Ileal Interposition with Sleeve Gastrectomy for the Treatment of Type 2 Diabetes

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ABSTRACT

Metabolic syndrome and two of its most important components, obesity and type 2 diabetes, have reached pandemic proportions threatening the entire world. Initial treatment options indicating life style changes including diet and exercise have failed to achieve desired results for an important portion of patients and eventually considerable numbers of patients have become worse than the pre-treatment status due to reactive weight regain. Currently, the most effective treatment for obesity and type 2 diabetes is, without doubt, surgical procedures. There is no treatment option that can achieve remission for the entire compounds of metabolic syndrome with over 90% efficiency. However, it should be known that there are numerous methods used for the surgical treatment of metabolic syndrome and all have advantages, disadvantages, and restrictions of their own. Also, each has its own rate of efficiency. This article aimed to provide a brief understanding on the mechanisms of action and analyze the outcomes of diverted sleeve gastrectomy with ileal transposition (DSIT) as a mode of functional restrictive therapeutic option for obese and non-obese patients with type 2 diabetes.

Key Words: Metabolic surgery, sleeve gastrectomy, ileal transposition

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METABOLIC SURGERY

The original description of metabolic surgery is “the treatment of any metabolic disease by surgical means”. In this respect, splenectomy used for the treatment of hematological disorders like ITP, Idiopathic Thrombocytopenic Purpura, is accepted within the concept of metabolic surgery. However, when metabolic surgery is mentioned in clinical practice, what is meant is the treatment of non-morbidly obese type 2 diabetic patients with surgical procedures. To this end, the only surgical method applied to overweight type 2 diabetic patients from the start has been ileal transposition (IT)⁷,⁸). However, recent popular approach is to adapt obesity surgery procedures like gastric bypass to overweight patients and name them as “Metabolic Surgery”. The purpose of this article was to discuss surgical procedures with specific emphasis on IT and review possible solutions against probable scenarios awaiting us in the future.

“FUNCTIONAL RESTRICTION” and SURGICAL SUCCESS

Currently, the most widespread procedures in obesity surgery are gastric bypass and sleeve gastrectomy. Unfortunately, the third most widespread procedures in terms of frequency are revision operations. Sadly, the word “revision” represents the disability and inefficiency of the operations performed. Just like any other field in surgery, obe-
Ileal transposition: A challenging option?
IT associated with a diverted sleeve gastrectomy has been blamed for its complexity and named as a challenging operation. However, recently published evidence suggest that IT, compared to sleeve and bypass, has a slightly higher, but acceptable complication (6.1%) and mortality (0.27%) rates, and can be safely performed within the hands of well trained and dedicated teams(14).

Ileal transposition: Do we really need it?
IT with diverted sleeve gastrectomy technique offers the possibility to provide us caloric restriction, duodenal exclusion and enhanced early ileal stimulation, without significant malabsorption, which makes the IT operation different from BPD and DS where the entire jejunum is bypassed (Figure 1). BPD and DS do have the capability to provide same opportunities with the expense of a marked malabsorption. Surgeons should question the extent of the consequences of daily clinical practice and keep away from ending one form of addiction, while triggering another one. Since only proximal 50 cm of the jejunum is bypassed in IT, the technique provides this facility without causing a marked malabsorption. Preoperative and postoperative analysis of patients undergoing IT has demonstrated that iron deficiency anemia and vitamin D deficiency dropped from 6.7% and 24.2% to 6.1% and 19.7%, respectively(14).

Figure 1. Schematic demonstration of the operation. A. Sleeve gastrectomy, B. Duodenal transection, C. Inframesocolic transfer of the sleeve, D. Interposition of the ileal segment between distal stomach and the proximal jejunum.
PATHOPHYSIOLOGY of TYPE 2 DIABETES and IT

Type 2 diabetes is a dynamic, heterogeneous and multifactorial disease. In the novel paper by Ralph De Fronzo, eight mechanisms have been pointed out for the development and progression of type 2 diabetes, which are shown in Table 1. In morbidly obese diabetics, the excess fat (adipotoxicity) takes the central place, whereby in non-morbidly obese individuals, beta cell failure associated insulin insufficiency and disrupted insulin release plays the central effect. In other words, in morbidly obese diabetics, the main problem is insulin resistance, and in non-morbidly obese individuals, the main denominators of surgical success are insulin sensitivity and beta cell glucose sensitivity. From this point of view, clamp studies can guide with respect to disease pathophysiology\(^{16,17}\).

CLAMP STUDIES

Insulin Sensitivity

Insulin sensitivity in clamp method is calculated as the whole body insulin-mediated glucose uptake (M value, mol.min\(^{-1}\).kg\(^{-1}\)ffm\(^{-1}\)) during the last forty min of the clamp normalized to fat-free mass. 6,6-2 [H5] glucose (titrated glucose) data is analyzed to calculate glucose rates of appearance (Ra) and disappearance (Rd) in the fasting state and during the clamp. Endogenous glucose production (EGP) is obtained as the difference between the time-course of Ra and exogenous glucose infusion rate.

Beta-Cell Function

Beta-cell function during MTT is resolved using a mathematical model describing the relationship between insulin secretion and glucose concentration. In brief, the model consists of three blocks: firstly, glucose concentration profile is stabilized; secondly, dependence of insulin (or C-peptide) secretion on glucose concentration is stabilized; and thirdly, C-peptide kinetics are individually adjusted to the subject's anthropometric data.

Insulin Kinetics & Efficiency

The dependence of insulin secretion rate on absolute glucose concentration at each time point during MTT is described by a dose-response function relating the two variables. The main characteristic parameter of the dose-response, the mean slope within the observed glucose range, is denoted as beta-cell glucose sensitivity by analogy with insulin sensitivity (slope of the dose-response of insulin-mediated glucose uptake vs. insulin concentrations). The dose-response function is modulated by a time-dependent potentiation factor, indexed as the ratio of its value at 2 h into the MTT to the corresponding basal value. The dependence of insulin secretion rate on the rate of change of plasma glucose levels is denoted as rate sensitivity.

MECHANISMS of ACTION in IT

It has been previously documented that IT is associated with significant increase in rate sensitivity, disposition index, glucose dependent C-peptide release, and insulin sensitivity index (Figures 2-5). Furthermore, IT leads to significant elevations in beta cell glucose sensitivity, insulin sensitivity, hepatic resistance index, and muscular sensitivity index (Figures 6-8).

WEIGHT LOSS

IT operation has been performed on a wide variety of patients with BMI ranging from 25 to > 40 kg/m\(^2\). Therefore, weight loss after IT has been evaluated in terms of BMI ranges. Briefly, patients were grouped into four categories: BMI 25-30, 30-35, 35-40 and > 40 kg/m\(^2\). Change in BMI according to these groups were 6.27, 7.91, 10.41, and 13.2 kg/m\(^2\) and percentage of excess BMI loss (EBMIL\%) was 22.4, 24.64, 27.98, and 30.3%, respectively\(^{14}\). These data demonstrate that the more the preoperative excess weight, the more weight loss has been achieved by IT operation. This operation provides an early contact of ingested nutrients to the interposed distal ileum and an early and significant rise of glucagon-like peptide is observed. This step corrects the defective early phase of insulin secretion and leads to prolonged satiety.

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**Table 1. Mechanisms involved in the occurrence and progression of type 2 diabetes**

1. Inadequate insulin release from beta cells, disrupted early phase insulin effect
2. Insulin Resistance (IR) in peripheral tissues
3. Increased endogenous glucose production (hepatic/intestinal glucose output)
4. Adipocytes
5. Gastrointestinal tract (incretion insufficiency/resistance)
6. Alpha cell (hyperglucagonemia)
7. Kidney (glucose reabsorption)
8. CNS (insulin resistance-others)
Figure 2. Changes in rate sensitivity after IT.

Figure 3. Changes in disposition index after IT.

Figure 4. Changes in glucose dependent C-peptide release after IT.

Figure 5. Changes in insulin sensitivity after IT.
Mechanisms of action in insulin sensitivity and beta cell functions after II-SG

Figure 6. Changes in beta-cell glucose sensitivity in lean, overweight and obese patients after IT.

Increase in Insulin Sensitivity According to BMI Values

Figure 7. Changes in insulin sensitivity in lean, overweight and obese patients after IT.

Time Based Evaluation (3 years) of Insulin Sensitivity After II-SG in T2DM Patients with BMI < 35

Figure 8. Changes in hepatic resistance index (left) and muscular sensitivity index (right) in lean, overweight, obese and morbidly obese patients after IT.
SUMMARY
Bariatric and Metabolic Surgery is still an evolving concept and there will always be a search for “the best” technique. Although BPD and DS provide the highest rates of remission in terms of weight control and glycemic regulation, they are still being practiced by less than 3% of the bariatric community. Bariatric surgery and complex medical therapy, may eventually necessitate a revisional surgery in the field of Bariatric and Metabolic Surgery are listed below (7,8,18):
1. Caloric restriction and weight adjustments
2. Increased gastric emptying and decreased Ghrelin levels
3. Early contact of the “non-digested” food with the ileal mucosa and “ileal nutrient sensing”
4. Correction of glucose dependent insulin response due to GIP effect (Duodenal Exclusion)
5. Correction of the glucagon suppression (Duodenal Exclusion + Ileal Proximalisation)
6. Decrease in hepatic and peripheral insulin resistance
7. Decrease in Hepatic Glucose Output

Data demonstrated in the present paper documents that it operation provides all the above mentioned steps without causing long term malabsorption and supplement requirement. The major problem associated with it is its technical difficulty and complexity which can be overcome by well-organized education and training models.

REFERENCES
Tip 2 Diyabet Tedavisinde İleal Transpozisyon ve Sleeve Gastrektomi

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Metabolik sendrom ve bunun en önemli iki bileşeni olan obezite ve tip 2 diyabet artık tüm dünyayı tehdit eden bir pandemi haline gelmiştir. Diyet ve egzersiz uygulamaları içeren yaşam tarzı değişiklikleri hastaların önemli bir kısmında istenen tedavi hedeflerine ulaşamamış ve hatta reaksiyonel geri dönüşlere bağlı olarak hastaların bir kısmında tedavi öncesinde durumdan daha kötü bir hale gelmelerine neden olmuştur. Günümüzde obezite ve tip 2 diyabet konusunda en etkili tedavi hiç tartışmasız cerrahi uygulamalarıdır. Metabolik sendromun tüm bileşenleri üzerinde %90’ın üzerinde remisyon sağlayan başka bir tedavi yöntemi bulunmamaktadır. Ancak, bilinmelidir ki metabolik sendromun cerrahi tedavisinde kullanılan çok sayıda yöntem bulunmaktadır ve tüm bu yöntemlerin kendisine has avantaj, dezavantaj ve kısıtlılıkları vardır. Ayrıca, her yöntem etkinlik düzeyi de farklıdır. Bu makalenin amacı bu eylemin mekanizmaları hakkında kısa ve öz bir anlayış oluşturuma ve obez ve obez olmayan tip 2 diyabet hastalarını için fonksiyonel kısıtlama sağlayan bir tedavi yöntemi olarak Diverted Sleeve Gastrektomi + İleal Interpozisyon ameliyatının sonuçlarını analiz etmekti.

Anahtar Kelimeler: Metabolik cerrahi, sleeve gastrektomi, ileal transpozisyon