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Evaluation of hormonal changes in obese individuals with constipation problems

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Abstract

Aim: Constipation is frequently seen in obese individuals. It is still not fully known whether the constipation in these individuals is related only to excess weight or due to other reasons. It is limited that the hormones secreted from the gut can play an important role in constipation. In this study, we think that hormones such as intestinal peptide YY, somatostatin, GLP-1, GLP-2 and Oxyntomodulin, which are known to have effects on bowel movements, may have effects on constipation. In this study, it will be tried to determine how the changes in the levels of the mentioned hormones with constipation in individuals who are obese and have constipation problems.

Materials and Methods: 22 obese and 22 obese+constipated individuals aged 20-64 years with BMI>30 who would sign the voluntary consent form were included in the study. Individuals with chronic diseases such as diabetes and hypertension in addition to obesity, those who received psychiatric treatment and those who used alcohol were not accepted. The demographic information of the individuals was determined by the face-to-face survey method. GLP-1, GLP-2, somatostatin, peptide YY, serotonin, oxyntomodulin levels were determined with the help of commercial ELISA kit in fasting blood samples taken from obese and obese+constipated individuals in the morning.

Results: The levels of oxyntomodulin, PYY, somatostatin did not differ in obese and constipated individuals ($p>0.05$). GLP-1, GLP-2, serotonin levels were found to be significantly higher in obese individuals than in constipated individuals ($p<0.01$).

Conclusion: In our study, high levels of GLP-1, GLP-2, and serotonin, which have conflicting results in the literature, and positive correlations between these hormones can be considered as important findings in our study.

Introduction

The prevalence of obesity has increased rapidly in recent years, thus becoming a serious global public health problem [1]. It has been reported that obesity causes systemic chronic inflammation, which plays a role in both the onset and progression of cardiovascular diseases, type 2 diabetes, non-alcoholic fatty liver disease, and cancer [2]. It has also been suggested that obesity is strongly associated with some chronic gastrointestinal disorders, especially constipation [3]. Obesity depends on both food intake and nutrient absorption, and these processes are related to gastrointestinal motility. Therefore, changes in gastric motility are likely to affect appetite and satiety. It has also been shown that nutrient absorption in the small intestine can be affected by changes in gastrointestinal motility [4]. While health professionals define constipation as defecation less than three times a week, patients often define constipation as a feeling of incomplete evacuation, straining, hard stool, insufficiency in bowel movements, and defecation that requires effort [5]. Although constipation and obesity have similar risk factors, not much is known about the occurrence of constipation and associated factors in highly obese individuals [6]. A high prevalence of constipation is often observed in obese individuals. A worrying intestine health profile has also been identified in these individuals, with low weekly defecation frequency, hard stools, and the need to exert excessive effort to evacuate [7]. Various gastrointestinal hormones are involved in the regulation of colonic motility, with hormones known to increase intestinal motility, such as motilin, gastrin, and cholecystokinin (CCK), or inhibit intestinal motility, such as somatostatin [8]. In addition to this hormone, it is thought that serotonin, secretin, CCK, gastric inhibitory polypeptide and somato-

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statin cells in the proximal small intestine and serotonin, Peptide YY (PYY), oxyntomodulin (enteroglucagon) and somatostatin secreting cells in the distal small intestine also affect motility [9]. An increase in the density of PYY cells has been observed in irritable bowel syndrome, and it has been reported that the increase in PYY cell density causes constipation by slowing down ileal motility, increasing water absorption, and slowing down intestinal transit by reducing the secretion of intestinal fluid [10]. When the literature is considered in general, it comes to mind that hormones that have effects on the gastrointestinal system may be related to constipation problem in obese individuals.

This study was planned to determine whether there is a difference in serum levels of hormones such as somatostatin, PYY, serotonin, GLP-1, GLP-2 and oxyntomodilin, which have effects on the gastrointestinal system, between obese and obese+constipated individuals.

Materials and Methods

Study design and ethical aspects

Our study was approved by the Inonu University Faculty of Medicine Malatya Clinical Research Ethics Committee (dated 26.01.2022, protocol number 2022/04). The individuals included in the study were selected from among patients who applied to the Inonu University Turgut Ozal Medical Center Endocrinology Department obesity clinic with complaints of obesity and constipation. The number of individuals in the groups was calculated using the http://biostatapps.inonu.edu.tr/ software system (Type I error amount (alpha) 0.05, power of the test (1-beta) 0.8, effect size 0.89 and alternative hypothesis (H1) two-sided, and the minimum sample size required to find a significant difference using this test was calculated as 20 obese and 20 obese+constipated individuals in each group (44 in total). Obese individuals aged between 24 and 64 years with a BMI (Body Mass Index) value ≥30 according to World Health Organization (WHO) age-specific and gender-specific references >18 were included in the study. Individuals who had chronic diseases such as diabetes and hypertension in addition to obesity, those receiving psychiatric treatment, those with infectious diseases, those using prescription drugs for any reason, or those using alcohol were excluded from the study. Individuals who met the inclusion criteria were included in the study after approving the informed consent form. Blood samples of the individuals participating in the study were taken after at least 8 hours of fasting and centrifuged, the serum portion was separated and stored at -80°C degrees until the day of analysis.

Experimental procedures

Serum levels of all hormones were measured with commercial ELISA kits (BT LAB, China) according to the kit protocol. Quantitative data were summarized as mean±standard deviation, and qualitative data were summarized as number (percentage). In order to compare the variables examined between groups with one-way variance analysis, compliance with normal distribution and homogeneity of variances (Levene test) were checked. When these assumptions were met, the difference between group means for the relevant variables was measured using one-way variance analysis, and in cases where normality assumptions were not met, the Mann Whitney U Test was used. The $p<0.05$ value was considered statistically significant.

Results

Age, height, water consumption and BMI values of obese and obese+constipated individuals are given in Table 1. When the groups were compared, only the BMI value was found to be lower in obese+constipated individuals than in obese individuals ($p<0.05$).

The correlation between the lifestyle and nutritional behaviors of obese and obese+constipated individuals was evaluated (Table 2). Gender, fast food consumption

Table 1. Quantitative statistics of survey data.

Variable	Obese	Obese+Constipation	p
Age	42.9545^{a}±9.9593	44.381^{a}±11.6468	0.6678
Size	1.605^{a}(0.12)	1.63^{a}(0.09)	0.2131
BMI	40.082^{a}±5.4237	36.7103^{b}±4.4789	0.0322
Water Consumption	2^{a}(0.375)	2^{a}(1)	0.7911

In the comparison of quantitative data obtained from the survey study between groups, variables that provided the normal distribution assumption were summarized as mean±SD. p<0.05 was accepted as significant.

Table 2. Statistics of survey data.

	Pearson correlation coeffecient	p
Gender	-0.04	0.801
Fast food consumption efficiency	0.161	0.303
Family history of obesity	-0.115	0.461
Genetic predisposition	-0.115	0.461
Chronic disease	0.118	0.45
Frequency of exercise	0.007	0.962
Vegetable consumption frequency	0.045	0.775
Fruit consumption frequency	0.111	0.478
Regular breakfast	0.139	0.373
Having a regular lunch	-0.051	0.746
Having a regular dinner	-0.019	0.905

Pearson correlation coefficient values were taken to compare the qualitative data obtained from the survey between groups (p<0.05 was considered significant).

Table 3. Relationship between hormone levels between the Obese and Obese+Constipated groups.

	Obese	Obese+Constipation	p value
GLP-1(pmol/L)	9.165^{a}±2.502	14. 356b±5.21	<0.001
GLP-2(ng/L)	196. 265^{a}±20.695	226. 116b±47.919	0.017
Somatostatin (ng/L)	73.729^{a}±9.938	80. 981^{a}±16.576	0.111
Serotonin (ng/ml)	111.663^{a}±9.38	127. 269^{b}±21.765	0.008
Peptid YY(pg/ml)	123.305^{a}±26.309	120. 287^{a}±27.922	0.734
Oxyntomodulin (ng/ml)	1.742^{a}±0.256	1. 883^{a}±0.591	0.347

ELISA results of serum PYY, SS, serotonin, oxyntomodulin, GLP-1, GLP-2 hormones were evaluated, variables that provided the normal distribution assumption were summarized as mean±SD. p<0.05 was accepted as significant. Different letters in group categories ındicate meaningful differences.

frequency, family history of obesity, genetic predisposition, chronic disease status, frequency of doing sports, frequency of consuming vegetables and fruits, breakfast, lunch and dinner habits were compared. No significant relationships/changes were found between obese and obese+constipated individuals between these environmental and nutritional behavior differences that may cause constipation ($p>0.05$).

Somatostatin, PYY, serotonin, oxyntomodulin, GLP-1, GLP-2 serum levels of obese and obese+constipated individuals are given in Table 3. Serum GLP-1, GLP-2, serotonin levels of obese+constipated individuals were observed to be statistically significantly higher than serum hormone levels of obese individuals ($p<0.05$).

Discussion

Obesity is defined by the WHO as the excessive increase of adipose tissue in the body that negatively affects human health [11]. Obesity has become a global problem that is increasing both in the world and in our country. Obesity negatively affects many systems in the body, not only physically, but also causes many health problems [12]. Constipation, which is commonly seen among gastrointestinal system disorders, is a metabolic disorder frequently seen in obese individuals. Constipation is used to describe various symptoms such as hard stools, excessive straining, infrequent bowel movements, bloating and abdominal pain [13]. Diagnosis and treatment of constipation in obese individuals are especially important and can prevent the development of gastrointestinal disorders due to constipation. It is important for health professionals to evaluate constipation in severely obese individuals [14]. The etiology of constipation in obese individuals is not clear. Such individuals may have an irregular eating pattern and less physical activity, which are factors that may affect their bowel movements [15]. In addition, studies suggest that the main reason why constipation is more common in obese individuals is related to a diet devoid of fruits and vegetables and low in fiber [16].

The level of constipation is associated with age and smoking, and the lack of whole grain consumption are risk factors for constipation. Using the Rome III criteria, it is confirmed that childhood constipation is more common in obese children. It has been shown that the increased frequency of childhood constipation is not due to decreased colonic motility, as only a small proportion of obese children had prolonged intestinal transit time. The observed constipation could not be explained by differences in dietary fiber or fat intake. Therefore, further studies are needed to elucidate the relationship between constipation and obesity in children, as other factors such as hormones and exercise are known to play a role [17]. A recent study conducted on constipated individuals with high levels of obesity in grades II and III also indicated that obesity level, physical activity level, consumption of fiber-rich foods and water intake were not associated with constipation in obese individuals [18]. In our study, when the nutritional behaviors of obese and obese+constipated individuals were evaluated, we evaluated that the gender, fast food consumption frequency, family history of obesity, genetic predisposition, chronic disease status, frequency of doing sports, frequency of consuming vegetables and fruits, and breakfast, lunch and dinner habits of obese+constipated individuals did not have an effect on constipation. Our findings suggest that these factors may cause obesity but do not have a clear effect on constipation. It suggests that endocrine secretions may play a role in constipation observed in obese individuals. Intestinal peptides, which play a role in the regulation of gastrointestinal motor and sensory functions, may be the cause of constipation other than nutritional behavior.

It has been reported in the literature that somatostatin inhibits gastrointestinal smooth muscle motility [19]. Some studies have shown that somatostatin levels are higher not only in plasma but also in the sigmoid colon in patients with Irritable Bowel Syndrome [20]. In another study conducted to examine the possible inhibitory effect of somatostatin on colorectal motility in the lumbo-sacral spinal defecation center, contrary to what is known, intrathecal somatostatin application to the L6-S1 region of the spinal cord was shown to increase colorectal motility. It was observed that intravenous and/or intrathoracic application of somatostatin had no effect on colorectal motility and increased colorectal motility without neural interaction with the supraspinal region [21]. In another study, it was suggested that changes in colonic somatostatin levels may cause decreased intestinal secretion and cause constipation, a common symptom in diabetes, together with a slow gastrointestinal system [22]. When the studies are evaluated, it is among the data obtained that somatostatin increases in plasma in case of constipation, but the hormone shows contradictory results in the defecation center. The effect of somatastatin on the role of intestinal motility is not fully known. In our study, although somatostatin was found to be higher in obese+constipated individuals than in obese individuals, the difference was not found to be statistically significant. It should be considered together with other factors affecting constipation. In addition, evaluating the difference between obese and normal weight individuals may also be important for explaining the role of somatostatin.

During the fasting period, glucagon hormone, which increases, acts on AgRP and POMC, which regulate feeding behaviors, on the central nervous system [23]. AgRP and POMC show their effects on food intake as well as motility and gastric emptying. Food intake increases insulin secretion 30-40 minutes later. It has been found that increased insulin levels, apart from their effects on body weight and β-cell function, increase GLP-1 levels. It has been suggested that increased GLP-1 reduces gastrointestinal motility and achieves this effect particularly by reducing gastric emptying rate and food intake [24]. On the contrary, it has been suggested that GLP-1 has an inhibitory effect on gastrointestinal motility at high serum levels and that GLP-1 is a mediator of the inhibitory ileal brake mechanism [25]. These studies, which demonstrate the relationship between increased GLP-1 secretion and constipation, are also consistent with our study data. In obese individuals, high insulin levels increase GLP-1 levels, leading to slowing down of intestinal motility. The significantly higher GLP-1 levels in obese+constipated individuals in our study findings may be related to this pathway,

which inhibits intestinal movement and causes constipation.

GLP-2 is secreted from L cells in the intestine and preproglucagonergic neurons in the brain. Peripheral GLP-2 is effective in regulating absorption efficiency and blood flow in the intestines, maintaining intestinal homeostasis by supporting the immune system, and treating gastrointestinal diseases [26]. Studies have shown that GLP-2 increases the absorption of carbohydrates, amino acids, and lipids. Increases in nutrient absorption with GLP-2 may be independent of simultaneous increases in blood flow. When GLP-2 levels are infused (in doses higher than the circulating GLP-2 levels after meals), it has been shown to inhibit gastrointestinal motility and gastric acid secretion in rodents, pigs, and humans [27]. When studies are evaluated, it has been shown that GLP-2 slows down motility. Our study suggests that the serum level of GLP-2 increases in cases of constipation and therefore may be a cause of constipation, which is frequently observed in obese individuals.

Synthesized from enteroendocrine L cells in the small intestine and colon, PYY is an important hormone that has been recently studied. Studies have shown that PYY inhibits gastrointestinal motility and electrolyte secretion and also interacts with the intestinal microbiota [28]. PYY functions as satiety factors, slows down gastrointestinal transit of chyme, prevents further food intake, and alters metabolic and energy homeostasis. In addition to regulating hormonal digestive secretions and energy homeostasis secreted from the intestine, PYY also has an effect on emotional eating behaviors. Since these actions partially occur in the brain, it has been concluded that PYY can send signals to the brain [29]. In a study conducted in individuals with chronic idiopathic slow-transit constipation, a common clinical problem, an increase in the number of colonic PYY-secreting cells and PYY synthesis was observed in cases of chronic severe constipation that were not relieved by bulking agents, prokinetic drugs, or other laxative treatments. As a result, the increase in PYY decreased the secretion of water and electrolytes by increasing absorption, and prevented intestinal motility leading to constipation by strengthening the ileal brake [30]. Although no clear relationship was found between PYY hormone levels and constipation in our study, there may be a relationship between constipation, especially in obese individuals.

Oxyntomodulin consists of a basic octapeptide extending from the entire glucagon sequence and its C-terminus. It is secreted into the circulation by L cells in the ileum and colon and is released into the circulation by intraluminal stimulation of glucose and other nutrients [31]. Infusion of oxyntomodulin in the fasting state strongly inhibited postprandial gastric acid secretion and basal acid secretion. Since oxyntomodulin is a pancreatic GLP-1 hormone derived from the distal intestine, when meal-induced gastroduodenal and pancreatic functions were investigated, both peptides were reported to inhibit gastric acid secretion in humans [32]. Recent studies have reported that GLP-1 causes a similar delay in gastric emptying in patients with diarrhea-predominant IBS [33]. In our study, although the differences in oxyntomodulin serum levels were not statistically significant, they were higher in obese+constipated individuals. Evaluating serum oxyntomodulin hormone levels in more obese individuals and constipated individuals with normal body index may provide more accurate results in evaluating the relationship between constipation.

Serotonin is best known as one of the neurotransmitters that modulates neural activity and a wide range of neuropsychological processes. 95% of serotonin, which is important for cognitive function, is synthesized in the intestines, and intestinal microorganisms play an important role in serotonin synthesis [34]. Serotonin regulates numerous biological processes in the gastrointestinal system, including slowing down, bladder control, and intestinal motility [35]. Peptides and amines localized in cells in the colonic mucosa have important regulatory functions in controlling motility. While somatostatin, PYY, and glucagon have inhibitory properties, serotonin has both stimulatory and inhibitory effects on gastrointestinal motility [36]. However, in one study, a slight increase in the number of serotonin-containing epithelial cells in the descending colon of constipated individuals was noted. Increased serotonin levels were shown in whole wall samples taken from the sigmoid colon of constipated patients. However, it was observed that there was no significant relationship between peptide contents and age in the control group that could be considered relevant [37]. In our study, the increase in serotonin serum levels in obese+constipated individuals compared to obese individuals was significant. Considering that the results in our study indicate that constipation will be affected by serotonin hormone levels, comprehensive studies should be conducted on this subject. In this case, serotonin hormone levels in individuals with high levels of obesity and constipation, according to obesity and chronic constipation, may offer a different perspective in terms of early diagnosis and increasing the quality of life of the individual.

Conclusion

In conclusion, although there are conflicting results in the literature, high GLP-1, GLP-2, and serotonin levels in obese individuals with constipation complaints can be considered as important findings in our study. Although the lack of evidence on constipation in obese or morbidly obese individuals limits our study in terms of comparison, it provides new data to the literature regarding the idea that endocrine disorders may also play an active role among the causes of constipation. In addition, the evaluation of the hormones we examined in obese and obese+constipated individuals may be effective in elucidating their effects on nutrition and gastrointestinal motility. At the same time, this may be a therapeutic approach for the treatment of constipation, which is commonly observed in obesity. However, it is seen that more comprehensive studies are needed on these issues. Considering the relationship between constipation observed in obese individuals and high medical costs; increasing constipation should be effectively prevented, and individuals at risk should be carefully identified and treated. In addition to providing individuals with healthy eating and physical activity habits at the treatment point, hormonal adjustments should also be taken into consideration. Treating both constipation

and obesity can speed up the treatment process at much lower costs by intervening before other more serious diseases worsen or emerge.

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Ethical approval

Our study was approved by the Inonu University Faculty of Medicine Malatya Clinical Research Ethics Committee (dated 26.01.2022, protocol number 2022/04).

References

1. Malik VS, Hu FB. The role of sugar-sweetened beverages in the global epidemics of obesity and chronic diseases. Nat Rev Endocrinol. 2022;18(4):205-18.
2. Andersen CJ, Murphy KE, Fernandez ML. Impact of Obesity and Metabolic Syndrome on Immunity. Adv Nutr. 2016;7(1):66-75.
3. Le Pluart D, Sabaté JM, Bouchoucha M, Hercberg S, Benamouzig R, Julia C. Functional gastrointestinal disorders in 35,447 adults and their association with body mass index. Aliment Pharmacol Ther. 2015;41(8):758-67.
4. Chen JD, Yin J, Wei W. Electrical therapies for gastrointestinal motility disorders. Expert Rev Gastroenterol Hepatol. 2017;11(5):407-18.
5. Bharucha AE, Lacy BE. Mechanisms, Evaluation, and Management of Chronic Constipation. Gastroenterology. 2020;158(5):1232-49.e3.
6. Bouchoucha M, Fysekidis M, Julia C, Airinei G, Catheline JM, Reach G, Benamouzig R. Functional Gastrointestinal Disorders in Obese Patients. The Importance of the Enrollment Source. Obes Surg. 2015;25(11):2143-52.
7. Wang GN, Zhang K, Xiong YY, Liu S. The relationship between functional constipation and overweight/obesity in children: a systematic review and meta-analysis. Pediatr Res. 2023;94(6):1878-86.
8. Tomita R, Igarashi S, Fujisaki S, Tanjoh K. The effects of neurotensin in the colon of patients with slow transit constipation. Hepatogastroenterology. 2007;54(78):1662-6.
9. El-Salhy M, Mazzawi T, Hausken T, Hatlebakk JG. Interaction between diet and gastrointestinal endocrine cells. Biomed Rep. 2016;4(6):651-6.
10. Noh HK, Kwon BS, Kim YH, Lee NK, Choi KU, Suh DS, et al. Peptide YY producing strumal carcinoid tumor of the ovary in a postmenopausal woman: a rare cause of chronic constipation. Obstet Gynecol Sci. 2017;60(6):602-7.
11. Sağlık Bakanlığı Sağlik İstatistikleri Yilliği. Ankara2020. 35-98 p.
12. Perdomo CM, Cohen RV, Sumithran P, Clément K, Frühbeck G. Contemporary medical, device, and surgical therapies for obesity in adults. Lancet. 2023;401(10382):1116-30.
13. Aziz I, Whitehead WE, Palsson OS, Törnblom H, Simrén MJErog, hepatology. An approach to the diagnosis and management of Rome IV functional disorders of chronic constipation. 2020;14(1):39-46.
14. Hong Y, Chen X, Liu J. Analysis of factors associated with constipation in the population with obesity: Evidence from the National Health and Nutrition Examination Survey. Obes Facts. 2024.
15. Miron I, Dumitrascu DL. GASTROINTESTINAL MOTILITY DISORDERS IN OBESITY. Acta Endocrinol (Buchar). 2019;15(4):497-504.
16. Sav NM, Sungur MA, Kiliçaslan Ö, Karaca SE. Obez Çocuklarda Uyku Kalitesi ve İşeme Fonksiyonunun Değerlendirilmesi. Online Türk Sağlık Bilimleri Dergisi. 2022;7(3):446-52.
17. vd Baan-Slootweg OH, Liem O, Bekkali N, van Aalderen WMC, Rijcken THP, Di Lorenzo C, Benninga MA. Constipation and Colonic Transit Times in Children With Morbid Obesity. Journal of Pediatric Gastroenterology and Nutrition. 2011;52(4):442-5.
18. Silveira EA, Santos A, Ribeiro JN, Noll M, Dos Santos Rodrigues AP, de Oliveira C. Prevalence of constipation in adults with obesity class II and III and associated factors. BMC Gastroenterol. 2021;21(1):217.
19. Shamsi BH, Chatoo M, Xu XK, Xu X, Chen XQ. Versatile Functions of Somatostatin and Somatostatin Receptors in the Gastrointestinal System. Front Endocrinol (Lausanne). 2021;12:652363.
20. Zhang H, Yan Y, Shi R, Lin Z, Wang M, Lin L. Correlation of gut hormones with irritable bowel syndrome. Digestion. 2008;78(2-3):72-6.
21. Naitou K, Shiina T, Nakamori H, Sano Y, Shimaoka H, Shimizu Y. Colokinetic effect of somatostatin in the spinal defecation center in rats. The journal of physiological sciences : JPS. 2018;68(3):243-51.
22. Milosavljevic T, Popovic DD, Mijac DD, Milovanovic T, Krstic S, Krstic MN. Chronic Constipation: Gastroenterohepatologist's Approach. Dig Dis. 2022;40(2):175-180.
23. Tanbek K, Yilmaz U, Gul S, Koç A, Gul M, Sandal S. Effects of glucagon as a neurohormone on the central nervous system and glucose homeostasis. Eur Rev Med Pharmacol Sci. 2024;28(1):163-79.
24. Hellström PMJAp. GLP-1 playing the role of a gut regulatory compound. 2011;201(1):151-6.
25. O'Brien R, O'Malley D. The Glucagon-like peptide-1 receptor agonist, exendin-4, ameliorated gastrointestinal dysfunction in the Wistar Kyoto rat model of Irritable Bowel Syndrome. Neurogastroenterol Motil. 2020;32(2):e13738.
26. Guan X, Shi X, Li X, Chang B, Wang Y, Li D, Chan L. GLP-2 receptor in POMC neurons suppresses feeding behavior and gastric motility. American journal of physiology Endocrinology and metabolism. 2012;303(7):E853-64.
27. Drucker DJ, Yusta B. Physiology and pharmacology of the enteroendocrine hormone glucagon-like peptide-2. Annual review of physiology. 2014;76:561-83.
28. El-Salhy M, Hatlebakk JG, Hausken T. Possible role of peptide YY (PYY) in the pathophysiology of irritable bowel syndrome (IBS). Neuropeptides. 2020;79:101973.
29. Holzer P, Reichmann F, Farzi A. Neuropeptide Y, peptide YY and pancreatic polypeptide in the gut-brain axis. Neuropeptides. 2012;46(6):261-74.
30. El-Salhy M, Mazzawi T, Gundersen D, Hatlebakk JG, Hausken T. The role of peptide YY in gastrointestinal diseases and disorders (review). International journal of molecular medicine. 2013;31(2):275-82.
31. Schalla MA, Taché Y, Stengel A. Neuroendocrine Peptides of the Gut and Their Role in the Regulation of Food Intake. Compr Physiol. 2021;11(2):1679-730.
32. Stanley S, Wynne K, Bloom S. Gastrointestinal satiety signals III. Glucagon-like peptide 1, oxyntomodulin, peptide YY, and pancreatic polypeptide. American journal of physiology Gastrointestinal and liver physiology. 2004;286(5):G693-7.
33. Rao AS, Wong BS, Camilleri M, Odunsi-Shiyanbade ST, McKinzie S, Ryks M, et al. Chenodeoxycholate in females with irritable bowel syndrome-constipation: a pharmacodynamic and pharmacogenetic analysis. Gastroenterology. 2010;139(5):1549-58, 58.e1.
34. Liu N, Sun S, Wang P, Sun Y, Hu Q, Wang X. The Mechanism of Secretion and Metabolism of Gut-Derived 5-Hydroxytryptamine. Int J Mol Sci. 2021;22(15).
35. Berger M, Gray JA, Roth BL. The expanded biology of serotonin. Annual review of medicine. 2009;60:355-66.
36. Li CP, Ling C, Biancani P, Behar J. Effect of progesterone on colonic motility and fecal output in mice with diarrhea. Neurogastroenterol Motil. 2012;24(4):392-e174.
37. Sjölund K, Fasth S, Ekman R, Hulten L, Jiborn H, Nordgren S, et al. Neuropeptides in idiopathic chronic constipation (slow transit constipation). 1997;9(3):143-50.