducted to filial anthropometric data, age, sex, lipid profile, and drug history. The cases were selected based on inclusion criteria (patients over 18 years and both genders) and exclusion (previous diagnosis of T2DM, current pregnancy or lactation, treatment with metformin for any reason and incomplete anthropometric data on file).

Databases were provided by Aguilar, Carlos MD, Mehta, Roopa MD and Gulías, Alfonso MD. Also values of insulin and glucose curves for 3 and 5hours performed in 2013 were included.

We considered only one curve of glucose and insulin for each patient. Both basal values of glucose - insulin and values after 75g glucose load at 30, 60, 90, 120, 180, 240 and 300min was taken. With which we cataloged each case according to the criteria of the ADA for its status of glucose tolerance (normal: fasting blood glucose <100mg/dl and 2hours glucose <140mg/dl; Impaired Glucose Fasting (IGF): fasting glucose 100 to 125mg/dl; Impaired glucose tolerance (IGT): 2hours glucose above 140mg/dl; IGF+IGT: fasting glucose above 100 mg / dl glucose and/or 2-hour glucose between 140 and 199 mg/dl; DM clinic: fasting blood glucose ≥126mg/dl and/or 2 hours glucose ≥200mg/dl). We also calculated indices that evaluate insulin secretion. Early insulinogenic index (EII) (2): Delta0-30 insulin/delta 0-30glucose min; HOMA B: 20x insulin (mUI/ml)/glucose (mg/dl)-3.5.

Indices that evaluate the action of insulin:

i. HOMA IR: Basal Insulin (mUI/ml) x fasting glucose (mg/dl)/405;

ii. Quicki index: 1/.log (fasting insulin U/ml)+log (fasting glucose, mg/dl);

iii. MATSUDA index: $10000/\sqrt{}$(fasting glucose (mg/dl) x basal insulin (uU/ml)) x (mean OGTT glucose x mean insulin OGTT);

iv. 1/Insulin: 1/Basal Insulin

v. Oral Glucose Insulin sensitivity (OGIS) available at http://www.isib.cnr.it/ogis/;

Finally we calculated the indices that together evaluate the function of the beta cell thanks to the product of an index of secretion by index of action of insulin

Beta cell function indexes

Oral disposition index (ODI): EII x 1/basal insulin;

IS/IR index: EII x MATSUDA;

We considered as confounding variables in the analysis: age in years, gender expressed as men and women, BMI calculated based on the formula weight (kg)/height (m²) classified subjects according to the WHO 2013 underweight: <19; Normal Weight: 19-24.9; Overweight: 25-29.9; Obesity>30.

For statistical analysis, the Kolmogorov-Smirnov test was used to assess the distribution of (normal or abnormal) variables: all quantitative continuous variables had non-normal distribution, so the descriptive statistic used was median and interquartile range to determine the clinical and demographic characteristics of patients. While in the qualitative or nominal variables, frequency and percentage were used.

To determine differences in beta cells secretion and insulin action indexes between medians according to gender, status of glucose tolerance and weight categories the Mann-Whitney and Kruskal-Wallis test were used. For the analysis of correlation and concordance between indexes, negative values of Early insulinogenic index were excluded.

In the multivariate analysis: we calculated Spearman correlation coefficient between the components of the known and the new proposed oral disposition indexes. Finally we calculated the correlation between ODI and our index. We determined value of concordance (kappa) between oral disposition indexes with the values of the 75th percentile of each one. To analyze these data, the SPSS version 20 was used.

Results

Of the 2097 patients just 1619 patients met selection criteria. The median age of the population was 43years (31-53), median weight was 83kg (64-96), median BMI of 32 (26-36), median values of SBP and DBP were normal 118 and 77mmHg, respectively.

The basal blood glucose level was 92 (83-99)mg/dl and 122(95-139)mg/dl after 2hours. Fasting insulin was 13(6-15)µU/ml and 85 (37-102)µU/ml at 120min. The median value of triglycerides was 133(101-164)mg/dl, median cholesterol value was 183 (159-206) mg/dl, HDL 43(35-49)mg/dl, LDL 114(92-133)mg/dl and non-HDL cholesterol 140(117-160)mg/dl (Table 1). 73%(1177) were women and 27%(442)men, their general characteristics are presented in Table 2. The median weight value was significantly higher in men 96kg (p<0.00), but no significant differences in BMI were found. The values of SBP and DBP also showed significant differences between genders with higher values in men with SBP 123mmHg and DBP 79mmHg (p 0.00). Baseline values of glucose and insulin were higher in men with glucose 93mg/dl and insulin 15IU/L (p 0.00), while the values of both glucose and insulin at 2hours afterload were not significantly different.

Table 1 Overview of the study population

	Variables	Median	Interquartile range
n=1619	Age(Years)	39	29-50
	Weight(kg)	75	64-94
	BMI(kg/m²)	29.5	26-36
	SP(mmHg)	120	110-120
	DP(mmHg)	80	70-80
	Basal Insulin(µUI/ml)	8,8	14-Jun
	Insulin 2hs(µUI/ml)	52	32-84
	Basal glucose(mg/dl)	87	81-92
	Glucose 2hs(mg/dl)	105	88-119
n=1099	TG(mg/dl)	124	95-160
	CHOL(mg/dl)	178	155-204
	HDL(mg/dl)	42	35-50
	LDL(mg/d)	108	90-131
	No HDL(mg/dl)	134	113-158

Table 2 Description of study population according to sex

	Variables	Women		Men		P
	%/Cases	1177(73%)		442(27%)		
n=1619	Age	43	32-53	42	30-52	0,99
	Weight	73,5	63-90	88	72-111	0,00
	BMI	30	26-36	31	26-37	0,31
	Basal Insulin	9,6	6,3-15	9,4	18-Jun	0,01
	Insulin 2hs	63	37-101	61	34-108	0,26
	Basal Glucose	91	83-99	91	84-100	0,00
	Glucose 2hs	116	97-139	117	93-139	0,51
	%/cases	822(75%)		277(25%)		
n=1099	TG	128	99-163	134	107-169	0,00
	CHOL	183	161-207	176	150-202	0,52
	HDL	43	36-51	37	33 – 43	0,00
	LDL	111	93-133	107	90-131	0,20
	No HDL	139	117-159	135	114-161	0,04

In the lipid profile, the values of total cholesterol and LDL cholesterol were not significantly different between genders. In men triglyceride levels were higher compared with women (p 0.00).

In women the values of HDL cholesterol were not higher relative to men (p 0.00), whereas HDL cholesterol levels were significantly lower (p 0.00).

816 (50%) had a BMI >30, 500(31%) were considered overweight, 285(18%) and 18 normal-weight (1%) were underweight. Their characteristics are shown in Table 3.

The group of subjects with low weight showed the lowest median age of 34years (24-37; p 0.00). The group of overweight subjects showed the highest median age 45 (34-55; p 0.00), also the highest median cholesterol value of 187mg/dl (161-208; p 0.00), LDL cholesterol 116mg/dl (95-135; p 0.00), non-HDL cholesterol 143mg/dl (119-163; p 0.00).

The group of obese subjects had the highest median SBP 121mmHg (110-130; p 0.00), DBP 79mmHg (70-85; p 0.00), fasting glucose 93mg/dl (84- 100; p 0.00), two hours post-load glucose 126mg/dl (101-143; p 0.00), basal insulin 16µUI/ml (9-20, p 0.00), two hours post-load insulin 98µUI/ml (45 to 121; p 0.00), triglycerides 136mg/dl (106-167; p 0.00). They also had the lowest median value of HDL cholesterol 41mg/dl (34-48; p 0.00).

1039 (64%) were categorized as normal glucose tolerance, 175 (11%) with IFG, 194 (12%) with IGT, 139 (9%) with IGT + IFG and finally 72 (4 %) with T2DM (Table 4).

Table 3 Description of the study population according to BMI

	Variables	Low weight		Normal weight		Over weight		Obesity		p
	Cases /%	18 (1%)		285 (18%)		500 (31%)		816 (50%)		
n=1619	Age	27	24-37	45	30-56	45	34-55	40	31-50	0,00
	Basal Glucose	86	79-87	89	81-96	90	84-99	92	84-100	0,00
	Glucose 2 hs	102	79-129	111	88-134	115	95-137	119	101-143	0,00
	Basal insulin	5	7-Feb	6	9-Apr	8	12-Jun	13	20-Sep	0,00
	Insulin 2 hs	60	37-99	42	26-62	60	36-91	76	45-121	0,00
	Cases/ %	13 (1%)		186 (17%)		338 (31%)		562 (51%)		0,00
n=1099	Triglycerides	192	73-151	118	82-156	131	103-164	133	106-167	0,00
	Cholesterol	161	156-175	184	158-208	186	161-208	177	157-203	0,00
	HDL	49	47-59	43	37-53	43	37-50	40	34-48	0,00
	LDL	86	81-97	110	92-132	113	94-135	111	91-132	0,00
	No HDL	113	100-117	136	112-158	141	119-163	138	117-159	0,00

Table 4 Description of population by status of glucose tolerance

	Variables	IFG	IGT	IFG+IGT	DM	Normal	p
	# CASES/%	175(11%)	194(12%)	139(9%)	72(4%)	1039(64%)	
N=1619	Age	45	45	50	49	39	0,00
		38-55	35-53	41-58	36-57	29-49	
	Weight	75	78	85	79	75	0,00
		68-98	67-92	70-102	60-100	63.93	
	BMI	30	31	33	31	30	0,00
		27-36	27-36	28-41	28-37	25-35	
	Basal Insulin	11	11	13	13	9	0,00
		18-Aug	16-Aug	21-Sep	21-Aug	14-Jun	
	Insulin 2 hs	62	100	95	96	52	0,00
		42-153	71-179	70-160	50-141	31-84	
		123(11%)	132 (12%)	94 (9%)	44 (4%)	706 (64%)	
N=1099	Triglycerides	132	149	148	144	124	0,00
		107-162	115-176	108-172	115-175	95-160	
	Cholesterol	184	191	185	188	178	0,00
		164-210	162-210	161-203	158-212	155-204	
	HDL	41	42	40	35	42	0,00
		36-49	36-50	35-46	31-44	35-50	
	LDL	116	114	113	124	108	0,02
		101-135	96-140	95-130	89-139	90-131	
	No HDL	142	144	141	153	134	0,00
		125-167	121-167	126-162	121-173	113-158	

Subjects with normal glucose tolerance had the lowest median value of age (40years) (p <0.00), lower BMI (31) (p=<0.00) relative to other status, in addition to lower median values triglycerides, LDL cholesterol and non-HDL (p 0.00).

The status of IFG cases in this group had total cholesterol and higher LDL cholesterol. On the status of IGT presented the highest afterload insulin value at 2hours and the highest triglyceride value.

The status of IFG + IGT had highest median value of age in the population and values higher SBP and DBP was evident with respect to the other status is presented.

In the group whose values in the OGTT were consistent with DM2 the highest median value of basal insulin and glucose afterload were present. They also had the lowest HDL cholesterol value. Calculating insulin secretion indexes was performed and showed significant differences by sex, BMI and status of glucose tolerance (Table 5).

Table 5 Indexes of insulin secretion in the study population by sex, BMI and status of glucose tolerance

Variables	Women		Men		P	
EII	1.09	0.7-1.8	1.03	0.6-1.8	0.28	
HOMA B	2.2	1.5-3.3	2.3	1.5–3.8	0.04	
Variables	Low Weight		Normal Weight	Over Weight	Obesity	P
EII	0.97		0.88	1.02	1.15	0,00
	0.7-1.9		0.5-1.5	0.6-1.7	0.7-2.1	
HOMA B	0.94		1.44	1.95	2.96	0,00
	0.6-1.5		0.5-1.5	1.4-2.8	2.1-4.4	
Variables	IFG	IGT	IFG + IGT	DM2	Normal	P
EII	0.99	0.91	0.7	0.37	1.25	0,00
	0.6-1.6	0.5-1.5	0.4-1.1	0.2-0.7	1.8-2.2	
HOMA B	2.26	2.54	2.48	2.41	2.13	0,00
	1.5-3.5	1.7-3.8	1.8-3.8	1.6-4.1	1.4-3.3	

Indexes of insulin action (HOMA IR, QUICKI, 1/INSULIN, MATSUDA, OGIS) was calculated and its value was stratified by sex, BMI and glucose tolerance status (Table 6).

Table 6 Indices of insulin action in the study population by BMI and status of glucose tolerance

Variables	Low weight		Normal weight	Over weight	Obesity	P
Cases/ %	18 (1%)		285 (18%)	500 (31%)	816 (50%)	
HOMA IR	0.78		1.35	1.91	3.05	0,00
Quicki	0.4		0.37	0.35	0.32	0,00
1/Insulin	0.3		0.2	0.12	0.07	0,00
Matsuda	7		6	4	3	0,00
OGIS2	456		442	404	369	0,00
Vablesria	IFG	IGT	IFG+IGT	DM2	Normal	P
Cases/ %	175(11%)	194(12%)	139 (9%)	72 (4%)	1039 (64%)	
HOMA IR	2.99	2.34	3.5	4	1.95	0,00
Quicki	0.32	0.34	0.32	0.31	0.35	0,00
1/Insulin	0.09	0.09	0.08	0.07	0.11	0,00
Matsuda	2.8	2.98	2.3	2.3	4.6	0,00
OGIS2	352	375	323	324	425	0,00

For analysis of correlation and concordance between indexes, EII negative values were excluded. Within the study population, 30 subjects had a negative early insulinogenic index, their general characteristics at Table 7.

EII negative cases were also classified according to BMI and glucose tolerance status (Table 8).

Table 7 Description of the population with early insulinogenic index with negative values

	Women	Men	P
Cases/%	19 (63%)	11 (37%)	
Age(Years)	39 (30-44)	31 (19-46)	0,103
Weight	78 (59-104)	88 (69-107)	0,158
BMI	32 (26-35)	31 (25-35)	0,966
Basal Glucose	92 (82-98)	98 (87-104)	0,307
Glucose 30min	93 (73-95)	113(74-132)	0,307
Fasting Insulin	12 (5-14)	36 (6-42)	0,200
Insulin 30min	51 (29-72)	66 (33-83)	0,471

Table 8 Categorization EII negative patients by sex, BMI, and glucose tolerance status

| Variables	Clasification	Women	Men
Weight Categories	Low Weight	0	1
	Normal Weight	2	1
	Over Weight	9	4
	Obesity	8	5
Status of glucose tolerance	IFG	1	1
	IGT	0	1
	IFG+IGT	0	0
	DM2	3	2
	NORMAL	15	7

Of the 30 subjects with negative EII, 15 subjects had the glucose delta 0-30min negative thus indicating that glucose values in OGTT return earliest form even lower than the baseline status and tolerance glucose was normal.

While 4 subjects showed delta insulin 0-30 negative, which mean low beta cell response to glucose stimulation, 3 subjects had DM2 status and only one had normal tolerance (female, 41years with BMI 27.7). The correlation between the oral disposition indexes and the possible new indices proposed (Table 9) Figure 1.

Table 9 Correlation between known disposition indexes (ODI - IR/IS) and proposed new indexes

Variables	ODI	p	IR/IS	P
HOMA B x 1/Insulin	0,422	0,00	0,519	0,00
HOMA B x Matsuda	0,213	0,00	0,470	0,00
EII x OGIS 2	0,773	0,00	0,808	0,00
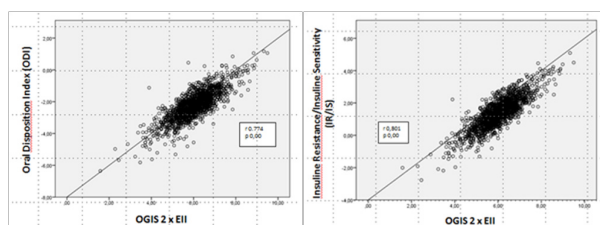
**Figure 1** Correlation between known disposition indexes (ODI-IR/IS) and EII x OGIS 2.

The correlation between disposition indexes was stratified by BMI and status of glucose tolerance (Tables10&11), (Figures 2&3).

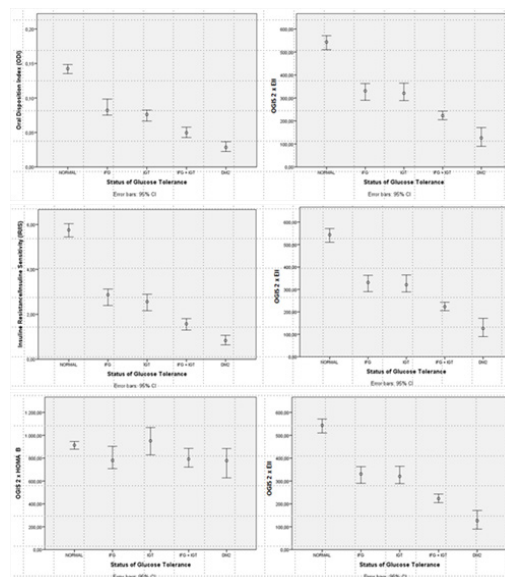**Table 10** Disposition indexes in the study population according to BMI

Variables	Low weight	Normal weight	Over weight	Obesity	P
Cases/ %	17 (1%)	282 (18%)	488 (31%)	804 (51%)	
ODI	0,33	0,14	0,12	0,09	0,00
	0,21-0,59	0,08-0,27	0,06-0,2	0,05-0,15	
IS/IR	10.2	5.7	4.2	3.5	0,00
	7,13-13,5	2,99-9,7	2,2-7,2	1,96-6,19	
HOMA B x 1/Insulin	0,24	0,23	0,23	0,23	0,00
	0,24-0,27	0,23-0,24	0,22-0,23	0,22-0,23	
HOMA B x Matsuda	7.18	8.9	8,1	8.5	0,00
	6,3-10,2	9-9,8	8,3-8,9	8,8-9,3	
HOMA B x OGIS2	503	627	764	1076	0,00
	314-681	457--892	550-1082	774-1508	
EII x OGIS2	502	393	379	433	0,04
	357-810	233-676	230-704	258-728	

Table 11 Disposition indexes in the study population according to status of glucose tolerance

Variables	IFG	IGT	IFG+IGT	DM2	Normal	P
Cases/%	173(11%)	193(12%)	139(9%)	67(4%)	1019(64%)	
ODI	0,08 0,09-0,13	0,076 0,05-0,11	0,05 0,03-0,08	0,03 0,006-0,098	0,14 0,09-0,23	0,00
IS/IR	2.8 1,8-4,2	2.6 1,7-3,7	1,6 0,99-2,14	0.83 0,25-2,59	5.7 3,6-9,5	0,00
HOMA B x 1/insulin	0,19 0,19-0,20	0,22 0,22-0,23	0,19 0,18-0,19	0,185 0,17-0,19	0,24 0,241-0,245	0,00
HOMA B x Matsuda	6,9 6,8-7,1	7,5 7,4-8,0	5,7 5,7-6,1	5,5 5,2-6	9.8 10-10,4	0,00
HOMA B x OGIS 2	766 533-1107	942 662-1374	780 596-1106	760 526-1073	910 621-1303	0,00
EII x OGIS 2	326 212-544	320 210-456	223 143-331	122 36-458	537 343-869	0,00
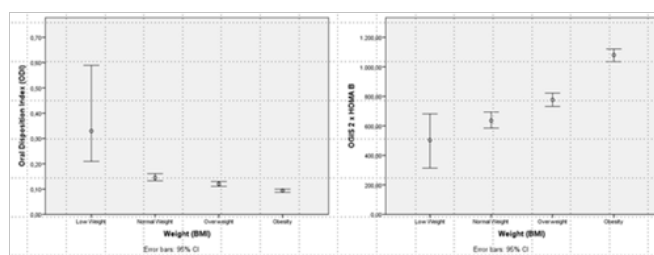
Figure 2 Disposition indexes in the study population according to BMI.

Figure 3 Disposition indexes in the study population according to status of glucose tolerance.

Finally the concordance between the known oral indexes and the proposed new index with better correlation (EII x OGIS) by calculating kappa was evaluated.

Table 12 Concordance between disposition indexes

Variables		ODI				IR/IS			
		p< 75	p>75	kappa	p	p<75	p>75	kappa	p
EII x OGIS 2	p<75	1053	146	0,518	0,025	1055	139	0,536	0,025
	p>75	140	252			138	259		

Discussion

In this study two new disposition indexes (OGIS x HOMA B and OGIS x EII) were evaluated and compared with the two available and known oral disposition indexes. Analyzing the OGTT and insulin curves 3 to 5hours was performed. 1619 curves were included in the final analysis.

There were a higher percentage of women (73%) in our study population. Men showed significantly greater weight (p 0.00), basal insulin values (p 0.01), glucose (p 0.00) and triglycerides (p 0.00) than women. Women as we expect showed significantly higher HDL cholesterol than men (p 0.00). The population was divided by weight class and found that only 18% had normal weight (BMI<25). The majority of subjects were overweight or obese (31% overweight and 50% obese).

This finding was expecting in hospital population like us with high risk to development type 2diabetes. The secretion insulin index, early insulinogenic index (EII), was similar between men and women. As we expected the highest value was associated with low weight in both genders.

We also find that value of EII fell in the presence of any abnormality in glucose tolerance (normal 1.6, IFG 1.2, IGT 1.1 and DM2 1.0; p 0.00). In contrast the value of HOMA B index was significantly higher in men (3.2 vs 2.8; p 0.036). Surprisingly, the highest values were found in the obese population (3.6vs1.7 in normal weight; p 0.00).

This result may be associated with increased insulin resistance in this population (basal insulin 16mUI/ml vs 7mUI/ml normal weight; p 0.00). Finally higher HOMA B was found in DM2 and IGT (3.3), this result may reflect the increase in fasting glucose and insulin.

In relation to insulin action indexes, our work shows results similar to those described in previous studies, where the HOMA IR values are higher in subjects with BMI >30 as well as lower values for Quicki, MATSUDA, OGIS2 and OGIS3 indexes. Our study showed that HOMA IR was higher in subjects with IFG+IGT and lowest in subjects with normal glucose tolerance (cannot assess HOMA IR in subjects with DM2).

The Quicki, 1/insulin, Matsuda and OGIS indexes showed a similar pattern with respect to glucose tolerance, with higher values in people with normal tolerance and lower in patients with T2DM. The only exceptions were OGIS and Matsuda with values in IFG+IGT cases lower than T2DM.

We recall that only 4% of the population was diabetic, this result may reflect the lack of n in this group. 30 subjects with EII negative were excluded, of which 19 (63%) were female and 11 (37%) were men, but no significant differences were found between them in terms of their general characteristics. These results may be associated with the value of n in this group.

We divided this subset by weight class and a similar number of overweight subjects.[13-15] and obesity (13) was found. In addition,

these subjects were divi Figure 1 Correlation between known disposition indexes (ODI-IR/IS) and EII x OGIS 2. ded by glucose tolerance: 12 subjects with normal tolerance, 3 prediabetics and 5 diabetic subjects were found.

This result agrees to the publication of Abdul-Ghani et al.[16] They suggest that subjects with EII negative and normal glucose tolerance have higher insulin sensitivity which explains why during OGTT glucose values return quickly under baseline. They propose that these patients are at low risk of progression to type 2 diabetes.[17-22]

Furthermore Mirjam V et al.[23] infer that subjects EII negative with insulin delta 0-30 negative indicating a low reserve of the beta cell and increased susceptibility to DM2.[24-28] BMI was considered the most important confounding factor. The best correlation was found between IR/IS and EII x OGIS 2; r 0.809 (p 0.00). The highest correlation value obtained according to the status of tolerance was in the DM2 group IR/IS and EII x OGIS2 (r 0.997; p 0.00). The concordance between the known oral disposition index IR/IS and OGIS2 x EII was 0.557 (p 0.00).

Limitations

The observational design did not allow tracking of subjects to establish the causal relationship between the different status of glucose tolerance and values of the proposed index.

The study group does not represent the general population, but allowed to identify the prevalence of different glucose tolerance status and describe their clinical characteristics.

The selection of patients represented the largest bias in our study, because at our institute, OGTT is applicate to subjects with high risk: dyslipidemia, obesity, hypothyroidism, chronic steroid use, menstrual abnormalities, hyperandrogenism or reactive hypoglycemia.

Conclusion

Our study showed that a new oral disposition index with EII as an insulin secretion index and OGIS as insulin action one has good correlation and concordance with known disposition indexes.

It is necessary to validate this index at prospective studies that allow us to evaluate their ability to discriminate individuals at high risk of progression to T2DM and compare it with values obtained in the clamp studies.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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