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Effect of Two Types of Diet on Cholecystokinin (CCK) Level in Three Groups of Males

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ABSTRACT

In response to a meal, the signals of satiety suppress the signals of hunger (meaning to finish the meal). These signals originate in the pancreas and gastrointestinal tract, transmitting information from the periphery to the brain (by the vagus nerve or the circulation). The study aimed to estimate whether the serum level of Cholecystokinin (CCK) in three male groups is influenced by their type of food. The current study included Sixty volunteers of adult males (normal-weight group n=20, overweight group n=20, and obese I group n=20) (21- 24 years). The blood samples were taken from subjects in the afternoon after (30 minutes–2 hours) from lunch was consumed, during March 2021 till June 2021. ELIZA kit was used to assay the serum concentration of the Cholecystokinin hormone. The anthropometric measurements were done, such as body weight and height, to calculate body mass index (BMI) by special formula, and the subjects were assorted depending on WHO body mass index (BMI) classification. Cholecystokinin showed a significant decrease ($p<0.05$) in obese I (311.201±21.542) and overweight (353.494 ± 43.915) as compared with the normal weight group (646.002 ± 46.344). A significant negative correlation was noticed between the hormone and body weight. Eating palatable food leads to uncontrolled ingesting behaviors due to the shift from homeostatic to hedonic regulatory mechanisms of food intake. These changes occur primarily in individuals with obesity and thus lead to an irregularity in the secretion of anorexigenic hormones.

1. Introduction

Obesity is caused by an excess of calorie intake in comparison to energy expenditure, not only that, but it can happen for some reasons including a high-calorie diet, a lack of physical activity, socioeconomic position, and genetic changes [1]. Obesity leads to an increase in associated diseases such as cardiovascular disease, type2 diabetes, numerous tumors, and psychiatric disorders. In this regard, a bidirectional communication system known as the gut brain axis plays an important role [2].
The Gut-brain axis is two-way communication between the gastrointestinal tract (GIT) and the central neurological system (CNS). Based on peptides expressed peripherally and/or centrally, both systems constantly share information about nutrient intake [3].

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The gastrointestinal tract (GIT) is considered a main sensory organ, which reacts to a variety of stimuli, including mechanical, nutritional, microbiota metabolites, pathogens, and toxins, and orchestrates a response that is important in order to maintain body homeostasis [4]. Following a meal, nutrients are transport from the stomach into the duodenum and jejunum leads to produce chemical and mechanical stimuli that the body can discover them. Enteroendocrine cells (EECs), which are specialized chemosensory cells that line the intestinal epithelium, are among the first sentinels to detect the presence of nutrients [5].

The hypothalamus and the brainstem are central structures in the central nervous system that regulate food intake. The vagus nerve, which connects the gut to the hindbrain, plays an important role in the gut brain and brain-gut relationship [6]. Cholecystokinin (CCK), Glucagon-like peptide (GLP-1), and Peptide YY (PYY) are food intake-regulating hormones that stimulate vagal afferent fibers that express respective receptors and project to the nucleus of the solitary tract (NTS), whence these signals are conveyed to the hypothalamus [7]. In

hypothalamus, each of paraventricular nucleus (PVN) and arcuate nucleus (ARC) are important for energy balance. When it comes to the motor and secretory activity, the stomach has a circadian rhythm that can lead to obesity if it is disrupted [8].

Food high in fat and sugar enhances food intake, indicating that the activity and expression of appetite-controlling signals will be balanced in favor of longer eating, activating the reward system and therefore influencing ingestive behavior. The behavior resulted via activating the reward system is to ‘‘get back for more’’ [9]. As a result, easy access to delicious food may lead to overeating, which is characterized via meal prolonging due to the overriding of the usually generated sensation of satiety, resulting in a gradual shift in the set point for energy balance and body weight. In the case of a healthy diet, reaching satiety is in an organized manner [10]. Figure 1 shows the effects of healthy and unhealthy diets on the expression of satiety peptides and brain response.

Cholecystokinin (CCK) is a peptide that reduces food intake. It is produced by intestinal cells in response to nutrient intake, particularly long-chain fatty acids reaching the duodenum and jejunum [11]. CCK release stimulates various parts of the CNS, including the brainstem, pons, hypothalamus, and motor cortex, causing the inhibition of food intake to be blocked [12].

There are no local studies that address the influence of food type on anorexigenic hormones in some individuals with gaining weight, to our knowledge, so this study was conducted. The goal of this study was to investigate how the type of diet affected the level of CCK hormone.

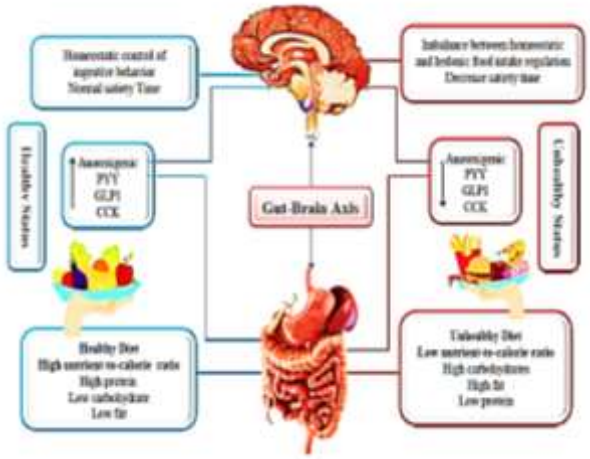

Fig 1: Proposed schematic diagram that connects the gut hormones changes. Left: Healthy diet leads to changes in hormone levels that lead to central nervous system response to inhibit eating. Right: Unrestricted Diet leads to changes in hormone levels leads to central nervous system response to more eating. Arrows show the respective change (↑ increase, ↓ decrease))Designed by me).

1. Methods and Procedures

2.1. Participants

The study was conducted in Anbar governorate, Iraq at Maternity and Children Teaching Hospital in Ramadi city, from March 2021 to June 2021. Study samples included 60 adults’ males who were close to the ages from 21 - 24 years. Subjects in this study were classified according to BMI as (normal-weight group n=20, overweight group n=20 and obese I group n=20). The males participating in the study did not have any gastrointestinal disease or symptoms or any other illnesses, or take any medication known to affect gastrointestinal motility or appetite.

2.2. Data Collection

The cross-sectional comparative study used data collected via a questionnaire including: age, length, weight, dietary, and lifestyle practices. Participants mentioned a diet diary through 21 before the study day to ascertain that their habitual energy and fat intake had not changed.

2.3. Protocol

On the day of the study, each group of subjects was given a different meal with different calories, and with different percentages of fat, carbohydrates and protein. Lunch meal is designed to match the meal each person in the three groups eats like a daily basis.

The first group was given a healthy lunch meal. At the same time, the second and third groups were given an unrestricted lunch meal. A detailed description of the two menus is given in Tables 1 and 2.

Each meal was consumed under medical supervision. Each person had consumed their meal at 1:00 pm. After 30 to 90 minutes of meal intake, blood samples were collected from each subject to measure serum CCK level.

Table 1: Nutrition facts of healthy lunch meal for normal-weight men.

Low-fat meal	Proteins (g)	Fat (g)	Carbohydrates (g)	Energy (kcal)
Raw Low Fat Beef)150g(	**35.7**	**10.5**	**0**	**228**
Olive oil 7 g	-	**6.99**	-	**63**
Medium slice of brown bread (15g)	**4**	**1.00**	**14**	**70**
Salad (200g) (Tomato+ Lettuce)	**1.2**	**0.2**	**5.1**	**23**
A cup of coffee	**0.3**	-	-	**1**
Total	**41.2**	**18.69**	**19.1**	**385**

Table 2: Nutrition facts of unrestricted lunch meal for overweight and obese class I men.

High-fat meal	Proteins (g)	Fat(g)	Carbohydrates (g)	Energy (kcal)
Raw High Fat Beef)200g(	**34.0**	**39.0**	**0**	**508**
Ghee 15 g	-	**14.00**	-	**130**
French fries (70g)	**2.44**	**9.84**	**24.96**	**192**
2 Medium slice of white bread (28g)	**4**	**2**	**30**	**140**
Coca-Cola (470ml)	-	-	**52**	**187**
Slice Chocolate cake(100g)	**5**	**15**	**53**	**371**
Total Energy (kcal)	**45.44**	**79**	**159.96**	**1.528**

3.Methods

3.1.Measurement of BMI

The body weight of each individual dressed in light clothing without shoes using a carefully calibrated electrical balance, the height of each individual was measured using vertical measuring rod. BMI was calculated as weight (kg) divided by squared height (m^2). The BMI was estimated with below formula, according to the World Health Organization classification (Table 2).

Body Mass Index(BMI) = Weight (kg)\Height (m)2

Table 3: WHO body mass index (BMI) Classification [13].

Groups	BMI
Underweight	**<18.5**
Normal weight	**18.5-24.9**
Overweight	**25-29.9**
Obesity class I	**30-34.9**
Obesity class II	**35-39.9**
Obesity class III	**≥40.0**

3.2. Determination of CCK hormone

The samples were collected and allowed to coagulate for serum separation using a centrifuge (4000 rpm) for 5 minutes. The sera were stored at -20˚C until the assay was done.
Cholecystokinin (CCK) level was measured by Enzyme Linked Immune Sorbent Assay kit of (Phoenix Pharmaceuticals, Belmont, CA) (intra-assay coefficient of variation <5% and interassay coefficient of variation <15%). The standard curve of CCK determination is shown in Figure 2:

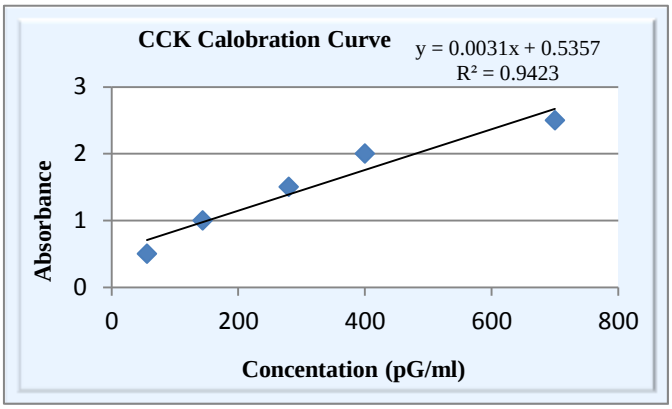

Fig 2: Representation Standard curve of CCK hormone.

3.3.Data Analysis

The data was analyzed using SPSS (version 18.0), and the results were presented as mean ± SD. A t-test and a nova were used to estimate statistical parameters for differences between the subjects tested. $p< 0.05$

4.Results

The results in Table 4 shows that there was no significant difference in age between normal-weight, overweight and obese groups. While BMI in the overweight and obese I group was significantly higher in comparison with the normal weight group. While BMI in obese I group was significantly higher than the overweight group.

Table 4: Mean and SD of BMI and Age in all study group.

Parameters	First Group (Normal Weight)		Second Group (Over Weight)		Third Group (Obesity class I)	
	Mean	S.D	Mean	S.D	Mean	S.D
BMI kg/m2	24.07	3.56	28.10	2.97	31.56	3.49
Age	22.13	8.13	23.34	1.63	21.45	2.20

The results in Table 5 show that the CCK level was significantly lower in both the overweight and obese I group; respectively, compared to the normal weight group.

Table 5: Mean and SD of CCK hormone in all study group.

Parameter	**Group**	**N**	**Mean ± S.D**	**95% confidence interval for mean**		**Sig. Value**
				Lower bound	**Upper bound**	
CCK (PG/ml)	**First Group**	**30**	**646.002 ± 46.344**	**631.912**	**660.092**	**.000****
	Second Group	**30**	**353.494 ± 43.915**	**340.142**	**366.845**	
	Third Group	**30**	**311.201± 21.542**	**241.720**	**354.871**	

* $p< 0.05$

5. Discussion

The current study has evaluated the effects of unrestricted diet on the CCK levels in overweight and obese I men compared with the effects of a healthy diet on CCK levels in normal-weight men. Consumption of an unrestricted diet (high calories diet) was associated with a decreased concentration of CCK, suggesting that exposure to this diet changes CCK secretion. Also, CCK signaling is blunted under obese conditions, possibly due to reduced excitability of the vagus nerve [14].

Overweight and obesity were associated with increased calories with participants in this study. This agrees with a study in Europe that found that the diet characterized by irregular calorie consumption is associated with weight gain[15].

The current study results agree with the study by Lasschuijt and his colleagues have reported that overweight and obese men show an attenuated CCK response to unrestricted intake meals compared with normal-weight men[16].

Taste-signaling mechanisms specified in the oral cavity have an important role in detecting the taste; stimulation of taste receptors triggers regulatory circuits, which are essential in controlling eating behavior and regulating energy homeostasis [17].

In the gut, nutrient detection is controlled mainly by enteroendocrine cells; upon sensing nutrients, a cascade of physiological phenomena is activated, including secretion of CCK for inhibition of gastric emptying and reduction in food intake, as shown in the results of the current study, but with different levels of CCK hormone depending on the type of meal [18] [19].

Food is an essential component for living a long and healthy life. The human need for food stems from the requirement to provide the body with the energy it requires to perform important functions such as heartbeat, breathing, digestion, and so on[20]. Obesity and many disorders connected with it, such as heart disease and cancer, are caused by an excessive increase in calories consumed by the person[21].

In the current study, men with a high BMI reported their cravings to eat large amounts of calorie-rich, unrestricted foods, as shown in Table 2, because of the greater responsivity of brain reward regions[22] [23].

Very appealing foods are more appreciated, preferred, and found to be more flavorful. Foods high in sugar and sweet flavor, highly processed foods high in saturated fats or high carbohydrate forming savory tastes, and combinations of food categories cooked in ways that improve the taste and value of such foods are examples of these [24].

As indicated in their lunch meal, as shown in Table 1, the first set of our study (Normal-weight men) participants were concerned about reducing energy intake by adopting healthy lifestyles and avoiding foods high in sugar, salt, or fat to prevent obesity and other diseases. These results are in agreement with a study by Mohammadbeigi and his team [25]

Unrestricted food has an effect on regular appetite regulation, which means it decreases the response to fullness signals and activates the reward system. This explains the rising obesity problem [26] [27].

6. Conclusion

We conclude that the ingestion of the healthy meal lead to stimulation of gut hormone release CCK have a decelerating effect on gastric emptying, conversely, when ingestion of unrestricted meal.

7. Limitations

In this study, we studied effects of type of diet on CCK levels in three groups. In future studies, the type of food should be more specific and number of samples more.

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تأثير نوعين من النظام الغذائي على مستوى الكوليسيستوكينين (CCK) في ثلاث مجموعات من الذكور

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الخلاصة:

استجابةً للوجبة ، تقوم إشارات الشبع بقمع إشارات الجوع (بمعنى إنهاء الوجبة)، وتنشأ هذه الإشارات في البنكرياس والجهاز الهضمي، ثم تنتقل هذه المعلومات من المحيط إلى الدماغ (عن طريق العصب المبهم أو الدورة الدموية). هدفت الدراسة إلى تقدير ما إذا كان مستوى مصل دم الكوليسيستوكينين (CCK) في ثلاث مجموعات من الذكور البالغين يتأثر بنوع طعامهم. شملت الدراسة الحالية ستين ذكرا بالغا مقسمين بالتساوي على ثلاثة مجموعات (مجموعة الوزن الطبيعي 20، مجموعة الوزن الزائد 20 ومجموعة الاشخاص المصابين بالسمنة 20) تتراوح اعمارهم ما بين (21 الى24 سنة). وقد تم أخذ عينات الدم من الأشخاص في فترة ما بعد الظهر بعد تناول وجبة الغداء لفترة من (30 دقيقة الى ساعتان)، من مارس 2021 الى يونيو 2021. وقد استخدمت مجموعة ELIZA لفحص تركيز هرمون الكوليسيستوكينين في الدم، وتم اخذ قياسات الجسم البشري مثل؛ وزن الجسم والطول لحساب مؤشر كتلة الجسم وتم تصنيف الذكور اعتمادًا على مؤشر كتلة الجسم لمنظمة الصحة العالمية. أظهر كوليسيستوكينين انخفاضًا معنويًا (p <0.05) في مجموعة السمنة (311.201 ± 21.542) وزيادة الوزن (353.494 ± 43.915) مقارنة بمجموعة الوزن الطبيعي (646.002 ± 46.344) ، كما لوحظ وجود علاقة سلبية معنوية بين هرمون الكوليسيستوكينين مع وزن الجسم. يؤدي تناول الطعام المستساغ إلى سلوكيات ابتلاع غير منضبطة، وذلك بسبب التحول من آليات التنظيم المتوازنة إلى اللذة في تناول الطعام. تحدث هذه التغييرات في المقام الأول لدى الأفراد المصابين بالسمنة، وبالتالي تؤدي إلى عدم انتظام في إفراز هرمونات فقدان الشهية.