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## Effects of Sleeve Gastrectomy as a Bariatric Surgery on Weight of Dietary Induced Obese Rats.

## ARTICLE INFORMATION

## ABSTRACT

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**Background:** Obesity is becoming the healthcare epidemic world wide. Obesity is associated with reduced life expectancy, increased morbidity and mortality, and greater healthcare costs.

Bariatric surgery is the only effective treatment for morbid obesity and is gaining increasing popularity. There has been a steady rise in the numbers and types of bariatric operations done worldwide in recent years but none of prove to be ideal. Animal studies and use of animal models are significant element in the evolution of medical knowledge and the use of animals as a model for bariatric surgery is of importance to study the mechanisms of these operations and also help to develop new technique in management of obesity.

**Objectives:** Study of effects of sleeve gastrectomy as bariatric surgery procedures on weight of dietary induced obese rats (DIO).

**Methods:** Eighteen adult rats with diet induced obesity (DIO) divided into two groups, the first (n=9) group exposed to sleeve gastrectomy (SG) under general anesthesia, the second (n=9) is the sham (control) group. Postoperative care of the animals done as required and the weight of the rats were measured weekly for 6 weeks.

**Results:** Follow up for 6 weeks post-operative. Four rats from SG group were died: two in the first day, second and 6th post operative day. Postmortem done with evidence of gastric leak in two of them. Two sham operated rats were died. The dead rats were cancelled from the study when body weight calculated. Average weight were 425gram and 420gram for SG and Sham respectively before surgery. Both groups experience some weight loss in the first week after surgery while the SG group start losing more weight, while the sham group are starting to maintain its normal weight until the end of the experiment.

**Conclusions:** Sleeve Gastrectomy as a bariatric procedure are successfully reduce the weight of DIO rats. Development of animal model for bariatric procedure is of great importance to test the effects of different bariatric procedures on the weight, and translate these procedures on human.

### Introduction:

Obesity is considered as major health problem and is associated with sever comorbidities and has major impacts on health and economy<sup>1,2</sup>

Obesity associated with increased risk of developing type 2 diabetes and cardiovascular disease<sup>3-6</sup> also obesity associated with other comorbidities like sleep apnea, musculoskeletal disorders, infertility and cancer<sup>7-10</sup>

Bariatric surgery is the only effective treatment for morbid obesity and is gaining increasing popularity for its ability

to produce potent and long-term changes in body weight. Additionally, bariatric surgery reduces overall mortality despite surgical risks<sup>11-13</sup> which prove to have positive effects on diabetes control<sup>13-15</sup>.

Bariatric surgical techniques share two fundamental designs: intestinal malabsorption and gastric restriction. Malabsorptive operations shorten the functional length of the intestinal surface for nutrient absorption, while restrictive procedures decrease food intake by creating a small neogastric pouch and the outlet<sup>16,17</sup>.

The goals of surgery are to achieve and maintain significant weight loss and to reverse or prevent many of the obesity-induced comorbidities. The ideal bariatric procedure must be safe, durable, and effective and performed with relative ease. Consequently, there has been a steady rise in the number of bariatric operations done worldwide in recent years with the Roux-en-Y gastric bypass (gastric bypass) being the most commonly performed operation is (at least in the United States) the most frequently performed bariatric procedure, it has both restrictive and malabsorptive aspects<sup>18,19</sup>.

A (restrictive) gastric pouch is created and separated from the remainder of the stomach. The continuity is then restored by a Roux-Y-limb, which is connected to the jejunum. Sleeve gastrectomy and gastric banding are commonly used procedures. Laparoscopic sleeve gastrectomy (LSG) is gaining more popularity, has been in use for approximately 7 years. Sleeve gastrectomy (SG), also known as partial gastrectomy, longitudinal gastrectomy, or vertical gastrectomy, is a relatively new bariatric surgery which is gaining popularity. It was initially performed in 1998, and was then first performed laparoscopically in 1999<sup>20</sup>. More recently, LSG has been advocated as a primary operation for all stages of morbid obesity. Today, LSG is accepted as a first-line treatment for the super-obese (body mass index > 45-50 kg/m<sup>2</sup>), before attempting more complicated procedures. In addition, surgeons have begun using it as a stand-alone definitive therapy<sup>21</sup>. Animal studies and using of animals as models has significant element in the evolution of medical knowledge and the use of animals as a model for bariatric surgery is of importance to study the mechanisms of these operations. And also help to develop new technique in management of obesity<sup>22,23</sup>.

### Methods:

Eighteen adult rats fed with high fat calorie diet for 12 weeks and maintained in 6 cages under controlled temp, with 12 hour day and night cycle. Those rats were maintained on the same diet after bariatric surgery and sham surgery. Individual rats are weight and then subdivided into 2 groups. First (n=9) underwent open sleeve gastrectomy and the second (n=9) underwent sham operation (control). The net weight of 2 groups were taken prior to surgery.

#### Preoperative preparations

Animals were fasted for 12 hours and only allowed access to water until one hour to the surgery to avoid dehydration and to prevent leak. All surgeries were done under general anesthesia by the use of mix 8.75 ml of ketamine (100 mg/ml) and 1.25 ml of xylazine (100 mg/ml). Administer 0.05-0.10 ml/100 g IP Repeat as required with 1/3 to 1/2 doses at a time (approximately every 30 min). The abdomens are shaved with trimmer. Alcohol with betadine used

as skin disinfectant. Sterile towels are used to cover the surgical field.

Sleeve gastrectomy procedure (SG): ( three to four cm incision done in the upper abdomen). Identification of stomach, ligation of greater curvature vessels with absorbable 6/0 suture. Transection of stomach with excision of greater curvature with gastric fundus starting 3-4 mm above the pylorus. That will leave about 4 mm width from lesser curvature and reducing 70-80% of stomach volume. Closure of the cut line with same suture and reinforced with interrupted sutures as required.

Layers of the abdomen were closed with 4/0 vicryl and the skin closed with 4/0 interrupted silk.

#### Sham operation:

The sham group is the control. Same preoperative preparations was done. Abdominal incision was the same. Access to the stomach with a longitudinal incision along the greater curvature without excision of any part from the stomach. Then closed in same manner with same kind of suture used for SG. The Abdominal layers are not closed until proper time passed almost equal to the time spent for completion of SG to reduce the difference in metabolic stress between the groups.

#### Postoperative care:

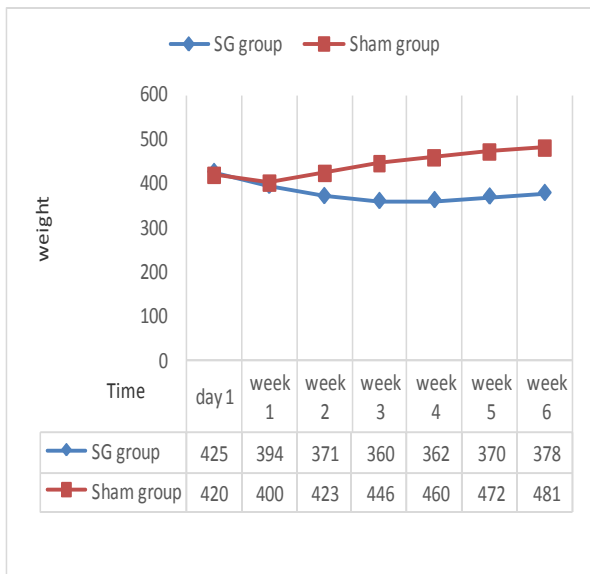
After surgery rats were left to recover spontaneously in controlled environment with special attention to avoid hypothermia. Liquid diet were allowed in the 3rd postoperative day. Meanwhile 10 ml of normal saline given intraperitoneally daily until the 3rd day. Body weight of individual rats were recorded using sensitive scale for 6 weeks, after that all animals are euthanized as recommended.

### Results:

Follow up for 6 weeks after surgery. Four rats were died from the SG group, postmortem dissection revealed anastomotic leak in 2 of the rats, the other 2 rats no pathology could be seen.

Two sham rats are died intraoperative and in the first operative day, the rest survived until the end of experiment. Stiches were removed for both groups in the 10<sup>th</sup> postoperative day.

The rats that were submitted to SG showed a decrease in weight when compared to sham rats (P-value= 0.01, DF=11 which is significant) fig 1. All rats are lost weights in the first week in both groups. Then the SG group continue losing weight until the 4<sup>th</sup> week when its started to gain weight to the end of experiment but never reach its original weights. Sham operated group were started to gain weight from week 1 until the end of experiment.



**Figure 1;** Weight of the rats in grams after GS surgery or Sham operation

### Discussion:

This is the first animal model for bariatric surgery conducted in Iraq and was based on experiences gained from the work in the animal lab / University of California. And we consider it an important step in developing our knowledge and experience in the translational studies. Rodents usually used as a model for bariatric surgery as well as in dietary induced obesity. We used rats in spite of its small size organs because the anatomy of the rat GI tract is strikingly similar to humans. The rat stomach has a cardia or forestomach which is continuous with the esophagus and is lined by squamous epithelium. It is thinner and relatively non-motile. The fundus and pylorus (glandular stomach) have a similar anatomy as human<sup>24</sup>. We used almost the same technique for sleeve gastrectomy that described by Lopez et al<sup>25</sup>, Wang<sup>26</sup> and Panagiotis Patrikakos et al<sup>27</sup>. but we performed the sleeve with hand sewn not by staple which is proved to be applicable. Both groups loss weight during the first week this may be due to catabolism resulted from surgical trauma. The SG group continue losing weights in spite of high calorie diet and this is observed by lower food intake which is not recorded in our study. That weight loss continue until the fourth week of study then the rats started gaining weight but never reach their initial weight prior to surgery. High death rate in both groups is expected because of small organs and unlike human the rats are adversely affected by anesthesia, the pain they feel and even smallest degree of blood loss. Any of these stresses placed upon the animal usually results in death<sup>30</sup>.

In conclusion, SG were reduced weight of DIO rats and we successfully performed rat model for bariatric surgery

procedure in Iraq in spite of the high mortality. This will open the door widely for further studies on effects of different bariatric procedures on the rodents and to test the effects of these surgeries in many aspects. This will help to develop novel technique to treat obesity that will be translated on human.

### Conclusions:

Sleeve Gastrectomy as a bariatric procedure are successfully reduce the weight of DIO rats. Development of animal model for bariatric procedure is of great importance to test the effects of different bariatric procedures on the weight, and translate these procedures on human.

### References:

- 1- Colditz G. Economic costs of obesity and inactivity. *Medsci Sports Exerc.* 1999;31(suppl):S663-S667.
- 2- Yan LL, Daviglius ML, Liu K, Stamler J, Wang R, Pirzada A, Garside DB, Dyer AR, Van Horn L, Liao Y, Fries JF, Greenland P: Midlife body mass index and hospitalization and mortality in older age. *JAMA* 2006, 295:190-198.
- 3- Rimm, E.B., Stampfer, M.J., Giovannucci, E., Ascherio, A., Spiegelman, D., Colditz, G.A., Willett, W.C., 1995. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *Am. J. Epidemiol.* 141 (12), 1117-1127.
- 4- Kahn SE, Hull RL, Utzschneider KM. Mechanisms linking obesity to insulin resistance and type 2 diabetes. 2006. *Nature.* 2006 Dec 14;444(7121):840-6.
- 5- Frchetti KJ, Goldfine AB. Bariatric surgery for diabetes management. *Curr Opin Endocrinol Diabetes Obes.* 2009;16(2):119-124.
- 6- Rimm, E.B., Stampfer, M.J., Giovannucci, E., Ascherio, A., Spiegelman, D., Colditz, G.A., Willett, W.C., 1995. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. *Am. J. Epidemiol.* 141 (12), 1117-1127.
- 7- Must A, Spadano J, Coakley EH, Field AE, Colditz G, Dietz WH. The disease burden associated with overweight and obesity. *JAMA.* 1999;282:1523-1529.
- 8- Bolúmar F, Olsen J, Rebagliato M, Sáez-Lloret I, Bisanti L, European Study Group on Infertility and Subfecundity. Body mass index and delayed conception: a European multicenter study on infertility and subfecundity. *Am J Epidemiol.* 2000;151:1072-9.
- 9- Olson AL, Zwillich C (2005) The obesity hypoventilation syndrome. *Am J Med* 118:948-956.
- 10- Samanic C, Gridley WH, Chow J, Lubin RN, Hoover RN, Fraumeni JF Jr. Obesity and cancer risk among white and black United States veterans. *Cancer Causes Control.* 2004;15(1):35-43
- 11- Christou, N. V., Sampalis, J. S., Liberman, M., Look, D., Auger, S., McLean, A. P. H., Surgery decreases long-term mortality, morbidity and health use in morbidly obese patients. *Annals of Surgery,* 240, 416-424.
- 12- Maggard MA, Shugarman LR, Suttrop M, et al. Meta-analysis: surgical treatment of obesity. *Ann Intern Med.* 2005;142:547-59.

- 13- Adams, T.D., Gress, R.E., Smith, S.C., Halverson, R.C., Simper, S.C., Rosamond, W.D., Lamonte, M.J., Stroup, A.M., Hunt, S.C., 2007. Long-term mortality after gastric bypass surgery. *N. Engl. J. Med.* 357 (8), 753-761.
- 14- Pattou F, Beraud G, Arnalsteen L, et al. Restoration of  $\beta$ -cell function after bariatric surgery in type 2 diabetics: a prospective controlled study comparing gastric banding and gastric bypass. *Obes Surg.* 2007;17:1041-3.
- 15- Schernthaner G, Kopp H-P, Brix JM, et al. Cure of type 2 diabetes by metabolic surgery? A critical analysis of the evidence in 2010. *Diabetes Care.* 2011;34:S355-60.
- 16- Schneider BE & Mun EC. Surgical management of morbid obesity. *Diabetes Care* 2005;28:475-480.
- 17- Deitel M, Crosby RD, Gagner M (2008) The First International Consensus Summit for Sleeve Gastrectomy (SG). *Obes Surg* 18:487-496
- 18- Santry HP, Gillen DL, Lauderdale DS. Trends in bariatric surgical procedures. *Journal of the American Medical Association* 2005;294:1909-1917.
- 19- Buchwald, H. & Oien, D.M. Metabolic/bariatric surgery Worldwide 2008. *Obes. Surg.* 19, 1605-1611 (2009).
- 20- Gumbs AA, Gagner M, Dakin G, Pomp A (2007) Sleeve gastrectomy for morbid obesity. *Obes Surg* 17:962-969.
- 21- Deitel M, Crosby R, Gagner M. The first international consensus summit for sleeve gastrectomy (SG), New York City, October 25-27, 2007. *Obes Surg.* 2008;18:487-96.
- 22- Monteiro MP, Monteiro JD, Aguas AP et al. A Rat model of restrictive bariatric surgery with gastric banding. *Obes Surg* 2006; 16: 48-51.
- 23- Bozbora A, Coskun H, Barbaros U et al. The effect of gastric bands of different synthetic materials on the gastric and esophageal mucosa: an experimental study. *Obes Surg* 2004; 14: 246-52.
- 24- Wingerd BD. The digestive system. In *Rat dissection manual.* 2008; p. 522 41-48.
- 25- Lopez PP, Nicholson SE, Burkhardt GE, et al. Development of a sleeve gastrectomy weight loss model in obese Zucker rats. *J Surg Res.* 2009;157:243-50.
- 26- Wang Y, Liu J. Sleeve gastrectomy relieves steatohepatitis in high-fat-diet-induced. *Obese Rats* *Obes Surg.* 2009;19:921-5.
- 27- Patrikakos P, Toutouzias KG, Perrea D, Menenakos E, Pantopoulou A, et al. (2009) A surgical rat model of sleeve gastrectomy with staple technique: long-term weight loss results. *Obes Surg* 19: 1586-90.
- 28- Rao RS, Rao V, Kini S. Animal models in bariatric surgery - a review of the surgical techniques and postsurgical physiology. *Obes Surg.* 2010;20:1293-305.
- 29- Endo Y, Ohta M, Kai S, Kitano S. An obese rat model of bariatric surgery with gastric banding. *Obes Surg.* 2007;17:815-9.
- 30- Tichansky DS, Boughter JD, Harper J, et al. Gastric bypass surgery in rats produces weight loss modeling after human gastric bypass. *Obes Surg.* 2008;18:1246-1250.