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BRIEF COMMUNICATION

Is Early Reimplantation of the Duodenal–Jejunal Bypass Liner Viable?

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Abstract

The endoscopically implanted duodenal–jejunal bypass liner (DJBL) is an impermeable fluoropolymer device which prevents food making contact with the proximal intestine, thus inducing weight loss and improvement of type 2 diabetes mellitus (T2DM). However, weight and HbA1c levels generally increase post explantation. This study investigated the safety and feasibility of early DJBL reimplantation in five patients with obesity whose glucose levels had relapsed post explantation, examining the effect of reimplantation on weight loss, BMI and T2DM management. All DJBL implantation and explantation procedures were performed without complications. Despite reduction of T2DM medications, reduction in body weight and HbA1c levels resumed after reimplantation. In conclusion, early reimplantation of DJBL appears feasible, safe and effective.

Keywords Obesity · Type 2 diabetes · Duodenal–jejunal bypass liner · Weight loss · Glycaemic control · Obesity surgery

Introduction

Obesity has become a worldwide epidemic. It is estimated that in 2030, 2.2 billion people worldwide will be overweight and 1.1 billion will be affected by obesity, accounting for over 30% of the entire world population [1, 2]. One of the major complications of obesity is the development of diabetes, which results in considerable mortality and morbidity and enormous health care costs [3].

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At present, bariatric surgery is the only effective treatment delivering sustainable weight loss and glycaemic control in patients with obesity and diabetes. Roux-en-Y gastric bypass (RYGB) remains one of the most favoured bariatric procedures in patients with type 2 diabetes mellitus in the context of obesity. Hyperglycaemia has been shown to improve within a few days of surgery and even before significant weight loss has occurred, suggesting a role of weight-independent mechanisms in enhancing glucose metabolism [4, 5].

The duodenal–jejunal bypass liner (DJBL, GI Dynamics, Lexington, MA, USA) is an endoscopically implantable and removable 60-cm-long impermeable fluoropolymer device anchored in the bulbus duodeni. Functionally, the DJBL mimics some of the physiological effects of RYGB, including the exclusion of food from the proximal small intestine and the mixing of pancreatic and biliary juices after food passes through the sleeve. Several clinical trials analysing patients over a duration of 6–12 months following implantation have shown a total body weight loss of between 11.9 and 23.6%, accompanied by improvements in diabetes including reduction of HbA1c and normoglycaemia [6–8].

However, both body weight and HbA1c levels have been reported to increase within 6 months of explantation. This has prompted the question as to whether the DJBL can be reimplanted and how reimplantation would affect BMI and diabetes management. One initial study by Koehestanie et al. recently demonstrated reimplantation of DJBL 18 months after its

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first removal to be feasible [9]. In view of this success, and since, as stated above, weight loss and HbA1c are known to increase even within 4 to 6 months of explantation, an even earlier reimplantation of the device would seem advantageous [7].

The aim of this study was therefore to investigate the safety, feasibility and effectiveness of early (4-month) reimplantation of the DJBL in patients who show an early relapse in BMI and HbA1c after DJBL explantation.

Patients and Methods

This retrospective, observational study was conducted at the Department of Surgery and Gastroenterology at the Obesity Centre based at DGD Clinics Frankfurt-Sachsenhausen, Germany, between 2014 and 2016. Ethical approval was given by the ethics committee of the regional regulatory institution, LÄK Hessen (FF 24/2017).

After the first implantation, DJBLs had remained in situ for 12 months. During this period, up to and including 6 months after reimplantation, all patients took part in a follow-up monitoring program. Outcomes of the full study cohort of 20 patients from the initial implantation phase up to November 2014 were published previously [4].

Five patients with T2DM and obesity who completed the follow-up program and underwent explantation after 12 months were selected for reimplantation according to the inclusion and exclusion criteria set out below. All five patients gave written informed consent for reimplantation and data analysis. Intensification of diabetes-related pharmacotherapy was not permitted after explantation in these patients, in order to avoid drug-induced enhancement of biochemical parameters in the context of the study. The participants received nutritional and diabetes counselling including dietary advice on avoiding weight gain. Weight loss, BMI and HbA1c were analysed before and 12 months after reimplantation.

Inclusion criteria for study participation were age 18–65 years, BMI between 28 and 35 kg/m^2, T2DM with two different oral medications or insulin and previous uncomplicated DJBL implantation and explantation. Additionally, the patients were required to have achieved weight loss and improvement of glycaemic parameters and to have shown full commitment to the follow-up schedule during the first implantation period of at least 12 months.

Exclusion criteria were pregnancy, use of non-steroidal anti-inflammatory drugs (NSAIDs), anticoagulation therapy, weight loss medication, substance abuse, active *Helicobacter pylori* infection and gastrointestinal tract abnormalities observed during the first implantation or explantation.

Patients were advised to consume only liquids and pureed fruit for 7 days after reimplantation and soft, moist or pureed foods during days 8–14. All patients received a proton pump inhibitor (omeprazole 40 mg twice daily) during DJBL treatment to prevent ulceration. Peri-procedural diabetes medications were adjusted based on the medical advice of a specialist endocrinologist.

Follow-Up

After the first DJBL implantation, follow-up visits were performed after 1, 3, 6 and 12 months. After the device was explanted, reimplantation was performed 4 months later and patients were monitored again at months 17, 19 and 22. After 28 months, the DJBL was explanted for a second time. Assessments during the visits included safety and follow-up laboratory parameters, body weight, blood pressure and adverse events. All patients received nutritional and diabetes counselling.

Statistics

Data were collected prospectively using a computerised database and analysed using SPSS 24.0 for Windows. Mean, standard error and range for each parameter were calculated. No additional statistical analysis was performed. The graphics were created using GraphPad Prism 5.02 (GraphPad Software, Inc.).

Results

Five patients were included in this observational study (Table 1), one female and four male, with a mean age of 48.6 (± 21.2) years and a mean BMI of 40.9 (± 10.3) kg/m^2. Although, in some cases, pseudopolyps were visible in the duodenal bulb prior to reimplantation, it was possible to reimplant the DJBL 4 months after explantation without any complications. Likewise, no complications arose during reexplantation. Implantation was performed under general

Table 1 Patient characteristics at baseline and changes at 12 months after the first implantation and 4 months after the first explantation

$n = 5$	Baseline	12 months after the first implantation	Δ	4 months after the first explantation	Δ
Age (years); gender	48.6 ± 21.2; 1 male, 4 female				
Weight (kg, mean)	115.8	95.0	− 20.8	97.3	+ 2.3
BMI (kg/m^2, mean)	40.9	29.2	− 11.7	33.9	+ 4.7
HbA1c (%)	9.1	6.7	− 2.4	7.8	+ 1.1

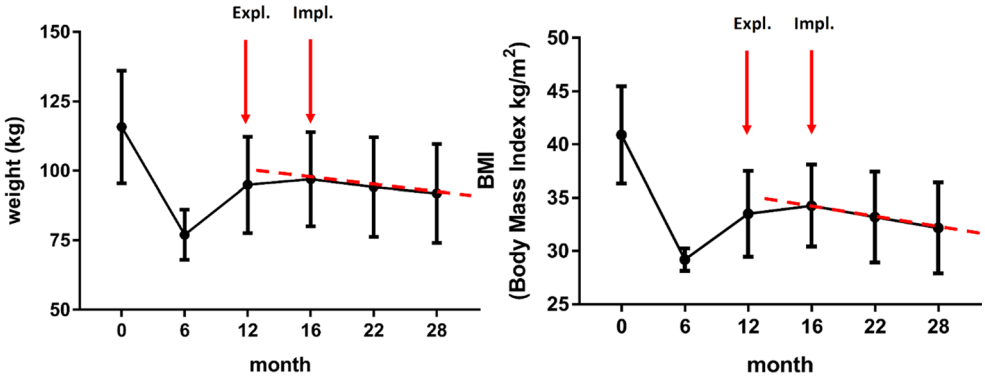

Fig. 1 Results—body weight/BMI

anaesthesia with tracheal intubation. The first implantation of the DJBL took 26 (20–39) min in mean, whereas reimplantation was performed in an average time duration of only 15 (10–17) min, in line with current primary implantation times.

During the first implantation phase, mean (± SD, range) body weight decreased significantly from 115.8 (45.4; 88–196) to 93.0 (38.8; 72–164) kg, and mean BMI (± SD, range) decreased from 40.9 (10.3; 35.3–59.2) to 33.5 (9.0; 29.5–49.5) kg/m^2 (Figs. 1 and 2), while mean levels of glycated haemoglobin (HbA1c) decreased from 9.1% (1.3; 8–10.7) to 6.7% (0.9; 5.9–7.8). Three months after the first explantation, body weight, BMI and HbA1c increased to 97.0 (37.8; 72–164) kg, 34.5 (8.6; 29.5–49.5) kg/m^2 and 7.7% (1.6; 5.9–7.8), respectively. After reimplantation, all three parameters diminished once more, follow-up results at 12 months for the same parameters being 91.9 (39.8; 73–161) kg, 32.8 (9.5; 28.8–48.4) kg/m^2 and 7.1% (0.67 3.9–6.8) (Figs. 1 and 2).

The majority of patients were taking metformin, gliflozins and liraglutide; one patient required insulin before reimplantation. Twelve months after device reinsertion, approximately half of the patients had reduced or discontinued at least one of the drugs (Table 2).

Discussion

Trials in Europe and Latin America have shown DJBL to be an effective and safe therapy for patients with obesity and T2DM [8]. Reports of liver abscesses in patients treated with DJBL in the sham-controlled US ENDO trial [10] are probably attributable to a lack of suitable study selection criteria in a land where obesity therapies are expensive and inaccessible, and many study patients therefore had not only severe obesity but also severe and numerous comorbidities including poorly managed T2DM. Although the DJBL works conceptually, both weight and HbA1c levels have been reported to increase within 6 months of explantation. This has prompted the question as to whether the DJBL can be reimplanted, and how reimplantation would affect BMI and diabetes management. A pilot study by Koehestanie et al. recently demonstrated that reimplantation can be safely carried out 18 months after the first removal of the DJBL [9]. In view of this success, and since, as stated above, weight loss and HbA1c are known to increase during the first 4 to 6 months after explantation, even earlier reimplantation of the device would be advantageous [7].

Our observational study demonstrated for the first time that it is technically possible to reimplant the DJBL within 4 months of explantation. While only a small group of patients were evaluated, our results indicate that early reimplantation is not only viable, but seems also to be safe and effective. Reimplantation showed a similar efficacy in terms of body weight and metabolic parameters as initial DJBL implantation. Compared to the study of Koehestanie et al., our patients showed even better results, possibly due to the earlier reimplantation of the device and the longer implantation period.

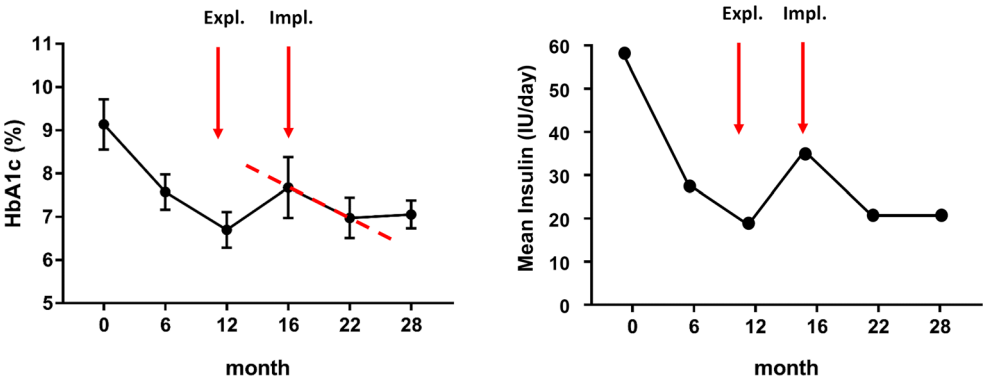

Fig. 2 Insulin/glycated haemoglobin A1c (HbA1c)

Table 2 Diabetic medication at baseline and after device explantation

Medication	At baseline (*n*)	After device explantation (*n*)			
		↑	→	↓	Ø
Dapagliflozin	3	0	1	0	2
Empagliflozin	1	0	1	0	0
Insulin	2	0	0	2	0
Liraglutide	3	0	1	1	1
Metformin	5	0	2	1	2

↑, increased; →, no change; ↓, decreased; Ø, discontinued

However, only patients who responded to the device during the first implantation period, achieving weight reduction as well as lower HbA1c levels and improved glycaemic control, were chosen to participate in this study. In these patients, device reimplantation again showed positive effects on weight and glucose levels, while at the same time allowing daily medication to be reduced. Therefore, while larger studies are required to substantiate the data presented here, DJBL reimplantation may be considered in this patient group. Whether reimplantation is worthwhile in patients whose results were less favourable during the first DJBL implantation period remains unclear and requires further studies.

Conclusion

This observational study (in a small group of patients) shows promising results for early reimplantation of DJBL after 4 months in patients with T2DM who did well during their first implantation. Reimplantation of the DJBL only 4 months after explantation is feasible and seems to be safe. Furthermore, reintroduction of the DJBL resulted in additional weight loss and further enhancement of glycaemic control, despite a substantial reduction in medication.

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Author Contributions All authors made substantial contributions to the conception and design of the article and to acquisition, analysis and interpretation of data. Jürgen Stein drafted the manuscript. All authors reviewed the manuscript for important intellectual content and approved the final version for publication.

Compliance with Ethical Standards

Ethical approval was given by the ethics committee of the regional regulatory institution, LÄK Hessen (FF 24/2017). All five patients gave written informed consent for reimplantation and data analysis.

Conflict of Interest The authors declare that they have no conflicts of interest.

References

1. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA. 2006;295(13):1549–55.
2. Kelly T, Yang W, Chen CS, et al. Global burden of obesity in 2005 and projections to 2030. Int J Obes. 2008;32(9):1431–7.
3. Haslam DW, James WP. Obesity. Lancet. 2005;366(9492):1197–209.
4. Guenthert SJ, Stier C, Weiner RA, et al. Improvement in glucose metabolism after bariatric surgery: comparison of laparoscopic Roux-en-Y gastric bypass and duodenojejunal bypass liner. Gastroenterology. 2015;148(4):S900.
5. Sugerman HJ, Wolfe LG, Sica DA, et al. Diabetes and hypertension in severe obesity and effects of gastric bypass-induced weight loss. Ann Surg. 2003;237(6):751–6. discussion 757-758
6. Force ABET, Committee AT, Abu Dayyeh BK, et al. ASGE Bariatric Endoscopy Task Force systematic review and meta-analysis assessing the ASGE PIVI thresholds for adopting endoscopic bariatric therapies. Gastrointest Endosc. 2015;82(3):425–38. e425
7. Patel N, Mohanaruban A, Ashrafian H, et al. EndoBarrier(R): a safe and effective novel treatment for obesity and type 2 diabetes? Obes Surg. 2018;28(7):1980–9.
8. Jirapinyo P, Haas AV, Thompson CC. Effect of the duodenal-jejunal bypass liner on glycemic control in patients with type 2 diabetes with obesity: a meta-analysis with secondary analysis on weight loss and hormonal changes. Diabetes Care. 2018;41(5):1106–15.
9. Koehestanie P, Betzel B, Aarts EO, et al. Is reimplantation of the duodenal-jejunal bypass liner feasible? Surg Obes Relat Dis. 2015;11(5):1099–104.
10. Gersin KS, Rothstein RI, Rosenthal RJ, et al. Open-label, sham-controlled trial of an endoscopic duodenojejunal bypass liner for preoperative weight loss in bariatric surgery candidates. Gastrointest Endosc. 2010;71(6):976–82.