Original Research Article

Fasting insulin level and Homatest IR as a predictors of Hepatic encephalopathy in critically ill patients

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Abstract

Several methods have been used for diagnosing insulin resistance in humans. Glycemic clamp continues to be the gold standard procedure; however, its complexity limits its application in daily medical practice. Several methods using glycemia and insulinemia measurements, both during fasting or after oral or endovenous glucose overload, have been proposed. The purpose of this study was to identify the fasting insulin level and insulin resistance detected by HOMA-IR test in ICU patients as predictors for hepatic encephalopathy. This was a case-control study. The study was done in the medical intensive care unit (ICU) of the Faculty of Medicine Cairo University, 319 ICU patients were included in the study. Control subjects without acute illness were recruited from the local community, stratified by age and gender to approximate the sepsis cohort. In our study we found that hepatic encephalopathy is associated with statistically significant less fasting insulin levels and less insulin resistance than patients without hepatic encephalopathy. This may be explained by that end stage liver disease is associated with hypoglycaemia due to defective hepatogluconeogenesis which causes reduction in calculation of HOMA test. Our present observations indicate that patients with hepatic encephalopathy are associated with statistically significant less fasting insulin levels and less insulin resistance than patients without hepatic encephalopathy.

Keywords: Fasting insulin level, Hepatic encephalopathy, Homatest IR

INTRODUCTION

Several methods have been used for diagnosing insulin resistance in humans. Glycemic clamp continues to be the gold standard procedure; however, its complexity limits its application in daily medical practice (Leonetti et al., 2004). Several methods using glycemia and insulinemia measurements, both during fasting or after oral or endovenous glucose overload, have been proposed (Vaccaro et al., 2004; Yeckel et al., 2004). Due to the simplicity of its determination and calculation, insulin resistance assessment by the homeostatic assay (HOMA-IR) has been the most frequently employed technique both in clinical practice and in epidemiological studies. HOMA-IR, as proposed by Matthews et al. (1985), shows significant correlation to glycemic clamp in non-diabetic patients and has been widely utilized in NAFLD clinical studies (Aguilera et al., 2002; Katz et al.,

Table 1. Demographic data for whole group

		Mean / N	SD / %	Median (IQR)
Gender	Male	121	37.9%	
	Female	198	62.1%	
Age		46.15	19.44	48 (27 - 63)
Smoking	No	252	79.0%	
	Yes	67	21.0%	

2000; Lansang et al., 2001). In these studies, however, cut values of HOMA-IR to identify IR have been arbitrarily set and show great variety among authors. Moreover, these values were obtained in case-control studies or in trials performed with a small number of control subjects (Duseja et al., 2007; Duvnjak et al., 2007; Song et al., 2007; Ybarra et al., 2005).

The purpose of this study was to identify the fasting insulin level and insulin resistance detected by HOMA-IR test in ICU patients as predictors for hepatic encephalopathy.

Study Design

This was a case-control study. The study was done in the medical intensive care unit (ICU) of the Faculty of Medicine Cairo University, 319 ICU patients were included in the study.

Control subjects without acute illness were recruited from the local community, stratified by age and gender to approximate the sepsis cohort. Prospectively defined exclusion criteria

METHODOLOGY

Included patients were subjected to the following: Written consent (by the patient or his relatives), detailed history, full clinical assessment, laboratory tests on admission and follow up including urea, creatinine, sodium, potassium, random blood sugar, complete blood count, coagulation profile, liver function tests; fasting insulin level and Homatest IR.

Estimation of IR was done using HOMA-IR which wascalculated as fasting glucose (mmol/L) fasting insulin (mU/mL)/22.5. According to the instructions of themanufacturer, samples were collected in the morningafter 12 h fasting. The collected samples were centrifuged and the plasma was separated from the cells.Samples were assayed immediately or stored at -70 Cor below.

Data Management and Analysis

The collected data was revised, coded, tabulated and

introduced to a PC using Statistical package for Social Science (SPSS 25). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

Descriptive statistics

1. Mean, Standard deviation (± SD) and range for parametric numerical data, while Median and Interquartile range (IQR) for non-parametric numerical data.
2. Frequency and percentage of non-numerical data.

Analytical statistics

1. Student T Test was used to assess the statistical significance of the difference between two study group means.

RESULTS AND DISCUSSION

319 ICU patients were included in the study .22 of them developed hepatic encephalopathy fasting insulin and Homa IR were done to find if insulin resistance and fasting insulin level is related to hepatic encephalopathy and can be a good predictors or not .

Many studies showed that there is a significant correlation between DM and liver cirrhosis (Ampuero et al., 2013) and insulin resistance and liver cirrhosis (Kawaguchi et al., 2011; Cavallo-Perin et al., 1985).

In our study we found that hepatic encephalopathy is associated with statistically significant less fasting Insulin levels (47.05 ± 10.51, 53.15 ± 16.2 respectively) (p value 0.021) and less insulin resistance (11.42 ± 2.62,12.87 ± 3.98 respectively) (p value 0.027) than patients without hepatic encephalopathy. This may be explained by that end stage liver disease is associated with hypoglycaemia due to defective hepatogluc-oneogenesis which causes reduction in calculation of HOMA test.

Table 1. Lab investigations for whole group

	Mean / N	SD / %	Median (IQR)
Urea	111.51	99.92	102 (16 - 164)
Creatinine	3.95	3.57	3 (0.8 - 5.6)
Uric acid	8.14	7.46	6.95 (4.95 - 9.7)
ALT	69.75	176.63	20 (17 - 43)
AST	88.22	219.20	26 (19 - 59)
Hb	10.48	2.72	11 (8.34 - 12.8)
WBCs (x10_3)	11.78	14.19	8.6 (6.1 - 14.8)
Platelet (x10_3)	251.16	130.55	261 (150 - 354)
Ca	8.15	1.23	8.5 (7.4 - 8.9)
PO4	4.89	2.24	4 (3.5 - 5.9)
25 (OH) Vit. D (ng/ml)	22.77	10.75	21 (12 - 33)
PTH (15 – 65 Pg/mL)	67.63	17.63	69 (50 - 82)
Fasting glucose mg/dl	95.50	7.64	94 (90 - 101)
Fasting Insulin level	41.77	20.65	40 (19.4 - 58)
Homatest IR	9.99	5.18	9.8 (4.3 - 13.3)

Table 3. Descriptive for control group
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	Mean / N	SD / %	Median (IQR)
Weight /kg	65.82	8.03	65 (60 - 72)
ESR	4.14	1.93	4 (3 - 5)

Table 4. Past history and Co-morbid diseases for cases group
.

		Mean / N	SD / %	Median (IQR)
	Male	82	37.4%	
	Normal	50	22.8%	
Menstrual history	Irregular	3	1.4%	
	Menopausal	83	37.9%	
	2ry amenorrhea	1	0.5%	
Days of hospital to ICU		3.56	4.96	2 (1 - 5)
Systolic BP		118.89	39.90	110 (90 - 140)
Diastolic BP		72.21	22.69	70 (60 - 90)
GCS		13.00	3.17	15 (12 - 15)
BMI		26.31	6.10	25.3 (22 - 30)
DM		92	42.0%	
DM duration		12.69	8.47	10.5 (5.5 - 18)
HTN		130	59.4%	
HTN duration		8.91	7.56	6 (3 - 12)
CKD		91	41.6%	
CKD duration		8.01	13.79	3 (2 - 6)
Viral hepatitis	No	175	79.9%	
	HCV +ve	44	20.1%	
Duration of hepatitis C		16.20	24.52	5.5 (3 - 16.5)
Hepatic encephalopathy		22	10.0%	
Hematemesis / Oesphgealvarices	No	180	82.2%	
	Hepatic	20	9.1%	
	Non-hepatic	19	8.7%	
Other Co-morbidity		152	69.4%	
DURATION		8.60	14.79	4 (2 - 9)

Table 5. Lab investigations for cases group

	Mean / N	SD / %	Median (IQR)
Albumin	2.58	0.63	2.6 (2.2 - 3)
Na	131.91	9.00	133 (128 - 137)
K+	4.67	2.88	4.4 (3.8 - 5.2)
Mg	2.10	0.45	2.1 (1.8 - 2.4)
follow up creat AFTER 48hrs	4.73	2.53	4.3 (2.5 - 6.4)
follow up creat AFTER 96hrs	4.36	2.42	4.5 (2.28 - 6.05)

Table 6. Correlation between Fasting insulin level and hepatic encephalopathy
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		Fasting Insulin level (pmol/L)	Student t-test	
			P-value	Sig.
Hepatic encephalopathy	No	53.15 ± 16.2	0.021	S
	Yes	47.05 ± 10.51		

Table 7. Correlation between Homatest IR and hepatic encephalopathy
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		Homatest IR	Student t-test	
			P-value	Sig.
Hepatic encephalopathy	No	12.87 ± 3.98	0.027	S
	Yes	11.42 ± 2.62		

CONCLUSION

Our present observations indicate that patients with hepatic encephalopathy are associated with statistically significant less fasting insulin levelsand less insulin resistance than patients without hepatic encephalopathy.

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