Curr Obes Rep
DOI 10.1007/s13679-012-0015-x

OBESITY TREATMENT (AM SHARMA, SECTION EDITOR)

Utilization of Temporary Controllable Intragastric Pseudobezoars for the Treatment of Obesity

Marlena G. Deneva · Orly Yadid-Pecht · Michel Fattouche · Martin P. Mintchev

Abstract The growing worldwide obesity epidemic has prompted the development of two main treatment streams: 1) conservative approaches and 2) invasive techniques. However, only invasive surgical methods have delivered significant and sustainable benefits. Therefore, contemporary research exploration has focused on the development of gastric volume reduction methods having noninvasive administration and termination, while featuring a safe but reliable and long-term sustainable weight loss effect similar to the one delivered by bariatric surgeries. This antiobesity approach is based on placing external devices in the stomach ranging from intragastric balloons to temporary pseudobezoars for a predetermined amount of time. The present review examines the evolution of these techniques from invasively positionable and removable units to completely noninvasive patient-controllable implements. Comparative discussion over the available pilot and clinical studies related to temporary controllable pseudobezoars outlines this new concept as an alternative gastric volume reduction antiobesity strategy. Available short-term studies reported an average weight loss of 6% for a 1-month period. The beneficial features of this method include patient-specific design, performance flexibility, full controllability, and particularly low level or lack of side effects. More multicenter, placebo-controlled, long-term studies on a significant number of patients and further technological improvements of the design of the pseudobezoars are required before the technique can be considered a reliable alternative to present-day bariatric surgeries.

Keywords Bezoars · Pseudobezoars · Gastric volume reduction · Bariatric surgery · Obesity

M. G. Deneva
Institute of Catalysis, Bulgarian Academy of Sciences,
Acad. G. Bonchev Str., Bldg. 11,
Sofia 1113, Bulgaria

O. Yadid-Pecht · M. Fattouche · M. P. Mintchev (✉)
Department of Electrical and Computer Engineering,
University of Calgary,
2500 University Drive NW,
Calgary, AB T2N 1N4, Canada
e-mail: mintchev@ucalgary.ca

M. P. Mintchev
Department of Surgery, University of Alberta,
2D4.06 Walter Makenzie Centre,
Edmonton, AB T6G 2B7, Canada

Published online: 14 March 2012

Introduction

This paper reviews a new and emerging obesity treatment involving temporary, controllable pseudobezoars—orally introduced, non-nutritional foreign bodies in the stomach that can reside in the organ for several days, invoking satiety and leading to significantly reduced food consumption. The most recent publications and patents related to this innovative method are discussed.

Obesity as a Worldwide Health Problem

The World Health Organization (WHO) recently announced that worldwide obesity has increased more than twice since 1980 [1]. WHO statistics reported 1.5 billion overweight adults in 2008 worldwide. A significant percentage of them were obese: nearly 300 million women and over 200 million men. An earlier report [2] revealed a diminishing initial age

of obesity onset, with nearly 43 million overweight children under the age of 5 years [1]. Obesity is an important key factor for comorbidities and related mortality and is also increasingly considered as a type of cellular malnutrition and noncommunicable disease [3]. The WHO Global Strategy on Diet, Physical Activity, and Health for 2008 to 2013 [4] provides a roadmap to improve dietary and physical activity patterns at the population level. Along with that, the global scientific community has been developing diverse obesity treatment approaches.

Current Obesity Treatments

Contemporary obesity treatment approaches can be divided into two main streams: conservative—represented by diets [5, 6], pharmacotherapy, and/or behavior modification [7, 8]; and invasive—represented by bariatric surgery [9, 10], gastrointestinal electrical stimulation [11, 12], and a variety of endoscopic techniques, including intragastric balloons and temporary bezoars [13, 14]. Unfortunately, of these approaches only gastric volume reduction associated with bariatric surgery has offered a sustainable long-term reduction of body weight, while the endoscopic techniques for gastric volume reduction within the organ have been considered either dangerous or still being in their infancy.

The recently proposed temporary controllable pseudobezoar concept [15–18, 19••, 20, 21, 22••] can be considered a bridge between the two main obesity treatment streams—starting as a completely conservative, noninvasive approach, this therapy literally grows in the human stomach to an intragastric bezoar-based treatment featuring the capability to be discontinued in a controllable, noninvasive fashion. This new antiobesity method is the subject of the present review. Since the technique can be regarded as a link between the noninvasive and the invasive obesity treatment approaches, a brief summary of both is also presented.

Bezoars and Bezoar Formation

Gastric Bezoars

Bezoars are collections, concretions, foreign bodies that accumulate, coalesce, and are retained in the gastrointestinal tract, most frequently within the stomach [23••]. The nature of the comprising materials defines several types of bezoars: phytobezoars (including diospyrobezoars) [24], trichobezoars [25], pharmacobezoars [26], and lactobezoars [27].

Bezoar formation is commonly predisposed by postoperatively induced: 1) atony, dysmotility, and delayed gastric emptying; 2) stenosis; 3) poor gastric mixing; 4) decreased secretion of acid and pepsin; and 5) increased mucus production. Furthermore, partial gastrectomy, antrectomy, pyloroplasty, Roux-en-Y gastric bypass, and even laparoscopic adjustable gastric banding have been associated with phytobezoars, fungus balls, and bezoar formation in general [23••].

Many bezoars are asymptomatic. However, when they are not, some typically appearing symptoms include the following: vague epigastric discomfort (up to 80% of cases); nausea, vomiting, and early satiety; weight loss, anemia, and anorexia; and bleeding, pain, and gastric outlet obstruction [23••].

Since anemia and weight loss are typical accompanying conditions related to bezoar formation [25], the latter sparks interest as a possible obesity treatment technique.

Temporary Pseudobezoars

The global quest for noninvasive, yet long-term sustainable antiobesity treatment methods has lead to an impressive progress in intraluminal weight loss devices. They have been seriously improved in terms of technical precision, location, traumatism, anesthesia assistance, etc. The volume of the last-generation intragastric balloons can be adjusted by the patient [28]. Despite these improvements, balloons are still inserted and removed endoscopically and different levels of sedation and anesthesia are needed for both procedures. Moreover, these devices have been associated with a notable mortality and morbidity [28–30], and have not been approved for clinical use in the United States.

Responding to the global quest for weight loss novelties other than invasive intragastric balloons, several implementations were announced as novel approaches for gastric volume reduction based on ideas borrowed from the effect naturally occurring bezoars have on appetite: 1) “butterfly”-type bezoars [31, 32]; 2) expandable gastroretentive systems [33, 34]; and most recently; 3) controllable temporary pseudobezoars [15–18, 19••, 20, 21, 22••].

Hashiba et al. [31, 32] reported experimental designs of artificial bezoars made of digestive-resistant polyethylene. A more than 30-m-long strip, previously divided into loops of 40 cm, is folded in the middle. It is in a partially compacted configuration during the instrumental insertion in the gastric lumen. Inside the stomach the device expands sufficiently to be retained there for a long time without passing through the pylorus into the intestines. A subsequent modification of this device improved its compactness while inserting. It is implemented by a significantly shorter (3-m), but wider polyethylene flexible tube, compressed over a plastic tube that is used as a guide and a pusher. It is deployed into the stomach after intraluminal endoscopically controlled manipulations. Animal testing revealed effective weight loss over a several-month period [31]. The device was inserted into the gastric lumens of 10 pigs for a

period of 49 days. The average initial weight was 27.8 kg (25.0 ÷ 31.2 kg). At the end of the testing period, the animals reached an average weight of 34.5 kg (29.5 ÷ 39.0 kg). It is significantly less than the weight gain observed in similar animals without inserted artificial bezoar. The anticipated weight for the animals at the end of the period was accepted to be 57 kg, due to the normal expected growth for these animals [31]. Compared to balloons, this device seems to have several advantages: does not need to be inflated; has the opportunity for size adjustment; does not have valves to retain fluids; and does not require static positioning in the stomach. Unfortunately, the effectiveness of the device for obese patients has been referred to future studies [35], which to date have not been published.

Expandable gastroretentive therapeutic systems [33, 34], which have been designed primarily to control active substance release in the gastrointestinal tract by gastric emptying delay, represent another pseudobezoar design opportunity. Such a system usually consists of an element that controls the active-compound release, as well as a polymer cover. The release controllability can be performed in different ways. One of them is via a substance that expands on contact with the gastric juice due to the acidity of the latter. Long-term retainment in the stomach is claimed to be achieved noninvasively due to an appropriate design and composition, although no experimental work has been reported. The individual volume of the device does not exceed 10 mL, and its utilization as an appetite/hunger suppressant is considered possible due to its expandability and its subsequent solid food–like behavior. However, weight loss data obtained with this technique have not been reported. In addition, its disintegration is not controllable independently of its drug-delivery feature [33].

A novel temporary, controllable pseudobezoar weight loss concept was formulated recently [15–18, 19••, 20, 21, 22••]. It propounds artificial, temporary pseudobezoars that are intended to combine the noninvasiveness of the conservative therapies with the long-term sustainable weight loss effect of the invasive antiobesity approaches. The artificial temporary, controllable pseudobezoars are designed as orally ingested, intragastric, self-expandable units and consist of biocompatible, sac-like carriers filled with cellulose-based expandable fibers. They fit into standard gelatin capsules. Ingested with an abundant amount of water, they expand rapidly in the stomach thus forming non-nutritional volume in it. Post-expansion dimensions of these pseudobezoars prevent their expulsion through the pylorus and they are retained in the stomach for a controlled time period. Their regular intake reduces gastric volume similarly to the way intragastric balloons do, thus invoking constant feeling of satiety. This new approach for noninvasive manipulation of gastric volume is reviewed in greater details below.

Temporary, Controllable Pseudobezoars

Pseudobezoar Design

The main of idea of the temporary, controllable pseudobezoar concept [19••] is to create an artificial bezoar (pseudobezoar, pseudofood chunk) that invokes weight loss through gastric volume reduction from inside the stomach without any endoscopic or surgical interventions. Mimicking pathologically formed bezoars and aiming their effect on weight loss, such an implement was required to be: 1) ingestible, but non-nutritional, ideally designed as a standard capsule for oral intake; 2) expandable—to grow rapidly in the stomach while in contact with gastric juices; 3) retainable—to expand to a size and stiffness that prevent its expulsion through the pylorus, ensure its retainment in the stomach, and stimulate gastric mechanoreceptors the same way real food would; 4) residable—to preserve its integrity in the stomach for a predetermined period; 5) temporary—to have self-disintegration capabilities after several days retention in the stomach and to leave the gastrointestinal tract without endoscopic or surgical assistance; 6) controllable—to quickly, noninvasively, and preferably by pH change disintegrate on demand; 7) safe—to be gentle enough not to injure gastric mucosa while residing in the stomach, not to create obstructions anywhere in the gastrointestinal tract, and not to cause any significant side effects while in place; 8) permeable to fluids and gases to avoid possible gastrointestinal obstructions; 9) identifiable— to allow identification and monitoring by noninvasive methods (eg, sonographically).

Several optimization rounds of laboratory and animal tests, as well as pilot and clinical studies [19••, 20, 21, 22••], led to a pseudobezoar design that met the outlined functional requirements. The first artificial, temporary, controllable pseudobezoar for dynamic gastric volume reduction from inside the organ was designed and manufactured as a dietary supplement “Zalak B” (EatLittle Bulgaria Ltd., Sofia, Bulgaria; licensed from EatLittle Inc., Calgary, Alberta, Canada). The product consists of a granulated, expandable, nonirritating polymer mixture that fills a biocompatible, permeable oxycellulose carrier. The pseudobezoar is inserted in a standard hard gelatin capsule (DB–type, size AAA; Capsugel, Greenwood, SC, USA) with an overall length of 22.5 mm and dry volume before ingestion of 1.44 mL.

This pseudobezoar design successfully embeds the following important features: 1) swelling in contact with gastric liquids and water to a volume of approximately 15 mL; 2) reaching final expanded volume upon ingestion within 15 min; 3) presenting sufficient post-swelling stiffness sufficient to ensure pseudobezoar dimensions higher than 1.5 cm in all directions when subjected to simulated dynamic gastric forces (compression of 1.5 N) [36]; 4) providing adequate weight and heaviness of the expanded pseudobezoars to

ensure their sinking to the antral area of the stomach; 5) ensuring compact integrity and volume for several days; 6) providing structural permeability for liquids and gases for maximal safety; 7) and providing a complete pH-based controllability to a level of disintegration to safe, constituent natural fibers.

Based on a 6 capsules-per-day schedule, the optimized temporary pseudobezoars have demonstrated their objective ability to displace dynamically, non-nutritionally and daily an intragastric volume of about 90 mL [19••, 20, 21, 22••]. Thus, in several days, the pseudobezoar accumulation delivered a substantial gastric volume reduction achievable without surgical or endoscopic intervention. Two levels of pseudobezoar safety were achieved: 1) despite their stability in pH 1 to 3, the pseudobezoars gradually self-disintegrate within several days due to losing their rigidness in the stomach; 2) at pH greater than 5 the pseudobezoars disintegrate within several hours, which ensures maximal safety in the small and large intestines or when antacid-assisted disintegration in the stomach is sought on demand.

Clinical Studies

Since the introduction of the temporary, controllable pseudobezoar concept, the first implements have been tested in two pilot human studies [19••, 20, 21] and in a blind, placebo-controlled, cross-over study of 16 volunteers [22••]. All studies demonstrated the feasibility and the legitimacy of the approach as a new alternative weight loss method for gastric volume reduction from inside the stomach.

Pilot Studies

The first pilot research of temporary controllable pseudobezoars on humans was performed as chronic studies of overweighed healthy volunteers motivated to reduce their weight. Both studies were divided to three distinct, 1-month periods: baseline, therapy, and washout. During the baseline and washout periods volunteers ingested 300 to 500 mL of water, a half hour before meals, without pseudobezoar administration. During the therapy period, 2 pseudobezoar capsules, 3 times a day, a half hour before meals with 300 to 500 mL of water were administered. The aim of the studies was to examine the feasibility of the new method and evaluate its effectiveness without any restrictions in the everyday life of the volunteers. Participants were asked not to change their daily routines, eating habits, and physical activity. No low-calorie diet was recommended. Daily measurements of body weight (BW), hip circumference (HC), and the sense of satiety evaluated by the satiety scale of Haber [35], as well as stool consistency, regularity, and notable side effects were registered. The retainment of the pseudobezoars in the stomach during the therapy and their clearance from the stomach at the end of the treatment was monitored by three-dimensional abdominal ultrasound tests (GE Voluson E8, Fairfield, CT, USA) at the end of both, the therapy and the washout months.

The first pilot human study [19, 20] involved two overweight healthy male adults (2 M, BW=84.3±7.6 kg, body mass index (BMI)=27.7±2.3 kg/m^2, HC=91.7±5.0 cm). Significant weight loss and girth reduction during the therapy period were registered and the final values were BW=79.7±6.0 kg and HC=88.3±3.7 cm. Significantly increased ($P \leq 0.05$) scores on the satiety scale of Haber were registered as well: 8.9±0.1 during the therapy versus 6.5 +/−0.1 in the baseline and the washout periods.

The second pilot study [21] included four human volunteers (2 M, 2 F, BW=76.7±12.3 kg; BMI=27.2±2.3 kg/m^2, HC=81.2±6.8 cm). The pseudobezoars were administered according to the same protocol as in the previous study [19••, 20]. After the therapy month, significantly reduced BW and HC were registered: 72.2±10.8 kg and 78.0.2±6.2 cm, respectively. Haber satiety scale scores increased significantly ($P \leq 0.05$) during the pseudobezoar treatment and reached an average value of 9.2±0.3, compared to 6.5±0.2 for the other 2 months.

Both pilot studies have independently and clearly demonstrated that the oral administration of temporary controllable pseudobezoars, their expansion, and retainment in the stomach for a long-term period of time, and finally, their peristaltic expulsion through the pylorus and the gut are entirely possible. Two important findings were verified sonographically: the location and accumulation of the pseudobezoars in the area of the lesser gastric curvature, and the fact that the stomachs were collapsed around the pseudobezoars but not distended. The obtained results in terms of weight loss, HC reduction, and increased satiety confirmed the feasibility, the efficacy, and the safety of the temporary controllable pseudobezoar concept. However, placebo-controlled studies exploring the method were lacking.

Blind, Placebo-Controlled Study

Further investigation of the effectiveness of the temporary pseudobezoar therapy was performed for a period of 2 months in the first blind, placebo-controlled, crossover chronic human study. A total of 16 healthy but overweight and/or obese subjects (3 M, 13 F, mean age 44.0±12.0 years, BW=93.8±21.9 kg, BMI=33.3±5.6 kg/m^2, waist circumference [WC] 103.3±13.8 cm, and HC=114.3±12.3 cm) were engaged according to predetermined inclusion/exclusion criteria [22••]. They were randomly distributed into two groups (denoted as A and B) of 8 participants. Group A (8 F) started with the pseudobezoar product therapy, while Group B (3 M, 5 F) started on placebo. The administration

schedule during the entire study period was unified: 3 times a day oral intake of 2 pseudobezoar or placebo capsules, 15 to 30 min before principal meals with at least 300 mL of room temperature water. After the first month the groups were crossed over for another month of study. All subjects were recommended and provided with low-calorie, biweekly dietary schemes. All participants registered daily their BW, HC, WC, Haber scale satiety scores, and side effects if any.

The 1-month pseudobezoar treatment of all participants resulted in a statistically significant increase in satiety (Haber scores 4.2±1.3 vs 3.8±1.1 in placebo, $P \leq 0.05$) and greater reduction in BW (3.5% vs 2.6%), BMI (3.5% vs 2.7%), and WC (3.4% vs 2.4%) compared to placebo ($P \leq 0.01$). At the end of the pseudobezoar therapy 31.3% of the volunteers had more than 3% BMI reduction (vs 18.7% on placebo) and 25% registered more than 5% BMI reduction (vs 12.5% on placebo, achieved in the post-pseudobezoar therapy month for Group A only). Both groups produced greater body parameter reduction during their pseudobezoar therapy, compared to their corresponding placebo periods. For Group A the reduction in BW is 3.3% versus 1.9%, in BMI is 3.3% versus 2.0%, and in WC 2.6% versus 1.7%. All participants from that group did not regain weight and continued their weight loss with an additional 3.3% during the subsequent placebo month. During the therapy month and compared to the previous placebo month, Group B resulted in BW, BMI, WC, and WHR reductions of 3.7% versus 1.9%, 3.5% versus 2.0%, 4.2% versus 1.7%, and 1.3% versus 1.4%, respectively. The results explicitly demonstrate pseudobezoar effectiveness superior to placebo. However, the reduction of the basic anthropometric parameters is far from the desirable and further optimization of the pseudobezoars, their administration, as well as schemes of combined diet-involving therapy could improve effectiveness.

Table 1 summarizes the available studies of the temporary, controllable pseudobezoar on humans. The safety of this pseudobezoar method was confirmed during all three studies and the volunteers did not report any notable side effects. Due to the reported bloating and heaviness in the stomach, as well as the small inconveniences related to the large capsule size, the required administration scheme, and water intake requirement, high attrition rate was reported in the blind, placebo-controlled study (33 subjects were involved initially, only 16 completed it). This problem seems manageable through controlled administration schedules and counseling.

Discussion

The focus of the present review was gastric volume reduction methods having noninvasive administration and termination. Temporary intragastric pseudobezoars, initially developed as drug delivery platforms [33], appear to have the potential to develop into an effective method for weight control. However, only a limited number of studies have explored this technique. The studies by Hashiba at al. [31, 32] utilized an endoscopically positionable and removable, butterfly-like bezoar device, which, however, was tested on animals only. Further studies explored the possibility to make the positioning and the removal of the pseudobezoars not only noninvasive, but also externally controllable to avoid possible obstructions or severe side effects [15–18, 19••, 20, 21, 22••]. The most comprehensive study on the subject [22••] reported the results of the first blind, placebo-controlled, crossover chronic human study of the impact of the pseudobezoar therapy as an antiobesity treatment on a statistically viable number of overweight or obese volunteers ($n=16$). Although the results of the study explicitly demonstrated that the pseudobezoar treatment could be regarded as an alternative weight loss method that can be designed to be patient-specific, could be fully controllable, and has minimal to no side effects, the reported 5% to 6% weight loss in the placebo-controlled study [22••] is in no way superior to what can be achieved with conservative weight management even over years.

Table 1 Summary of the existing human studies involving temporary pseudobezoars

Study	Type of study	Number and gender of subjects	Overall duration, *mo*	Duration of active therapy, *mo*	Overall weight change, %	Overall HC change, %	Overall WC change, %	Significantly increased satiety during therapy[b]
Mintchev et al. [19••]	Pilot, chronic	2 M	3	1	5.5[a]	3.7[a]	Not measured	Yes
Mintchev et al. [21]	Extended pilot, chronic	2 M, 2 F	3	1	6.0[a]	4.1[a]	Not measured	Yes
Marintchev et al. [22••]	Blind, placebo-controlled, cross over, chronic	3 M, 13 F	2	1	6.0[a]	4.3[a]	5.6[a]	Yes

[a] Reduction, compared to the initial values

[b] $P<0$ .05

HC hip circumference; *WC* waist circumference

As every "temporary" treatment results in relapse, the role of pseudobezoars in long-term management has to be further explored. At the moment, it is clearly nowhere close to the 20% to 30% sustainable weight loss seen with bariatric surgery. Therefore, optimization of the pseudobezoars is desirable. Such optimization can be in several directions: 1) to take greater volume from inside of the stomach; 2) to expand rapidly and ensure retainment in the stomach; 3) to last longer before disintegration while being retained in the stomach; and 4) to become harder upon expansion so that the contact with the gastric mechanoreceptors is more pronounced. Naturally, the concept of controllability of the pseudobezoars for the purpose of immediate discontinuation of the therapy on demand must also be preserved for safety reasons. With the rapid progress in new, chemically controllable, safe, and biocompatible materials, improvement in the directions outlined above is inevitable and is a matter of time, development, and testing.

None of the volunteers in the published pilot and clinical studies [19••, 20, 21, 22••] reported any notable side effects. Of course, bloating and heaviness in the stomach could be expected, particularly during the sometimes long, stubborn, and tedious process of changing eating habits [37, 38]. For this reason, it has been suggested that biweekly counseling might be quite helpful [6]. It should be noted that while patients who have undergone bariatric surgeries do not have a choice but to put up with very similar symptoms, inconveniences, and discomfort [9, 39], the noninvasiveness of the controllable pseudobezoar therapy provides a significant freedom of choice to patients to discontinue it because of even the mildest possible discomfort. Thus, higher levels of attrition associated with this novel therapy can be expected [22••]. Therefore, some controlled administration schedules might be needed to impose the therapy in a clinically stricter fashion, if need be. Most importantly, future studies should provide some innovative administration ideas to increase the effectiveness of this therapy and test them on a statistically significant number of patients. Therefore, in the absence of long-term studies, temporary controllable pseudobezoars can perhaps be best described as a promising experimental treatment that warrants further study in terms of indications, outcomes, safety, and cost-effectiveness.

Conclusions

Current antiobesity research focus shifts toward new, simple, minimally traumatic and reproducible nonsurgical weight loss methods. The present paper reviews the recently proposed pseudobezoar therapy as a possible approach for noninvasive gastric volume reduction from inside the organ. Further optimization of the intragastric temporary controllable pseudobezoars can increase their effectiveness and competitiveness compared to the wide variety of long-term sustainable, but invasive weight loss methods.

Acknowledgments This study was supported in part by EatLittle Inc., Alberta, Canada.

Disclosure Conflicts of interest: M.G. Deneva: has received a consulting fee or honorarium, support for travel to meetings for the study or other purposes, employment, and grant support from EatLittle Bulgaria, Ltd.; O. Yadid-Pecht: has board membership with EatLittle, Luxmux; has been a consultant for different companies; is employed at the University of Calgary; has received grant support from iCORe and NSERC; has received payment for lectures including service on speakers bureaus (University presentations); has several patents from different institutions in different areas and receives royalties for these; has received payment for development of educational presentations; and has stock/stock options in EatLittle Inc., other companies; M. Fattouche: is a Board Member and Shareholder of EatLittle Inc.; is employed by Co-CEO of EatLittle Inc., Calgary, Alberta, Canada; has four patent applications on the pseudobezoar technology filed with the WIPO; and is a Shareholder in EatLittle Inc., Calgary, Alberta, Canada; M.P. Mintchev: has received support for travel to meetings for the study or other purposes for the scientific conference of the European Obesity Society; is a Board Member and Shareholder of EatLittle Inc.; is President and Co-CEO of EatLittle Inc., Calgary, Canada; has received grant support from EatLittle Bulgaria EOOD; has four patent applications on the pseudobezoar technology filed with the WIPO; is a Shareholder in EatLittle Inc., Calgary, Alberta; has received travel/accommodations/meeting expenses unrelated to activities listed for travel to a scientific conference of the European Obesity Society, 2011.

References

Papers of particular Interest, Published Recently, have been highlighted as:

•• Of major importance

1. Obesity and overweight. In: Fact sheet No. 311. World Health Organization. 2011. http://www.who.int/mediacentre/factsheets/fs311/en/. Accessed 16 Nov 2011.
2. McTigue KM, Garret JM, Popkin BM. The natural history or the development of obesity in a cohort of young U.S. adults between 1981 and 1998. Ann Int Med. 2006;136:857–64.
3. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham LB and Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health. 2009;9:88–107.
4. WHO. 2008–2013 Action plan for the global strategy for the prevention and control of noncomunicable diseases. 2008. http://www.who.int/nmh/Actionplan-PC-NCD-2008.pdf. Accessed 16 Nov 2011.
5. Hite AH, Berkowitz VG, Berkowitz K. Low-carbohydrate diet review: shifting the paradigm. Nutr Clin Pract. 2011;26:300–8.
6. Grace C. A review of one-to-one dietetic obesity management in adults. J Hum Nutr Diet. 2011;24:13–22.
7. Kaplan LM. Pharmacologic therapies for obesity. Gastroenterol Clin North Am. 2010;39(1):69–79.
8. Powell AG; Apovian CM; Aronne LJ. New drug targets for the treatment of obesity. Clin Pharmacol Ther. 2011; 90:40–51.
9. Padwal R, Klarenbach S, Wiebe N, Hazel M, Birch D, Sharma AM, Manns B, Tonelli M. Bariatric surgery: a systematic review of

the clinical and economic evidence. J Gen Intern Med. 2011;26:1183–94.
10. Brethauer SA, Chand B, Schauer PR, Thompson CC. Transoral gastric volume reduction for weight management: technique and feasibility in 18 patients. Surg Obes Relat Dis. 2010;6: 689–94.
11. Hasler WL. Methods of gastric electrical stimulation and pacing: a review of their benefits and mechanisms of action in gastroparesis and obesity. Neurogastroenterol Motil. 2009;21:229–43.
12. Sallam HS; Chen JD. Colon electrical stimulation: potential use for treatment of obesity. Obesity. 2011;19:1761–7.
13. Familiari P, Bokoški I, Marchese M, Perri V, Costamagna G. Endoscopic treatment of obesity. Expert Rev Gastroenterol Hepatol. 2011;5:689–701.
14. Swidnicka-Siergiejko A, Wróblewski E, Andrzej D. Endoscopic treatment of obesity. Can J Gastroenterol. 2011;25:627–33.
15. Mintchev MP, Yadid-Pecht O. Controlled degradation of expandable polymers in gastric volume reduction treatment. PCT International Application No. CA2005/001693, Nov. 04, 2005.
16. Mintchev MP, Yadid-Pecht O, Fattouche M. Ingestible implement for weight control. PCT International Application No. CA2007/000512, Mar. 03, 2007.
17. Mintchev MP, Yadid-Pecht O, Fattouche M. Device for delivery of a substance. PCT International Application No. CA2007/002336, Dec. 18, 2007.
18. Mintchev MP, Yadid-Pecht O, Fattouche M. Bezoar forming units for weight control. PCT International Application No. CA2009/000598, Apr. 28, 2009.
19. •• Mintchev MP, Deneva MG, Aminkov BI, Fattouche M, Yadid-Pecht O, Bray RC. Pilot study of temporary controllable gastric pseudobezoars for dynamic non-invasive gastric volume reduction. Phys Meas. 2010; 31:131–44. *This paper describes the first pilot study of temporary, controllable gastric pseudobezoars on two volunteers, including the design of the pseudobezoars and their short-term impact.*
20. Mintchev MP, Deneva MG, Aminkov BI, Fattouche M, Yadid-Pecht O, Bray RC. Pilot studies of temporary controllable gastric pseudobezoars (pseudofood) as an alternative to bariatric surgery for the treatment of obesity. Gastroenterology. 2010; 138(5/1):S755.
21. Mintchev MP, Deneva MG, Yadid-Pecht O, Fattouche M, Bray RC. Pseudofood (temporary controllable gastric pseudobezoars) as an alternative to intragastric balloons for the treatment of obesity: results from a chronic human study. In: Proceedings of the 28th Annual Meeting of the Obesity Society, San Diego, CA, Oct 8–12, 2010.
22. •• Marintchev A, Deneva MG, Fattouche M, Yadid-Pecht O, Bray RC, Mintchev MP. Temporary controllable pseudobezoars as a non-invasive alternative to surgical gastric volume reduction for the treatment of obesity. 2011. http://www.eatlittle.com/Zalak_B_clinical_study.pdf Accessed 30 Dec 2011. *This paper describes a 2-month, blind, placebo-controlled, crossover study of temporary controllable pseudobezoars on 16 volunteers.*
23. •• Ersoy YE, Ayan F, Ersan Y. Gastro-intestinal bezoars: Thirty-five year experience. Acta Chir. Belg. 2009; 109 (2): 198–203. *This paper describes a long-term experience in identifying, classifying, management, symptoms, and treatment of gastrointestinal bezoars, including tricho- and phytobezoars.*
24. Fu CY, Chu CH, Liu TP, Hong ZJ, Hsu KF, Liu YC, Lu TC, Chan DC, Yu JC. The relationship between acid-suppressing drugs and phytobezoar formation: a retrospective analysis and discussion of phytobezoar formation. Acta Chir Belg. 2010;110:595–7.
25. Mehta P, Bhutiani R. The Rapunzel syndrome: is it an Asian problem? (case report and review of literature). Eur J Gastroenterol Hepatol. 2009;21:937–40.
26. Simpson SE. Pharmacobezoars described and demystified. Clin Toxicol (Phila). 2011;49 (2):72–89.
27. Corzine M. Radiology case study. Gastric lactobezoar. Neonatal Netw 2011;30:180–1, 183–7.
28. Tsesmeli N, Coumaros D. Review of endoscopic devices for weight reduction: old and new balloons and implantable prostheses. Endoscopy. 2009;41:1082–9.
29. Koutelidakis I, Dragoumis D, Papaziogas B, Patsas A, Katsougianopoulos A, Atmatzidis S, Atmatzidis K. Gastric perforation and death after the insertion of an intragastric balloon. Obes Surg. 2009; 19: 393–6.
30. Cubattoli L, Barneschi C,Mastrocinque E, Bonucci P, Giomarelti PP. Cardiac arrest after intragastric balloon insertion in a super obese patient. Obes Surg. 2009;19:253–6.
31. Hashiba K, Surit VC. Intragastric Device for Treating Obesity. U. S. Patent 7,066,945 B2, issued Jun. 27, 2006.
32. Hashiba K. Endoscopic bariatric procedures and devices. Gastrointest Endoscopy Clin N Am. 2007;17:545–557.
33. Asmussen B, Cremer K, Hoffman H-R, Ludwig K, Roreger M. Expandable gastro-retentive therapeutic system with controlled active substance release in the gastro-intestinal tract. U.S. Patent 6,290,989, issued Sep. 18, 2001.
34. Marco D, Eckhouse S. Bio-erodible, self-deployable intragastric implants. U.S. Patent 7,699,863, issued April 20, 2010.
35. Haber GB, Heaton KW, Murphy D, Burroughs LF. Depletion and disruption of dietary fibre: effects on satiety, plasma glucose and serum-insulin. Lancet. 1977;310:679–682.
36. Kong F, Singh RP. A model stomach system to investigate disintegration kinetics of solid foods during gastric digestion. J Food Sci. 2008;73:E202–210.
37. Heiner KB, Unverdorben S, Degenhardt R et al. Effect of a cellulose-containing weight-loss supplement on gastric empting and sensory functions. Obes.2008;16:2272–80.
38. Ernst B, Thurnheer M, Wilms B and Schultes B. Differential changes in dietary habits after gastric bypass versus gastric banding operations. Obes Surg.2009;19:274–280.
39. Hamdan K, Somers S, Chand M. Management of late postoperative complications of bariatric surgery. Br J Surg 2011; 98: 1345–1355.