

Research

An Update on Bariatric Surgery with Long Term Efficacy and Its Utilization for Medical Therapy Development from the Different Mechanism of Action and Other Short Comes to Be Outcome

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Introduction

Obesity is increasing markedly and according to WHO there are 2.3 billion overweight people globally, of which 700 million people are obese [1]. There is need for long term effective treatment. In our previous work on obesity we have tried to cover the various aspects of aetiopathogenesis of obesity, medical treatment and further updates on medical therapy and how long term treatment with medical treatment is required but yet no effective medical treatment is found [2-7]. Here we try to provide an update on Bariatric Surgery (BS) and how it may be effective in tackling morbid obesity in adolescents as well and its long-term benefits along with overcoming problems associated with BS.

Methods

We carried out a pubmed database search for the same and have tried to review the articles found on BS relating to morbidly obese adolescents, longterm effects of BS, complications and mechanism of action of the same till 2018.

Results

We found a total of 6136 articles. We excluded duplicate articles and selected 65 articles pertaining to the topic, 10 articles on morbidly obese adolescents undergoing BS, 5 articles on long-term effect of BS, 2 on nutritional complications and further on other conditions like IIH, Nephrolithiasis, venous thromboembolism (VTE) and 15 articles on mechanism of action which have been used for this update. No meta-analysis was done.

Bariatric Surgery (BS)

Bariatric Surgery (BS) by definition is a group of surgical procedures performed to facilitate substantial weight loss by resecting the size of stomach and or limiting absorption in small intestine as per American

Society for Metabolic and BS [8]. Metabolic Surgery is defined as the operative manipulation of a normal organ system to achieve a biological result or a potential health gain. Evolution of BS should always be viewed in the following ways-i.e. BS always will be and remains a metabolic surgery [9]. BS has been shown to be the most effective type of approach for achieving and sustaining weight loss in morbidly obese people [10].

The total number of bariatric procedures was estimated at 304768 in 2011 [11]. The most commonly performed procedures were Roux-Y gastric bypass (46.6%), vertical sleeve gastrectomy (SG) (27.8%), adjustable gastric banding (AGB) (17.8%) and biliopancreatic diversion with duodenal switch (2%). The largest number of operations were performed in the US and Canada together (101645), followed

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by Brazil(65000),France(27648),Mexico(19,000), Newzealand (12000),UK(10000). No other nation performed 10,000 or more operations in 2011 [11]. Arterburn and Coucoulas 2014 reviewed the historical evolution of various procedures and compared the various systematic and other reviews comparing effectiveness of BS with nonsurgical management [12].

Although it is a highly effective treatment for extreme obesity,BS patients recurrently report difficulty in initiating and maintaining healthy behavioral changes following surgery [13]. Most post operative BS patients are strictly placed on liquid diet during the early post operative phase and are practically unable to consume larger quantities of food in one sitting on taking solid protein within the first month which put them at a higher rates of developing protein malnutrition [14]. Hence post surgical multivitamin and high protein supplementation is important to avoid any nutrient deficiency [15]. These high protein supplements in general are inexpensive ,widely distributed ,and commonly used in patients who need protein supplementation while recovering from a illness or post BS [15]. Hence post surgical multivitamin and high protein supplementation is important to avoid any nutritional deficiency [15]. High protein supplements are mainly rich in proteins, and supplemented with minerals, vitamins. Protein supplementation is an effective approach in ensuring that post BS patients maintain muscle mass and healthy levels of these nutrients and body composition [15]. In its absence weight loss achieved by surgery may present a systematic issue =>higher fat percentage and lack of these elements , since these are essential for the function of the human physiology. The imbalance of such essential body composition and nutrients can also cause pathological and irreversible conditions.

Thus Al- Shamani et al tried to investigate the efficacy of protein supplementation in reducing the risk of developing protein malnutrition, and muscle wasting in post BS patients in Qatar. They are studying 160 post BS patients in Doha's Department of bariatric and metabolic surgery for which they have randomized these patients to be followed up 6 mthly in which both male and female obese subjects having a BMI >35kg/m2 between 18-69 yrs are included .They excluded subjects having renal or liver disease or those with past history of BS from final analysis. Protein supplement(Cubitan,Nutricia,Netherlands)which contains daily intake of 20g of protein is to be taken orally 3times a day throughout the study period. The placebo group is to receive identical ampoules containing zero protein with exact instructions as per the intervention group. Body weight, muscle and fat mass ,total protein, albumin, Vit B12,Mg and zinc will be measured at baseline and every follow up /study visit. Study variables will be compared between 2 groups at different stages of the trial including baseline using sample t test (paired and unpaired)and significant levels will be confirmed with the 95% Confidence limit with alpha error set to 0.05.

The major strength of their study was that Qatari obese population was a distinctive one where results from international studies may not apply

to the local unique context .Thus their study would give health providers in Qatar for ensuring good clinical practice and healthy and sustainable wt loss following BS. The limitations is the slight discrepancy in caloric content of the intervention and placebo(250and 100cal respectively). However it is the intervention with the higher caloric content in which case it may not influence results of their hypothesis that protein supplementation=>lower fat mass and higher muscle mass. Other limitations were that both intervention and placebo are not objectively measured .Although they are making efforts for ensuring compliance as well as reporting of consumption of products. Also they could be lost to follow up .Patients may cease to participate especially once they have lost significant weight and gained the fitness to consume any of the food which they desire [16].

Wellbourn 2014 showed that 53.9%of men and 41.4%of women had 4 or more obesity related diseases at the time of primary surgery as per the UK national bariatric register [17]. But significant resolution of comorbidities occur within 2 years of bariatric surgery [18-20], with long term cost savings ,as treatment is not jut obesity but obesity related illnesses [17]. Though weight loss is not the most important outcome of BS ,the aim is to support resolution of obesity related illnesses, but it is considered to be important secondary factor of surgical options [17]. Gilhooty et al tried to explore the predictors of short term and longer term poor weight loss after BS. In a single centre postoperative cohort pilot study ,in patients undergoing BS, they assessed the accuracy (discrimination and calibration) of 2 previously validated risk prediction models(the physiological and operative severity score for the enumeration of Morbidity and Mortality(POSSUM Score) and the obesity surgical mortality risk score(OS-MS) for postoperative outcome(post operative morbidity survey(POMS).They tested the relationship between test of morbidity and longer term weight loss outcomes adjusting for known patient risk factors .

They collected completed data on 197 patients who underwent surgery for obesity or obesity related illnesses between mar2010 and sep 2013,and found that POSSUM and ORMS were less accurate at predicting POMS defined morbidity on day 3 than defining prolonged length of stay due to poor mobility and for POMS defined morbidity. Having fewer than 28days alive and out of hospital within 30days of surgery was predictive of poor weight loss at 1year independent of POSSUM defined risk(odds ratio 26%;95%confidence interval 1.28-5.24).Thus they concluded POSSUM may be used to predict patients who will have prolonged postoperative length of stay(LOS) after BS due to morbidity or poor mortality. But independent of POSSUM Score having <than 28days alive and out of hospital predicted poor weight loss outcomes at 1year .This added to the literature that post operative complications are independently associated with poor longer term surgical outcomes [21].

Role of Robotics in BS

Reviewing the role of robotics in foregut and BS Toro et al 2015 found robotic procedures were associated with better ergonomics for the surgeon, better visualization of the anatomy ,easier fine dissection(i.e lymphadenectomy)when required and higher cost .In foregut surgery ,the robotic system is significantly associated with considerable lower rate of mucosal perforation in Heller myotomy as compared to laparoscopy . In BS the clinical advantages have not been well documented yet, however it seems robotics shortens the learning curve in this area ,the clinical outcomes of robotic surgery are the same as standard lapaoscopy .However use of robotics in selected cases may have specific advantages and may overcome the limitations of laparoscopic surgery. More research is needed ,mainly larger well designed RCT's to elucidate the exact condition [22].

Role of BS in IIH

Effective treatment is not there for idiopathic intracranial hypertension(IIH),a condition where there is increased intracranial pressure(ICP),and papilloedema and is found primarily in obese women. Weight loss and lowered BMI have been shown to lower ICP and improve symptoms in IIH ,however it is typically not maintained i.e symptoms return .The IIH Weight trial(IIHWT)would assess whether BS is an effective longterm treatment for patients with a BMI>35kg/m2 and quantifying comorbidity. Although IIH is not considered a comorbidity ,Oltridge et al conducted a multicentre open label randomized control trial of 64 participants with active IIH and BMI>35kg/m2 .Participants were to be randomized in which a 1:1 ratio of BS or a dietary weight loss programme and follow up for 5yrs. The primary outcome measures is ICP at 12months.Secondary outcome measures include ICP at 24,and 60 months and IIH symptoms, visual function, papilloedema, headache, quality of life and cost effectiveness at 12,24 and 60 months [23].

For understanding why there is so low utilization of BS(<1%)undergoing it)despite it being cost effective treatment for severe obesity,Funk et al tried to identify both the patient and referral provider characteristics which were likely to make the patient undergo BS. On reviewing 7212 reports from 1998-dec 2014of which 53 were included in full text review ,they carried out metaanalysis in 9 .In 4/9 studies it was found that there is an association between female gender and > willingness to undergo BS. Lack of knowledge alone was a barrier in 2 studies.5/9 studies quoted patient concerns about the outcome/safety of BS as a barrier to undergoing it. Patients are more likely to persue BS when it was recommended by referring provider .Providers who believed obesity treatment should be covered by insurance were more likely to recommend BS. Thus they concluded that patient and referring provider knowledge about safety and effectiveness of BS are important barriers to BS utilization. Future efforts focused on improving knowledge and identification of the critical determinants of obesity treatment decision making from both the provider and patient perspectives would have an important public health impact [24].

BS and Complications

Nephrolithiasis

Riberiro dos Santos et al tried to identify complications associated with BS especially occurrence of nephrolithiasis. They analyzed studies to address this from 2005-2013.Retrospective studies with minimal follow up of 3yrs showed 7.65% in surgery patients and 4.63%in non surgery had nephrolithiasis (p<0.05).Prospective studies (8/10) showed large percentage of calculi appearing and significant increase in oxaluria. Thus they concluded there was a correlation between BS and nephrolithiasis [25].

Venous Thromboembolism (VTE)

To determine in obese patients undergoing BS who are high risk for VTE development ,if there is need for weight adjusted doses of LMW or high fractionated heparin or that standard doses are enough for thromboprophylaxis, Ikeraos et al reviewed 6studies,1RCT ,4cohort studies and 1 quasi experiment trial having 1858 patients for the systematic review. They found post BS patients receiving weight adjusted doses of heparin products ,had an in hospital rate of VTE of 0.54%(95% CI:0.2-1%)as compared to 2%(95% CI:0.1-6.4%) for those that did not weight adjust dosage. Rates of major bleeding were similar for both groups;1.6%(95%CI:.6-3%)for patients receiving weight adjusted dosing ,as compared to 2.3%(95%CI:1.1-3.9%)for those receiving standard doses of heparin products. Thus they concluded that adjusting doses of heparin products, for throbo prophylaxis post BS seems to be associated with lower rate of hospital VTE, as compared to strategy of not adjusting the dose although this did not reach statistical significance. This practice does not=>an increase in adverse major bleeding events [26].

Longterm Effects of BS

Macejewsky et al to study the long term durability of weight loss following BS carried out a cohort study and studied the differences upto 10years after surgery in a retrospective study of 1787 veterans who underwent RYGB from jan 2000-sept 2011 where 573/700 were eligible i.e 81.9% with 10 years follow up and 5303 nonsurgical matches 1274/1889-i.e 67.4% eligible with 10years follow up in a mixed effects model. Differences in weight changes up to 4years were compared among veterans undergoing RYGB(n=1785),SG(n=379)and AGB(n=246). Data analysis was performed from sep 2014-feb 2016.

Of the 1787 patients undergoing RYGB mean age(SD) was 52.1years(8.5) yrs as compared to 5305 nonsurgical patients having 52.2(8.4)years. Patients undergoing RYGB had a mean BMI of 47.7% while that of controls having 47.1%,of which 1306(73.1%) and3911(73.7%) in each group were predominantly male respectively. Patients undergoing RYGB lost 21 %(95% CI,11%-31%)more of their baseline weight at10yrs than nonsurgical matches. A total of 405/564(71.8%)had more than 20%estimated weight loss, and 224/564(39.7%)had more than 30%

estimated weight loss at 10years as compared to 134/1247(10.8%) and 48/1247(3.8%) respectively of nonsurgical matches. Only 19/564 patients undergoing RYGB(3.4%) regained weight back to within estimated 5% of their baseline weight by 10yrs. At 4years patients undergoing RYGB lost 27.5%(95% CI,23.8-31.2%) of their baseline weight ,patients undergoing AGB lost 10.6%(95% CI,0.6-20.6%) and patients undergoing SG lost 17.8%(95%CI,9.7-25.9%).Patients undergoing RYGB lost 16.9%(95%CI,6.2-27.6%)more of their baseline weight than patients undergoing AGB and 9.7%(95%CI,0.8-18.6%)more than patients undergoing SG. Thus they concluded that patients in veterans health care administration healthcare lost substantially more weight as compared to nonsurgical matches and sustained most of this weight loss in long-term .RYGB induced significantly greater weight loss among veterans than SG or AGB at 4yrs. These results give further evidence of beneficial association between BS and long-term weight loss which has been shown in short term studies of younger predominantly female populations [27].

Laparoscopic RYGB is considered a gold standard in BS, achieving long term weight loss along with improvements in obesity related comorbidities. Recently the laparoscopic mingastric bypass(LMGB)has received popularity allover world, both in terms of weight loss as well as comorbid resolution. In view of lack of RCT comparing LMGB and LRYGB Kraljevic etal 2017designed a randomized patient and observer blinded trial in a single centre. To show that LMGB is not inferior to LRYGB in terms of excess weight loss(EWL),the study was conducted as a noninferiority trial with the sample size calculation performed accordingly.EWL 12mths after surgery is the primary endpoint ,while 3yrs EWL, morbidity, mortality ,remission of obesity related comorbidities, quality of life(QOL) and hormonal and lipid profile changes are secondary endpoints.80 patients ,18yrs or older and with a BMI between 39 and 50kg/m2 who meet the Swiss guidelines for the surgical treatment of morbid obesity will be randomized .Endpoints and baseline measurements are at discharge and at time points 6weeksand 12 and 36mths postoperatively .With its 3yr follow up time this RCT will give important data on impact of LMGB and LRYGB on EWL, remission of comorbidities, QOL and hormonal and lipid profile changes [28 clinical trial GOV no NCT02601092.]

Shah et al 2017 studied patients with prior RYGB operation for weight loss, which present reconstruction challenges during a pancreatoduodenectomy (PD).With over 60,000 RYGB done annually RYGB increasing odds of encountering such patients during a PD make it imperative to understand the RYGB anatomy and anticipate reconstruction options

They reviewed their PD options compared them to what had been described in literature and derived from internal conferences comprising bariatric and hepatobiliary surgeons to describe known reconstruction options. In general reconstruction options can include one of the 3 options i)remnant gastrectomy ii)preservation of gastric remnant iii)reversal of gastric bypass. Thus they concluded how individualized reconstruction options for RYGB patients undergoing PD can be tailored to the need of the patient [29].

LSG and LRYGB are the most commonly performed bariatric procedures. Major differences exist between LSG and LYRGB during postoperative period .Optimization of the postoperative care might be achieved by using enhanced recovery after surgery(ERAS) protocol which allows earlier functional recovery postoperative care conducted in accordance with ERAS protocol among pts after LSG and LRYGB.

Data concerning patients treated for morbid obesity were prospectively gathered in one academic center. Patients were divided into 2grps,LSG(n=364,63.4%) and LYRGB(n=210,36.59%).Multiple factors were used as endpoint to determine the influence of the type of bariatric procedure on postoperative course. They found that the rate of postoperative nausea and vomiting and incidence of i/v fluids administration during the operation was higher in LSG grp. LYRGB patients were able to tolerate higher oral fluid intake volumes during the first and 2nd postoperative day. Mean diuresis during the 2nd and 3rd post operative day was significantly higher in a LRYGBgrp. Administration of diuretics and pain killers was comparable between grps, while the risk of fever after the operation was higher in LRYGB grp. Mean length of stay was higher in LSG grp(LRYGB vs LSG,3.46days+ 1.58 vs 3.64+ 4.41,P=.039). Thus they concluded postoperative treatment after LSG requires more supervision and longer time until functional recovery is achieved [30].

Since BS has increased exponentially in 1990'sin Netherlands ,to improve quality of BS, the nationwide Dutch Audit for treatment of obesity(DATO) got established in 2014. The audit was coordinated by the Dutch Institute of Clinical Auditing(DICA).Thus Poelmeijer in 2018 reviewed the process in establishing this nationwide registry.

In collaboration with the DATO's scientific committee and other stakeholders, an annual list of several external quality indicators was formulated. This list consists of volume, process and outcome indicators. Besides the annual external indicators the database permits individual hospitals to analyze their own data. The dashboard provides several standardized reports and detailed quality indicators ,which are updated on a weekly base. They found since the start ,all18Dutch bariatric centres participated in this nationwide audit. A total of 21,941 cases got registered within 2015and 2016..By 2016, the required variables were registered with 94.3% of all cases. A severely complicated course was seen in 2.8%,and mortality in 0.05% in 2016.The first year followupshows a >20%TWL in 86.1% of the registered cases .Thus DATO has become rapidly a mature registry. The well organized structure of the national audit institution DICA and government funding was essential. However the most important were the bariatric teams themselves. With the reporting of results from the registry already more knowledge got contributed besides the acceptance by other healthcare providers as per the authors [31].

BS in Morbidly Obese Adolescents

A systematic review and metaanalysis done by Paulus et al in 2015,revealed 37 studies evaluated effect of Laparoscopically Adjustable gastric banding(ADGB),RYGB,and laparoscopic sleeve gastrectomy(LSG)

in patients under 18yrs of age.15/37 studies were prospective including IRCT.Mean BMI loss after LAGB was 11.6kg/m2(95%CI-9.8-13.4)VS 16.6kg/m2(95% CI-13.4-19.8)after RYGBand 14.1kg/m2(CI-10.8-17.8) after LSG.2 unrelated deaths were reported after 495 RYGB procedures. All3 bariatric procedures caused substantial weight loss and improvement of comorbidity with an acceptable complication rate ,which indicates that surgical intervention is applicable in properly selected Morbidly Obese Adolescents(MOA) [32].

Further review by Paulus et al in 2016 in a retrospective analysis of gastric banding for >5yrs In a single centre study in patients <18yrs or younger was analyzed .Wt loss, complication ,reoperations and comorbidity reductions were assessed as well as health status ,food behavior and personality. They found BMI loss in 10adolescents was 10.7kg/m2(0.9-12.9kg/m2) after a median follow-up of 64mths(52-84mths),the major part of weight loss occurred after the 1st year. In 4 patients the gastric band was removed after 3.5-5.5yrs.2/3 patients effectively lost wt after conversion to a by pass procedure.1pt is maintaining a stable healthy weight after band removal. Thus concluding that LAGB has a failure rate of 40%in morbidly Obese Adolescents, but was successful in rest 60%,without major side effects. Long term follow up was essential for proper evaluation of weight loss and reoperation rates [33].

Similarly Inge et al for the Teen –LABS Consortium prospectively enrolled 242 Adolescents, who underwent wt loss surgery at 5 US centres. Patients undergoing RYGB(n=161)or SG(n=67)were included in the analysis. Changes in body weight, coexisting conditions ,cardiometabolic risk factors and weight related quality of life and post operative complications were evaluated for 5yrs following the procedure. They found mean (SD+-) was 17+-1.6yrsand mean BMI was 53,75% participants were female and 72%were white. At 3 yrs following the procedure remission of type2 diabetes mellitus (T2DM) occurred in 95%(95%CI-85-100)of participants who had had the condition at baseline, remission of abnormal kidney function occurred in 86%(95% CI-72-100),remission of prediabetes in 76%(95%CI-56-97),remission of elevated BP in 74%(95%CI-64-84) and dyslipidemia in 66%(CI-57-74).Weight related QOL also improved significantly. However at 3yrs after BS hypoferritinemia was found in 57%(95%CI-50-65)of the participants and 13%(95%CI-9-18)of the participants had undergone one or more additional intraabdominal peocedures. Thus concluding that in this multicenter prospective study of BS in adolescents, they found significant improvements in wt, cardiometabolic health and wt related quality of life(QOL) at 3yrsafter the procedure. Risk associated with surgery include specific micronutrient deficiencies and the need for additional abdominal procedures [34].

Shah et al reviewed the role of BS with T2DM in inducing remission since T2DM in adolescents may progress in adulthood with multisystemic health consequences and may not respond even to aggressive medical therapy. Outcomes and complications of BS in adolescents with DM, recommending future directions for use ,like taking care of deficiencies

resulting and preventing repeated abdominal operations as in TEEN-LABS study and preventing cholecystectomy commonly seen [35].

Acanthosis nigricans (AN),once was considered a rare paraneoplastic dermatoses ,but now being frequently observed in obese adolescents. It is associated with insulin resistance and has a unique role in secondary prevention. Ng 2017 reviewed comprehensively AN in obese adolescents, discussing its history ,current knowledge, clinical significances, management challenges and future research. Although BS is an option ,it remains a last resort, considering its irreversibility, lack of long term pediatric data, risk of nutritional deficiencies and possible need if reoperstion [36].

Elhag et al 2018 evaluated a narrow range of anthropometric ,nutritional and cardiometabolic parameters among morbidly obese adolescents before and after LSG. They retrospectively reviewed medical charts of all obese adolescents who underwent LSG at Hamad medical corporation, Qatarbetween jan 2011-june2015(n=102).They assessed preoperative levels and postoperative levels in 4 anthropometric , 15nutritional and 10 cardiometabolicparameters. The study sample had 79patients with complete information(36 males, mean age 15.99+-1.1yrs).At a mean of 24.2mths post LSG,they observed significantly reduced BMI by 51.82+-28.1Kg and 17+_6.24kg/m2 respectively; the highest percentage of post LSG deficiencies pertained to vitamin D, albumin and ferritin (89.2,38 and 33.3%)respectively; low hemoglobinlevels(29.3%)only in females; trace elements were not deficient; significant reductions in percentage of adolescents with increased LDL from 66.1%to38.9%), alanine aminotransferase (from 45.3 to 10.9%)and aspartate amino transferase(from 24.1to8.6%)levels;100% remission of prediabetes cases and 80% of T2D cases. Thus they concluded LSG achieved significant wt loss and improvement of cardiometabolic risk factors among adolescents. However the slight worsening of preexisting nutritional deficiencies warrants careful preoperative surveillance and appropriate postoperative nutritional supplementation [37].

Mechanism of Action

As reviewed by Shin and Berthoud et al BS has superior efficacy and how one can know how obesity surgery works and how exactly we can use it for developing newer medical therapies[38]. Changes in gut brain signaling, hormones ,bile acids and still other unidentified factors remain an important factor. Both Roux –en Y gastric bypass surgery (RYGB) and sleeve gastrectomy result in increased levels of circulating bile acids [39-42],which can signal through the membrane receptor TGR5 and nuclear receptor FXR to a number of organs [43-46]. The conjugated bile acid taurodeoxycholic acid(TUDCA) which decreases endoplasmic stress is a potent leptin sensitizer of body weight set point directly. Also the feedback control loop that regulates the total pool of bile acids also involves FXR mediated stimulation of FGF 9 in humans and FGF15 in mice [43] and the levels of FGF21 as wellas FGF19 are altered significantly following RYGB surgery [43] and further FGF21 is known to improve

glucose and body weight homeostasis through multiple pathways [47-50]. Besides that the powerful body weight lowering effect of monoclonal antibodies the FGF 1c R that have partial agonistic activity [51] suggest the possibility that the bile acid FGF signaling pathway maybe crucial for the success of RYGB and sleeve gastrectomy .Further bile acid signaling through the membrane receptor TGR5 has been found to increase brown fat thermogenesis [52] and glucagon like peptide 1(GLP1) secretion [53]. By increasing brown fat thermogenesis it helps in increasing energy expenditure besides improving the glycaemic profile withGLP1 achieving both in terms of fat reduction as well as improved glucose homeostasis. By resensitizing homeostatic regulating circuits in the hypothalamic hedonic processing in the corticolimbic to internal signals BS could=>a state of being content with less [54,55].

Why BS is more effective is not clear .If it is true that reduced food intake and body weight are secondary to restriction and malabsorption, then BS patients should show the normal signs of starvation and suppression of satiation mechanisms, which includes GIT hormone secretion.

One would not expect these starvation responses if BS were to lower the defended body weight levels. Clinical studies in Roux-en Y gastric bypass patients provide some support for both explanations .Most people who undergo BS have lost the will to eat and preoccupation with food and food cues [56-59] and have decreased appetite as shown by large and sustained reduction of food intake [60-62]. The increased craving of fatty foods in obese patients ,do fight feeling of hunger and food craving [63], resistance in weight loss or significant regain of weight [64]. Lot of studies show that basal metabolic rate(BMR) is reduced rather than increased although the decrease appears to be <than the expected weight loss [65,66detail review]. Also evidence against a starvation/restriction mechanism is shown by the marked raised levels of GIT hormones like GLP1 andPYY3-36,which occur both in human and rodents after gastric bypass surgery but not following caloric restriction [67,68].

Various rodent studies further support against the restriction/starvation hypothesis ,favoring the defense of a lower body weight explanation .Rats having vertical gastric sleeve gastrectomy which are additionally food restricted will increase food intake and regain body weight to prerestriction but not beyond [69]. Rats with RYGB have become hyperphagic and obese by chronically blocking brain Mc4 receptors signaling return to pretreatment body weight, which proves that food intake is not restricted and that a lower level of body weight appears to be defended [70]. In comparison to human studies ,most rodent studies display an increased BMR following RYGB series, proving that increased energy expenditure seems to be an important mechanism for defending the lower body weight level. Mumphrey et al from the lab of Berthoud HR further tried to get the support for this hypothesis i.e. reprogramming defended body weight rather than passive restriction of energy intake is a functional mechanism of RYGB. They studied male C57 BL6J mice who reached different obesity degrees on HFD, either with adlibitum or with

caloric restriction(weight restricted) who underwent RYGB.

They found RYGB induced weight loss and fat mass was proportionate to presurgical levels ,with moderately obese mice losing < body wt and fat as compared to very obese mice. But mice which were weight reduced to the level of chow controls before surgery ,gained weight immediately following surgery ,which was mainly accounted by lean mass gain. Thus concluding that reprogramming of a new defended body weight is an important principle by which RYGB surgery lastingly suppresses body weight .RYGB appears to selectively abolish defense of a higher fat mass level ,while remaining sensitive to the defense of lean mass. Still the molecular and physiological mechanisms underlying this reprogramming have to be worked out [71].

Conclusions

Thus BS is effective not only in short term but maintaining weight loss in long-term. RYGB surgery has proven to be the most effective. To prevent any post operative complications in view of liquid diet and inability to eat ,there is need for protein supplementation containing vitamins and minerals.

There is need to weight adjust the dosage of enoxaprin to prevent VTE in the morbidly obese group.

A Slightly higher incidence of nephrolithiasis has been found .The reason incidence of BS is so low despite it being effective appear to be because of cost ,scare of complications and referral provider ,whether it Is covered by insurance.

The mechanism of action appears more in resetting the defended body weight besides alterations in GIT hormones,PYY,GLP1,ghrelin and bile acid secretions changes help in trying to utilize for development of newer most efficacious medical therapies.

The long term hospital stay besides POSSUM Score predicts the long term efficacy of BS which lowers the side effects ,giving a better chance ,thus importance of good perioperative care to prevent resurgery and decrease morbidity and mortality.

Further the importance of BS in morbidly obese adolescents is considered in great detail.

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