ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Is there a difference between patients with functional dyspepsia and irritable bowel syndrome in headache manifestation?

Ana Starčević[1,2], Marija Marjanović-Haljilji[3], Ljiljana Milić[1,4], Branka Filipović[1,3]

[1]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[2]Niko Miljanić Institute of Anatomy, Belgrade, Serbia;
[3]Dr Dragiša Mišović – Dedinje Clinical and Hospital Center, Department of Gastroenterology, Belgrade, Serbia;
[4]Zvezdara Clinical and Hospital Center, Department of Surgery, Belgrade, Serbia

SUMMARY
Introduction/Objective The objective was to explore whether there is a difference in headache manifestation and level of its intensity in patients with functional dyspepsia and irritable bowel syndrome.
Methods We assessed a cohort of 420 participants out of which 300 satisfied the recruiting criterion of the presence of irritable bowel syndrome (148) or functional dyspepsia (152). Diagnoses of irritable bowel syndrome and functional dyspepsia were made according to Rome IV criteria. Intensity of headaches was estimated in irritable bowel syndrome and functional dyspepsia participants using visual analog scale. All the patients underwent subsequent testing by Hamilton's Depression Inventory and anxiety scale.
Results Our results showed that males with headaches are more susceptible to functional dyspepsia, statistical significance in the group of patients with irritable bowel syndrome with high scores on the visual analog scales, in relation to Hamilton's anxiety scores in the group of patients with irritable bowel syndrome. Gender and visual analogue scale scores were determinants to show whether the patient falls within the group of functional dyspepsia or irritable bowel syndrome. Scores of visual analogue scale where the patient felt the best was statistically borderline (p = 0.061) and its higher values pinpointed which of those patients fall into irritable bowel syndrome group.
Conclusion Gender and level of headache intensity as a extraintestinal manifestation showed to be the main variables to make a difference between patients with functional dyspepsia and irritable bowel syndrome where irritable bowel syndrome had higher scores and greater dominance in differential diagnosis if the headache was determining variable.
Keywords: headaches; functional dyspepsia; irritable bowel syndrome

INTRODUCTION

Migraine is a primary headache typically characterized by unilateral pulsating head pain that is aggravated by routine physical activity and may be accompanied by a variety of autonomic, cognitive, and emotional disturbances [1]. Headaches are reported to be evaluated as one of the top rated self-reported physical disorders [2]. Estimated one-year prevalence of migraine is approximately 14% in the general population and the association between headache and gastrointestinal complaints increased with increasing headache frequencies. Chronic migraine-like headache was reported in about 30% patients with functional dyspepsia (FD), but the pathophysiology is still not fully understood [3, 4]. Functional gastrointestinal and motility disorders are a group of disorders of gut–brain interaction, which are categorized by Rome diagnostic criteria as symptom-based diagnostic criteria for each category [5]. Due to the fact that the prevalence of functional digestive disorders and irritable bowel syndrome (IBS) are still underestimated with the currently applied diagnostic tools, some other improved criteria or point of view are needed as the treatment is still not very efficient and satisfactory. IBS presents a neurogastroenterological functional disorder that shares some environmental risk factors with migraine (predominately affecting the female sex and younger individuals). It is a group of bowel disorders with specific abdominal discomfort or pain correlated with bowel habit irregularities. FD refers to pain or specific discomfort in the topographic region of the upper abdomen. IBS and FD share many somatic and psychiatric comorbidities [6]. Except for the headaches as one of the most prominent extraintestinal neurological manifestation, GH presents one of esophageal disorders manifesting as a sensation of a lump or tightness in the throat, which also can be attributed to psychogenic cause i.e., somatoform or anxiety disorder [7].

The objective was to explore whether there is a difference in headache manifestation and to evaluate the level of its intensity in patients with FD and IBS.

Correspondence to:
Ana STARČEVIĆ
Institute of Anatomy
Faculty of Medicine
University of Belgrade
Dr Subotića 4/2
11000 Belgrade, Serbia
ana.starcevic22@gmail.com

METHODS

We assessed a cohort of 420 participants, out of which 300 (174 females and 126 males) satisfied a recruiting criterion of the presence of IBS (148) or FD (152). The participants were 18–80 years old and were referred to the gastroenterology unit of the Dr Dragiša Mišović – Dedinje Clinical and Hospital Center from January to December of 2019. Diagnoses of IBS and FD were made according to Rome IV criteria [5]. The participants satisfied the following inclusion criteria: 1) older than 18 years; 2) no evidence of organic disease on the upper and lower endoscopy examination; 3) normal findings on abdominal ultrasonography; 4) no history of abdominal surgery; 5) absence of any cardiovascular or metabolic disease to avoid vasculoprive or headaches related to the impaired metabolism or endocrine function; and 6) no evidence about prior neuropsychiatric treatment.

Participants underwent a clinical interview and physical and neurological examinations by experienced neurologists in order to exclude headaches associated with neurological disorders and to assess for presence of migraine-like migraine. A migraine has been diagnosed according to International Classification of Headache Disorders 3rd edition [8].

The intensity of headaches has been estimated in IBS and FD participants using visual analogue scale (VAS), where 0 is the absence of pain and 10 is the worst possible pain. VAS scale was used to assess pain in three states: pain when the patient was at his/her best (VAS best), baseline pain (VAS typical), and pain when the patient was at his/her worst (VAS worst). It is important to note that we reanalyzed the data from our two groups (IBS, n = 148, and FD, n = 152) to determine the mean of VAS pain intensity rating and changes scores on 10-cm-rating scale, 0–0.4 cm signified no pain; 0.5–4.4 cm signified mild pain, 4.5–7.4 cm moderate pain, and 7.5–10 cm severe pain.

Participants underwent psychiatric examination including psychiatric interview/evaluation by the specialist of psychiatry in order to assess the presence of depressive or anxiety disorder and to exclude other psychiatric comorbidities. The patients underwent subsequent testing by Hamilton's anxiety (HA) and depression (HD) 21-item inventory, Serbian version [9]. Typically, Hamilton Depression Inventory contains items related to gastrointestinal symptoms and weight loss. Please note that these were omitted because the mentioned symptomatology is part of the illness. The diagnosis of globus hystericus (GH) has been made according to the 10th revision of the International Classification of Diseases (ICD-10) criteria for the diagnosis code F 45.8 [7]. The presence of GH was assessed by routine questionnaire used during the first visit to the gastroenterologist.

Statistical analysis

We used Pearson's χ^2 test with likelihood ratio correction to compare groups among categorical data when necessary.

For those variables expressed with the scores, testing was performed to verify if the normal distribution exists and, in that case, we used the Kolmogorov–Smirnov test. Non-parametric test methods were used for further analysis. The Mann–Whitney test was used to compare the parameters on the scale to determine the difference. A binomial logistic regression analysis, the stepwise backward method, was used to define the determining variables that may be influencing the prediction of group affiliation. We used the software program IBM SPSS Statistics, Version 27.0 (IBM Corp., Armonk, NY, USA) with a significance threshold of p = 0.05.

The protocol involving human data was in accordance with national and institutional guidelines and the Declaration of Helsinki. All the participants were informed about the study protocol and they provided written consent. The study was approved by the Ethics Committee of Dr. Dragiša Mišović – Dedinje Clinical and Hospital Center (18-6685/2019).

RESULTS

Demographic data imply that examined groups were of similar size (p = 0.808), gender-balanced with slightly more women within examined groups (p = 0.122). The manifestation and occurrence of headaches is less pronounced according to our results but not statistically significant (p = 0.073). Manifestation of GH and scores of HA were almost completely uniform within the observed categories (p = 0.755 and p = 0.949, respectively). The HD scores were mostly uniform and did not show a statistically significant difference (p = 0.271). The scores of HD, HA, VAS, as well as the ages of the examined patients did not have a normal distribution, therefore we used non-parametric tests and based our results on the Mann–Whitney test. In all cases, the groups were uniform (p > 0.05) and at the very beginning did not differ according to the observed parameters (Tables 1 and 2).

Demographic data showed no statistical difference between FD and IBS groups (p > 0.05) (Table 1).

VAS score and Hamilton's scales showed no difference between the examined groups when Mann–Whitney test was done, but when we made a separation into groups of those who did experience headaches and those who did not, the statistical significance was shown in male patients with FD, which is shown in Table 2.

Since headache was found as one of the dominant determinant variables in logistic regression analysis, the influence of the determining variable between the examined groups and observed variables was measured (Table 3).

Sex (gender) had an impact on FD and IBS when related to headache, as seen in Table 4. Males with headaches were more susceptible to FD, HR = 1.829 (1.043–3.206).

GH, HD, HA show no statistical difference between the groups if headache is observed as a determining variable (p > 0.05).

Table 1. Group comparisons by category parameters

Parameters			FD	IBS	Total	p
			Group			
Sex	Male	n (%)	49 (56.3)	38 (43.7)	87 (100)	0.122
	Female	n (%)	99 (46.5)	114 (53.5)	213 (100)	
Headache	Yes	n (%)	51 (57.3)	38 (42.7)	89 (100)	0.073
	No	n (%)	97 (46)	114 (54)	211 (100)	
Globus	Yes	n (%)	63 (50.4)	62 (49.6)	125 (100)	0.755
	No	n (%)	85 (48.6)	90 (51.4)	175 (100)	
HD	None	n (%)	7 (43.8)	9 (56.3)	16 (100)	0.271
	Mild	n (%)	39 (47.6)	43 (52.4)	82 (100)	
	Moderate	n (%)	52 (44.8)	64 (55.2)	116 (100)	
	Heavy	n (%)	50 (58.1)	36 (41.9)	86 (100)	
HA	None	n (%)	9 (56.3)	7 (43.8)	16 (100)	0.949
	Mild	n (%)	75 (49.3)	77 (50.7)	152 (100)	
	Moderate	n (%)	22 (47.8)	24 (52.2)	46 (100)	
	Heavy	n (%)	42 (48.8)	44 (51.2)	86 (100)	
Total		n (%)	148 (49.3)	152 (50.7)	300 (100)	

FD – functional dyspepsia; IBS – irritable bowel syndrome; HA – Hamilton's anxiety; HD – Hamilton's depression

Table 2. Group comparisons by score parameters

Parameters	FD		IBS		p
	Group				
	Median	IQR	Median	IQR	
Age	42.5	25	45	22	0.333
VAS now	0	4	0	2	0.815
VAS best	0	0	0	0	0.168
VAS typical	0	5	0	4	0.170
VAS worst	0	8	0	8	0.430
HD	21	13	21	9	0.242
HA	15.50	12	16	12	0.391

FD – functional dyspepsia; IBS – irritable bowel syndrome; HA – Hamilton's anxiety; HD – Hamilton's depression; IQR – interquartile range; VAS – visual analogue scale

Table 3. Logistic regression, stepwise backward method, for Group predictions and determined parameters

Parameters	HR	95% CI LL	95% CI UL	p
VAS Best	1.438	1.042	1.985	**0.027**
HA	1.040	1.001	1.080	**0.043**
Headache (No)	3.307	1.599	6.839	**0.001**
Constant	0.186			0.005

HA – Hamilton's anxiety; VAS – visual analogue scale

Table 4. Determined Headache parameter and comparison of the parameters Sex and Groups

Headache			FD	IBS	Total	p
			Group			
Yes	Sex	Male	n (%) 27 (71.1)	11 (28.9)	38 (100)	**0.024**
		Female	n (%) 24 (47.1)	27 (52.9)	51 (100)	
	Total		n (%) 51 (57.3)	38 (42.7)	89 (100)	
No	Sex	Male	n (%) 22 (44.9)	27 (55.1)	49 (100)	0.863
		Female	n (%) 75 (46.3)	87 (53.7)	162 (100)	
	Total		n (%) 97 (46%)	114 (54)	211 (100)	

FD – functional dyspepsia; IBS – irritable bowel syndrome

In VAS scores (worst and best) there was a statistical significance between FD and IBS where IBS had higher scores if the headache is the determining variable. In contrast to this, in a situation without headache only HA scale showed some upper limits in IBS group of patients as statistically significant (p < 0.05) (Table 5.)

In the group of those who had headache, logistic regression showed determining variable within each examined group and sex (gender), VAS best, VAS typical, and VAS worst determined whether patient falls within the group of FD or IBS. VAS best was statistically borderline (p = 0.061). Higher VAS best score shows HR = 1.410 (0.984–2.020), which pinpoints that those patients fall into the IBS group. VAS typical shows less hazard to be IBS if scores are higher HR = 0.577 (0.377–0.884). VAS worst shows a more important role to determine the IBS group with HR = 2.191 (1.273–3.771).

In situations without headache, the only important variable is HA, where HR score shows to fall within the scope of IBS with higher values HR = 1.092 (1.022–1.166) (Table 6)

DISCUSSION

There is a significant overlap between FD and IBS clinical manifestations. Headaches, especially migraines, present one of the most important and disabling manifestations in above mentioned gastrointestinal disorders, proving a very important and powerful role of the brain–gut axis [4, 10].

In our study, we used the presence of headaches and relation to their specific intensity (VAS scale scores) based on which we made a separation between the patients with FD and those with IBS.

Migraine-like headaches present a very disabling condition, often recurrent and severe with concomitant gastrointestinal features and affect women more frequently than men [11]. It was also shown that FD affects women more than men in daily life [12].

Our results showed that gender had an impact on FD and IBS when related to headache, showing that males with headaches are more susceptible to FD. When we made a separation into groups of those who did experience headaches and those who did not, the statistical significance was shown in the group of male patients with FD. In previous studies conducted related to gender differences in migraines it was shown that man tend to have longer remission periods than women and that headache attack frequency and their intensity are similar to both genders with severe migraines persisting longer in women [13].

The VAS evaluates the severity of subjective symptoms in patients, especially in measuring pain. Our results showed that there is statistical significance in the group of patients with IBS who had high scores on the VAS, which correlates with previous studies.

Migraine headaches have a higher prevalence in patients with IBS compared to the general population. Li et al. [14]

Table 5. Determined Headache parameter and comparisons with parameters Score and Groups

Parameter	Group	Headache									
		Yes					No				
		n	Mean	Median	STD	p	n	Mean	Median	STD	p
Age	FD	51	41.41	33	15.478	0.549	97	44.61	43	13.610	0.557
	IBS	38	41.03	41.50	11.554		114	45.63	45	13.415	
VAS Now	FD	51	4.73	5	2.601	0.123	97	0.05	0	0.508	0.142
	IBS	38	5.18	6	2.415		114	0.29	0	1.480	
VAS Best	FD	51	0.63	0	1.183	**0.028**	97	0	0	0	0.191
	IBS	38	1.21	0	1.492		114	0.04	0	0.295	
VAS Typical	FD	51	6.06	6	1.580	0.943	97	0.12	0	0.869	0.351
	IBS	38	5.97	6	1.602		114	0.25	0	1.209	
VAS Worse	FD	51	8.47	8	1.206	**0.023**	97	0.27	0	1.517	0.423
	IBS	38	9.03	9	1.150		114	0.50	0	2.138	
HD	FD	51	28.61	28	4.976	0.656	97	16.74	17	5.553	0.748
	IBS	38	28.53	27	4.607		114	16.82	18	5.508	
HA	FD	51	26.61	30	8.139	0.403	97	15.70	15	4.895	**0.035**
	IBS	38	27.82	30	7.665		114	17.31	15	6.046	

FD – functional dyspepsia; IBS – irritable bowel syndrome; HA – Hamilton's anxiety; HD – Hamilton's depression; VAS – visual analogue scale

Table 6. Logistic regression, stepwise backward method, by determining parameter Headache to identify prediction variables to identify the groups

Headache	Parameters	HR	95% CI LL	95% CI UL	p
Yes	Sex (male)	0.253	0.089	0.718	**0.010**
	VAS Best	1.410	0.984	2.020	0.061
	VAS Typical	0.577	0.377	0.884	**0.011**
	VAS Worse	2.191	1.273	3.771	**0.005**
	Constant	0.028			0.055
No	HA	1.092	1.022	1.166	**0.009**
	Constant	0.613			0.402

HA – Hamilton's anxiety; VAS – visual analogue scale

showed that patients with reported chronic headaches are more likely to have IBS.

Our results also showed statistical significance in relation to HA scores in the group of patients with IBS. Anxiety presents a psychiatric disorder which attacks individuals with IBS and therefore might worsen their condition. The reason lies in the fact that colon as an anatomical substrate is under control of nervous system responding to stress. Affected hypothalamic-pituitary axis (HPA) activates a stress biochemical cascade, which triggers the immune system as well, playing a significant role. Although anxiety itself mostly does not cause a gastrointestinal disorder, these patients are more emotional to everyday life stressors.

When we analyzed all significant variables in the group of patients with headaches, our results showed that gender, VAS best, VAS typical, and VAS worst were determinants whether a patient falls within the group of FD or IBS. VAS best was statistically borderline and higher VAS best score pinpointed which of those patients fall into the IBS group. Generalized inflammatory response rather than isolated bowel inflammation may play the key role in the pathogenesis of the extra-intestinal manifestations of IBS.

The activation of HPA was associated with stress and the increase of IL-6 in the peripheral blood. There is also a link between inflammation and mental disorders in patients with anxiety and depression that had immune response correlated to increased levels of serum C-reactive protein and other inflammatory mediators [15, 16, 17].

Patients with overlapping IBS and FD symptoms had more severe psychological problems and problems with anxiety and depression as an independent factor [18].

It has been hypothesized that the underlying pathophysiology for both IBS and migraine is a genetically established hypersensitive or hyperexcitable brain [19]. Environmental, psychological, and immunological factors may increase sensitization in the enteric nervous system and brain gut axis in IBS. Increased amygdala activity, demonstrated in IBS, could also be linked with the conversion dysphagia, also known as GH and subsequent influence to the emotional zones [20]. Abnormalities in emotion regulation and connectivity have been identified in non-symptom studies about conversion disorders, potentially pointing to a diathesis or vulnerability: two studies found an abnormal emotion–motor connectivity, and a failure of normal habituation [21].

Many researchers debated about precise pathophysiological mechanisms of migraines and one of them is vascular due to the vasodilatation of the middle meningeal artery and middle cerebral artery on the side of the brain where the pain occurs, or bilaterally if the pain attacks from both sides. It is widely considered that the inflammation is the core mechanism and that the inflammatory mediators play the main role. Among the others the most important and the oldest are histamine and tumor necrosis factor alpha [17].

The link between depressive and anxiety symptomatology with functional gastrointestinal disorders' clinical symptoms may refer to a low concentration of serotonin (5-HT), which correlates to greater nociception of trigeminal neurons, which also produces a clinical correlation with different migraine intensities in pain [22]. Serotonin 5-HT1F receptor agonists are on the list of prophylactic drugs for migraine, implying that a lower concentration of serotonin decreases the stimulation of the mentioned receptors which are hypothesized to have an important role in migraine genesis [23, 24]. Moreover, probiotics are

believed to be of potential benefit in the treatment of migraine, as well as IBS and FD [25].

The results from a double-blind randomized controlled experimental investigation showed based evidence of correlation between IBS and migraine showing expressed immunoglobulin G antibodies reduced the frequency and the level of migraine attacks after specific food deprivation and reduction, which pinpoints the growing significance of the gut–brain axis [26].

There is also evidence showing a correlation between pain-related functional gastrointestinal disorders and migraine in pediatric population, as well as much evidence based on association of anxiety, depression, and FD [27].

Finally, migraine in functional disorders of the gastrointestinal tract is interpreted as disrupted balance of microbiota in the gut and its influence to pain sensations and impaired brain–gut axis [15]. The concept of microbiota gut–brain axis refers to a significant role of the modulated enteric and central nervous system function disrupting mood and affection by modifying serotonin, which plays a key role in both gastrointestinal tract and in the brain [28, 29].

Gut microbiota in correlation with the gut–brain axis defines itself as the main new to-be-defined axioma in functional sense of evidence-based functional substrate on precise explanation of neuropsychiatric and functional gastrointestinal disorders interaction. Management options of headaches which are typically diagnosed very late impact the quality of life of a patient and therefore the development of treatment regime with less potentional side effects correlated with patients with functional gastrointestinal disorders is of huge importance. Defining morphological anatomical substrate is the main step in defining an illness or disorder, but in this case we must be aware of the fact that the systems and their interaction understanding present the main step in defining functional gastrointestinal disorders and migraine attacks [30].

Study strengths

The study largely contributes to the development and improvement of differential diagnosis and treatment of patients diagnosed with neuropsychiatric intestinal problems.

Study limitations

An important limitation is that this is a referred sample. Physicians referred patients to participate in the study. This may be justified by the fact that these are hard-to-reach groups due to social cultural stigma. As these patients were 'referred,' we acknowledge that there is a significant risk of selection bias (choosing a large number of people with similar characteristics or views to the initial individual identified). Data about pain intensity in migraine are depending on sincerity of the patients. GH is a symptom, thus it is a subjective feeling and might be interpreted differently by patients and physicians. Nonetheless, the criteria from ICD-10 are attenuating, and not eliminating, the subjectivity. Psychiatrists were not blinded to the patients' diagnosis, because psychiatric evaluation is the part of routine treatment of IBS and FD patients.

CONCLUSION

In conclusion, according to our results, headaches and their intensity are more related to males with FD but higher VAS scores showed great significance in diferentiating between patients with FD and IBS, where IBS had higher scores if the headache was a determining variable. Both functional gastrointestinal disorders probably induce morphological and functional brain alterations due to impaired metabolism of serotonin with extraintestinal manifestations, but more different tests should be performed in this field of investigation.

ACKNOWLEDGMENT

Conflict of interest: None declared.

REFERENCES

1. Grassini S, Nordin S. Comorbidity in Migraine with Functional Somatic Syndromes, Psychiatric Disorders and Inflammatory Diseases: A Matter of Central Sensitization?. Behav Med. 2017;43(2):91–9. [DOI: 10.1080/08964289.2015.1086721] [PMID: 26431372]
2. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2163–96. [DOI: 10.1016/S0140-6736(12)61729-2]. Erratum in: Lancet. 2013;381(9867):628. AlMazroa, Mohammad A [added]; Memish, Ziad A [added]. [DOI: 10.1016/S0140-6736(12)61729-2] [PMID: 23245607]
3. Lankarani KB, Akbari M, Tabrizi R. Association of Gastrointestinal Functional Disorders and Migraine Headache: a Population Base Study. Middle East J Dig Dis. 2017;9(3):139–45. [DOI: 10.15171/mejdd.2017.64] [PMID: 28894515]
4. Aurora SK, Shrewsbury SB, Ray S, Hindiyeh N, Nguyen L. A link between gastrointestinal disorders and migraine: Insights into the gut-brain connection. Headache. 2021;61(4):576–89. [DOI: 10.1111/head.14099] [PMID: 33793965]
5. Futagami S, Yamawaki H, Agawa S, Higuchi K, Ikeda G, Noda H, et al. New classification Rome IV functional dyspepsia and subtypes. Transl Gastroenterol Hepatol. 2018;3:70. [DOI: 10.21037/tgh.2018.09.12] [PMID: 30363705]
6. Di Stefano M, Pucci E, Miceli E, Pagani E, Brondino N, Nappi G, et al. Prevalence and pathophysiology of post-prandial migraine in patients with functional dyspepsia. Cephalalgia. 2019;39(12):1560–8. [DOI: 10.1177/0333102419857596] [PMID: 31203636]
7. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry. 1960;23(1):56–62. [DOI: 10.1136/jnnp.23.1.56] [PMID: 14399272]
8. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013;33(9):629–808. [DOI: 10.1177/0333102413485658] [PMID: 23771276]

9. Timotijevic I, Paunovic VR. Instruments of the clinical evaluation in psychiatry. [Serbian]. Belgrade: Naucna knjiga; 1992. pp. 78–90 and 326–7.
10. Wang C, Fang X. Inflammation and Overlap of Irritable Bowel Syndrome and Functional Dyspepsia. J Neurogastroenterol Motil. 2021;27(2):153–64. [DOI: 10.5056/jnm20175] [PMID: 33795538]
11. Tonini MC. Gender differences in migraine. Neurol Sci. 2018;39(Suppl 1):77–8. [DOI: 10.1007/s10072-018-3378-2] [PMID: 29904873]
12. Narayanan SP, Anderson B, Bharucha AE. Sex- and Gender-Related Differences in Common Functional Gastroenterologic Disorders. Mayo Clin Proc. 2021;96(4):1071–89. [DOI: 10.1016/j.mayocp.2020.10.004] [PMID: 33814075]
13. T Noghani M, Rezaeizadeh H, Fazljoo SM, Keshavarz M. Gastrointestinal Headache; a Narrative Review. Emerg (Tehran). 2016;4(4):171–83. [PMID: 27800536]
14. Li C, Yu S, Li H, Zhou J, Liu J, Tang W, et al. Clinical features and risk factors for irritable bowel syndrome in Migraine patients. Pak J Med Sci. 2017;33(3):720–25. [DOI: 10.12669/pjms.333.12379] [PMID: 28811802]
15. Arzani M, Jahromi SR, Ghorbani Z, Vahabizad F, Martelletti P, Ghaemi A, et al. Gut-brain Axis and migraine headache: a comprehensive review. J Headache Pain. 2020;21(1):15. [DOI: 10.1186/s10194-020-1078-9] [PMID: 32054443]
16. Wauters L, Talley NJ, Walker MM, Tack J, Vanuytsel T. Novel concepts in the pathophysiology and treatment of functional dyspepsia. Gut. 2020;69(3):591–600. [DOI: 10.1136/gutjnl-2019-318536] [PMID: 31784469]
17. Beurel E, Toups M, Nemeroff CB. The Bidirectional Relationship of Depression and Inflammation: Double Trouble. Neuron. 2020;107(2):234–56. [DOI: 10.1016/j.neuron.2020.06.002] [PMID: 32553197]
18. Aybek S, Nicholson TR, O'Daly O, Zelaya F, Kanaan RA, David AS. Emotion–motion interactions in conversion disorder: an FMRI study. PLoS One. 2015;10(4):e0123273. [DOI: 10.1371/journal.pone.0123273] [PMID: 25859660]
19. Aybek S, Nicholson TR, Zelaya F, O'Daly OG, Crig TJ, David AS, et al. Neural correlates of recall of life events in conversion disorder. JAMA Psychiatry. 2014;71(1):52–60. [DOI: 10.1001/jamapsychiatry.2013.2842] [PMID: 24258270]
20. Liu P, Wang G, Zeng F, Liu Y, Fan Y, Wei Y, et al. Abnormal brain structure implicated in patients with functional dyspepsia. Brain Imaging Behav. 2018;12(2):459–66. [DOI: 10.1007/s11682-017-9705-z] [PMID: 28353135]
21. Sayuk GS, Gyawali CP. Functional Dyspepsia: Diagnostic and Therapeutic Approaches. Drugs. 2020;80(13):1319–36. [DOI: 10.1007/s40265-020-01362-4] [PMID: 32691294]
22. Jia Z, Yu S. Grey matter alterations in migraine: A systematic review and meta-analysis. Neuroimage Clin. 2017;14:130–40. [DOI: 10.1016/j.nicl.2017.01.019] [PMID: 28180071]
23. Robson MJ, Quinlan MA, Blakely RD. Immune System Activation and Depression: Roles of Serotonin in the Central Nervous System and Periphery. ACS Chem Neurosci. 2017;8(5):932–42. [DOI: 10.1021/acschemneuro.6b00412] [PMID: 28345868]
24. Gałecki P, Mossakowska-Wójcik J, Talarowska M. The anti-inflammatory mechanism of antidepressants - SSRIs, SNRIs. Prog Neuropsychopharmacol Biol Psychiatry. 2018;80(Pt C):291–4. [DOI: 10.1016/j.pnpbp.2017.03.016] [PMID: 28342944]
25. Liu RT, Walsh RFL, Sheehan AE. Prebiotics and probiotics for depression and anxiety: A systematic review and meta-analysis of controlled clinical trials. Neurosci Biobehav Rev. 2019;102:13–23. [DOI: 10.1016/j.neubiorev.2019.03.023] [PMID: 31004628]
26. Aydinlar EI, Dikmen PY, Tiftikci A, Saruc M, Aksu M, Gunsoy HG, et al. IgG-based elimination diet in migraine plus irritable bowel syndrome. Headache. 2013;53(3):514–25. [DOI: 10.1111/j.1526-4610.2012.02296.x] [PMID: 23216231]
27. LenglarT L, Caula C, Moulding T, Lyles A, Wohrer D, Titomanlio L. Brain to Belly: Abdominal Variants of Migraine and Functional Abdominal Pain Disorders Associated With Migraine. J Neurogastroenterol Motil. 2021;27(4):482–94. [DOI: 10.5056/jnm20290] [PMID: 34642268]
28. Esterita T, Dewi S, Suryatenggara FG, Glenardi G. Association of Functional Dyspepsia with Depression and Anxiety: A Systematic Review. J Gastrointestin Liver Dis. 2021;30(2):259–66. [DOI: 10.15403/jgld-3325] [PMID: 33951117]
29. Margolis KG, Cryan JF, Mayer EA. The Microbiota-Gut-Brain Axis: From Motility to Mood. Gastroenterology. 2021;160(5):1486–501. [DOI: 10.1053/j.gastro.2020.10.066] [PMID: 33493503]
30. Eller M, Cheng S. Migraine management: an update for the 2020s. Intern Med J. 2022;52(7):1123–8. [DOI: 10.1111/imj.15843] [PMID: 35879242]

Постоји ли разлика у манифестацији главобоље између болесника са функционалном диспепсијом и синдромом иритабилног црева?

Ана Старчевић[1,2], Марија Марјановић-Хаџиљи[3], Љиљана Милић[1,4], Бранка Филиповић[1,3]

[1]Универзитет у Београду, Медицински факултет, Београд, Србија;
[2]Институт за анатомију „Нико Миљанић", Београд, Србија;
[3]Клиничко-болнички центар „Др Драгиша Мишовић – Дедиње", Одсек гастроентерологије, Београд, Србија;
[4]Клиничко-болнички центар „Звездара", Одсек хирургије, Београд, Србија

САЖЕТАК
Увод/Циљ Циљ овог истраживања је да утврди да ли постоји разлика у манифестацији главобоље и степену њеног интензитета код болесника са функционалном диспепсијом и синдромом иритабилног црева.
Методе Група испитаника сачињавала је 420 болесника од којих је 300 задовољило укључујуће критеријуме у виду присуства синдрома иритабилног црева (148) или функционалне диспепсије (152). Дијагнозе синдрома иритабилног црева и функционалне диспепсије постављене су у складу са критеријумима Рома IV. Интензитет главобоља процењен је у групама болесника са синдромом иритабилног црева и функционалном диспепсијом помоћу визуелно-аналогне скале. Сви болесници подвргнути су тестирању помоћу Хамилтонове скале депресије и скале анксиозности.
Резултати Наши резултати показују да су мушкарци са главобољом подложнији функционалној диспепсији, као и да постоји статистички значајна разлика у групи болесника са иритабилним синдромом црева који су имали веће резул-

тате на визуелно-аналогној скали и статистички значајна разлика у погледу резултата скале анксиозности у групи болесника са синдромом иритабилног црева. Пол и резултати на визуелно-аналогној скали били су детерминанте одређивања да ли болесник припада групи функционалне диспепсије или синдрома иритабилног црева. Резултати на визуелно-аналогној скали где су болесници навели да се најбоље осећају били су гранично статистики значајни ($p = 0.061$) и њихова већа вредност истакла је оне болеснике који припадају групи са синдромом иритабилног црева.
Закључак Пол и ниво интензитета главобоље као екстраинтестиналне манифестације представљају главне варијабле за утврђивање разлике између болесника са функционалном диспепсијом и синдромом иритабилног црева, где синдром иритабилног црева има веће резултате и доминацију у диференцијалној дијагнози уколико је главобоља детерминишућа варијабла.

Кључне речи: главобоље; функционална диспепсија; синдром иритабилног црева