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The efficacy of liraglutide combined with intragastric balloon on weight loss

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SUMMARY

OBJECTIVE: Intragastric balloon placement is an effective method for weight reduction. The aim of this study was to evaluate the efficacy of combining liraglutide with intragastric balloon.

METHODS: Initially, demographic data of patients such as age, gender, comorbid diseases, adverse events, initial weight, height, body mass index, percent body fat, and waist-hip ratio were collected. Weight, body mass index, percent body fat, and waist-hip ratio were measured in the second, third, fourth, fifth, and sixth months. Then, intragastric balloon was removed and liraglutide was stopped.

RESULTS: A total of 50 patients were included in the study, of whom 28 (56%) were in Group A (intragastric balloon) and 22 (44%) were in Group B (plus liraglutide). Weight change at the time of balloon removal was higher in Group B [median weight change 13.8 (7.8 min to 16.8 max) versus 7.9 (4.8 min to 11.8 max); p<0.01]. When the weight, percent body fat, body mass index, and waist-hip ratio changes were compared according to gender, no significant difference was observed in the groups. Comorbid diseases were hypertension in 7 patients (4 in Group A and 3 in Group B) and diabetes in 9 patients (5 in Group A and 4 in Group B). No statistical significance was found.

CONCLUSION: Liraglutide has benefits in terms of weight, percent body fat, and body mass index reduction when administered with intragastric balloon.

KEYWORDS: Glucagon-like peptide 1. Gastric balloon. Liraglutide. Obesity. Body weight changes.

INTRODUCTION

Intragastric balloon (IGB) is an effective minimally invasive procedure for patients with body mass index (BMI) over 35[1]. Up to 35% success has been reported in obesity control[2]. Minimized gastric volume, increased satiety, and increased gastric emptying time are thought to be related to this weight reduction technique[3,4].

Liraglutide is a glucagon-like peptide-1 receptor agonist (GLP1-RA). Medical treatment has become an alternative method with the development of GLP1-RA. Subcutaneous use of liraglutide has been found to be successful for weight loss in adults and approved for overweight and obese in combination with reduced calorie foods and regular physical activity[5]. Appropriate groups are adults with a BMI≥30 or ≥27 kg/m² with weight-related comorbidities (e.g., hypertension, diabetes, or dyslipidemia)[2]. GLP-1 is an incretin hormone secreted by the L cells of the gastrointestinal tract in response to nutrients digested in the gastrointestinal lumen. GLP1-RA stimulates insulin secretion and reduces glucagon secretion from the pancreas in a glucose-dependent manner. Additionally, it induces a dose-dependent weight loss by decreasing calorie intake through delayed gastric emptying and activation of GLP-1 receptors in the brain[6].

In a small number of studies investigating the efficacy of liraglutide combined with IBG, it has been observed that, when liraglutide is started after balloon removal, it has an additional benefit in terms of efficiency and reduction in body fat[6], the average weight loss is greater after balloon removal and even 6 months later, it does not increase complications[7,8], and it may be effective in preventing weight regain[9]. The effect of combining endoscopic IGB insertion with liraglutide on weight reduction remains unknown despite these reports. In this study, we aimed to evaluate the efficacy of combining the GLP1-RA to endoscopic IGB insertion on weight reduction.

METHODS

This study was retrospectively performed with the data collected between August 2020 and August 2021. The study was approved by the Local Ethics Committee (with decision number 2023/97 on 12.04.2023), and written informed consent was obtained from all patients. All patients were adults aged above

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20 years with a BMI over 27 kg/m² and they were unable to reduce weight with lifestyle modifications and diet. They were presented to the General Surgery Clinic with the requisition of IBG insertion for weight reduction.

Patients who preferred only IBG were classified as Group A and patients who additionally accepted liraglutide as Group B. In Group A (GrA), only IGB (MedSil®, Belgium) was applied. In Group B (GrB), liraglutide (Saxenda, Novo Nordisk, Bagsvaerd, Denmark) was added 0.6 mg/day, subcutaneously for 6 months to the treatment schedule. All IGBs were removed 6 months after the insertion. There was no adverse event causing the early withdrawal of IGB. All patients tolerated both IGB and liraglutide during the study. All IBG insertions and withdrawals were performed by a certified general surgeon.

Demographic data of patients such as age, gender, comorbid diseases, adverse events, initial weight, height, BMI, percent body fat (PBF), and waist-hip ratio (WHR) were collected. Patients' weight, BMI, PBF, and WHR were measured in the second, third, fourth, and fifth months by a dietician and nurse. Finally, in the sixth month, the same parameters were evaluated, IGB was removed with the same physician, and liraglutide was stopped.

Patients were informed about diet and lifestyle modifications. A clear liquid diet was approved in the first week, following the IGB insertion. A full liquid diet in the second week, a soft diet with high protein content in the third week, and a regular high-protein diet with 80% calories of the basal metabolic rate in the fourth week and beyond were applied, respectively. Side effects of liraglutide were noted monthly on visits.

Insertion and removal of intragastric balloon

The MedSil® is designed as a nonadjustable saline-filled balloon with a maximal volume of 700 mL and approved for 6 months. It was applied in the endoscopy unit in the left-lateral position with monitorization. Normal saline was used for inflation under direct visualization endoscopically. Removal of IGB was also carried out in the endoscopy unit. The balloon was deflated in the sixth month by puncturing with an endoscopic needle. All saline was suctioned out and the balloon was extracted from the esophagus by a grasper. Patients may complain of nausea, vomiting, pain, and gastroesophageal reflux disease (GERD) after IGB insertion. Antiemetics and antispasmodics were offered in such cases. A proton pump inhibitor is prescribed routinely once daily with the duration of IGB.

Application of liraglutide

Potential side effects of the drug such as nausea, constipation, headache, and diarrhea were informed to the patients. The initial and maintenance dose was 0.6 mg/day applied subcutaneously on the abdomen, thigh, or upper arm. The drug was started 1 month after IGB insertion and discontinued with removal in the sixth month.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics, version 23.0 (SPSS Inc., Chicago, USA). Descriptive statistics were reported as mean±standard deviation and median (minimum to maximum) according to the distribution of variables. The difference between the baseline and sixth month values between the groups was evaluated using the independent samples t-test or the Mann-Whitney U test. The limit of significance was accepted as $p<0.05$.

RESULTS

A total of 50 patients were included in this study. The mean age was 32.5 (26–41) years in GrA and 35.5 (19–55) years in GrB. A total of 28 patients (56%; 19 females and 9 males) were treated with IGB and 22 (44%; 17 females and 5 males) with IGB plus liraglutide, respectively. Comorbid diseases were hypertension in seven patients (four GrA and three GrB) and diabetes in nine (five GrA and four GrB). No statistical significance was found according to the distribution of comorbid diseases in groups. Adverse events of IGB and liraglutide were abdominal pain in four patients (two GrA and two GrB), nausea and vomiting in seven (four GrA and three GrB), and GERD in four (two GrA and two GrB). None of the patient's balloon was removed, with liraglutide being stopped, or excluded because of side effects. There was no statistically significant difference in the distribution of adverse events according to the groups (Table 1).

When the weight, PBF, BMI, and WHR changes of the patients were compared according to the months. The initial and second month PBF values ($p=0.001$ and $p=0.006$) as well as fifth and sixth month BMI values ($p=0.026$ and $p=0.031$) were statistically significant in GrA and GrB, respectively (Table 1).

Patients in GrB lost more weight in the sixth month than GrA. Weight reduction at the time of balloon removal was higher in GrB [median weight change 13.8 (7.8 min to 16.8 max) versus 7.9 (4.8 min to 11.8 max); $p<0.01$]. The median PBF change in Gr A was 9.5 (5 min to 9.5 max), and in GrB, it was 7 (4.5 min to 9.5 max); $p<0.001$. The mean BMI change at the time of balloon removal in GrA was 3.13±0.51, and in GrB, it was 4.9±0.87; $p<0.001$. The median WHR change in GrA was 5 (5 min to 5 max), and in GrB, it was 5 (2 min to 9 max), which was statistically nonsignificant ($p=0.471$) (Table 2). When the changes in the weight, PBF, BMI, and WHR of patients were compared according to gender, no significant difference was observed in groups.

Table 1. Demographic data of patients such as age, gender, comorbidities and adverse events, and baseline and subsequent values of weight, percent body fat, body mass index, and waist-hip ratio measurements.

		Group A (IGB)			Group B (IGB plus liraglutide)			p
Age		32.5			34.5			
Gender		19 females, 9 males 28 (56%)			17 females, 5 males 22 (44%)			
Comorbid diseases	Hypertension	4			3			>0.05
	Diabetes, prediabetes, insulin resistance	5			4			>0.05
Adverse events	Abdominal pain	2			2			>0.05
	Nausea, vomiting	4			3			>0.05
	GERD	2			2			>0.05
		Median	Minimum	Maximum	Median	Minimum	Maximum	p
Weight	Initial weight	78	68	112	82	70	133	0.882
	Weight 2nd month	76.4	66.4	108.4	78.4	65.3	127.0	0.522
	Weight 3rd month	74.8	64.3	107.3	76.3	62.3	124.3	0.449
	Weight 4th month	74.1	63.1	105.1	74.1	60.1	121.1	0.392
	Weight 5th month	71.8	62.8	103.8	72.2	57.8	119.6	0.175
	Weight 6th month	70.2	59.2	100.2	71.1	55.2	116.2	0.148
PBF	Initial PBF	40.5	40.5	40.5	37.6	29.8	42.5	**0.001**
	PBF 2nd month	37.1	37.1	37.1	36.1	27.1	40.1	**0.006**
	PBF 3rd month	34.6	34.6	34.6	34.6	26.6	39.6	0.712
	PBF 4th month	32.9	32.9	32.9	32.9	25.9	38.9	0.712
	PBF 5th month	31.9	31.9	31.9	31.9	25.9	37.9	0.292
	PBF 6th month	31.0	31.0	31.0	31.0	23.0	36.8	0.169
BMI	Initial BMI	30.3	25.8	33.4	29.9	26.0	35.0	0.516
	BMI 2nd month	29	25	32	29	25	33	0.906
	BMI 3rd month	29	24	32	28	24	33	0.455
	BMI 4th month	28	24	31	27	23	32	0.230
	BMI 5th month	28	23	30	27	22	31	**0.026**
	BMI 6th month	27	23	30	26	21	31	**0.031**
WHR	Initial WHR	0.93	0.93	0.93	0.93	0.88	1.11	0.736
	WHR 2nd month	0.92	0.92	0.92	0.92	0.87	1.08	0.712
	WHR 3rd month	0.91	0.91	0.91	0.91	0.87	1.06	0.471
	WHR 4th month	0.89	0.89	0.89	0.89	0.88	1.03	0.049
	WHR 5th month	0.89	0.89	0.89	0.89	0.85	1.02	0.712
	WHR 6th month	0.88	0.88	0.88	0.88	0.84	1.02	1.000

IGB: intragastric balloon; GERD: gastroesophageal reflux disease; PBF: percent body fat; BMI: body mass index; WHR: waist-hip ratio. Bold indicates statistically significant values.

DISCUSSION

Intragastric balloons are recommended to be removed in the sixth month after insertion[10]. The effectivity of IGB is associated with its gastric volume reducing feature. It also diminishes caloric intake and increases the feeling of satiety by delaying gastric emptying. The effectivity of IGB will probably lost and patients desire eating more for satiety with the removal of the balloon. Therefore, measures that can prevent eating and weight regain behavior should be determined and their medical effectiveness should be revealed[3,4]. Liraglutide reduces calorie intake and lowers body weight by causing a delay in gastric emptying[5]. Due to this feature, it was thought that it could be beneficial for weight regain after the removal of the IGB. Weight regain was reported as a major problem after IGB removal up to 35%

Table 2. Change in weight, percent body fat, body mass index, and waist-hip ratio levels between groups.

	Group A (IGB)	Group B (IGB+Liraglutide)	p-value
	Mean±SD Median (min–max)	Mean±SD Median (min–max)	
Weight	7.9 (4.8–11.8)	13.8 (7.8–16.8)	**<0.001**
PBF	9.5 (9.5–9.5)	7 (4.5–9.5)	**<0.001**
BMI	3.13±0.51	4.9±0.87	**<0.001**
WHR	0.5 (0.5–0.5)	0.5 (0.2–0.9)	0.471

PBF: percent body fat; BMI: body mass index; WHR: waist-hip ratio. Descriptive statistics were reported as mean±standard deviation in normally distributed data and median (minimum to maximum) in non-normally distributed data, according to the distribution of variables. Only BMI change was normally distributed, and mean±standard deviation was used. Bold indicates statistically significant values.

as seen after metabolic surgeries[11,12]. The factors that affect weight regain following the IGB removal are not well understood. Hormonal changes, dietary incompatibility, inadequate physical exercises, mental problems, alcohol consumption, and sleep disturbances may cause weight regain[10].

In the first study evaluating liraglutide plus IGB, the mean weight loss was found as 10.2±6.7 kg at the time of IGB removal. After 6 months, the mean weight loss was decreased to 2.7±4.1 kg. This shows that the effectiveness of liraglutide and IGB gradually decreases in the follow-up period[7]. In a nonadjustable IBG study, the weight loss of patients was diminished seriously 5 years after removal (23.9–7.3 kg)[13]. Notably, 78.7% of patients regained weight and have been candidates for metabolic surgeries 3.3 years after IGB removal[14].

The efficacy of liraglutide plus IGB compared with placebo was also studied at different daily doses of 1.2, 1.8, 2.4, or 3.0 mg in randomized controlled trials, and weight loss was found, respectively, as 4.8, 5.5, 6.3, and 7.2 kg after 20 weeks[15]. Another study investigated weight loss following the removal of nonadjustable IGB at 12 months. Weight loss was found to be significantly higher in those using 1.2 mg liraglutide (17.4±3.8 versus 10.7±4.1; p<0.001)[9]. IGB plus 0.6–3 mg/day different doses of liraglutide were evaluated compared with IGB alone. A significant weight loss was found at the sixth month (18.3 versus 22.2 kg; p<0.001) in the combined group[8]. In our study, we did not increase the dose and 0.6 mg liraglutide was used daily throughout the study. No other study combining IGB with low dose liraglutide has been observed in the literature. BMI and weight change at the end of 6 months suggest that a dose as low as 0.6 mg may be effective.

A total of 3,731 nondiabetic patients with BMI≥30 or ≥27 kg/m² with dyslipidemia or hypertension were randomized to receive 3.0 mg/day subcutaneous liraglutide or placebo plus diet and exercise in another study. Weight loss at week 56 was significantly higher with liraglutide compared with placebo. In addition, blood pressure and prevalence of prediabetes were decreased in patients receiving liraglutide, and 76% of patients receiving liraglutide lost more than 5% of their weight[16]. Different daily doses of liraglutide combinations have been applied to prevent weight regain after all weight-reducing treatments, including bariatric surgeries[17-20]. Pharmacotherapy with liraglutide was reported as having lower risk and resulted in significant improvement in hypertension and dyslipidemia[18]. Therefore, daily subcutaneous injection of liraglutide is an alternative option to treat weight gain in eligible patients[18]. Different studies emphasized the beneficial effects of liraglutide on reducing body fat composition and distribution, and improvements in metabolic and cardiovascular tests[21]. In a study examining body fat loss, a significantly greater loss of PBF was found in the liraglutide group compared with the IGB group[6] as in our study. Acute pancreatitis, acute cholecystitis, bowel obstruction, epigastric pain, nausea, and GERD are reported complications of IGB[22]. Similarly, abdominal pain, nausea, vomiting, and GERD were observed in our study.

The meaning and impact of each factor in preventing weight regain are likely different. As patients lose weight, mechanisms in body weight regulation that act to resist weight loss make it more difficult to maintain weight loss and create a higher risk for weight gain. A lifestyle change, including dietary restriction, exercise program, and regular sleep, is strictly recommended after balloon replacement for the effectiveness of the weight loss procedure in obese patients[6,7]. One or two monthly follow-ups with a team including weight loss counselors, personal fitness trainers, dietitians, nurses, and doctors may be beneficial in preventing weight regain as we do. Also, close follow-up protocols may be applied following the IGB removal to prevent weight regain. Mobile applications that give instructions to all patients about exercise, diet, and lifestyle changes can be developed, and mobile communication support groups such as WhatsApp and Telegram can be used more effectively.

The important limitation of this study is that it was retrospective and did not evaluate the weight gain processes after the balloon was removed and liraglutide was stopped. In addition, adaptation processes and lifestyle changes are far from being measurable and remained at the recommendation level. Also, the use of liraglutide was carried out in accordance with the wishes and financial possibilities of the patients and not in accordance with the randomization rules.

More randomized controlled trials with larger numbers of patients with longer follow-ups are needed to evaluate

the effect of liraglutide on weight gain with appropriate duration and dosage, along with metabolic and cardiovascular effects.

CONCLUSION

This study showed that the change in weight, PBF, and BMI is greater in patients receiving additional liraglutide compared with baseline values. There were no significant side effects that required discontinuation of liraglutide. Lifestyle change should also be recommended in all patients as it may positively affect the results of endoscopic IGB placement.

AUTHORS' CONTRIBUTIONS

AY: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Methodology, Project administration. **SH:** Supervision, Validation, Visualization. **GD:** Software, Writing – original draft, Writing – review & editing. **OK:** Investigation, Resources.

REFERENCES

1. Moura D, Oliveira J, Moura EG, Bernardo W, Galvão Neto M, Campos J, et al. Effectiveness of intragastric balloon for obesity: a systematic review and meta-analysis based on randomized control trials. Surg Obes Relat Dis. 2016;12(2):420-9. https://doi.org/10.1016/j.soard.2015.10.077
2. Martins Fernandes FA, Carvalho GL, Lima DL, Rao P, Shadduck PP, Montandon ID, et al. Intragastric balloon for overweight patients. JSLS. 2016;20(1):e2015.00107. https://doi.org/10.4293/JSLS.2015.00107
3. Machytka E, Brooks J, Buzga M, Mason J. One year adjustable intragastric balloon: safety and efficacy of the Spatz3 adjustable balloons [version 1; peer review: 2 approved with reservations]. F1000Research. 2014;3:203.
4. Vargas EJ, Rizk M, Bazerbachi F, Acosta A, Abu Dayyeh BK. Changes in gastric empty ing with the Spatz3 adjustable intragastric balloon are associated with increased weight loss: a prospective study. Surg Obes Relat Dis. 2018;14:118.
5. Konwar M, Bose D, Jaiswal SK, Maurya MK, Ravi R. Efficacy and safety of liraglutide 3.0 mg in patients with overweight and obese with or without diabetes: a systematic review and meta-analysis. Int J Clin Pract. 2022;2022:1201977. https://doi.org/10.1155/2022/1201977
6. Badurdeen D, Hoff AC, Barrichello S, Hedjoudje A, Itani MI, Farha J, et al. Efficacy of liraglutide to prevent weight regain after retrieval of an adjustable intra-gastric balloon-a case-matched study. Obes Surg. 2021;31(3):1204-13. https://doi.org/10.1007/s11695-020-05117-8
7. Mosli MM, Elyas M. Does combining liraglutide with intragastric balloon insertion improve sustained weight reduction? Saudi J Gastroenterol. 2017;23(2):117-22. https://doi.org/10.4103/1319-3767.203362
8. Fittipaldi-Fernandez RJ, Hoff AC, Barrichello SA. Intragastric balloon treatment in association with liraglutide: a novel approach in the excess weight treatment. Gastrointest Endosc. 2019;89:AB271.
9. Hoff AC, Fittipaldi-Fernandez RJ, Barrichello SA. Impacts of liraglutide use in weight maintenance after balloon retrieval: a 12-month follow up. Gastroenterology. 2019;156:1172-3.
10. Sander B, Arantes VN, Alberti L, Neto M, Grecco E, Souza T. 550 long-term effect of intragastric balloon in the management of obesity. Gastrointest Endosc. 2017;85:AB83. https://doi.org/10.1016/j.gie.2017.03.113
11. Aune D, Vatten LJ. Diabetes mellitus and the risk of gallbladder disease: a systematic review and meta-analysis of prospective studies. J Diabetes Complications. 2016;30(2):368-73. https://doi.org/10.1016/j.jdiacomp.2015.11.012
12. Velapati SR, Shah M, Kuchkuntla AR, Abu-Dayyeh B, Grothe K, Hurt RT, et al. Weight regain after bariatric surgery: prevalence, etiology, and treatment. Curr Nutr Rep. 2018;7(4):329-34. https://doi.org/10.1007/s13668-018-0243-0
13. Kotzampassi K, Grosomanidis V, Papakostas P, Penna S, Eleftheriadis E. 500 intragastric balloons: what happens 5 years thereafter? Obes Surg. 2012;22(6):896-903. https://doi.org/10.1007/s11695-012-0607-2
14. Haddad AE, Rammal MO, Soweid A, Shararra AI, Daniel F, Rahal MA, et al. Intragastric balloon treatment of obesity: long-term results and patient satisfaction. Turk J Gastroenterol. 2019;30(5):461-6. https://doi.org/10.5152/tjg.2019.17877
15. Astrup A, Rössner S, Gaal L, Rissanen A, Niskanen L, Hakim M, et al. Effects of liraglutide in the treatment of obesity: a randomised, double-blind, placebo-controlled study. Lancet. 2009;374(9701):1606-16. https://doi.org/10.1016/S0140-6736(09)61375-1
16. Pi-Sunyer X, Astrup A, Fujioka K, Greenway F, Halpern A, Krempf M, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. N Engl J Med. 2015;373(1):11-22. https://doi.org/10.1056/NEJMoa1411892
17. Thakur U, Bhansali A, Gupta R, Rastogi A. Liraglutide augments weight loss after laparoscopic sleeve gastrectomy: a randomised, double-blind, placebo-control study. Obes Surg. 2021;31(1):84-92. https://doi.org/10.1007/s11695-020-04850-4
18. Horber FF, Steffen R. Correction to: reversal of long-term weight regain after roux-en-Y gastric bypass using liraglutide or surgical revision. A prospective study. Obes Surg. 2021;31(7):3386. https://doi.org/10.1007/s11695-021-05426-6
19. Pajecki D, Halpern A, Cercato C, Mancini M, Cleva R, Santo MA. Short-term use of liraglutide in the management of patients with weight regain after bariatric surgery. Rev Col Bras Cir. 2013;40(3):191-5. https://doi.org/10.1590/s0100-69912013000300005
20. Stanford FC, Alfaris N, Gomez G, Ricks ET, Shukla AP, Corey KE, et al. The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: a multi-center study. Surg Obes Relat Dis. 2017;13(3):491-500. https://doi.org/10.1016/j.soard.2016.10.018
21. Feng WH, Bi Y, Li P, Yin TT, Gao CX, Shen SM, et al. Effects of liraglutide, metformin and gliclazide on body composition in patients with both type 2 diabetes and non-alcoholic fatty liver disease: a randomized trial. J Diabetes Investig. 2019;10(2):399-407. https://doi.org/10.1111/jdi.12888
22. Said F, Robert S, Mansour EK. Pancreatitis and intragastric balloon insertion. Surg Obes Relat Dis. 2016;12(3):e33-4. https://doi.org/10.1016/j.soard.2015.12.015