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Cohort Study

Lipoabdominoplasty and the leptin hormone

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ABSTRACT

Background: Obesity contributes to a chronic disease with lethal complications. Leptin as an adiponectin interacts with fat metabolism. Surgical extra fat resection is an interventional approach to control obesity. We aimed to evaluate how body contouring surgery would influence on leptin plasma level.
Methods: Females candidate for body contouring surgery were allocated in to two groups included abdominal wall liposuction alone and in combination with abdominoplasty from 2018 to 2020. Demographic data was registered. Serum plasma level of leptin with the ELISA method was measured on the day before the operation and also after 3, 6, and 12 months after surgery with 8 h fasting prior to blood sampling. Finally the amounts of resected fat, type of surgical approach, and plasma level of leptin were analyzed.
Results: Total 124 females with mean age of 37 ± 10.1 years underwent abdominal wall liposuction (58%) and liposuction + abdominoplasty (42%) respectively. Mean weight and BMI significantly decreased postoperatively for both groups ($p < 0.01$). Although in both groups leptin concentration was higher in all triple blood sampling following operation in compared to preoperative measurement, changes were not significantly considerable ($p = 0.6$). Coefficient of correlation between amounts of resected fat and plasma level of leptin was directly positive and calculated 0.4 ($p = 0.03$).
Conclusion: Leptin interacts independently from abdominal wall contouring surgery. However it could be a marker for amounts of resected fat after operation.

1. Introduction

Obesity (BMI≥30) as a worldwide expanding medical challenge is the mainstay component of the metabolic syndrome involves cardiovascular and neuroendocrine systems. It leads to type 2 diabetes mellitus, hypertension, heart disease, and death [1]. Growth of the adipose tissue results in obesity which is influenced by different metabolic mediators and enzymatic cycles originating in almost all body tissues. Adipocytes are one of the main biologically active cellular structures which directly affect fat metabolism through production of wide variety of endocrine metabolic hormones and mediators, called adipokine. For the latter, adiponektin, tumor necrotizing factor-alpha, interleukin-6, resistin, and leptin are some familiar instances [2]. Leptin is a small 16 KD protein synthesized by ob-gene in adipocyte cytoplasm. Therefore, it is expected to have more fat storage when higher level of leptin is measured in plasma [3]. The goal of leptin is to regulate total body fat weight by reducing adipocytes lipid resources. The hormone plays its role by both inhibition of lipogenesis and stimulation of lipolysis. Leptin also signals feeling of satiety to hypothalamus gland and therefore postpones the desire of eating [4]. However, this regulatory system just executes in specific plasma level of leptin. Since the plasma level of hormone rises exceedingly (in case of elevated body mass index--BMI≥40) adipocytes manifest resistance to the hormone and aforementioned regulatory pathway deteriorates accordingly. Logically, elimination of peripheral fat tissue volume could lead to break this resistance and prevents obesity progression [4]. Some studies showed that fat tissue removal by surgical approaches through omentectomy, liposuction, mammoplasty, and abdominoplasty have decreased both plasma level of leptin and broke resistance to leptin and insulin which is a key point to reverse metabolic syndrome characteristics [5–7].

We supposed that surgical fat removal also could enhance remained fat tissue counter action to leptin and the hormone then prevents weight regain in patient with BMI<40 who isn't resistant to the hormone. Since body contouring surgery alone absolutely doesn't warrant weight loss steadily for long time we focused on leptin to evaluate its probable contributive chronic effect on weight. Current study pursued change of

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BMI and plasma level of leptin as a contributing agent of body fat mass following body contouring intervention.

2. Materials and method

This study was performed as a cohort research from February 2018 to May 2020 under supervision of department of general surgery of medical college after obtaining university ethics committee approval with trial registration code IRT201807131102C12 which is available at www.irct.ir. Females were included by randomly simple selection from patients consecutively referred to our surgical clinic seeking consult to manage their obesity ($30 \leq$ BMI<40). Three medical interns who were blind to the study randomly selected 124 (two of three) numbers from total 186 consecutive registered eligible patients at the end of every weekly clinic time. Written consent form was signed by all participants after orally description of study procedure. Inclusion criteria were:

a) Having no change in physical activity for 3 consecutive months in one year before surgery.
b) Continuation of physical activity for 12 months after surgery similar to preoperative pattern.
c) Having regular type of diet for 12 months after surgery similar to preoperative time.
d) Considering 20–25 calories/kg as mean daily energy intake for 12 months after surgery.
e) Negative history for consumption of oral contraceptive pills (OCP), anti-hyperlipidemic, and hormonal agents for at least 6 months before surgery.
f) Negative medical history for chronic disease like diabetes mellitus, liver, heart, lung, and kidney disease.

Exclusion criteria were included regular smoking, addiction, alcohol drinking, BMI >40 kg m^{-2}, chronic disease needing medication to be controlled, consumption of OCP, anti-hyperlipidemic or other hormonal agents (like spironolactone, finastride, letrozole, etc), psychiatric disorders, previous history of bariatric or endocrine surgery.

Demographic data included age, weight, height, and BMI was registered pre-operatively and also 3, 6, and 12 months after surgery. Surgical body contouring in this study represented as transdermal abdominal liposuction followed by abdominoplasty in selected patient. Liposuction performed with transdermal injection of large equal amount of tumescent solution to emulsify fat tissue prior to material suction in every individual. Following liposuction for some of participant additional abdominoplasty was implemented. Abdominoplasty contained abdominal fat and regional skin resection. All interventions were performed mainly by two general surgeons who were members of department of general surgery. Intraoperative amount of suctioned ± resected fat in according to type of procedure i.e. liposuction alone (for patients with $30 \leq$ BMI<35 kg m^{-2}) or liposuction with concurrent abdominoplasty (for patients with $35 \leq$ BMI<40 kg m^{-2}) were recorded for every patient. It should be mentioned that in case of abdominoplasty we ignored the weight of epidermis of resected tissue and considered each 1 kg of resected fat equal to 1 L of suctioned fat. This was accepted by authors because injection of same volume of tumescent for liposuction to all patients makes the mean density of dermal fat relatively equal for every individual.

Plasma level of leptin (ng/mL) was measured by the ELISA method on the day before and also 3, 6, and 12 months after surgery with 8 h fasting prior to take blood sample (Human Leptin ELISA Kit, Proteintech CO., Wuhan, China). All samples were analyzed by hospital reference biochemical lab. One year follow up period was accomplished by three visits in 3rd, 6th, and 12th months after the theatre.

Data analysis was performed using the SPSS v.19. Central statistical parameters, percent, mean, and standard deviation were calculated for study variables. We used paired *t* and Mann-Whithney *U* test to analyze means. We also applied Peasron's correlation coefficient method to investigate correlation between variables. Significant level of differences was regarded as $p < 0.05$. This study also was written in lined with STROCSS criteria [8].

3. Results

Finally 124 appropriate females underwent body contouring intervention. From all, 72 (58%) and 52 (42%) patients experienced liposuction alone (for patients with $30 \leq$ BMI<35 kg m^{-2}) and liposuction + abdominoplaty (for patients with $35 \leq$ BMI<40 kg m^{-2}) respectively. Mean age of all was 37 ± 10.1 years old. Significant change for weight and BMI was maintained during 12 months after intervention ($p < 0.001$). Table 1 shows findings about weight and BMI of all clients in this study. Analysis showed normal distribution for age, weight, and BMI whether for each group or for all participants.

Considering normal levels of the leptin (normal range: 2.5–21.8 ng/mL) however the hormone increased postoperatively both after liposuction alone and liposuction + abdominoplasy the change was not remained considerable 12 months after operation. Table 2 reveals attenuated data in this regard.

Mean change of plasma level of leptin according to Table 2 was significant neither for liposuction nor for liposucation + abdominoplasty group. The latter might be due to existence of relative leptin resistance, even partial, in $30 \leq$ BMI<40 kg/m^2.

Total resected fat was calculated 4.5 ± 1.3 and 4.9 ± 1.8 L for liposuction and liposuction + abdominoplasty, respectively. Analysis for volume of resected fat and change in plasma level of leptin illustrated no significance ($p = 0.3$) although there was a directly positive correlation with coefficient 0.432 between amount of the removed fat and increasing in plasma level of leptin. In follow up visits no considerable side effects or unexpected/long lasting events was remarkable to present.

4. Discussion

Obesity is defined as elevated BMI associated with several chronic disease including of hypertension, diabetes mellitus, and metabolic syndrome facing patients to lethal complications [9]. Therefore it is highly recommended to control obesity by modifying life-style and using medical and/or surgical approaches. Abdominal contouring surgery is principally based up on removing subcutaneous fat tissue through surgical suction and/or excision [10,11]. Following such interventions biochemical change could appear including elevation of anti-inflammatory agents. Some of these agents like leptin are suspected for helping body to confront obesity more efficiently [12,13]. Liposuction is a procedure in which emulsified fat is suctioned by specific devices. Abdominoplasty is defined as reconstruction of abdominal shape with resection of pannus of abdomen consisting of dermal abdominal fat and skin layers. Probable complication of these procedures in literature are regional skin flap necrosis, vascular thromboembolic events, splenic rupture, chronic pain, decreased body energy expenditure, decreased daily physical activity, increased occupational disorder, and feeling embarrassment [14,15]. Considering leptin effect on obesity, contouring surgery is expected to break leptin resistance especially in hypothalamic cells which is followed by enhancement of negative feedback on fat accumulation [16]. The hormone is originated by transcription of the obesity (ob) gene in adipocyte which contains 167 amino-acid and half-life 24.9 ± 4.4 min [17]. In addition to regulatory role of leptin on energy metabolism and inhibitory effects on fat tissue expansion, it has roles in sexual growth, reproduction, hematopoiesis, immune and gastrointestinal systems, angiogenesis, and bone formation as well [16]. Leptin is influenced by amounts of insulin, corticosteroid derivatives, sexual hormones, physical activity, and body energy expenditure [18].

Considering above, current study showed after a 12-months period from abdominal contouring intervention weight and BMI favorably remained constant whether abdominal liposuction alone or concurrent

Table 1
Measured weight and BMI of subjects during the study.

	Preoperative			Postoperative				Mean Changes (%)	p*
	LA[1] (N:72)	L + A[2] (N:52)	Total (N:124)	Sampling time (month)	LA (N:72)	L + A (N:52)	Total (N:124)		
Weight (kg)	79.8 ± 9.3+	96.8 ± 12.7	88.3 ± 11.1	3rd	74.8 ± 1.8	82.4 ± 7.1	78.6 ± 4.4	10.9 ± 6	<0.001
				6th	76.1 ± 2.5	83.6 ± 5.6	79.8 ± 4	9.6 ± 6.3	
				12th	74.4 ± 1.9	85.7 ± 6.5	80.1 ± 5.1	9.2 ± 5.4	
				Total mean	75.1 ± 2.1	83.9 ± 6.4	79.5 ± 4.5	9.9 ± 5.8	
BMI(kg/m2)	29.6 ± 4.3	35.2 ± 3.1	32.4 ± 3.8	3rd	27.7 ± 3.1	26,8 ± 5.8	27.2 ± 4.4	16 ± 1.5	<0.001
				6th	28.1 ± 4.1	29.5 ± 4.4	28.8 ± 4.2	11.2 ± 1	
				12th	27.6 ± 3	30.1 ± 5.1	29.2 ± 4	9.8 ± 0.5	
				Total mean	27.8 ± 3.4	28.8 ± 5.1	28.4 ± 4.2	12.3 ± 0.7	

1 Liposuction Alone, 2 Liposuction + Abdominoplasty, *paired *t*-test, +mean ± standard deviation.

Table 2
Perioperative changes of leptin.

Type of surgery	Participants Number (%)	Resected fat(L)	Plasma Leptin Level (mg/dL)					p[a]
		Intraoperative	Preoperative	Postoperative (months)				
				3rd	6th	12th	Total mean	
Liposuction	72 (58)	4.5 ± 1.3+	54.1 ± 22.7	52.5 ± 21.4	53.2 ± 20.7	55.8 ± 23.5	53.8 ± 21.7	0.5
Liposuction + abdominoplasty	52 (42)	4.9 ± 1.8	49.4 ± 21.8	52.1 ± 30.3	54.6 ± 31.3	53.3 ± 33.2	53.3 ± 31.6	0.8
Total	124 (100)	4.7 ± 1.5	52 ± 22	52.3 ± 27.6	53.4 ± 26.5	54.7 ± 27.3	53.5 ± 27.1	0.6

[a] Mann-Whithney *U* test, +mean ± standard deviation.

with abdominoplasty were conducted. Similar to other investigations, we also found no significant increasing in plasma level of leptin in a 12-months period postoperatively [19–23]. Opponents in previous studies revealed decreasing of plasma level of leptin at 7 and 12 weeks after surgery [7,24,25]. It is while other author has claimed that despite significant decreasing in BMI, no sensible change was found in plasma level of leptin 4 months after abdominal liposuction [26]. Interestingly another study showed that elevation in plasma level of leptin remained significant even one year after abdominal contouring surgery [27]. These variety of findings may contribute to samples size, patient selection method, differences in demographic characteristic of subjects, and conducted surgical approaches that eventually make leptin and other metabolic pathways to be affected.

Postoperative acute increasing in plasma level of leptin could refer to cellular destruction of fat tissue and releasing of hormone in to the blood stream [28]. Another reason for increasing of plasma level of leptin could point to hormone over-construction just after intervention. For explain the latter, when amount of fat mass decreases through surgical resection, interactions between cellular mediators lead to acute intraoperative elevation of pro-inflammatory cytokines such as interleukin-6, C-reactive protein, and resistin that is a clue for decreasing in plasma level of anti-inflammatory factors like adiponektin -leptin. The result is conduction of a message to responsible end organs particularly hypothalamus which senses that leptin is inactivated and finally makes exaggerated orders to synthesize leptin more than the usual although it lasts temporarily [29]. The above mentioned hypotheses are introduced for acute phase elevation in plasma level of leptin however data for describing pathophysiologic changes in late phase is lack. In current study no significant long-lasting elevation in plasma level of leptin was demonstrated. Acute postoperative elevated hormone concentration might be due to releasing of hormone from destructed fat tissue to the blood stream. On the other hand minimal change in plasma level of leptin in a 12-months period after surgery could attribute to activated feedback counter actions targeted to weight regain in order to save sufficient energy for next possible such critical condition. The final outcome of the latter was hyperactivity, hypertrophy, and hyperplasia of adipocyte tissue that decreased plasma level of leptin with constant slope. According to available data and ours, it seems any increasing in plasma level of leptin is temporary after abdominal contouring intervention. Additionally, because of hormone inability to remain steadily elevated in long term postoperatively it should not be expected to confront weight regain.

Conclusively, this study showed the following results: there was no direct obvious relationship between amount of surgically ablated fat and plasma level of leptin in a long term follow up, leptin had not enough potency to decrease body fat amount, relative leptin resistance was probable in BMI 30–40 kg m^{-2}, and it is not recommended to focus on leptin agonists/antagonists to control body weight. Considering lack of pathophysiologic concept for introducing the long term metabolic changes after abdominal contouring surgery and the requirement to find solutions for keeping favorable results of surgery conduction of more prospective studies with concentration on details of metabolism of mediators is highly recommended in this regard.

5. Limitations

This cohort study was performed in a crossed section of time among limited numbers of participants in also a single medical center. According to type of the study there was no control group to compare. Plasma level of leptin was measured just three times through 12 months postoperatively that made further tracking of hormone changes limited. Although patients with chronic disease including of overt diabetes mellitus were excluded evaluation of other metabolic profile and lipid indexes was not implemented.

6. Conclusion

Abdominal contouring intervention including of liposuction alone or with concurrent abdominoplasty was not enough competent to increase plasma level of leptin significantly in a 12-months period after surgery. Considering leptin agonist/antagonist as medications to confront weight regain is not recommended. Postoperative measurement of plasma level of leptin could directly determine amount of removed abdominal fat since the higher postoperative plasma level of leptin is associated with more volume of resected fat mass.

Ethical approval

This study was conducted under ethics committee consult and approval of the Kashan University of Medical Sciences with national trial

registration code IRT201807131102C12 which is available at www.irct.ir.

Availability of data and material

The surgical data used to support findings of this study is available in medical file archive unit of University of Medical Sciences, Kashan, Iran.

Author contribution

LG: study design, supervision, interpret results. VE: study design, data collection. AF: study design, data collection. AH: study design, data collection, data analysis, interpret results, drafting article.

Consent

Obtaining data from medical files was implemented followed by giving written consent form from the chief of forensic unit of the university.

Registration of research studies

This study was conducted under supervision of the Kashan University of Medical Sciences with national trial registration code IRT201807131102C12 which is available at www.irct.ir.

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Declaration of competing interest

Authors did not have any conflicts of interest in writing this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102633.

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