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LITERATURA REVIEW

The domestic pig (*Sus scrofa domestica*) as a model for evaluating nutritional and metabolic consequences of bariatric surgery practiced on morbid obese humans

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Abstract

M. Gandarillas, and F. Bas. 2009. The domestic pig (*Sus scrofa domestica*) as a model for evaluating nutritional and metabolic consequences of bariatric surgery practiced on morbid obese humans. Cien. Inv. Agr. 36(2):163-176. The prevalence of obesity has increased dramatically over the last 20 years. Moreover, morbid obese patients routinely suffer from serious medical problems, especially cardiovascular disease. Medical therapy for morbid obesity offers no substantial long-term benefit, and thus the first choice therapy for severe obesity is effectively surgery. Gastrointestinal surgery for obesity, also called bariatric surgery, alters the digestive process by limiting food intake and facilitating malabsorption of nutrients from the diet. This article reviews the types and evolution of morbid obesity surgery performed in humans and proposes the pig model as an alternative when practicing new surgical techniques or improving actual procedures, as well as to evaluate the metabolic consequences of these procedures. Based on similarities between humans and pigs in terms of their anatomical, physiological and metabolic characteristics, the pig also provides an opportunity to develop, evaluate specific techniques in open and laparoscopic surgery. Finally, a complete review of macronutrient digestion and absorption between pigs and humans is done in order to justify the use of this model. Therefore, the objective of this article was to illustrate the use of the pig as a model for studying nutrient digestion and absorption in humans who undergo bariatric surgery and to review how, through digestibility trials, a digestion and absorption assessment of nutrients should complement classical human assessments with surgery.

Key words: Bariatric surgery, human obesity, obesity, pig nutrition, swine nutrition.

Introduction

Obesity is a multifactorial disease; the excess body fat is related to genetic predisposition and, mainly, environmental factors. Patients with severe obesity often suffer from serious illnesses as well as physical and psychological disabilities that markedly increase mortality and morbidity (Alvarez-Leite, 2004). The prevalence of obesity has increased dramatically over the last 20 years, with 64.5% of the general population in the United States now being considered overweight. The percentage of adults in the U.S. meeting the criteria of morbid obesity, defined as a body mass index (BMI) ±40 kg·m^{-2}, has also increased from 2.9% in 1988 to 4.7% in 2000 (Flegal *et al.*, 2002). In the case of Chile, 61.3% of the population is overweight, and within this group, 1.3% is morbid obese (Vio, 2005). Mor-

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bidly obese patients routinely suffer from serious medical problems, especially cardiovascular disease (Bray, 1998; Must *et al.*, 1999), and have much higher mortality rates than non-obese individuals (Allison *et al.*, 1999).

Unfortunately, medical therapy offers no substantial long-term benefit (Greenway, 1996). Certainly, the first-choice therapy for severe obesity is a non-surgical intervention that integrates behavioral modifications, adequate physical activity and psychological support. However, in many cases of severe obesity, non-operative treatment fails to provide sustained weight loss, and surgical treatment can be indicated in some specific cases (body mass index ≥ 40 or ≥ 35 with co-morbidities) (Alvarez-Leite, 2004). In 1991, the National Institute of Health (Anonym a, 1991) issued a consensus statement supporting the use of surgery as an effective therapy in morbid obesity. The NIH supported surgery for morbid obese subject who remained severely obese after trying nonsurgical approaches or for people who have an obesity related disease.

There are several recent studies showing rapid improvement of complications of major obesity following bariatric surgery (Brolin *et al.*, 2000; Arribas del Almo *et al.*, 2002; Dixon and O'Brien, 2002a,b; Pinkney and Kerrigan, 2004). Postoperatively, 15 to 40% of patients depending on the surgical procedure performed fail to maintain adequate weight loss. However, patients with successful weight loss make this challenging surgery worthwhile, with alleviation of devastating diseases and marked improvement in quality of life (Deitel, 1998).

Pigs have been used extensively in human nutrition research (Miller and Ullrey, 1987). The digestive system of swine has some anatomical similarities and some differences compared to that of humans. Pigs and humans have comparable gastrointestinal tract (GIT) anatomy, morphology and physiology. The GIT of a 30- to 40-kg pig is similar in total length to that of an adult human, and the relative sizes of the sections of human and pig GIT are alike with similar digestive physiology (USDA, 2000). Swine are true omnivores, as are humans. Furthermore, there is nearly complete agreement between humans and pigs in their dietary requirements for nutrients, although the quantitative requirements for each nutrient differ between the two species. For example, the total requirement of crude protein in terms of dry matter is higher for piglets than for adult infants due to a higher growth rate in piglets (National Research Council, Anonym b, 1998). Surgically prepared pigs provide a powerful tool for investigating the digestion and absorption of nutrients (Yen, 2000). Several types of surgeries have been carried out using the porcine model to test their applicability to human surgery, to try new equipment, or to develop the necessary skills in surgeons. More recently, endoscopic and laparoscopic surgical models have been developed and used extensively in pigs. Therefore, the objective of this article is to show that the use of the pig as a model for studying nutrient digestion and absorption in human status post bariatric surgery is feasible due to their similar characteristics in terms of nutrient absorption and digestive physiology. Additionally, nutritional and metabolic evaluations during the postoperative period of pigs submitted to bariatric surgery provide new insights through postoperative digestibility trials; in this way, digestion and absorption process assessments of nutrients are complementary to classical human evaluations.

Bariatric surgery for morbid obese humans

Gastrointestinal surgery for obesity, also called bariatric surgery, alters the digestive process. The operations can be divided into three types: restrictive, malabsorptive, and combined restrictive/malabsorptive. Restrictive operations limit food intake by creating a narrow passage from the upper part of the stomach into the larger lower part, reducing the amount of food the stomach can hold and slowing the passage of food through the stomach. Malabsorptive operations do not limit food intake but instead exclude most of the small intestine from the digestive tract so that fewer calories and nutrients are absorbed (Horbal and Vázquez, 2005). Procedures like the Roux en Y gastric bypass and the Biliopancreatic Diversion (described below) promote weight loss due to combined restrictive/malabsorptive effects (Adami *et al*., 2003; Stoeckli *et al*., 2004). Malabsorptive operations, also called intestinal bypasses, are no longer recommended because they result in severe nutritional deficiencies (NIH, 1991). Combined operations use stomach restriction and a partial bypass of the small intestine.

Procedures that combine restriction and malabsorption (gastric bypass or GPB, described below) were first described in 1967 and have undergone many modifications since then. GPB exists as a hybrid operation and has been extensively scrutinized and evaluated in comparison to other operations for the treatment of obesity. Co-morbidities secondary to severe obesity are usually ameliorated or arrested after the weight loss from GPB. The average percentage excess weight loss with gastric bypass is 70%. The success rate, defined as 50% excess body weight (EBW) loss after at least two years of follow-up, is 85% per Fobi *et al.* (1998).

Evolution of the GPB operation for the treatment of obesity

The original jejunocolic bypasses were abandoned because of severe diarrhea, electrolyte imbalances, and liver failure. Jejunoileal (JI) bypasses (Figure 1) were widely performed during the 1960s and 1970s. Weight loss in the long-term varied, but a mean loss of 50% of EBW was maintained in 65% of patients. Unfortunate sequelae, however, required the constant availability of the surgeon. Hepatic failure occurred unless sufficient protein was consumed, diarrhea persisted after ingestion of fatty foods, with perianal corrosion, and electrolyte imbalance required continuous replacement therapy (Deitel, 1989).
Mason and Ito (1969), after an extensive labora-

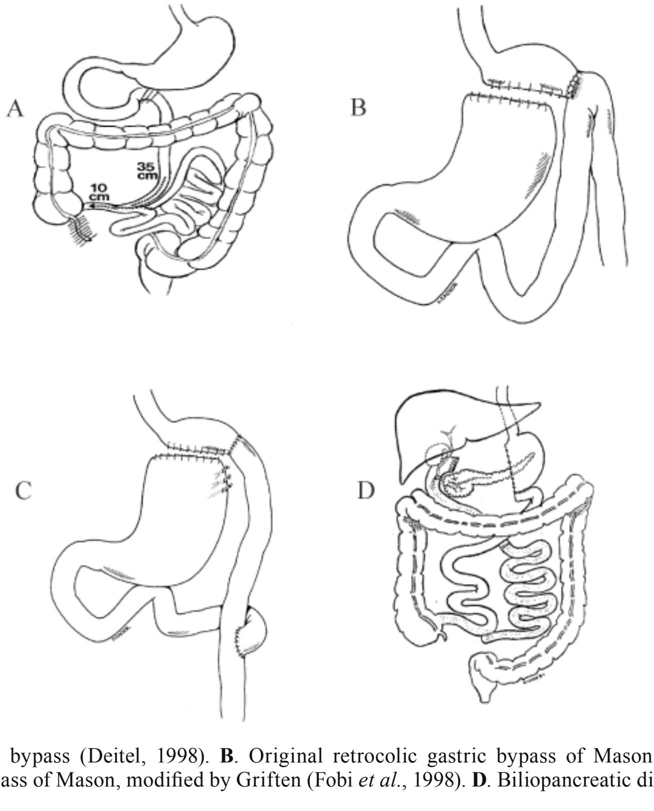

Figure 1. **A**. Jejunoileal bypass (Deitel, 1998). **B**. Original retrocolic gastric bypass of Mason (Fobi *et al*., 1998). **C**. Roux en Y gastric bypass of Mason, modified by Griften (Fobi *et al*., 1998). **D**. Biliopancreatic diversion of Scopinaro (Scopinaro *et al*., 1998).

tory investigation, first reported the use of GBP in humans in 1967 for the treatment of obesity. The operation has undergone a host of subsequent modifications. In short, the stomach is transected horizontally across the upper fundus, totally separating the distal stomach from the proximal gastric pouch; this pouch is then anastomosed to a loop of jejunum. Alden (1977) introduced the use of the staple instrument for bariatric surgery to provide an in-continuity division between the upper pouch and the distal stomach, in contrast to the suture technique (Fobi *et al.*, 1998). This change simplified the operation and made it technically less involved and safer. Griffen *et al.* (1977) used a Roux-en-Y gastrojejunostomy instead of a loop (Figure 1C). The Roux-en-Y gastric bypass (RYGBP) has become the gold standard for bariatric surgery. A loss of $\geq$ 50% of excess body weight was maintained in approximately 60% of the patients at five years (Deitel, 1998). Biliopancreatic diversion (BPD), developed by Scopinaro *et al.* (1992), has some similarities to the distal RYGBP. The small bowel is divided 250 cm proximal to the ileocecal valve (Figure 1D), and a subtotal gastrectomy is performed. The distal (alimentary) limb is then anastomosed to the proximal gastric pouch, and the biliopancreatic conduit is anastomosed to the side of the distal limb 50 cm proximal to the ileocecal valve. Absorption of nutrients occurs in this distal 50-cm common channel, with malabsorption of fats and starches (Scopinaro *et al.*, 1998).

The RYGBP causes weight loss by restriction of food intake and by the dumping effect. Biliopancreatic diversion promotes weight loss principally via malabsorption of ingested nutrients. Both operations exclude parts of the gastrointestinal tract from alimentation, resulting in the potential to develop metabolic deficiencies secondary to malabsorption of certain nutrients, including protein, certain minerals and vitamins (Brolin and Leung, 1999).

Lately, the laparoscopic technique has been introduced for obesity surgery with the following known advantages: better access to the operative field, early recovery, early mobilization, less postoperative pain, almost no incisional hernia and improved respiratory function (De la Torre and Scott, 1999).

The importance of increasing the malabsortive component of the RYGBP

Roux-en Y gastric bypass is among the most commonly practiced bariatric alternatives, combining a restrictive component through the construction of a 15-30 ml gastric pouch with a malabsorptive mechanism through the creation of a 150 cm alimentary limb (Herron, 2004). Nevertheless, the ideal length of the alimentary and the common limb in order to achieve optimal metabolic results has been a matter of research. The question that remains unresolved is whether altering the limb lengths of the RYGBP will produce greater weight loss due to malabsorption or decreased ingestion of food. Of related concern is whether there are differences in the percentage of ingested total calories from carbohydrates, proteins or fat among different limb lengths (as might be evidenced by increasing or decreasing the alimentary limb).

Studies performed comparing different limb lengths in RYGBP done in morbid obese and super obese patients have shown that only the super obese (BMI > 50 $kg \cdot m^{-2}$) benefit from longer alimentary limbs and have a greater weight reduction (MacLean *et al.*, 2001; Choban and Flancbaum, 2002; Inabnet *et al.*, 2005). Among patients with a BMI < 50 $kg \cdot m^{-2}$, longer alimentary limbs did not result in a greater weight reduction, although they did lower the amount of weight regain. The metabolic impact of the malabsorptive mechanism is not clear, especially if nutritional supplementation is not provided. Nutritional deficiencies could also have a negative impact among age groups such as adolescent patients, among whom bariatric surgery is becoming more frequent (Deckelbaum and Williams, 2001; Surgeman *et al.*, 2003).

It seems that there is no consensus in the literature on which length is optimal to promote significant weight loss. However, the construction of longer alimentary limbs in RYGBP has also proven in some cases to reduce weight regain in morbid obese patients after long-term follow up. Brolin *et al.* (2002) compared weight progression in a five-year follow-up of morbid obese patients with alimentary limb lengths of 75 cm and 150 cm and a distal RYGBP with a common limb length of 75 cm. In this study, patients with the 150 cm alimentary limb and those who underwent distal RYGBP had less weight regain after five years. Even though long alimentary limbs have proven in human clinical trials not to present significant differences in excess weight reduction among morbid obese patients but just in the incidence of weight regain, longer limbs have controversial nutritional outcomes. Brolin *et al.* (1992) observed that morbid obese patients who underwent distal RYGBP presented with postoperative steatorrhea and nutritional deficiencies such as hypoalbuminemia in 13% of cases. In 1997, Sugerman *et al.* (1997) proved the presence of nutritional deficiencies and liver failure among super obese patients who were re-operated on undergoing RYGBP with common limbs of 50 cm and 150 cm.

Nutrient absorption assessment using pigs

Besides the difficulty of accurately assessing daily nutrient intake in humans, even more complex will be accounting for nutrients in the diet intake that are lost in the feces. From a practical point of view, the pig provides a suitable alternative to evaluate the metabolic consequences of these procedures based on similarities between humans and pigs in terms of anatomical, physiological and metabolic characteristics (USDA, 2000). The digestive system of pigs has some anatomical differences compared to humans; however, the physiology of digestion remains the same (USDA, 2000).

The porcine model in biomedical human research

Before discussing why pigs represent a suitable model for evaluating nutritional and metabolic outcomes of a particular kind of bariatric surgery, there are several studies in the literature that demonstrate the practical advantage of using the porcine model to evaluate nutritional consequences after any particular surgery.

The use of the pig in the biomedical research of nutrition and metabolic diseases has increased dramatically during the last decade. The proceedings of two somewhat recent symposia on the use of swine in biomedical research (Tumbleson, 1986; Tumbleson and Schook, 1996) underscore the extent of this trend. Swine are used as a general surgical model for most organs and systems, for cardiovascular research including atherosclerosis, for digestive system models, and in recent years, in transplantation and xerographic research (USDA, 2000). The neonatal pig has been widely used as a model for studying the nutrient requirements and digestive function of human infants. Examples include the role of colostrum in intestinal tract functional development (Burrin *et al.*, 1995; 1997) and the role of insulin-like growth factor I (IGF-1) in intestinal and digestive function (Donovan *et al.*, 1996).

Several types of surgeries have been carried out with the porcine model, to test their applicability to human surgery, to try new equipment or to develop the necessary skills of the surgeons. More recently, endoscopic and laparoscopic surgical procedure models have been developed and used extensively in the pig. The size and function of structures such as the biliary system and pancreatic duct make them suitable for studying with life-sized equipment and biomaterial implants. Surgical modifications have made the pig's intestinal tract amenable for the study of surgical and chronic fistulation procedures (Swindle and Swindle, 1998).

The pig in bariatric surgical treatment of morbid obese humans

In 1985, Coelho *et al.* (1985) evaluated the effectiveness and complications of gastric banding in miniature pigs using a Gore-tex or Dacron graft to encircle the stomach. Based on this simple operation in the treatment of the morbid obese patient, they concluded that gastric banding should be applied with caution. Later in 1987, a new method of gastroplasty began being used in operative treatment of extreme obesity in humans, placing a non-absorbable band on the stomach in order to form two reservoirs (one small upper and one large lower) connected by a narrow passage without having to open the stomach. These findings proved that in the surgical treatment of extreme obesity in humans, it is essential to not allow the pressure to build up excessively in the upper stomach reservoir.

The use of intragastric balloons as a noninvasive method for weight reduction was also observed in nine Yorkshire pigs by Yang *et al.* (1987). None of the animals lost weight, and their appetites were inhibited for only a short period of time. Also, there was significant dilatation of the stomach noted after balloon insertion resulting from increased food intake, thus obliterating the original effect of the intragastric balloons. At the same time, ulceration was seen in 83.3% of the animals that received balloons. They concluded that intragastric balloon therapy was not an effective approach for managing morbid obesity in human subjects.

A decade later, Frantzides *et al.* (1995) used a porcine model to pilot laparoscopic gastric bypass, in which laparoscopic gastric stapling and Roux-en-Y gastrojejunostomy were accomplished. Based on randomized prospective studies in humans, the Roux-en-Y gastric bypass has been shown to provide more effective weight loss than vertical banded gastroplasty for morbid obesity. Potvin *et al.* (1997) performed laparoscopic Roux-en-Y gastric bypasses to assess the feasibility of this procedure with conventional laparoscopic techniques and instruments. They suggested that a definite learning curve exists for this procedure primarily because of the extent of gastrointestinal reconstruction, but there was potential for its use in humans.

Based on the successful results of surgical treatment for sustained weight reduction, Marx and Halverson (1998) performed vertical banded gastroplasty, an adaptation of the standard open procedure to laparoscopic techniques. They developed an anterior wall banded gastroplasty in Yorkshire pigs in the laboratory laparoscopically. The procedure was difficult and was associated with a risk of staple line leak (i.e., anastomatic leake) as well as bleeding along the lesser curvature of the stomach. In the same experiment, 15 animals were then used to develop a new technique using a small gastric pouch from the anterior gastric wall. Once again, the pig model provided the information that this operation can be reproduced accurately; upon postmortem examination of the pigs, there were no anastomotic leaks.

Cagigas *et al.* (1999), in a preliminary report on a very small sample of animals, showed that a laparoscopic distal gastric bypass is feasible and could be performed with available instrumentation and advanced laparoscopic surgeons experienced in various techniques and procedures. Nevertheless, no nutritional follow-up was carried out on the animals. Scott *et al.* (2001) performed GPB (a mixed restrictive/malabsorptive surgery) laparoscopically in a porcine model. They concluded that the frailty of the porcine small intestine may limit one's ability to achieve intact anastomoses. Despite this anatomical limitation, the porcine model was well-suited for skill development and evaluation of surgical techniques. Compared to the subsequent human experience, performing anastomoses in the swine was considerably more difficult. After completion of this study, they were able to perform laparoscopic gastric bypass in 30 human patients with no anastomotic leaks.

Biliopancreatic diversion with a duodenal switch appeared as an emerging open procedure that was as effective as other bariatric operations. De Csepel *et al.* (2001), trying to determine the safety and feasibility of performing this procedure using a laparoscopic approach in the porcine model, anticipated that laparoscopic biliopancreatic diversion with a duodenal switch would be feasible and safe in humans. Substantial weight loss combined with the benefits of laparoscopic surgery could be expected.

Dilatation of the gastric pouch in a gastric bypass allowed the patient to increase food intake and resulted in weight regain after some years; with this in mind, Nocca *et al.* (2005) studied two groups of six pigs undergoing laparoscopic GBP as follows. In the first group, a non-adjustable silicone band was positioned 1 cm proximal to the gastrojejunal anastomosis. In the second group, the device used to stabilize the gastric pouch was an adjustable silicone band. Weight loss, complications and histological reactions were evaluated after three months. The overall mortality rate was 25% (cardiac arrhythmias in two pigs), and the conversion rate from laparoscopic to open surgery was 25%. They concluded that the use of silicone devices may be safe and effective in the prevention of pouch or outlet dilatation after GBP.

Laparoscopic Roux-en-Y gastric bypass (LRYGBP) is highly effective for morbid obesity, but the long-term effects in the bypassed segments are unknown. Bearing this in mind, Gentileschi *et al.* (2006) evaluated gastrin and histologic changes in bypassed segments after LRYGBP in ten 50-kg pigs. Preoperative weight and serum gastrin were compared with similar measures at six months postoperatively, when the pigs were euthanized. At necropsy, full-thickness gastric, duodenal, and jejunal biopsies were performed. Normal biopsies were obtained from a control group of ten pigs. One pig died three months postoperatively due to an intestinal intussusception, and the remaining nine pigs increased their weight after surgery from 52±2.2 kg to 55±1.9 kg. Serum gastrin was unchanged after surgery, and histological examinations showed no abnormalities from sections in all control pigs, and in seven of the LRYGBP pigs as well. In conclusion, LRYGBP was not associated with gastrin changes and major histological changes in the bypassed segments at six months postoperatively in the porcine model.

In summary, experimental models, specifically pigs, have mostly been used to prove the feasibility of the surgical techniques rather than to evaluate postoperative metabolic consequences (Cagigas *et al.*, 1999; Scott *et al.*, 2001). Swine is used in experimental surgery as an animal model because it is recognized as a suitable model for human disease based upon its comparative anatomy and physiology (Swindle and Swindle, 1998). Consequently, the information regarding the nutritional and metabolic consequences of surgically treating pigs should give surgeons and nutritionists some guidelines for a particular nutrient post surgical treatment.

The porcine model to measure and evaluate digestion and absorption post bariatric surgery

Digestion and balance studies in farm animals, especially in pigs, provide an accurate relationship between the input and the output of nutrients (Schneider and Flatt, 1975; Mclean and Tobin, 1987; Whittemore, 1990). Nutrient digestibility and absorption, the most direct and accurate sign of a successful procedure, are difficult to measure directly in humans.

Hence, animal models such as the pig have the ease and advantage of allowing repeated fecal and urine collections for nutrient analyses. To avoid possible experimental failure, it is important to conduct these assays when animals are completely recovered from the surgery and free of other possible injuries.

To determine relative nutrient absorption, quantities of each nutrient should be measured in the feed consumed as well as in fecal excretions. These assays complement and contrast the information obtained from plasma metabolite analyses (Batterham, 1994). Schneider and Flatt (1975) proposed digestibility trials for evaluating feedstuffs routinely fed to farm animals. This method provides information about the amount of a nutrient that is absorbed as a percentage of oral intake.

To conduct these analyses, swine must be kept in metabolic crates specially designed for this purpose. These crates allow the animal to remain static, facilitating total or partial collection of feces. At the front of the crate, previously measured quantities of feed are given, and nipple-type waterers fulfill water needs. At the other end, feces are collected.

For nutrient balance assays, urine should be also considered. A metabolic crate with a slat-type floor allows for urine collection. Beneath the floor, urine can be collected without being contaminated by contact with feed or feces.

It is essential that the pigs be adequately adapted to the crates and feed before beginning the assay. An adaptation period, usually three to seven days, is followed by the fecal (and urine if required) collection period of four to six days. In general, this adaptation period is used to establish the level of feeding that will be maintained throughout the collection period and to ensure that the fecal sample collected correspond to the test diet. As an example, 85% of the calculated, *ad libitum* intake of diet should be given during the following four to six collection days. Nutrient digestibility can then be determined by calculating the percentage of the nutrient that appears in the feces as:

$$\text{Fecal digestibility of nutrient (\%)} = [(I - F)\ I^{-1}] \times 100$$

where I = nutrient quantity in oral intake and F = fecal excretion of nutrient.

Validating the pig model by comparison to human digestive physiology

Despite some slight anatomical differences in the digestive systems of humans and pigs, pigs have been extensively used as a gastrointestinal model for humans. Most classical studies are closely related with nutritional studies, and work on metabolic functions, intestinal transports systems, motility, neonatal development of the gastrointestinal tract and nutrient absorption has made the pig a suitable model for research regarding human nutrition (USDA, 2000).

In humans, the functional maturation of the digestive system (e.g., digestive enzymes) progresses relatively slowly, but maturation also starts early, i.e., long before birth. At birth, the infant gastrointestinal tract (GIT) is sufficiently mature to digest significant amounts of non-milk carbohydrates and proteins. In contrast to humans, rodents (e.g., rats, mice) and carnivores (e.g., mink) have a very immature GIT at birth, and adult diets are poorly tolerated until shortly before weaning. Adult-type GIT functions in these animals develop rapidly, but not until quite late, e.g., postnatally. In the pig (and the other large domestic species), both the timing and the rate of GIT maturation fall in between those in precocious species (primates, guinea pigs) and altricial species (rodents, carnivores). Hence, the major developmental events occur in the immediate perinatal period, followed by more gradual changes postnatally.

These species-dependent patterns of GIT maturation are illustrated in Figure 2. At the time of birth, the pig becomes dependent on its own uptake of nutrients for the first time, and the functional characteristics of the GIT must either be sufficiently mature before birth or change rapidly after birth to meet this challenge. As already indicated in Figure 2, the maturation of some key GIT functions in the pig occurs quite rapidly shortly before and after birth, in association with the transition from placental (parenteral) nutrition to oral (enteral) nutrition. Rapid maturation at this time makes pigs and other large farm animals particularly vulnerable to disease when GIT development in the neonate is immature. It is therefore important to know the factors that influence GIT function in the neonatal pig (Sangild, 2001).

Nutrient digestion and absorption in humans and pigs

In both species, the internal surface layer that covers the stomach consists of epithelial cells that synthesize and release mucus, alkaline juices, and gastric acid into the luminal cavity. In the same surface, a number of pores exist, serving as drains from one or more gastric glands. In humans and pigs, the gastric mucosa is compartmentalized into four regions that differ in appearance and structure: esophageal, fundic, cardiac and pyloric regions. The first one, nonglandular, is a prolongation of the esophagus that extends into the proper stomach. Adjacent to the esophageal region is the cardiac gland region, which occupies one-third of the total luminal surface area. The fundic region has a mottled appearance and also lines one-third of the stomach, between the cardiac and pyloric regions. The pyloric region is close to the pyloric sphincter that separates the stomach from the small intestine (Berne, 1992; Frandson and Spurgeon, 1995; Brody, 1999). In terms of individual substances that are secreted into the gastric lumen, the four regions differ, and this secretion will be decreased and/or suppressed when gastric bypass

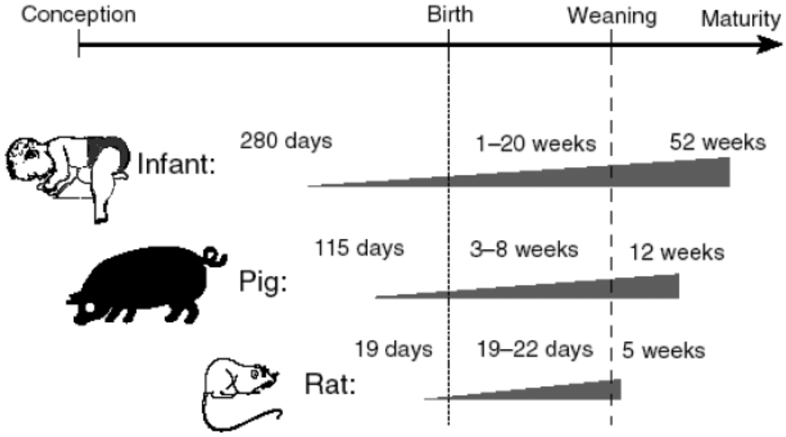

Figure 2. Progression of gastrointestinal maturation in three different species. In farm animals (e.g., pigs), GIT maturational changes occur mainly from shortly before birth to just after weaning. In humans, maturation is slower and starts relatively early (fetally); in the rat most changes occur relatively fast and late (postnatally) (Sangild, 2001).

is done in both humans and pigs (as a model) due to the 95% reduction made to the original dimension of the stomach. A 70-kg human with a normal stomach has an approximately 1.5 liter capacity in volume; at the same physiological stage, the pig has about 5.5 to 7 liters of total capacity (Mc Donald *et al.*, 1988; Frandson and Spurgeon, 1995).

The length of the small intestine is 4 m in an adult human subject and 16 to 21 m in the pig. The duodenum is 25 cm and 80 to 90 cm in length for humans and in the fully grown pig, respectively (Frandson and Spurgeon, 1995; Yen, 2000).

Macronutrient digestion and absorption: lipids, proteins, and carbohydrates

Lipids are consumed both in humans and pigs mainly as triglycerides. When the chemical stimulus begins, the proteolytic function of the stomach also promotes adequate segregation of dietary lipids from their original matrix, and the acidic condition allows for fat dispersion. Lipases present in the stomach are salivary lipase in the case of rats and mice and gastric lipase in swine and humans (Gargouri *et al.*, 1989; Brody, 1999). Bile composed of biliary salts, cholesterol, biliary pigments and phospholipids (mainly lecitine) is essential for the further absorption of triglycerides in the small intestine (Brindley, 1984; Berne, 1992). In both swine and humans, biliary salts are conjugated in the liver with taurine and glycine and use the cholesterol as a primer for their biosynthesis (Brody, 1999). The role of bile is essential for the proper digestion of lipids through micelle formation. Biliary salts give the fat globule a flat structure with polar and nonpolar ends; this detergent effect dissolves big globules into small droplets, which are further attacked by pancreatic enzymes (synthesized and delivered by the pancreas). This action done by biliary salts helps small droplets fats migration towards the brush border intestinal membrane. Pancreatic lipase attacks the sn-1 and n-3 link of a triglyceride, yielding a 2-monoglyceride and two non-esterified fatty acids. Colipase, fundamental for pancreatic lipase emulsification, then concludes the objective. Another important enzyme in lipid hydrolysis is cholesterol esterase; this enzyme produces instead a free fatty acid plus free cholesterol. Phospholipase A2 attacks the ester link of the lecithin, and the end-products are lysophospholipids, non-esterified fatty acids.

The absorption of lipids is mainly passive and is dependent on mixed micelle formation; these micelles are made up of biliary salts, monoglycerols and the end products of the remainder of lipids, like fat-soluble vitamins, cholesterol and a series of lipid-soluble substances. The majority of the free fatty acids and monoacyl glicerols are found in the duodenum and proximal jejunum, a trend that remains in the same in mammals (Drackley, 2000). Nevertheless, this process of digestion is not the same for all lipids; for example, the short chain fatty acids (less than 12 carbons) require bile for absorption. In the case of milk products, which are at least 30% short chain fatty acids (Maynard *et al.*, 1981), absorption will occur without biliary salts.

Additionally, biliary salts are reabsorbed in the distal ileum through a Na-dependent process called enteropathic circulation. In the ileum, biliary salts are actively transported to the liver for resynthesis and further storage in the gallbladder. A small portion of bile is excreted daily in feces (Drackley, 2000).

In gastric bypass surgery, it would be admissible to suppose that lipid digestion and absorption would be affected, mainly through the reduction in the portion of active stomach. Malabsorption will be also expected due to the bypassed region of the duodenum and part of the jejunum.

Protein digestion begins in the stomach, where G-cells stimulated by the chemical and cephalic phase segregate gastrin into the bloodstream. This hormone consequently stimulates parietal and chief cells to produce gastric acid and pepsinogen, respectively. Furthermore, due to the acidic condition of the stomach, pepsin (the activated form of pepsinogen) starts protein digestion by catalyzing the hydrolysis of peptide bonds, just as all pancreatic proteases do (Brody, 1999). In the intestinal lumen, digested food and the acid content stimulate secretin and CCK synthesis by the S- and I-cells of the gut epithelia. CCK and secretin then stimulate pancreatic duct cells to release bicarbonate and large amounts of fluids through the pancreatic duct, thus creating a suitable environment for further nutrient digestion. In addition, pancreatic enzymes (amylases, proteases and lipases) are segregated and released into the duodenum (Brody, 1999; Stipanuk, 2000; Kellems and Church, 2001). A small fraction of the polypeptides that contact the brush border of the small intestine are hydrolyzed by membrane-bound enzymes attached to the outside of the enterocytes. Trypsin, chymotrypsin, elastase, and carboxypeptidases then finish protein digestion by cleaving specific proteins at certain sites, leaving different amino acid residues (Krehbiel and Matthews, 2003).

Oligopeptides are the end product of the mixed action of these pancreatic proteases; in the small intestine, an average of 60% of digested protein appears as oligopeptides, with the remainder appearing as free amino acids (Alpers, 1994). Following initial digestion, oligopeptides are further degraded into small peptides (tri-, dipeptides plus amino acids), which are then further degraded by tri- and dipeptidases. Matthews (2000) has reported in detail on the absorption mechanism and some specific carriers for amino acids, dipeptides and tripeptides.

The jejunum is the most important part of the small intestine in terms of absorption of amino acids, as studied in cannulated pigs in the distal duodenum and proximal ileum (Matthews *et al.*, 1996). On the brush border of the small intestine, different kinds of carriers have been reported: IMINO, B and probably x^-, but no $B^{o,+}$. The active transport of cationic amino acids through enterocytes is Na-independent. Other *in vitro* experiments have shown that the pig jejunum has carriers for both amino acids and dipeptides, but no *in vivo* validations have been reported thus far (Matthews, 2000).

Pigs and humans have the same strategy for carbohydrate digestion and absorption. Both species consume similar ingredients in their diets, mostly starch from cereals, roots, and tubers. When food is in the mouth, being chewed and swallowed, salivary glands (mainly the parotid, sublingual and submaxillary glands) secrete saliva and mucus that contain alfa-amylase. Even though the quantity of this enzyme is quite low in contrast with pancreatic amylase, starch digestion starts in the mouth of both humans and pigs (Vonk and Western, 1984). Partially digested starches (dextrins) reach the small intestine as well as nondegraded starch, which are being attacked by pancreatic amylase. The rest of the carbohydrates currently ingested either by humans or pigs are lactose, sucrose and fructose. The first two are further degraded by brush border enzymes into glucose, fructose and galactose (Russell and Gahr, 2000). Glucose is absorbed in the small intestine by Na-dependent active transport; fructose instead crosses the mucosa by passive transport with a different carrier (Brody, 1999; Russell and Gahr, 2000).

Conclusions and further implications

The objective of this paper was to review the use of the pig as a model for studying nutrient digestion and absorption in humans who undergo bariatric surgery. The feasibility of this model is due to similarities in terms of anatomical, physiological and metabolic characteristics, mainly because of the parallel nutrient absorption and digestion physiology. Moreover, nutritional and metabolic evaluations during the postoperative period of pigs subject to bariatric surgery provide new insights through digestibility trials, as well as the assessment of nutrients in digestion and absorption processes. Digestibility trials all complementary to classical human evaluations, whereby only plasma metabolites are routinely utilized.

Additionally, the pig model allows for a good experimental approach when evaluating an advanced, open and/or laparoscopic technique, especially for training and testing new devices and equipment. This model is highly recommended since the frail nature of pig intestines relative to those of humans makes it considerably more difficult to perform anastomoses.

A description is also provided of pig digestion and nutrient absorption trials, which are useful for non-animal scientists and researchers who might find the pig model appropriate for their studies. In summary, this model can provide new insights into the live weight gain follow-up, feed intake capacity and nutrient digestion ability when performing and testing new and different types of bariatric surgeries.

Resumen

M. Gandarillas y F. Bas. 2009. El cerdo doméstico (*Sus scrofa domestica*) como modelo para estudiar las consecuencias metabólicas y nutricionales de la cirugía de la obesidad. Cien. Inv. Agr. 36 (2):163-176. La prevalencia de la obesidad ha aumentado dramáticamente durante las últimas dos décadas y más aún, pacientes con obesidad mórbida sufren habitualmente serios problemas médicos entre ellos, enfermedad cardiovascular. La terapia médica para la obesidad no ha dado buenos resultados en el tiempo y hoy día la Academia Nacional de las Ciencias ha aceptado como sano y efectivo el tratamiento quirúrgico como terapia para la obesidad. La cirugía bariátrica altera la anatomía y fisiología del tracto gastrointestinal como también el proceso digestivo debido a que incluye un componente restrictivo y/u otro malabsortivo. El presente artículo revisa los tipos y la evolución de la cirugía bariátrica realizada a humanos obesos y propone al modelo porcino como alternativa para practicar y probar nuevas técnicas quirúrgicas que en un futuro se realizarán a humanos. Así se muestra al cerdo como un modelo válido para evaluar consecuencias metabólicas y nutricionales de estos procedimientos, fundamentado en que el cerdo presenta similitudes en su anatomía, fisiología y bioquímica de su metabolismo. Finalmente se presenta una comparación sobre la digestión y absorción de macronutrientes. El objetivo de esta revisión es ilustrar el uso del modelo porcino para estudiar consecuencias metabólicas, digestión y absorción de nutrientes de pacientes humanos obesos que son sometidos a cirugía bariátrica y revisar cómo a través de estudios de digestibilidad de nutrientes sería posible estudiar dichos procesos.

Palabras claves: Obesidad, cirugía bariátrica, nutrición porcina, obesidad humana.

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