The effect of bariatric surgery on GLP-1,insulin resistance and metabolic parameters in patients with T2DM

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Abstract

Background The surgical treatment of obesity improves metabolic abnormalities in patients with type 2 diabetes.**The aim** of this study was to evaluate the immediate and late effect of bariatric surgery on GLP-1 , metabolic parameters and insulin resistance in patients with T2DM.
Methods fifty patients with T2DM ,obese at levels II and III(BMI more than or equal to 35) were evaluated for BMI , WC , BP , PPGLP-1 , fasting plasma glucose , fasting insulin and HOMA-IR before , 1w and 3m after intragastric ballon insertion , RYGBP and SG and evauated for Lipid profile , HbA1C , ALT and AST before and 3m after .**Results**: the study demonstrated significant increase of PPGLP-1 after RYGBP and SG with better results in RYGBP .No significant change noted after IGB insertion. The metabolic parameters significantly improved in the 3 groups with best results in RYGBP group then SG group followed by IGB group.**Conclusion**: Our data suggest that the RYGB and SG surgeries,beyond weight loss, induces early beneficial changes in PPGLP-1which favor glycemic control in type 2 diabetes.
Keywords RY gastric bypass. SG sleeve gastrectomy.IGB intra gastric ballon.Type 2 diabetes. GLP-1 glucagon like peptide -1.

Introduction:-

Glycemic control in diabetic patients improves markedly within days of bariatric surgery, which suggests that the procedures alter the hormones

that control insulin secretion (**Rubino et al ;2006).**The entero-insular axis includes the gut hormones glucagon-like peptide-1 (GLP-1) and glucose- dependent insulin-tropic peptide (GIP). These hormones, also known as incretins, are secreted by intestinal L and K cells, respectively, in response to nutrients and directly enhance insulin secretion (**Fetner *et* al ;2005).**

The aim:-

It was to evaluate the immediate and late effect of bariatric surgery on GLP-1 , metabolic parameters and insulin resistance in patients with T2DM.

Subjects and methods:-

This cross-sectional prospective study was carried out on 50 diabetic obese at levels II and III(BMI more than or equal to 35). patients from those attending the bariatric out patient clinc at Banha University Hospitals between February 2018 and October 2019 after approval of BenhaUniversity ethical committee.Among studied patients 15 were males and 35 were females . All the patients were subjected to full history taking with special stress on age,sex,type and duration of diabetes ,medications and complications, Complete physical examination with special stress on Height and weight , BMI, WC and BP, Post prandial plasma GLP-1 level,fasting plasma glucose,fasting insulin level,HbA1C,TC, LDL-c,HDL-c and TG levels,HOMA-IR,ALT and AST measurement.PPGLP-1 concentration was quantitatively measured using an Enzyme–Linked Immuno-Sorbant Assay (ELISA) kit (Quantikinehuman GA Immunoassay; R&D Systems, Minneapolis, MN, USA) according to manufacturers' instructions. Patients were classified into 3 groups *according to type of bariatric procedure done :*Group 1: that included 16 patients for whom intragastric balloons used.Group 2:that included 17 patients for whom RYGB operations used.Group 3: that included 17 patients for whom sleeve gastrectomy operations used .

Statistical analysis:- The collected data were tabulated and analyzed using SPSS version 16 soft ware (SpssInc, Chicago, ILL Company).

Categorical data were presented as number and percentages while quantitative data were expressed as mean ± standard deviation, an and range. Fisher's exact test (FET), was used to analyze categorical variables. Quantitative data were tested for normality using KolomogrovSmirnove test, using Student "t", if normally distributed, or Man Whitney U test, Krauskal Wallis test and Spearman's correlation coefficient (rho) if not normally distributed.

Statistical significance was accepted at P value <0.05 (S). A P value <0.001 was considered highly significant (HS) while a P value >0.05 was considered non-significant.

Results:-

Table 1. Effects of IGB on different parameters

	Mean ± SD	WSRT		
		P1	p2	p3
BMI(kg/m2) before	**39.62±4.24**	0.1	0.03	0.03
BMI(kg/m2)1w after	39.42±**4.21**			
BMI(kg/m2) 3m after	36.03±**2.85**			
	female male			
WC(cm) before	114.45± **1.69** 125.36±**1.14**	0.3	0.02	0.02
WC(cm) 1w after	113.95± **1.69** 124.71±**1.14**			
WC(cm) 3m after	108.36± **31.32** 120.6±**1.14**			
SBP(mmHg) before	**139.38±8.57**	1	0.03	0.03
SBP (mmHg)1w after	139.38±**8.47**			
SBP(mmHg) 3 m after	136.00±**9.61**			
DBP(mmHg) before	**88.13±6.87**	1	0.04	0.04
DBP (mmHg)1w after	88.13±**6.87**			
DBP (mmHg)3 m after	86.00±**6.85**			
FG(mg/dl) before	**270.81±44.70**	0.05	0.03	0.04

FG(mg/dl) 1w after	266.00±**44.64**			
FG (mg/dl) 3m after	229.94±**40.74**			
FI(micro IU /ml) before	15.75±**5.01**	0.05	0.03	0.04
FI(micro IU /ml) 1w after	13.45±**5.92**			
FI (micro IU /ml) 3m after	11.75±**5.92**			
HOMA-IR before	11.19±**5.41**	.04	0.02	0.03
HOMA-IR 1w after	7.84±**4.67**			
HOMA-IR 3m after	6.85±**5.54**			
PPGLP-1(P mol/L) before	12.38±**1.02**	0.3	0.1	0.1
PPGLP-1(P mol/L) 1w after	12.38±**1.02**			
PPGLP-1(P mol/L) 3m after	12.38±**1.02**			
HbA1C (%) before	10.00±**.56**		.05	
HbA1C (%) 3m after	8.70±**.56**			
TC (mg/dl) before	241.87±**45.15**		.05	
TC (mg/dl) 3m after	236.63±**44.19**			
	female male			
HDL-C (mg/dl) before	44.36±**7.56** **35.2±0.8**		.05	
HDL-C (mg/dl) 3m after	45.36± **7.52** **36.2±0.8**			
LDL-C (mg/dl) before	179.63±**55.51**		.05	
LDL-C(mg/dl) 3m after	174.63±**55.73**			
TG(mg/dl) before	224.69±**52.43**		.05	
TG(mg/dl) 3m after	217.69±**50.41**			
ALT(IU/L) before	94.31±**4.62**		.05	
ALT (IU/L) 3m after	90.31±**4.62**			
AST(IU/L) before	89.00± **4.17**		.05	
AST (IU/L) 3m after	87.00± **3.15**			

Table 1: Shows significant improvement of all parameters except for ppGLP-1 that did not show significant change after IGB

insertion.p1=before vs 1w after ,p2=before vs 3m after ,p3 = 1w after vs 3m .

Table 2. Effects of RYGB on different parameters.

	Mean ± SD	WSRT		
		P1	P2	p3
BMI(kg/m2) before	41.52±**3.21**	0.000	0.000	0.000
BMI (kg/m2) 1w after	39.52±**2.21**			
BMI (kg/m2) 3m after	34.52±**1.54**			
	Female male			
WC (cm) before	115.75±**2.73** **126.6±1.01**	0.000	0.000	0.000
WC (cm) 1w after	112.75±**2.74** **124.6±1.14**			
WC (cm) 3m after	100.94±**2.45** **112.6±1.14**			
SBP (mmHg) before	139.12±**8.36**	0.000	0.000	0.000
SBP (mmHg)1w after	137.12±**8.57**			
SBP (mmHg) 3 m after	129.12±**8.36**			
DBP(mmHg) before	85.94±**6.70**	0.000	.000	0.000
DBP (mmHg)1w after	84.88 **6.67**			
DBP(mmHg) 3 m after	79.94±**6.71**			
FG (mg/dl) before	269.00±**43.92**	0.000	.000	0.000
FG (mg/dl)1w after	189±**41.86**			
FG (mg/dl) 3m after	149.12±**44.13**			
FI(micro IU/ml) before	15.53±**5.09**	0.000	.000	0.000
FI (micro IU/ml) 1w after	8.52±**5.14**			
FI (micro IU/ml) 3m after	6.59±**4.95**			
HOMA-IR before	10.91±**5.36**	0.000	.000	0.000
HOMA-IR 1w after	4.54±**3.67**			
HOMA-IR 3m after	2.95±**2.94**			
PPGLP-1(P mol/L) before	12.42±**1.01**	0.000	.000	0.000
PPGLP-1(P mol/L) 1w after	20.42±**2.06**			
PPGLP-1(P mol/L) 3m	29.89±**4.12**			

after		
HbA1C (%) before	9.77±**.55**	.000
HbA1C (%) 3m after	6.77±**.55**	
TC (mg/dl) before	240.47±**44.72**	.000
TC (mg/dl) 3m after	220.47±**44.72**	
	female male	
HDL-C (mg/dl) before	44.83± **7.35** **35.2±0.8**	.000
HDL-C (mg/dl) 3m after	47.41±**8.75** **38.2±0.8**	
LDL-C(mg/dl) before	175.53±**56.34**	.000
LDL-C (mg/dl) 3m after	155.29±**56.23**	
TG (mg/dl) before	204.71±**31.88**	.000
TG (mg/dl) 3m after	184.71±**29.23**	
ALT(IU/L) before	104.00±**5.04**	.000
ALT (IU/L) 3m after	94.00±**5.66**	
AST (IU/L) before	92.71±**4.22**	.000
AST (IU/L) 3m after	85.71±**4.18**	

Table 2: Shows highly significant improvement of all parameters after RYGBP. p1=before vs 1w after ,p2=before vs 3m after ,p3 = 1w after vs 3m .

Table 3. Effects of SG on different parameters

	Mean ± SD	WSRT		
		P1	p2	p3
BMI (kg/m2) before	40.52±**5.64**	0.00	.00	.00
BMI (kg/m2)1w after	39.52±**4.63**			
BMI (kg/m2) 3m after	35.52±**2.31**			
	female male			
WC (cm) before	114.74±**2.73** **125.6±1.14**	0.01	.01	.01
WC (cm) 1w after	112.75±**2.73** **124.6±1.14**			
WC (cm) 3m after	105.74±**2.73** **116.6±1.14**			
SBP(mmHg) before	141.29±**8.54**	0.01	.01	.01
SBP (mmHg) 1w after	139.76±**8.47**			
SBP(mmHg) 3 m after	132.88±**8.31**			

DBP(mmHg) before	87.83±**7.74**	0.01 .01 .01
DBP (mmHg) 1w after	86.94±**6.70**	
DBP (mmHg) 3 m after	82.94±**6.08**	
FG (mg/dl) before	279.00±**40.92**	0.00 .00 .00
FG (mg/dl) 1w after	217.82±**42.13**	
FG (mg/dl) 3m after	178.82±**41.23**	
FI (micro IU/ml) before	16.53±**5.04**	0.01 .01 .01
FI (micro IU/ml) 1w after	10.58±**5.11**	
FI (micro IU/ml) 3m after	9.59±**5.11**	
HOMA-IR before	11.95±**5.59**	0.01 .01 .01
HOMA-IR 1w after	6.37±**4.43**	
HOMA-IR 3m after	5.36±**5.93**	
PPGLP-1(P mol/L) before	11.44±**1.15**	0.00 .00 .00
PPGLP-1(P mol/L) 1w after	18.42±**1.95**	
PPGLP-1(P mol/L) 3m after	26.84±**3.65**	
HbA1C (%) before	9.76±**.55**	.00
HbA1C (%) 3m after	7.16±**.55**	
TC (mg/dl) before	235.16±**43.99**	.00
TC (mg/dl) 3m after	222.24±**42.67**	
	Female male	
HDL-C (mg/dl) before	47.42±**6.8** **38.2±0.8**	.00
HDL-C (mg/dl) 3m after	49.76±**6.19** **40.2±0.8**	
LDL-C (mg/dl) before	172.53±**55.34**	.00
LDL-C (mg/dl) 3m after	161.94±**57.12**	
TG(mg/dl) before	221.47±**40.22**	.00
TG (mg/dl) 3m after	206.46±**37.12**	
ALT (IU/L) before	98.10±**4.55**	.00
ALT(IU/L) 3m after	90.24±**4.46**	
AST(IU/L) before	91.71±**4.22**	.00
AST (IU/L) 3m after	86.71±**4.20**	

Table 3: Shows significant improvement of all parameters after SG. p1=before vs 1w after ,p2=before vs 3m after ,p3 = 1w after vs 3m .

Discussion:- Obesity and related complications pose increasing health challenges worldwide **(Fallahi-Shahabad et al;2016)**. An impaired incretin effect is an early feature of T2D patho-physiology , however, in patients with T2D, this is thought to be a secondary phenomenon characterized by defective insulo-tropism due to beta cell dysfunction rather than impaired GLP-1 secretion(**Ahren,2013)**. The present study demonstrated a significant increase in PPGLP-1 with best results in RYGBP group followed by SG group, no significant change in PPGLP-1after IGB insertion. The change of the gut hormone incretins after GBP and their resulting effect on insulin or on glucagon secretion, could be the mediator of the greater improvement of glucose levels after GBP compared to diet or to gastric banding (**Laferrère et al; 2007 and 2008).**Cross sectional data from **Naslund et al.,1998** show a persistent increase fasting and post-prandial GLP-1 and GIP levels 20 years after DJB compared to obese non-operated controls . similar changes of PPGLP-1 following SG were seen in a small study by **Peterli et al. in 2012** ,Possiblly due to more rapid gastric emptying following SG and elevations in cholecystokinin (CCK). The present study demonstrated a significant reduction in BMI , WC , FG ,HbA1C ,HOMA-IR, FI, systolic and diastolic blood pressure, lipid prophile, ALT and AST with best results in RYGBP group then SG group followed by IGB group. **In 2016 ,Fallahi-shahabad** et al .in their prospective cohort study conducted from 2010 to 2013 on 60 consecutive patients who had body mass index (BMI) of more than 40 kg/m2 and met the surgical indication criteria of bariatric surgery. Upon discharge, patients were followed in outpatient clinic of Qaem Hospital, Mashhad, Iran, each 3

months for 12 months.Measurement of anthropometric and metabolic indices was done in each postoperative visit. Anthropometric indices including BMI and waist circumference significantly decreased after the surgery and sustained after 1 year of follow up. The study performed in 2011 by **Hutter et al.** showed that the average reduction in the mean BMI for patients undergoing LSG was 8.75 kg/m2at 6 months and 11.87 kg/m2 at 1 year post operation. Our results, and those of other similar studies(**Benaiges et al;2012 , Jimenez et al;2012 , Vidal et al;2013 and Li et al;2014**) suggest a greater weight loss and/or improvement in obesity-related co-morbidities including diabetes and hyperlipidemia. Greater weight loss and improvements in metabolic parameters are hypothesized to be related to both bypass of the proximal small intestine (upper intestinal hypothesis),which alone has been shown in rat models to improve glucose homeostasis, as well as increased nutrient delivery to the distal small intestine, additional studies in rodents have shown the latter mechanism alone to independently increase glucagon-like peptide-1 (GLP-1) and peptide YY to improve glucose homeostasis **(Thaler and Cummings,2009).**

In summary Our data suggest that the RYGB and SG surgeries,beyond weight loss, induces early beneficial changes in PPGLP-1which favor glycemic control in type 2 diabetes.

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