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ORIGINAL RESEARCH

Effect of Proton Pump Inhibitor Administration on Glycemic Parameters in Patients with Type 2 Diabetes Mellitus

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Abstract: Introduction: Proton pump inhibitors can influence glucose-insulin homeostasis by elevating plasma gastrin. Considering the few clinical trials and contradictory results of previous studies, we aimed to evaluate the effect of omeprazole, a proton pump inhibitor, on glucose-insulin homeostasis in patients with type 2 diabetes mellitus (T2DM). Materials and Methods: In this before-after clinical trial, 40 patients with T2DM received omeprazole treatment for 12 weeks. Patients were asked to continue their diet, lifestyle, and physical activity throughout the study period. Glycosylated hemoglobin (HbA1c), fasting plasma sugar (FBS), insulin level, C-peptide and 2 hours post prandial blood sugar (2hppBS) were measured at baseline and after 12 weeks. Homeostatic model assessment of Insulin resistance (HOMA-IR) and homeostatic model assessment of β-cell dysfunction (HOMA-B) indices were also calculated at baseline and after 12 weeks of omeprazole administration. Results: After 12 weeks of omeprazole administration, there was a clear decrease in the mean HbA1C before (8.11±0.96) and after (7.13±0.68) the treatment (P<0.001). Similarly, a decrease in mean FBS and 2HPPBS before and after treatment was observed, which was statistically significant for FBS (P=0.01) but not for 2HPPBS (P=0.1). There was a clear increase in the level of Insulin (P=0.001) and C-peptide (P=0.003). The mean activity index of HOMA-B before and after receiving omeprazole was 54.41±27.06 and 79.24±45.32, respectively (P=0.007). Also, HOMA-IR index was 5 before, and 6 after receiving omeprazole (P=0.001). Conclusion: Administration of omeprazole, increases insulin levels and decreases the levels of HbA1c, FBS, thus improving glycemic status and can be combined with other drugs used to manage DM, especially in patients with gastrointestinal problems; but more studies are needed.

Keywords: Diabetes mellitus; Gastrin; HbA1c; Proton pump inhibitors; omeprazole; glycemic control

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1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder that has a high prevalence worldwide. In 2019, 463 million people with DM lived worldwide, which is estimated to reach 700 million by 2045 (1). These predictions indicate a sharp increase in DM, especially in developing countries. In fact, we are facing a global epidemic.

DM is a chronic disease with complex pathophysiology that

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does not involve only insulin deficiency in type 1 DM and insulin resistance and progressive loss of pancreatic beta cells in type 2; but other pathophysiologies include increased lipolysis, decreased or resistance to incretin hormones, hyperglucagonemia, increased renal glucose uptake, and brain resistance to insulin (2). But ultimately hyperglycemia in type 1 and type 2 DM is the result of a partial or complete defect of pancreatic beta cells (3) and therefore research on pancreatic beta cell regeneration is being actively investigated.

The history of diabetes treatment and glycemic control shows that more than one treatment is often needed for patients at any one time, and effective treatment requires multiple medications; which is used in combination to correct different pathophysiological defects. Effectiveness of the drugs, their adverse effects, tolerability and cost-effectiveness are also important criteria for drug selection (4). Also, it should always be kept in mind that some drugs are not recommended because we do not have enough information about their side effects. Therefore, any new treatment strategy with the above characteristics can be a good event (3).

DM affects many organs with chronic microvascular complications (retinopathy, neuropathy, and nephropathy), macrovascular complications (Coronary artery disease, peripheral and cerebrovascular disease) and non-vascular complications including gastrointestinal, urogenital and skin involvement, cataract, glaucoma, hearing loss and infection (5).

Studies have shown that careful control and evaluation of blood sugar, proper treatment of DM and achieving plasma glucose in the normal range delays the onset and progression of micro and macrovascular complications (6, 7).

Therefore, glycosylated hemoglobin (HbA1C) is used as the gold standard for diagnosis (8) and evaluation of blood glucose and a criterion for estimating the severity of DM complications (9, 10). In HbA1C, the beta chains of hemoglobin A1 bind to glucose in a non-enzymatic reaction, showing the average blood glucose over the last 8 to 12 weeks (11, 12).

Gastrin, as the main endocrine-regulating hormone in response to secretory activities, after consumption of protein foods (13, 14) and is said to have a trophic effect on beta cells. In mice, gastrin induces neogenesis of pancreatic beta cells (15, 16). In vitro studies also showed that this hormone increase β cell mass (17).

The main site of gastrin secretion is the antrum of the stomach by G cells. But the other parts also secrete gastrin to a lesser extent in response to intestinal stimulation (presence of amino acids and amine-containing diet). Gastrin is the first released incretin hormone in response to oral glucose intake and enhances glucose-dependent insulin secretion (18). Because the amount of gastrin released by oral glucose to stimulate beta cell secretion is very low, the motivation for research on gastrin as an incretin hormone was diminished for decades until recent studies showed interference between gastrointestinal hormones. As well as gastrin can cause normoglycemic conditions in diabetic rats. But gastrin has been shown to affect insulin secretion many times in previous studies (19). On the other hand, proton pump inhibitors (PPIs) are drugs used to treat stomach acid-related diseases, especially gastroesophageal reflux disease. Other uses for PPIs include the treatment and prevention of NSAID-induced ulcers, gastritis, gastric ulcer and duodenal ulcer, part of Helicobacter pylori eradication therapy, hemorrhagic gastric ulcer, and functional dyspepsia (20, 21). They lower acid levels and therefore cause relative hypergastrinemia; which may cause better control of hyperglycemic status. Based on this hypothesis, the question arises as to whether PPI treatment is associated with better control of glycemic status in people with type 2 DM.

Safety in the long-term use of PPIs is more reported in omeprazole. Reports indicate that omeprazole has been safe for 15 years. However, there are some side effects including hypochlorhydria (15).

The risk of hypomagnesemia has also been reported in long-term use of PPI in some cases, and prolonged use of omeprazole has impaired the absorption of Vitamin B12 (20). Secondary hypergastrinemia caused by PPI can be considered a tumor carcinoid. However, long-term use (11 years) of omeprazole has been safe (22).

Recent studies have shown that gastrin, like other incretin hormones such as GLP1, stimulates pancreatic beta cell proliferation and neogenesis in animal and human cells, and also appears to increase insulin levels up to 2 times at the same time as glucose uptake (19, 23).

In one study, three days of intravenous injection of exogenous gastrin increased the beta cell mass of pancreatic islets in mouse samples and continued injection from 7 to 10 days later doubled the mass of beta cells which were examined by morphometry (15). In another study, they showed that the combination treatment of GLP 1 and gastrin expanded the mass of human beta cells implanted in diabetic immunodeficient mice and that it improved the hyperglycemic status. Improved hyperglycemia was associated with increased insulin levels in grafted pancreatic cells and was equally associated with increased plasma C-peptide levels (24). A study demonstrated that combination therapy of Dipeptidyl peptidase inhibitor 4 (DDPi4), such as sitagliptin, linagliptin which increase GLP1 levels, with PPIs, reversed type 1 DM in the non-obese diabetic (NOD) mouse model. Treatment with DDPi4 improved glycemic status in 38%, PPIs in 33%, and their combination improved glycemic status in 75% of them. Unlike administration of either alone, their combination showed a significant increase in C-peptide level (25).

Also, in 2011, the same study group demonstrated that com-

bination therapy with sitagliptin and pantoprazole induced neogenesis of grafted human beta cells in diabetic rats (25). After these basic studies on animals, several studies were performed on humans. In a cross-sectional study of 347 patients with type 2 DM, the HbA1C level in the group who took PPI was 7% and in the group who did not take PPI was 6%, which was significantly lower (22).

Boj-Carceller and co-workers in two separate studies, one study for people with type 1 and 2 poor control DM and the other study for people with controlled type 2 DM, both of which were cross-sectional studies performed on admitted patients, achieved similar results. In the first study, a smaller sample of 72 patients, 33.8% of whom had type 1 DM, showed that patients receiving PPI had lower HbA1C levels than those who did not. This was especially evident in people with type 2 DM who did not receive insulin (26). In the second study on 97 patients with controlled type 2 DM, 54 patients receiving PPI had HbA1C level of 6.7%, compared to 7.3% in 43 patients who did not receive PPI, which was statistically significant (27).

Another study on a small cross-sectional study on 42 people with type 2 DM who had gastrointestinal problems and had been on long-term treatment with esomeprazole in comparison with those who did not receive PPIs, achieved similar results; HbA1C decreased by 0.7% in patients with type 2 DM who received esomeprazole versus 0.2% reduction in patients with DM who did not receive PPIs. In patients with uncontrolled DM (HbA1C more than 9%), the beneficial effects of esomeprazole were more pronounced, showing a 1.2% decrease in HbA1C levels (P=0.004) (28).

Another study showed that omeprazole administration for 12 weeks was associated with a significant improvement in glycemic control based on the FBS and HbA1C level of the patients (29). In contrast, another study on patients with type 2 DM did not show a statistically significant difference between the PPI and control group and concluded that PPI addition does not affect glycemic control (30). Kruszelnicka and colleagues showed that PPI use is not associated with altered glycaemia in patients with cardiovascular disease based on baseline glucose levels and 2 hours post glucose intake levels of the patients (31).

Considering that few studies have been done in this field, most of them are retrospective studies and only studied the effect of PPI on HbA1C level and other parameters of glucose-insulin homeostasis (FPG, Insulin level, C-Peptide, HOMA-B , HOMA-IR) were not assessed in most of them, their contradictory results, and no similar study in Iran (considering its geographical, racial, cultural and nutritional and lifestyle differences), we decided to consider the effect of PPIs on glycemic control in a before-after clinical trial study on patients with type 2 DM referred to the endocrinology clinic of Imam Hossein Hospital. Among PPIs, omeprazole was used in the study because of its safety in long-term use (even up to 15 years) and has a lower cost for patients.

2. Materials and Methods

2.1. Study design

This study is a before-after clinical trial. It was performed on adult patients with type 2 DM referred to the endocrinology clinic of Imam Hossein Hospital during 2020. The sample size was calculated based on previous studies and their data were estimated to be 40 people. After providing explanations for the patient to participate in the research project, and mentioning that no fee would be received, informed consent was obtained and the study was approved by the Ethics Committee.

Inclusion criteria were adults of both sexes with diagnosis of type 2 DM according to World Health Organization criteria whose diabetes was not newly diagnosed and were on maintenance doses of oral anti-diabetic drugs, metformin or sulfonylurea, or both for at least one month.

Exclusion criteria were previous and current use of insulin, pioglitazone or treatment with incretins, history of liver failure (liver enzyme levels more than three times the normal limit), kidney disease (Creatinine>1.5), any complications of DM, alcohol consumption and drugs, hemoglobinopathies, pregnant and lactating women and people who already had used PPIs.

After obtaining the informed consent, questionnaires containing background and demographic information including age, sex, weight, height, body mass index (BMI), education level and place of residence (city/village) were recorded.

Enrolled patients were asked to go to the laboratory in the fasting state for measuring complete blood count (CBC), blood urea nitrogen (BUN), Creatinine (Cr), fasting blood sugar (FBS), hemoglobin A1c (HbA1C), C-peptide, and insulin level in the fasting venous blood sample. Two hours later, the patient underwent venous blood sampling for 2 hours post prandial blood sugar (2hppBS).

Patients were then given omeprazole 20 mg capsules twice daily orally and asked to continue their usual diet, lifestyle, physical activity, and medication during the study. Patient compliance was assessed based on their visits or telephone calls and the number of capsules consumed. Those who took more than 80% of the capsules were considered to have compliance and their test results were examined. Patients were prescribed omeprazole for 3 months and were asked to return to the clinic with the results of re-testing FBS, HbA1C, 2hppBS, C-peptide, and insulin level. To prevent glycolysis, plasma was isolated up to one hour after blood sampling and plasma glucose was measured enzymatically by glucose oxidase. HbA1c was also measured by Bronate Affinity Choromatography using NYCOCARD kit and fasting

insulin and c-peptide levels were assessed by Immunoreactive method.

Homeostatic model assessment of Insulin resistance (HOMA-IR) and homeostatic model assessment of β-cell dysfunction (HOMA-B) indices were also calculated based on the following formulas:

HOMA-IR=(Glucose×Insulin)/405

HOMA-B=(360×Insulin)/(Glucose-63)%

2.2. Statistical analysis

The data collected from the checklists were edited in SPSS software, version 18, and descriptively analyzed by paired and independent t tests. P values of 0.05 or less were considered statistically significant.

3. Results

In this study 40 patients participated, of which 8 (20%) patients were excluded (loss to follow-up) because of non-recurrence, testing and consumption of less than 80% of omeprazole capsules prescribed by the study. The time of evolution of DM in participants was up to 5 years. Of the remaining 32 patients (follow-up group), 12 (37.5%) were men and 20 (62.5%) were women. Their mean±SD age was 54.34±10.85 years (Figure 1).

Of the eight patients who discarded the study, 3 (37.5%) were men and 5 (62.5%) were women. Their mean±SD age was 52.87±8.32 years. The mean difference between the two groups was not statistically significant (P=0.724). Also, all other parameters including the mean initial values of BMI, FBS, 2HPPBS, C-peptide, and HbA1C and fasting Insulin level were not statistically different from the remaining group (Table 1). Table 2 shows the education level of all 40 study participants and the remaining 32 patients (follow-up group).

After 12 weeks of treatment with omeprazole, there was a clear decrease in the mean HbA1C before (8.11±0.96) and after (7.13±0.68) the treatment (P<0.001). Similarly, a decrease in mean FBS, 2HPPBS before and after treatment was observed, which was statistically significant in FBS (P=0.01) but not significant in 2HPPBS (P=0.1). There was a clear increase in the level of insulin (P=0.001) and C-peptide (P=0.003) (Table 3, Figure 2).

Changes in insulin level and HbA1c in the follow-up group is shown in Figure 3, both of which were significant (P=0.001). The mean activity index of HOMA-B before and after receiving omeprazole was 54.41±27.06 and 79.24±45.32, respectively (P=0.007). Also, HOMA IR index was 5 before, and 6 after receiving omeprazole (P=0.001) (Figure 4).

4. Discussion

The main goal of health care systems around the world is to promote the health and treatment of patients with the help of the most effective methods and treatments.

According to American Diabetic Association, in 2018, 34.2 million Americans or 10.5% of the population had DM which about 32.6 million had type 2 DM. Although DM may be underreported as a cause of death, it was the seventh leading cause of death in the United States in 2017 (32).

Statistics from the International Diabetes Federation also showed that in 2019, approximately 463 million adults were living with DM and this will rise to 700 million by 2045. The proportion of people with type 2 DM is increasing in most countries and 374 million people are at increased risk of developing type 2 DM. Also, DM caused 4.2 million deaths and at least 760 billion dollars in health expenditure in 2019 (1).

According to these statistics, controlling DM and its complications is the only way to deal with it. Studies have shown that careful control and evaluation of blood sugar, proper treatment of DM and achieving plasma glucose in the normal range delays the onset and progression of micro and macrovascular complications.

HbA1c is the best parameter for assessing glycemic status and evaluating the effect of anti-diabetic drugs. A meta-analysis showed that PPI administration may not generally have a significant effect on reduction of HbA1C level in patients with type 2 DM, but pantoprazole administration showed significant reduction of HbA1C level, which in turn demonstrates the effect of PPI type on its influence on glycemic control. However, none of the nine studies reviewed in this review addressed the effects of omeprazole, as a PPI, on glycemic control. Also, bias sources such as the exclusive inclusion of men were detected and the article itself pointed to the need for further studies (33).

Based on information available so far, our study was the first clinical trial study in Iran that was performed by Before- After method and investigated the effect of omeprazole treatment on glucose-insulin homeostasis in patients with type 2 DM.

In our study 40 people participated, of which 8 (20%) were excluded from the study for various reasons, including not performing the second test, not taking 80% of the prescribed omeprazole, discontinuation of the drug by the patient's family doctor due to lack of knowledge about the presence of the patient in our study, distance to return to the clinic and a case of drug intolerance. Since they were no more than 20% of the study population, and also there was no statistically significant difference compared with 32 remaining participants in terms of demographic characteristics and other parameters in our study, so their removal did not affect our study and we continued with the remaining 32 patients.

Omeprazole treatment for 12 weeks clearly reduced HbA1c levels by 0.97% and increased insulin levels by 4.01μU/ml, changes similar to those observed in a study by Singh and colleagues (18).

In our study, the mean HbA1c level decreased from 8.1±0.96

to 7.1±0.68, which was statistically significant (P<0.001). Also, in a study performed in India as a Double Blind RCT on 31 patients (16 in the pantoprazole group and 15 in the placebo group) HbA1c level decreased from 7.6±1.17 to 6.8±1.16 and was statistically significant (P<0.001) (18).

We also measured fasting insulin and blood sugar levels, HOMA-B cell and HOMA IR indices. In the previously mentioned study, similar results were obtained, but changes in gastrin levels were examined, which were not addressed in our study due to the high cost. However, C-peptide and 2HPPBS were considered in our study but they were not mentioned in theirs. Table 4 shows a complete comparison of the current study and the mentioned study. Many of the findings of our study are in line with Singh's study and to our knowledge, it is the only study similar to ours in terms of inclusion and exclusion criteria, but the rest of the studies did not follow these points.

One study was based on electronic records of patients with type 2 DM taking PPIs and those not taking them, and the HbA1C levels were reported 7.1% and 7.7%, respectively (34). This value was 8.1% vs. 7.1% in our study. However, they did not specify the duration of PPI use.

A previous cross-sectional study found similar results in patients with type 2 DM with gastrointestinal problems who had been on long-term treatment with esomeprazole and those who did not receive PPI, i.e., HbA1C reduction of 0.7% in patients with type 2 DM receiving esomeprazole versus reduction of 0.2% in patients with DM who did not receive PPI (28).

Other studies have been performed in this field but none of them examined FBS, 2HPPBs, Insulin, C-peptide and HOMA-B and HOMA-IR indices. And most of these studies were retrospective but the type of our study, before-after clinical trial, and the study of these parameters were the advantages over other studies.

Regarding HOMA-IR and HOMA-β indices that were discussed in our study and other studies except Singh's study, it should be said that these two valid and practical indices show insulin resistance and beta cell performance respectively, and are calculated based on fasting blood sugar and insulin through mathematical formulas.

The values attributed to these indicators have been expressed differently in various studies. In one of them, the HOMA-β cell index was expressed 100% in a young person under 35 years with normal weight. In the same study, the HOMA-IR index was expressed as less than 3 (normal resistance), 3 to 5 (moderate resistance), and higher than 5 (sever resistance) (35).

In our study, after 12 weeks of omeprazole, the HOMA-β cell index improved significantly, but the HOMA IR index also increased, which was also statistically significant. However, in one study, the changes in this index were not statistically significant (18). This difference may be due to racial influence and differences in the effect of omeprazole and requires further investigation.

But it is certain that the insulin resistance index in our patients was much higher than in Indian patients in Singh's study and was in the range of severe resistance. However, omeprazole was able to meet our expectations of improving beta cell function, which may be due to stimulation of gastrin secretion as an incretin hormone following omeprazole consumption and therefore the effect of this increase in gastrin level on stimulating beta cells and insulin secretion or beta cell proliferation.

In another study, administration of lansoprazole in Psammomys obesus mice with type 2 DM for 17 days in different doses and measurement of morning blood glucose, insulin, and gasterin, showed that gastrin levels increased by 9-fold, glucose levels decreased significantly, and insulin levels increased. Also, a 50% increase in the volume of beta-cell masses was reported which could further strengthen the idea that there is a close relationship between PPI and gastrin and glucose-insulin homeostasis (19).

Perhaps another reason for the effect of omeprazole in lowering HbA1c levels and improving glycemic status in our study is the effect of this drug and other PPIs in other studies on delayed gastric emptying following food intake. This leads to the timely delivery of glucose to the ileum and thus, if the environment is favorable, causes the secretion of incretin hormones, which in turn leads to a decrease in blood sugar levels after a meal (17). This was clearly seen in the improvement of 2HPPBs after 12 weeks of omeprazole use in our study. Other reasons for the improvement in glycemic status may be related to the direct effect of gastrin on glucose dependent insulinotropic peptide and the secretion of glucagon-like peptide 1 (GLP1) from small intestinal K and L cells, although this has not yet been proven. A 2 to 3-fold increase in plasma gastrin levels occurs after 24 to 32 weeks of PPI consumption (14). However, 12 weeks of pantoprazole treatment in Singh's study was associated with a 50% increase in plasma gastrin levels, which could lead to a further improvement in hyperglycemic status in longer use of PPIs.

One of the strengths of our study is that it is prospective and RCT, which distinguishes the current study from other retrospective studies, as well as accurate inclusion and exclusion criteria and review of various parameters that did not exist in other studies. But the before-after design and lack of placebo group is our limitation compared to other RCT studies.

5. Conclusion

Treatment with omeprazole increases insulin levels and decreases the levels of HbA1c, FBS, thus improving glycemic status and can be combined with other drugs used to man-

age DM, especially in patients with gastrointestinal problems, but more studies are needed. RCTs with placebo group, larger sample size, use of other PPIs, and if possible, plasma gastrin measurement is recommended.

6. Appendix

6.1. Acknowledgment

None.

6.2. Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

6.3. Funding support

None.

6.4. Author's contributions

All the authors have the same contribution.

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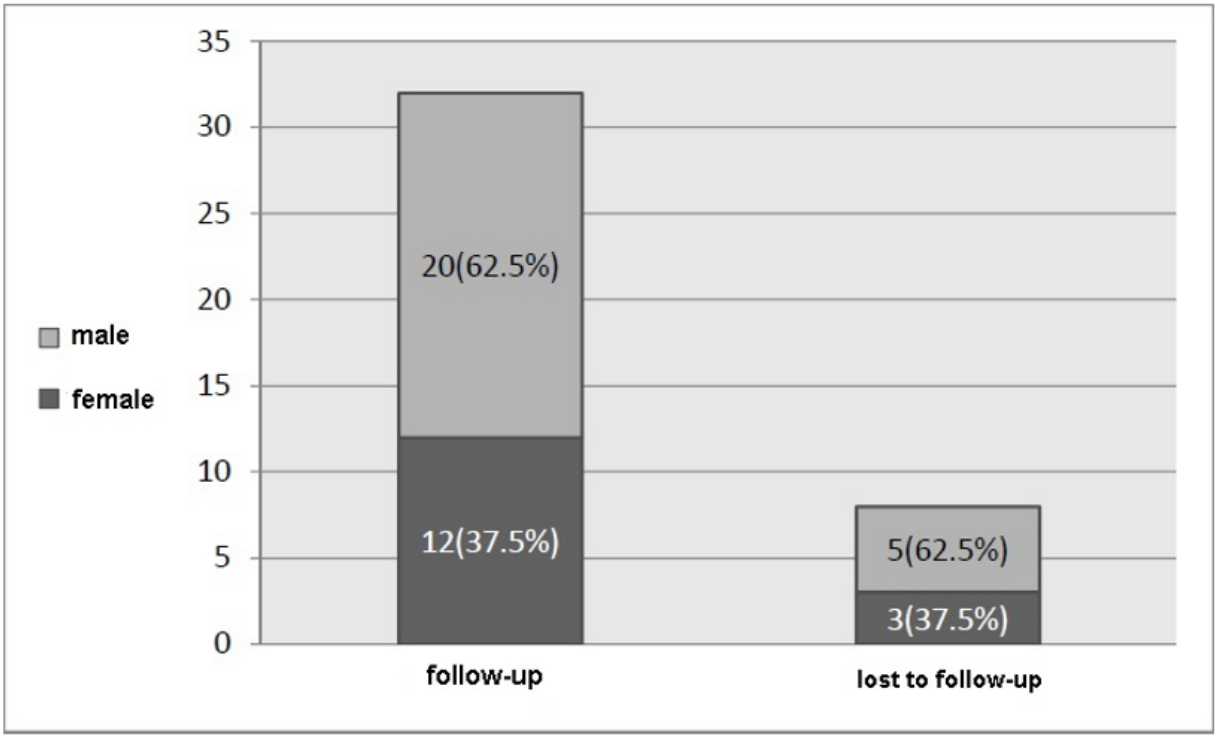

Figure 1: Gender demographic chart of the study participants.

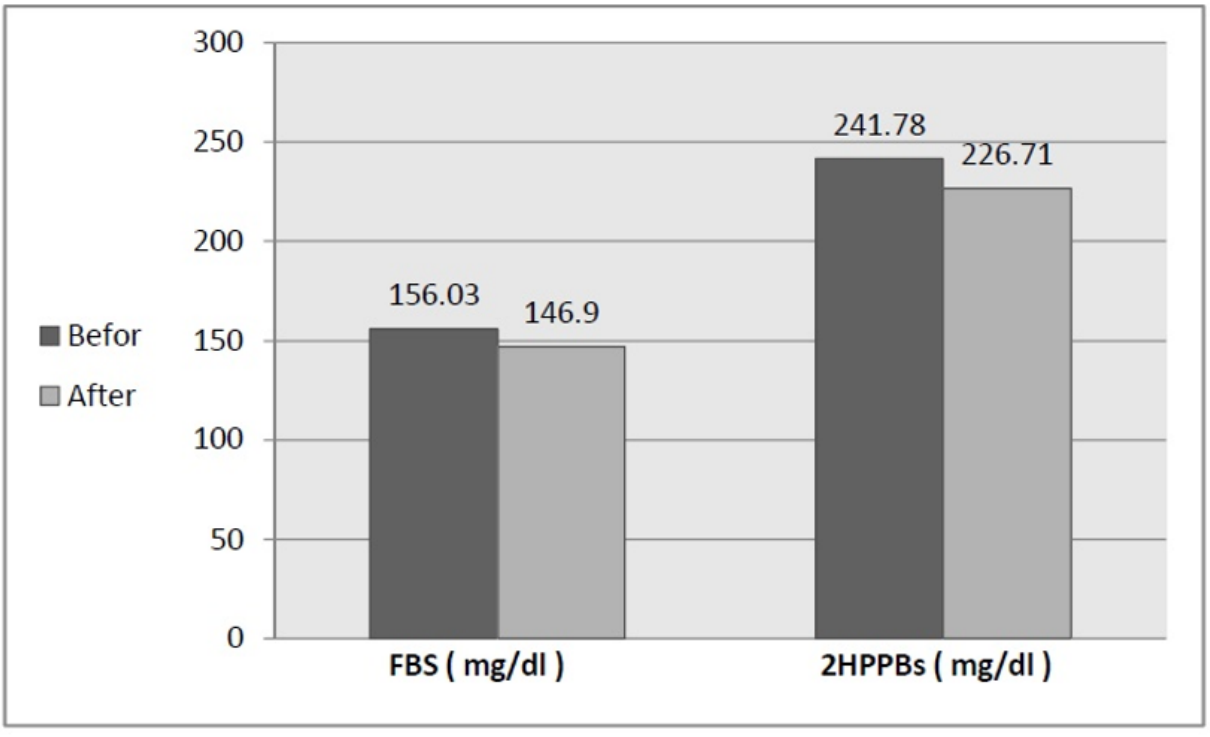

Figure 2: Comparison of mean fasting blood sugar and blood glucose 2 hours after meals before and after receiving omeprazole.

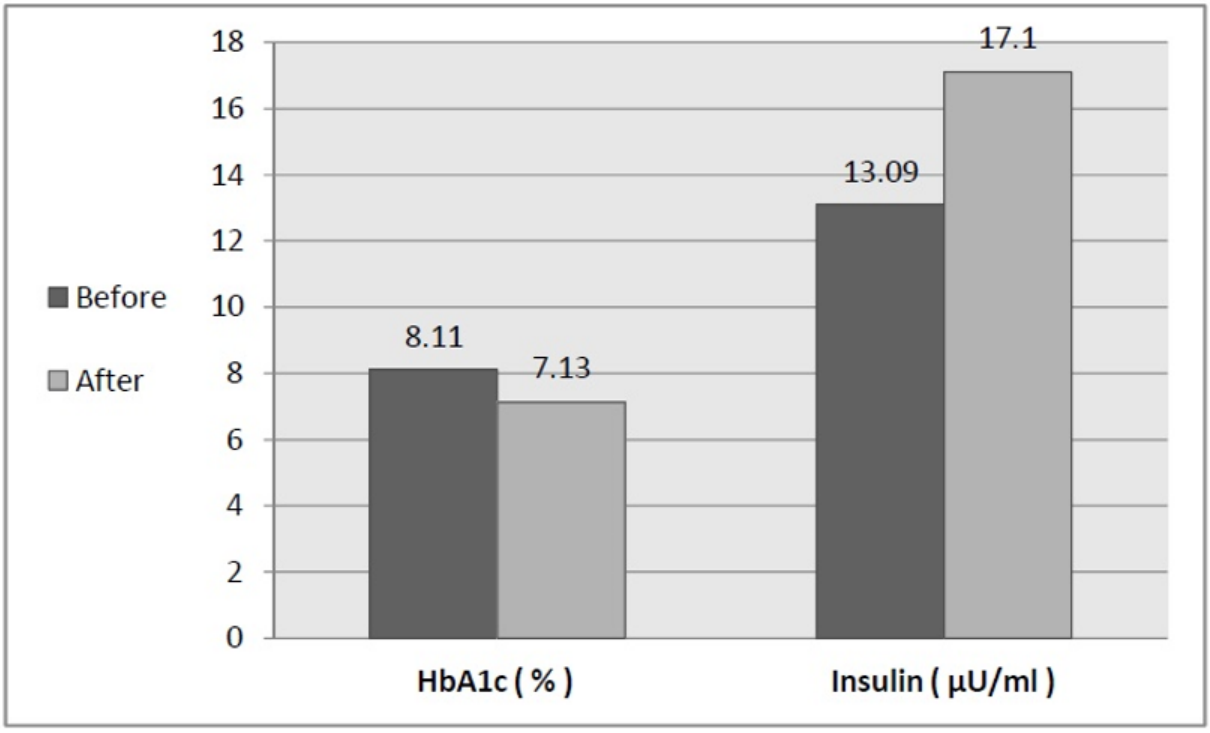

Figure 3: Changes in HbA1C and insulin level following 12 weeks of omeprazole therapy.

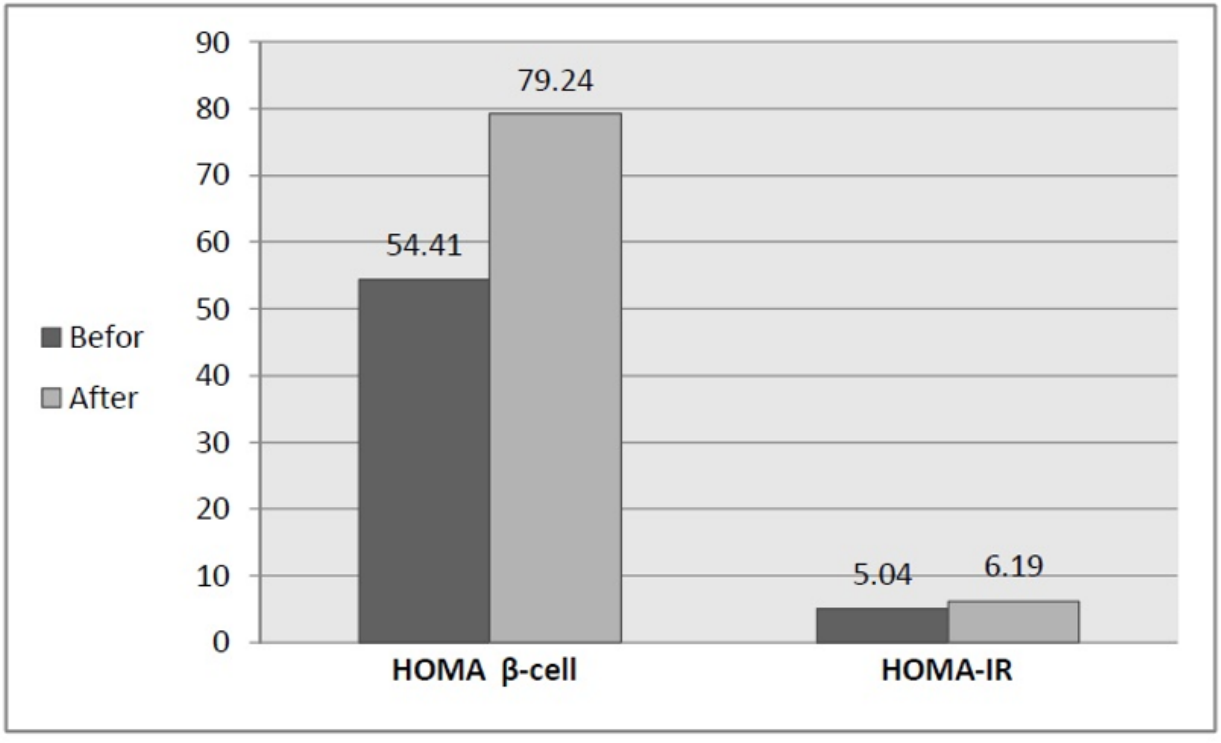

Figure 4: Comparison of Homeostatic model assessment of Insulin resistance (HOMA-IR) and homeostatic model assessment of β-cell dysfunction (HOMA-B) indices before and after omeprazole administration.

Table 1: Comparison of follow up group and loss of follow.

	Status	N	Mean	Std. Deviation	P-Value
Age	Follow-up	32	54.34	10.85	0.724
	Lost to follow-up	8	52.87	8.32	
BMI	Follow-up	32	29.00	2.74	0.905
	Lost to follow-up	8	28.87	2.03	
HbA1C. Before	Follow-up	32	8.11	0.96	0.298
	Lost to follow-up	8	7.73	0.58	
Insulin. Before	Follow-up	32	13.09	5.65	0.845
	Lost to follow-up	8	12.64	6.30	
C-Peptide. Before	Follow-up	32	2.94	0.98	0.548
	Lost to follow-up	8	2.70	1.02	
FBS. Before	Follow-up	32	156.03	30.87	0.817
	Lost to follow-up	8	153.25	26.76	
2hppBs. Before	Follow-up	32	241.78	64.35	0.715
	Lost to follow-up	8	232.75	50.34	

BMI: Body mass index; HbA1c: glycosylated hemoglobin; FBS: fasting plasma sugar; 2HppBS: 2 hours post prandial blood sugar.

Table 2: The education level of all study participants and the remaining follow up group.

Education level	study participants	Follow up group
None	3	2
Less than a high school diploma	20	16
High school diploma	12	11
Advance degree	5	3

Table 3: The effect of 12 weeks omeprazole therapy on glycemic parameters.

Parameter	Before Omeprazole	After Omeprazole	P Value
HbA1C (%)	8.11±0.96	7.13±0.68	0.001
FBS (mg/dl)	156.03±30.87	146.90±23.88	0.01
2HppBs (mg/dl)	241.78±64.35	226.71±48.45	0.16
Insulin (µU/ml)	13.09±5.65	17.10±7.16	0.001
C-Peptide (ng/ml)	2.94±0.98	3.40±1.30	0.003

HbA1c: glycosylated hemoglobin; FBS: fasting plasma sugar; 2HppBS: 2 hours post prandial blood sugar.

Table 4: Comparison of our study results with Singh and colleagues' study.

	Singh's study		Our study	
Parameter	Pantoprazole (Before)	Pantoprazole (After)	Omeprazole (Before)	Omeprazole (After)
HbA1c	7.9±1.2	6.8±1.2	8.11±0.96	7.13±0.68
FBS	126.3±10.3	109.2±13.0	156.03±30.8	146.90±23.8
2HppBs	———-	———	241.7±64.3	226.7±48.4
Insulin	10.5±4.0	13.9±4.5	13.09±5.65	17.10±4.16
C-Peptide	———-	———-	2.94±0.98	3.40±1.30
Gastrin	54.4±14.0	75.6±15.1	———-	———-
HOMA β-cell	75.0±55.8	105.1±52.9	54.41±27.09	79.24±45.32
HOMA-IR	3.9±1.4	3.8±1.7	5.02±2.42	6.19±2.52

HbA1c: glycosylated hemoglobin; FBS: fasting plasma sugar; 2HppBS: 2 hours postprandial blood sugar;
HOMA β-cell: homeostatic model assessment of β-cell dysfunction; HOMA-IR: Homeostatic model assessment of Insulin resistance.