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SINDROM IRITABILNOG CREVA: KLINIČKI PRISTUP I TERAPIJSKE STRATEGIJE

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Sažetak: Sindrom iritabilnog creva (engleski-Irritable bowel syndrome - IBS) je hronični funkcionalni poremećaj gastrointestinalnog trakta, koji karakteriše rekurentni bol u trbuhu udružen sa promenama učestalosti i konzistenciji stolice. Simptomi variraju u intenzitetu i učestalosti. IBS se klasifikuje u podtipove : IBS-D sa dijarejom, IBS-C sa zatvorom, mešoviti oblik IBS-M i neklasifikovani oblik IBS-U. Etiopatogeneza je multifaktorska, uključujući visceralnu hiperalgeziju, promene u obradi signala u centralnom nervnom sistemu, poremećaj motiliteta, imunološku aktivaciju, disbiozu mikrobiote i povećanu propustljivost crevne sluzokože. Psihološki faktori, stres i trauma u detinjstvu dodatno modifikuju simptome. Prevalencija IBS-a se procenjuje na 10–15% opšte populacije, sa većom učestalošću kod žena i osoba mlađih od 50 godina. Genetski i porodični faktori doprinose predispoziciji, dok akutni gastroenteritis i postinfektivni oblici predstavljaju važan etiološki okidač. Epidemiološki podaci ukazuju na stabilnost prevalencije tokom vremena, uz spontanu remisiju kod dela pacijenata. Dijagnostički pristup zasniva se na Roma IV kriterijumima i pozitivnoj dijagnozi, uz isključenje alarmnih simptoma i selektivnu laboratorijsku obradu. Terapija se individualizuje prema podtipu, dominantnim simptomima i psihosocijalnom opterećenju. Osnovne intervencije uključuju edukaciju, dijetetske mere i farmakoterapiju, dok neuromodulatori, probiotici i psihološke intervencije imaju važnu ulogu kod pacijenata sa izraženom visceralnom hipersenzitivnošću ili refrakternim simptomima. Razumevanje IBS-a kroz biopsihosocijalni model omogućava racionalan, personalizovan pristup dijagnostici i terapiji, sa ciljem smanjenja simptoma, poboljšanja funkcionalnog statusa i kvaliteta života pacijenata. Psihološke terapije i komplementarni pristupi, uključujući kognitivno-bihevioralnu terapiju, hipnoterapiju i tehnike redukcije stresa, doprinose dugoročnom poboljšanju kvaliteta života obolelih.

Ključne reči: sindrom iritabilnog creva, bol u trbuhu, opstipacija, dijareja

UVOD

Sindrom iritabilnog creva (IBS) predstavlja hronični poremećaj interakcije između gastrointestinalnog trakta i centralnog nervnog sistema, koji se klinički manifestuje rekurentnim bolom u trbuhu udruženim sa promenama u učestalosti i/ili konzistenciji stolice. Prema savremenoj klasifikaciji funkcionalnih gastrointestinalnih poremećaja, IBS pripada grupi poremećaja interakcije creva i mozga, kod kojih su simptomi prisutni u odsustvu strukturnih, biohemijskih ili inflamatornih promena koje bi ih u potpunosti objasnile. Dijagnoza se postavlja na osnovu kliničkih kriterijuma, uz isključivanje alarmnih znakova koji bi upućivali na organsku patologiju [1]. Iako se tradicionalno označava kao „funkcionalni“ poremećaj, savremena istraživanja ukazuju da IBS nije sinonim za odsustvo patofizioloških promena, već odražava poremećaj regulacije na više nivoa – neuralnom,

imunološkom, mikrobiološkom i neuroendokrinom. Upravo odsustvo jasnih morfoloških nalaza često je dovelo do potcenjivanja težine sindroma, iako je njegov uticaj na kvalitet života uporediv sa hroničnim inflamatornim bolestima creva i drugim dugotrajnim oboljenjima [2].

IBS je hronično stanje sa fluktuirajućim tokom, karakterisano periodima pogoršanja i remisije. Simptomi često uključuju nadimanje, osećaj nepotpunog pražnjenja, urgentnost ili naprezanje pri defekaciji, a njihova izraženost ne mora korelirati sa objektivnim nalazima. Upravo nesrazmera između subjektivnog intenziteta tegoba i minimalnih laboratorijskih ili endoskopskih promena predstavlja jedan od dijagnostičkih i terapijskih izazova u svakodnevnoj kliničkoj praksi.

Posebnu dimenziju sindroma čini visoka učestalost ekstraintestinalnih manifestacija. Kod obolelih se češće registruju hronični bolni sindromi, uključujući fibromijalgiju, hronični

IRRITABLE BOWEL SYNDROME: CLINICAL APPROACH AND THERAPEUTIC STRATEGIES

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Apstrakt: Irritable Bowel Syndrome (IBS) is a chronic functional gastrointestinal disorder characterized by recurrent abdominal pain associated with changes in stool frequency and consistency. Symptoms vary in both intensity and frequency. IBS is classified into subtypes: IBS-D (diarrhea-predominant), IBS-C (constipation-predominant), mixed IBS (IBS-M), and unclassified IBS (IBS-U). The etiopathogenesis is multifactorial and includes visceral hypersensitivity, alterations in central nervous system pain processing, motility disturbances, immune activation, gut microbiota dysbiosis, and increased intestinal permeability. Psychological factors, stress, and childhood trauma further modulate symptom expression. The prevalence of IBS is estimated at 10–15% of the general population, with higher incidence in women and individuals under 50 years of age. Genetic and familial factors contribute to susceptibility, while acute gastroenteritis and post-infectious states represent important triggers. Epidemiological data suggest relatively stable prevalence over time, with spontaneous remission occurring in a subset of patients. The diagnostic approach is based on the Rome IV criteria and a positive diagnostic strategy, with exclusion of alarm symptoms and selective laboratory evaluation. Treatment is individualized according to subtype, dominant symptoms, and psychosocial burden. Core interventions include patient education, dietary modification, and pharmacotherapy, while neuromodulators, probiotics, and psychological interventions play an important role in patients with marked visceral hypersensitivity or refractory symptoms. Understanding IBS through a biopsychosocial model enables a rational and personalized approach to diagnosis and therapy, aiming to reduce symptoms, improve functional status, and enhance quality of life. Psychological therapies and complementary approaches, including cognitive-behavioral therapy, hypnotherapy, and stress-reduction techniques, contribute to long-term improvement in patients' quality of life.

Key words: irritable bowel syndrome (IBS), abdominal pain, constipation, diarrhea

INTRODUCTION

Irritable Bowel Syndrome (IBS) is a chronic disorder of gut–brain interaction, clinically characterized by recurrent abdominal pain associated with changes in stool frequency and/or consistency. According to the modern classification of functional gastrointestinal disorders, IBS belongs to the group of disorders of gut–brain interaction, in which symptoms occur in the absence of structural, biochemical, or inflammatory abnormalities that would fully explain them. The diagnosis is based on clinical criteria, with exclusion of alarm features suggestive of organic disease [1].

Although traditionally labeled as a “functional” disorder, contemporary research indicates that IBS is not synonymous with the absence of pathophysiological changes, but rather reflects dysregulation at multiple levels—neural, immune, microbiological, and neuroendocrine.

The absence of clear morphological findings has often led to underestimation of the severity of the syndrome, despite its impact on quality of life being comparable to that of chronic inflammatory bowel diseases and other long-term conditions [2].

IBS is a chronic condition with a fluctuating course, characterized by periods of exacerbation and remission. Symptoms often include bloating, a sensation of incomplete evacuation, urgency, or straining during defecation, and their severity does not necessarily correlate with objective laboratory or endoscopic findings. This discrepancy between subjective symptom intensity and minimal diagnostic abnormalities represents one of the main challenges in everyday clinical practice.

A particular dimension of the syndrome is the high frequency of extraintestinal manifestations. Patients commonly report chronic pain

karlični bol i tenzionu glavobolju, kao i sindrom hroničnog umora, poremećaji temporomandibularnog zgloba, nekardijalni bol u grudima i urinarne tegobe. Anksiozni i depresivni poremećaji takođe su češći u ovoj populaciji. Ova komorbidnost ukazuje na zajedničke mehanizme centralne senzibilizacije i poremećaja obrade bola, što dodatno potvrđuje sistemsku prirodu poremećaja.

Savremeni pristup IBS-u pomera fokus sa isključivo gastrointestinalnih simptoma ka širem konceptu poremećaja regulacije osovine mozak–crevo. Interakcija između enteričnog nervnog sistema, autonomne regulacije, mikrobiote, imunološkog odgovora i psiholoških faktora oblikuje individualni fenotip bolesti. Ovakvo razumevanje ima neposredne terapijske implikacije, jer objašnjava zašto univerzalni terapijski pristup često daje ograničene rezultate i zašto je personalizacija lečenja od posebnog značaja [3]. Uprkos tome što IBS ne povećava mortalitet niti dovodi do progresivnog oštećenja creva, njegov javnozdravstveni značaj je veliki. Sindrom je povezan sa učestalim konsultacijama lekara, dijagnostičkim procedurama i smanjenom radnom produktivnošću. Psihološki teret, stigmatizacija i hronična priroda simptoma dodatno utiču na kvalitet života pacijenata. [4] Razumevanje IBS-a zahteva integrativni pristup koji objedinjuje kliničke kriterijume, epidemiološke podatke i savremena saznanja o patofiziološkim mehanizmima. U tom kontekstu, sindrom iritabilnog creva treba posmatrati ne kao jedinstvenu bolest, već kao heterogeni klinički entitet sa različitim dominantnim mehanizmima, što otvara prostor za precizniji dijagnostički i terapijski pristup.

Epidemiologija

Sindrom iritabilnog creva predstavlja jedan od najčešćih poremećaja digestivnog sistema u opštoj populaciji. Studije zasnovane na populaciji često procenjuju prevalenciju sindroma iritabilnog creva od 10% do 15%, i incidencu IBS na 1-2% godišnje. Prevalencija se značajno razlikuje među zemljama. Najniža prevalencija je u Francuskoj (1,1%), a najviša u Meksiku (35,5%); prevalencija od 7,1% je pronađena u SAD/Evropi/Australiji/Novom Zelandu. Približno 50% ljudi sa IBS-om prijavljuje simptome koji počinju pre 35. godine života. Adolescentkinje i mlade odrasle žene najčešće su pogođene IBS-om. U zapadnim

zemljama, žene imaju 2-3 puta veću verovatnoću da razviju IBS nego muškarci, iako na indijskom potkontinentu muškarci predstavljaju 70-80% pacijenata sa IBS-om [5]. Razlike u prevalenciji delimično su posledica metodoloških faktora, uključujući upotrebu različitih verzija Roma kriterijuma, ali i kulturnih i zdravstvenih obrazaca koji utiču na javljanje lekaru. Geografske varijacije su izražene, sa višom prevalencijom u pojedinim delovima Azije i u nekim evropskim zemljama, dok su u drugim regionima zabeležene niže stope. Razlozi ove razlike verovatno uključuju hormonske faktore, razlike u percepciji i obradi bola, kao i obrasce traženja zdravstvene zaštite. Sindrom se najčešće dijagnostikuje kod osoba mlađih od 50 godina, dok je prevalencija niža u starijoj populaciji. Ova razlika može odražavati spontanu remisiju simptoma kod dela pacijenata, ali i promene u percepciji tegoba ili obrascima javljanja lekaru. Najveća prevalencija je primećena kod obrazovanih, bogatih, studenata i mlađih osoba. [6]. Međutim, IBS je univerzalno prisutan poremećaj, bez obzira na etničku ili kulturnu pripadnost, što potvrđuje njegov multifaktorski karakter.

Porodična agregacija IBS-a ukazuje na genetsku komponentu, ali i na uticaj zajedničkih faktora sredine. Studije pokazuju da je sindrom približno dvostruko češći kod rođaka prvog stepena srodstva u poređenju sa opštom populacijom. Ipak, precizan doprinos genetskih faktora u odnosu na naučene obrasce ponašanja i zajedničke stresore ostaje predmet istraživanja.

Značajan epidemiološki entitet predstavlja postinfektivni IBS. Nakon akutnog gastroenteritisa, rizik razvoja hroničnih simptoma kompatibilnih sa IBS-om višestruko je povećan. Ovaj rizik je posebno izražen kod težih infekcija, produženog trajanja simptoma i prisustva psiholoških stresora u periodu oporavka. Pokrenut bakterijskim ili virusnim infekcijama, uključuje perzistentnu upalu niskog stepena, izmenjenu propustljivost creva i izmenjenu mikrobiotu i jasno demonstrira vezu između inflamacije, imunološke aktivacije i dugotrajnih promena u neuromišićnoj funkciji creva [7].

Psihosocijalni faktori imaju i epidemiološki značaj. Hronični stres, traumatska iskustva u detinjstvu i nepovoljni životni događaji povezani su sa većim rizikom razvoja IBS-a i težim tokom bolesti. Ovi faktori ne deluju

syndromes, including fibromyalgia, chronic pelvic pain, and tension-type headaches, as well as chronic fatigue syndrome, temporomandibular joint disorders, non-cardiac chest pain, and urinary symptoms. Anxiety and depressive disorders are also more prevalent in this population. This comorbidity suggests shared mechanisms of central sensitization and altered pain processing, further supporting the systemic nature of the disorder..

The modern approach to IBS shifts the focus from purely gastrointestinal symptoms toward a broader concept of dysregulation of the brain-gut axis. The interaction between the enteric nervous system, autonomic regulation, microbiota, immune response, and psychological factors shapes the individual disease phenotype. This understanding has direct therapeutic implications, as it explains why a universal treatment approach often yields limited results and why personalization of therapy is of particular importance [3].

Although IBS does not increase mortality nor lead to progressive intestinal damage, its public health impact is significant. The syndrome is associated with frequent medical consultations, extensive diagnostic workups, and reduced work productivity. The psychological burden, stigmatization, and chronic nature of symptoms further impair patients' quality of life [4].

Understanding IBS requires an integrative approach that combines clinical criteria, epidemiological data, and contemporary insights into pathophysiological mechanisms. In this context, irritable bowel syndrome should not be viewed as a single disease, but rather as a heterogeneous clinical entity with varying dominant mechanisms, which opens the door to more precise diagnostic and therapeutic strategies.

Epidemiology Irritable Bowel Syndrome (IBS) is one of the most common gastrointestinal disorders in the general population. Population-based studies estimate the prevalence of IBS at 10% to 15%, with an annual incidence of approximately 1–2%. Prevalence varies significantly between countries. The lowest prevalence has been reported in France (1.1%), while the highest has been reported in Mexico (35.5%); a prevalence of 7.1% has been observed in the USA, Europe, Australia, and New Zealand.

Approximately 50% of individuals with IBS report symptom onset before the age of 35.

Adolescent girls and young adult women are most commonly affected. In Western countries, women are 2–3 times more likely to develop IBS than men, whereas in the Indian subcontinent men account for 70–80% of IBS patients [5].

Differences in prevalence are partly explained by methodological factors, including the use of different versions of the Rome criteria, as well as cultural and healthcare-seeking behaviors. Geographic variation is evident, with higher prevalence in parts of Asia and some European countries, while lower rates have been reported in other regions. The reasons for these differences likely include hormonal factors, variations in pain perception and processing, and differences in healthcare utilization patterns.

The syndrome is most commonly diagnosed in individuals under 50 years of age, while prevalence is lower in older populations. This may reflect spontaneous remission in some patients, as well as changes in symptom perception or healthcare-seeking behavior. The highest prevalence has been observed among educated individuals, higher-income groups, students, and younger populations [6]. Nevertheless, IBS is a universally present disorder regardless of ethnic or cultural background, confirming its multifactorial nature. Familial aggregation of IBS suggests a genetic component, but also the influence of shared environmental factors. Studies show that IBS is approximately twice as common in first-degree relatives compared with the general population. However, the exact contribution of genetic factors versus learned behavioral patterns and shared stressors remains under investigation.

A significant epidemiological entity is post-infectious IBS. Following acute gastroenteritis, the risk of developing chronic IBS-like symptoms is markedly increased. This risk is particularly pronounced after severe infections, prolonged symptom duration, and the presence of psychological stressors during recovery. Triggered by bacterial or viral infections, it involves persistent low-grade inflammation, altered intestinal permeability, and microbiota changes, clearly demonstrating the link between inflammation, immune activation, and long-term alterations in neuromuscular gut function [7].

Psychosocial factors also have epidemiological importance. Chronic stress, childhood trauma, and adverse life events are associated with a higher risk of IBS development and a more

izolovano, već kroz modulaciju osovine mozak-crevo i percepcije visceralnih signala. [8].

Prirodni tok IBS-a je varijabilan. U populacionim studijama prevalencija pokazuje relativnu stabilnost tokom vremena, ali kod 10-40% pacijenata dolazi do remisije simptoma tokom višegodišnjeg praćenja. Sindrom retko prelazi u organsku bolest i nije povezan sa povećanim mortalitetom, ali je povezan sa značajnim smanjenjem kvaliteta života i povećanom potrošnjom zdravstvenih resursa. [9]

Etiopatogeneza

Etiopatogeneza sindroma iritabilnog creva (IBS) nije u potpunosti razjašnjena, ali se danas smatra rezultatom kompleksne interakcije genetskih, neurobioloških, imunoloških, mikrobioloških i psihosocijalnih faktora. Savremeni koncept zasniva se na biopsihosocijalnom modelu, prema kojem genetska predispozicija, u kombinaciji sa faktorima sredine – poput akutnih gastrointestinalnih infekcija, hroničnog stresa i nepovoljnih događaja u ranom detinjstvu – dovodi do poremećaja regulacije osovine mozak-crevo. IBS se stoga posmatra kao poremećaj regulacije, a ne strukture, pri čemu se patofiziološki mehanizmi razlikuju po intenzitetu i kombinaciji među pojedinim podtipovima pacijenata [10].

Jedan od centralnih mehanizama je **visceralna hipersenzitivnost**. Kod približno 60% pacijenata dokazan je snižen prag percepcije mehaničkih i hemijskih stimulusa u digestivnom traktu. Periferna senzibilizacija enteričnih neurona, ali i pojačana centralna obrada bola, dovode do intenzivnije percepcije inače fizioloških stimulusa. Slikovne studije centralnog nervnog sistema ukazuju na povećanu aktivaciju prednjeg cingularnog korteksa i amigdale – regija uključenih u emocionalnu obradu bola – uz smanjenu aktivaciju prefrontalnog korteksa, koji učestvuje u kognitivnoj modulaciji. Ove promene ukazuju na centralnu amplifikaciju visceralnih signala i objašnjavaju zašto bol kod IBS-a nije proporcionalan objektivnim nalazima [11].

Imunološka aktivacija niskog intenziteta predstavlja drugi važan mehanizam. Posebno je izražena kod postinfektivnog IBS-a, gde je dokumentovana povećana infiltracija T limfocita i mastocita u crevnoj sluzokoži. Mastociti, putem oslobađanja histamina, proteaza i citokina, doprinose senzibilizaciji

perifernih neurona i poremećaju barijerne funkcije epitela. Povećana koncentracija luminalnih proteaza dodatno pojačava aktivaciju enteričnog nervnog sistema. Ova mikroinflamacija, iako blaga, može imati dugotrajan efekat na neuromišićnu funkciju creva [12].

Poremećaji serotoninskog sistema takođe imaju značajnu ulogu. Serotonin (5-HT), koji se sintetiše u enteroendokrinim ćelijama, ključan je regulator motiliteta, sekrecije i senzorne funkcije creva. Kod pacijenata sa IBS-om opisan je poremećen metabolizam serotonina, što doprinosi promenama tranzita. Motorički poremećaji uključuju pojačanu aktivnost na gladno i postprandijalno, kao i izmenjen odgovor na stres. Ubrzan tranzit prisutan je kod približno polovine pacijenata sa dijarejnim podtipom (IBS-D), dok je usporen tranzit karakterističan za deo pacijenata sa konstipacionim podtipom (IBS-C). Kod oko četvrtine bolesnika sa IBS-D utvrđeno je povećano prisustvo žučnih kiselina u kolonu, što doprinosi povećanoj sekreciji i motilitetu, dok njihovo smanjeno fenotipa [13].

Mikrobiota predstavlja još jedan ključni element u patogenezi. Meta-analize su pokazale izmenjen sastav crevne mikrobiote kod pacijenata sa IBS-om u poređenju sa zdravim kontrolama, uz smanjenu raznovrsnost i promene u zastupljenosti pojedinih bakterijskih rodova. Disbioza može uticati na sintezu serotonina, modulaciju imunološkog odgovora, produkciju kratkolančanih masnih kiselina i integritet epitelne barijere. Studije koje pokazuju poboljšanje simptoma nakon primene određenih antibiotika ili probiotika dodatno podržavaju ulogu mikrobiote u razvoju sindroma. Povećana intestinalna permeabilnost, dokumentovana kod dela pacijenata, predstavlja važnu kariku između stresa, mikrobiote i imunološke aktivacije, omogućavajući povećani prolaz antigena i senzibilizaciju imunološkog sistema [14].

Psihološki faktori i stres imaju značajan modulacioni efekat. Hronični stres, traumatska iskustva u detinjstvu i maladaptivni obrasci suočavanja, poput straha od katastrofe i stalnog straha i opreza od opasnosti, povezani su sa povećanom percepcijom simptoma. Aktivacija ose hipotalamus-hipofiza-nadbubrežna žlezda dovodi do oslobađanja kortikotropin-oslobađajućeg faktora (CRF), koji utiče na autonomnu regulaciju, motilitet, sekreciju i imunološki odgovor. Eksperimentalni

severe disease course. These factors do not act in isolation but rather through modulation of the brain–gut axis and visceral signal perception [8]. The natural course of IBS is variable. In population studies, prevalence remains relatively stable over time, but 10–40% of patients experience symptom remission during long-term follow-up. IBS rarely progresses to organic disease and is not associated with increased mortality, but it is linked to significantly reduced quality of life and increased healthcare resource utilization [9].

Etiopathogenesis The etiopathogenesis of irritable bowel syndrome (IBS) is not fully understood, but it is now considered the result of a complex interaction between genetic, neurobiological, immunological, microbiological, and psychosocial factors. The contemporary concept is based on the biopsychosocial model, according to which genetic predisposition, combined with environmental factors such as acute gastrointestinal infections, chronic stress, and adverse early-life events, leads to dysregulation of the brain–gut axis. IBS is therefore viewed as a disorder of regulation rather than structure, with pathophysiological mechanisms varying in intensity and combination among different patient subtypes [10].

One of the central mechanisms is visceral hypersensitivity. In approximately 60% of patients, a reduced threshold for perception of mechanical and chemical stimuli in the gastrointestinal tract has been demonstrated. Peripheral sensitization of enteric neurons, as well as enhanced central pain processing, leads to increased perception of otherwise physiological stimuli. Neuroimaging studies of the central nervous system show increased activation of the anterior cingulate cortex and amygdala—regions involved in emotional pain processing—along with reduced activation of the prefrontal cortex, which is involved in cognitive modulation. These changes indicate central amplification of visceral signals and explain why pain in IBS is not proportional to objective findings [11].

Low-grade immune activation represents another important mechanism. This is particularly evident in post-infectious IBS, where increased infiltration of T lymphocytes and mast cells in the intestinal mucosa has been documented. Mast cells, through the release of histamine, proteases, and cytokines, contribute

to peripheral neuronal sensitization and disruption of epithelial barrier function. Increased luminal protease activity further enhances activation of the enteric nervous system. This microinflammation, although mild, may have long-term effects on neuromuscular gut function [12].

Disturbances in the serotonergic system also play a significant role. Serotonin (5-HT), synthesized in enteroendocrine cells, is a key regulator of intestinal motility, secretion, and sensory function. In IBS patients, altered serotonin metabolism has been described, contributing to changes in gastrointestinal transit. Motor disturbances include increased activity in fasting and postprandial states, as well as altered responses to stress. Accelerated transit is present in approximately half of patients with diarrhea-predominant IBS (IBS-D), while delayed transit is characteristic of a subset of patients with constipation-predominant IBS (IBS-C). In about one-quarter of IBS-D patients, increased colonic bile acid exposure has been observed, contributing to enhanced secretion and motility, while reduced bile acid availability is associated with a constipation phenotype [13]. The gut microbiota represents another key element in pathogenesis. Meta-analyses have demonstrated altered gut microbiota composition in IBS patients compared with healthy controls, with reduced diversity and changes in the abundance of specific bacterial taxa. Dysbiosis may affect serotonin synthesis, immune modulation, short-chain fatty acid production, and epithelial barrier integrity. Studies showing symptom improvement after administration of certain antibiotics or probiotics further support the role of the microbiota in the syndrome. Increased intestinal permeability, documented in a subset of patients, represents an important link between stress, microbiota, and immune activation, allowing increased antigen translocation and immune sensitization [14].

Psychological factors and stress have a significant modulatory effect. Chronic stress, childhood trauma, and maladaptive coping mechanisms—such as catastrophic thinking and persistent fear and hypervigilance—are associated with increased symptom perception. Activation of the hypothalamic–pituitary–adrenal (HPA) axis leads to the release of corticotropin-releasing factor (CRF), which influences autonomic regulation, motility,

modeli pokazuju da akutni stres povećava visceralnu osetljivost i propustljivost creva. Dominacija simpatičkog nad parasimpatičkim nervnim sistemom češće se registruje kod pacijenata sa izraženijim simptomima, iako uzročni odnos ostaje nedovoljno razjašnjen [15].

Genetska predispozicija predstavlja dodatni faktor rizika. Studije blizanaca pokazuju veću podudarnost simptoma IBS-a kod monozigotnih u odnosu na dizigotne blizance. Genomske analize identifikovale su varijante gena povezane sa funkcijom jonskih kanala, autonomnom regulacijom, kontraktilnošću glatkih mišića i mehaničkom osetljivošću. Kod manjeg broja pacijenata opisane su mutacije gena za enzim saharoza-izomaltaza, koje dovode do malapsorpcije ugljenih hidrata i kliničke slike slične IBS-u.

U celini posmatrano, IBS predstavlja heterogeni sindrom u kome se neuralni, imunološki, mikrobiološki i psihoneuroendokrini mehanizmi međusobno prepliću. Različite kombinacije i dominacija pojedinih patofizioloških puteva verovatno objašnjavaju kliničku raznolikost sindroma i različit terapijski odgovor. Ovakvo razumevanje etiopatogeneze otvara prostor za personalizovani terapijski pristup, zasnovan na identifikaciji dominantnog mehanizma kod pojedinačnog pacijenta.

Dijagnostički pristup

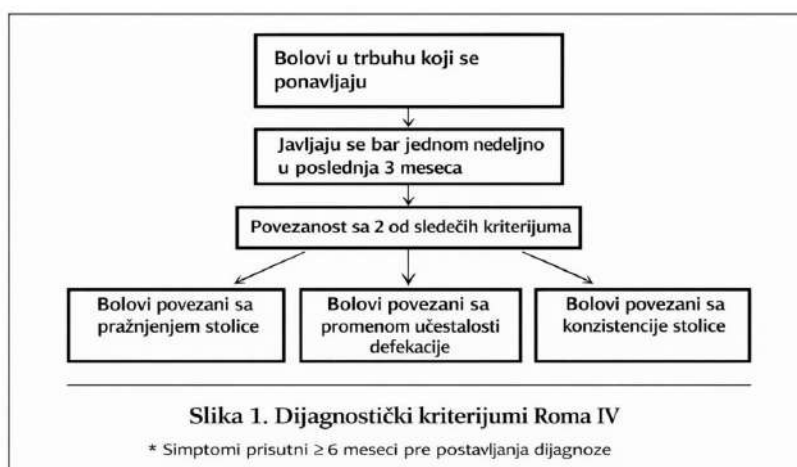
Savremeni dijagnostički pristup sindromu iritabilnog creva (IBS) zasniva se na konceptu postavljanja pozitivne kliničke dijagnoze, a ne isključivo na principu dijagnoze

isključenja. Ovakav pristup ima za cilj da smanji nepotrebne dijagnostičke procedure, skрати vreme do započinjanja terapije i umani anksioznost pacijenata.

Lečenje sindroma iritabilnog creva (IBS) zahteva temeljnu anamnezu i kliničku procenu, rezultate prethodnih dijagnostičkih testova i pažljivo praćenje. Polovina pacijenata sa IBS-om ima ekstraintestinalne simptome (glavobolja 23–45%, bol u leđima 27–81%, umor 36–63%, mijalgija 29–36%, dizurični simptomi 21–61%). Ekstraintestinalni simptomi su češći kod žena, posebno tokom menstruacije. U zavisnosti od težine simptoma i težine bolesti, pacijenti su podeljene u tri grupe prema skali težine simptoma IBS-a. Pacijenti u grupi sa blagim simptomima se obično leče na nivou primarne zdravstvene zaštite. Njihov kvalitet života nije značajno smanjen. Grupa sa umerenim simptomima se leči na nivou sekundarne zdravstvene zaštite, a grupa sa teškim simptomima se obično leči na tercijarnom nivou [16].

Dijagnoza se postavlja na osnovu **Roma IV kriterijuma** koji podrazumevaju kontinuirane tegobe pacijenta u poslednja 3 meseca, koje su se prvi put pojavile najmanje 6 meseci ranije. Osetljivost i specifičnost dijagnostičkih kriterijuma su 62,7% i 97,1%, respektivno.

To je rekurentni bol u trbuhu, prisutan u proseku najmanje jedan dan nedeljno u poslednja 3 meseca i povezan sa najmanje dva od sledećih kriterijuma: 1. pražnjenje stolice, 2. promena učestalosti stolice, 3. promena konzistencije stolice. Slika 1 [9].



Slika 1. Dijagnostički kriterijumi Roma IV

secretion, and immune response. Experimental models show that acute stress increases visceral sensitivity and intestinal permeability. Dominance of the sympathetic over the parasympathetic nervous system is more frequently observed in patients with more severe symptoms, although a causal relationship remains insufficiently defined [15].

Genetic predisposition represents an additional risk factor. Twin studies show higher concordance of IBS symptoms in monozygotic compared to dizygotic twins. Genome-wide analyses have identified gene variants associated with ion channel function, autonomic regulation, smooth muscle contractility, and mechanical sensitivity. In a smaller subset of patients, mutations in the sucrase-isomaltase gene have been described, leading to carbohydrate malabsorption and a clinical presentation resembling IBS.

Overall, IBS is a heterogeneous syndrome in which neural, immunological, microbiological, and psychoneuroendocrine mechanisms are interrelated. Different combinations and varying dominance of individual pathophysiological pathways likely explain the clinical heterogeneity of the syndrome and the variability in therapeutic response. This understanding of etiopathogenesis opens the possibility for a personalized therapeutic approach based on identifying the dominant mechanism in each individual patient.

Diagnostic approach

The modern diagnostic approach to irritable bowel syndrome (IBS) is based on the concept of establishing a positive clinical diagnosis rather

than relying solely on exclusion. This approach aims to reduce unnecessary diagnostic procedures, shorten the time to treatment initiation, and decrease patient anxiety.

Management of IBS requires a thorough medical history, clinical evaluation, review of previous diagnostic tests, and careful follow-up. Approximately half of IBS patients present with extraintestinal symptoms, including headache (23–45%), back pain (27–81%), fatigue (36–63%), myalgia (29–36%), and urinary symptoms (21–61%). Extraintestinal symptoms are more common in women, particularly during menstruation. Depending on symptom severity and disease burden, patients are divided into three groups according to an IBS symptom severity scale. Patients with mild symptoms are usually managed in primary care, as their quality of life is not significantly impaired. The moderate group is managed at the secondary care level, while patients with severe symptoms are typically treated in tertiary care centers [16]. Diagnosis is based on the Rome IV criteria, which require persistent symptoms over the last 3 months, with symptom onset at least 6 months prior to diagnosis. The sensitivity and specificity of these diagnostic criteria are 62.7% and 97.1%, respectively.

The defining feature is recurrent abdominal pain, occurring on average at least one day per week over the last 3 months, associated with at least two of the following criteria: (1) related to defecation, (2) associated with a change in stool frequency, and (3) associated with a change in stool form/consistency (Figure 1) [9].



Slika 1. Dijagnostički kriterijumi Roma IV

Other symptoms in addition to abdominal pain include: (1) abnormal stool frequency (<3 bowel movements per week or >3 bowel movements per day), (2) straining during defecation, (3)

urgency or a sensation of incomplete evacuation, and mucus discharge [17].

According to the predominant symptoms accompanying chronic abdominal pain over the

Drugi simptomi pored bola su: 1.abnormalna učestalost stolice (< 3 stolice nedeljno ili > 3 stolice dnevno), 2. naprezanje tokom defekacije, urgentnost defekacije ili osećaj 3. nepotpunog pražnjenja creva, iscedak sluzi [17]

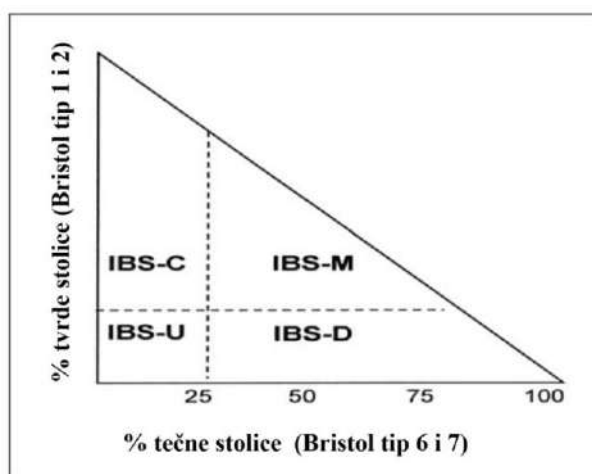
Prema prevladajućim simptomima koji prate hronični bol u trbuhu u poslednja 3 meseca, razlikujemo četiri **podtipa IBS-a**:

1. IBS sa pretežno zatvorom (IBS-C) – više od 25% pražnjenja creva sa rezultatom 1 ili 2 na Bristolskoj skali stolice i manje od 25% pražnjenja creva sa rezultatom 6 ili 7 na Bristolskoj skali stolice,

2. IBS sa pretežno dijarejom (IBS-D) – više od 25% pražnjenja creva sa rezultatom 6 ili 7 na Bristolskoj skali stolice i manje od 25% pražnjenja creva sa rezultatom 1 ili 2 na Bristolskoj skali stolice,

3. Mešoviti IBS (IBS-M) – više od 25% pražnjenja creva sa rezultatom 1 ili 2 na Bristolskoj skali stolice i više od 25% pražnjenja creva sa rezultatom 6 ili 7 na Bristolskoj skali stolice

4. Neopredeljeni IBS (IBS-U) – ispunjava dijagnostičke kriterijume za sindrom iritabilnog creva koji se ne može klasifikovati ni u jedan od navedenih podtipova . Slika 2 [9].



Slika 2. Podtipovi sindroma iritabilnog creva

Ključna komponenta inicijalne procene jeste identifikacija alarmnih simptoma koji mogu ukazivati na organsku bolest. U njih spadaju: neobjašnjeni gubitak telesne mase, gastrointestinalno krvarenje, anemija, noćni simptomi, porodična anamneza kolorektalnog karcinoma ili inflamatorne bolesti creva, kao i početak simptoma nakon 50. godine života. Prisustvo ovih znakova zahteva proširenu dijagnostiku, uključujući endoskopske i radiološke metode.

Kod pacijenata bez alarmnih simptoma preporučuje se ograničena inicijalna laboratorijska obrada. Ona obično uključuje kompletnu krvnu sliku, C-reaktivni protein (CRP) ili sedimentaciju eritrocita, kao i serološko testiranje na celijakiju, posebno kod bolesnika sa dijarejskim simptomima. Fekalni kalprotektin predstavlja koristan neinvazivni biomarker u diferencijaciji IBS-a od inflamatorne bolesti

creva, jer normalne vrednosti sa visokom verovatnoćom isključuju aktivnu inflamaciju [1].

Endoskopska evaluacija nije rutinski indikovana kod mlađih pacijenata bez alarmnih znakova. Međutim, kolonoskopija se preporučuje kod osoba starijih od 50 godina u skladu sa skrining preporukama za kolorektalni karcinom, kao i kod pacijenata sa perzistentnim ili atipičnim simptomima. Kod pacijenata sa hroničnom dijarejom treba razmotriti biopsiju kolona radi isključivanja mikroskopskog kolitisa, čak i u odsustvu makroskopskih promena.

Diferencijalna dijagnoza IBS-a zavisi od dominantnog kliničkog fenotipa. Kod IBS-D treba isključiti inflamatornu bolest creva, celijakiju, infekcije, kao i malapsorpciju žučnih kiselina. Kod IBS-C diferencijalno-dijagnostički dolaze u obzir primarni poremećaji motiliteta, hipotiroidizam i lekovima indukovana konstipacija. Sindrom bakterijskog prerastanja

last 3 months, IBS is classified into four subtypes:

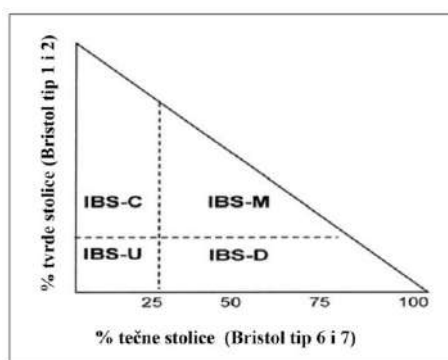
IBS with predominant constipation (IBS-C) – more than 25% of bowel movements with Bristol Stool Scale types 1 or 2, and less than 25% with types 6 or 7.

IBS with predominant diarrhea (IBS-D) – more than 25% of bowel movements with Bristol

Stool Scale types 6 or 7, and less than 25% with types 1 or 2.

Mixed IBS (IBS-M) – more than 25% of bowel movements with Bristol Stool Scale types 1 or 2, and more than 25% with types 6 or 7.

Unclassified IBS (IBS-U) – patients fulfilling diagnostic criteria for IBS that cannot be classified into any of the above subtypes (Figure 2). [9].



Slika 2. Podtipovi sindroma iritabilnog creva

A key component of the initial evaluation is the identification of alarm symptoms that may indicate organic disease. These include unexplained weight loss, gastrointestinal bleeding, anemia, nocturnal symptoms, a family history of colorectal cancer or inflammatory bowel disease, and onset of symptoms after the age of 50. The presence of these features requires an extended diagnostic workup, including endoscopic and radiological investigations.

In patients without alarm symptoms, a limited initial laboratory evaluation is recommended. This typically includes a complete blood count, C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR), as well as serological testing for celiac disease, particularly in patients with diarrhea-predominant symptoms. Fecal calprotectin is a useful non-invasive biomarker for differentiating IBS from inflammatory bowel disease, as normal values with high probability exclude active intestinal inflammation [1].

Endoscopic evaluation is not routinely indicated in younger patients without alarm features. However, colonoscopy is recommended in individuals over 50 years of age according to colorectal cancer screening guidelines, as well as in patients with persistent or atypical symptoms. In patients with chronic diarrhea, colonic biopsies should be considered to exclude microscopic colitis, even in the absence of macroscopic abnormalities.

The differential diagnosis of IBS depends on the dominant clinical phenotype. In IBS-D, inflammatory bowel disease, celiac disease, infections, and bile acid malabsorption should be excluded. In IBS-C, differential diagnoses include primary motility disorders, hypothyroidism, and drug-induced constipation. Small intestinal bacterial overgrowth (SIBO) remains a controversial diagnosis but may be considered in patients with prominent bloating and refractoriness to standard therapy.

An important aspect of the diagnostic process is the assessment of psychosocial factors. Anxiety, depression, and chronic stress do not represent merely comorbidities, but can also modulate symptom intensity and therapeutic response. Structured evaluation of psychological burden may help individualize the therapeutic approach. Overdiagnosis may have negative consequences, including increased healthcare costs and heightened health-related anxiety. Therefore, a rational, stepwise approach is of particular importance. After a careful medical history, physical examination, and basic laboratory testing, a reliable diagnosis of IBS can be established in patients without alarm features, allowing treatment initiation without additional invasive procedures.

The modern diagnostic concept of IBS thus reflects an understanding of the syndrome as a disorder of regulation, in which the clinical symptom pattern is of central importance. This

tankog creva (SIBO) ostaje kontroverzna dijagnoza, ali se može razmatrati kod izraženog nadimanja i refraktornosti na standardnu terapiju.

Važan aspekt dijagnostičkog procesa jeste procena psihosocijalnih faktora. Anksioznost, depresija i hronični stres ne predstavljaju samo komorbiditet, već mogu modulirati intenzitet simptoma i terapijski odgovor. Strukturisana procena psihološkog opterećenja može pomoći u individualizaciji terapijskog pristupa.

Preterana dijagnostika može imati negativne posledice, uključujući povećanje zdravstvenih troškova i pojačavanje zdravstvene anksioznosti. Stoga je racionalan, postepeni pristup od posebne važnosti. Nakon pažljivo uzete anamneze, fizikalnog pregleda i osnovnih laboratorijskih testova, kod pacijenata bez alarmnih znakova može se postaviti pouzdana dijagnoza IBS-a i započeti terapija bez dodatnih invazivnih procedura.

Savremeni dijagnostički koncept IBS-a time odražava razumevanje sindroma kao poremećaja regulacije, u kojem je klinički obrazac simptoma od presudnog značaja. Ovakav pristup omogućava bržu identifikaciju podtipa bolesti, smanjuje nepotrebne intervencije i predstavlja osnov za personalizovani terapijski plan.

Terapija sindroma iritabilnog creva

Terapijski pristup sindromu iritabilnog creva (IBS) zasniva se na kombinaciji edukacije pacijenta, dijetetskih mera, farmakoterapije i, po potrebi, psiholoških intervencija. Zbog heterogenosti patofizioloških mehanizama, terapija mora biti individualizovana i usmerena prema dominantnom podtipu bolesti (IBS-C, IBS-D, IBS-M, IBS-U), kao i prema izraženosti bola, nadimanja i psihosocijalnih faktora.

Opšti principi terapije

Osnov lečenja čini detaljna edukacija pacijenta. Objašnjenje benignog toka bolesti i uloge osovine mozak–crevo smanjuje anksioznost i poboljšava terapijsku saradnju. Važno je naglasiti da IBS ima hroničan, fluktuirajući tok i da je cilj terapije kontrola simptoma i poboljšanje kvaliteta života, a ne trajno izlečenje.

Dijetetske mere: pretpostavka da su simptomi IBS povezani sa ishranom, eliminacione dijetete i dodavanje dijetetskih vlakana retko poboljšavaju simptome na duži rok. Ishrana po principu FODMAP dijetete, koja ograničava fermentabilne oligosaharide, disaharide,

monosaharide i polihidroksialkohole u ishrani, može poboljšati simptome kod jednog od pet pacijenata smanjujući nadimanje i bol [18].

Individualna procena intolerancije na laktozu, fruktozu i druge fermentabilne ugljene hidrate može biti korisna. Preterano restriktivne dijetete treba izbegavati zbog rizika od nutritivnih deficita i negativnog uticaja na mikrobiotu.

Promene načina života (redovna fizička aktivnost, adekvatan san i upravljanje stresom) mogu doprineti ublažavanju simptoma. Kod pacijenata sa umerenim i teškim simptomima često je potrebna kombinacija farmakološkog i nefarmakološkog pristupa [9]. Farmakoterapija se bira prema dominantnom simptomu i podtipu bolesti.

Farmakološko lečenje IBS sa konstipacijom (IBS-C)

Ciljevi terapije su povećanje učestalosti i poboljšanje konzistencije stolice, uz redukciju bola i nadimanja.

Vlakna (psilijum, metilceluloza, kalcijum polikarbofil) predstavljaju terapiju prve linije. Meta-analize pokazuju umerenu efikasnost. Pšenične mekinje nisu pokazale značajnu korist.

Osmotski laksativi (PEG, magnezijumove mineralne vode) poboljšavaju konzistenciju stolice i smanjuju naprezanje, ali imaju ograničen efekat na bol i nadimanje. Laktuloza i sorbitol se ne preporučuju zbog nadimanja. Stimulativni laksativi (**sena, bisakodil**) se koriste kratkotrajno.

Kod pacijenata sa perzistentnim simptomima primenjuju se **sekretagogi i prosekretorni lekovi**:

Lubiproston (agonist ClC-2 kanala) poboljšava konzistenciju stolice i smanjuje bol; najčešći neželjeni efekti su mučnina i dijareja.

Plekanatid (agonist gvanilat ciklaze C) povećava sekreciju i istovremeno smanjuje visceralnu osetljivost; efikasan deluje i na bol.

Tenapanor (inhibitor Na⁺/H⁺ izmene) povećava sadržaj vode u stolici i smanjuje abdominalni bol.

Tegaserod (5-HT₄ agonist) može se razmotriti kod žena mlađih od 65 godina bez kardiovaskularnog rizika.

Prokinetik **prucaloprid** selektivni agonist 5-HT₄ receptora, stimuliše peristaltiku kolona, posebno kada postoje simptomi hronične opstipacije i loš odgovor na prethodne lekove

Kod izraženog bola i visceralne hipersenzitivnosti, naročito uz anksioznost ili

approach enables faster identification of disease subtypes, reduces unnecessary interventions, and forms the basis for a personalized therapeutic plan.

Treatment of Irritable Bowel Syndrome

Therapeutic management of IBS is based on a combination of patient education, dietary measures, pharmacotherapy, and, when necessary, psychological interventions. Due to the heterogeneity of pathophysiological mechanisms, treatment must be individualized and directed toward the dominant subtype (IBS-C, IBS-D, IBS-M, IBS-U), as well as the severity of pain, bloating, and psychosocial factors.

General principles of therapy

Patient education is the cornerstone of treatment. Explaining the benign nature of the condition and the role of the brain-gut axis reduces anxiety and improves adherence. It is important to emphasize that IBS has a chronic, fluctuating course and that the goal of therapy is symptom control and improvement of quality of life, rather than complete cure.

Dietary measures: The assumption that IBS symptoms are strictly diet-related is often overestimated, and elimination diets and fiber supplementation rarely provide long-term symptom improvement. A low-FODMAP diet, which restricts fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, may improve symptoms in about one in five patients by reducing bloating and abdominal pain [18].

Individual assessment of intolerance to lactose, fructose, and other fermentable carbohydrates may be useful. However, overly restrictive diets should be avoided due to the risk of nutritional deficiencies and negative effects on the gut microbiota.

Lifestyle modifications (regular physical activity, adequate sleep, and stress management) may contribute to symptom relief. In patients with moderate to severe symptoms, a combination of pharmacological and non-pharmacological approaches is often required [9].

Pharmacological treatment of IBS-C (constipation-predominant IBS)

The goals of therapy are to increase stool frequency and improve stool consistency, while reducing pain and bloating.

Fiber (psyllium, methylcellulose, calcium polycarbophil) is first-line therapy. Meta-analyses show moderate efficacy. Wheat bran has not demonstrated significant benefit.

Osmotic laxatives (PEG, magnesium-containing mineral waters) improve stool consistency and reduce straining, but have limited effect on pain and bloating. Lactulose and sorbitol are not recommended due to bloating. Stimulant laxatives (senna, bisacodyl) are used short-term. In patients with persistent symptoms, secretagogues and pro-secretory agents are used:

Lubiprostone (ClC-2 channel activator) improves stool consistency and reduces pain; common adverse effects include nausea and diarrhea.

Plecanatide (guanylate cyclase-C agonist) increases intestinal secretion and reduces visceral hypersensitivity, with beneficial effects on abdominal pain.

Tenapanor (Na⁺/H⁺ exchanger inhibitor) increases stool water content and reduces abdominal pain.

Tegaserod (5-HT₄ agonist) may be considered in women under 65 years without cardiovascular risk.

Prucalopride, a selective 5-HT₄ receptor agonist, stimulates colonic peristalsis and is particularly useful in chronic constipation with poor response to previous treatments.

For prominent abdominal pain and visceral hypersensitivity, especially in the presence of anxiety or depression, SSRIs (selective serotonin reuptake inhibitors) or SNRIs (serotonin-norepinephrine reuptake inhibitors) may be used, while TCAs (tricyclic antidepressants) can be beneficial in patients with pain and slow intestinal transit.

Irritable Bowel Syndrome (IBS)

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by recurrent abdominal pain associated with changes in stool frequency and/or stool consistency. Symptoms vary in intensity and frequency. IBS is classified into subtypes: IBS-D (diarrhea-predominant), IBS-C (constipation-predominant), mixed IBS (IBS-M), and unclassified IBS (IBS-U).

The etiopathogenesis is multifactorial, including visceral hypersensitivity, alterations in central nervous system processing of signals, motility disturbances, immune activation, microbiota dysbiosis, and increased intestinal permeability. Psychological factors, stress, and childhood trauma further modify symptom expression. The prevalence of IBS is estimated at 10–15% of the

depresiju, mogu se primeniti SSRI -selektivni inhibitori preuzimanja serotonina ili SNRI - inhibitori preuzimanja serotonina i noradrenalina, dok TCA - triciklični antidepresivi mogu biti korisni kod bola uz spor tranzit.

Farmakološko lečenje IBS sa dijarejom (IBS-D)

Dominantni simptomi su učestale, tečne stolice, urgentnost i bol.

Loperamid je terapija prve linije. Poboljšava konzistenciju stolice i smanjuje urgentnost, ali ima ograničen efekat na bol.

Eluksadolin (μ -opioidni agonist i δ -antagonist) smanjuje dijareju i bol. Kontraindikovano je kod pacijenata bez žučne kese i kod osoba sa povećanim rizikom od pankreatitisa.

Kod pacijenata sa sumnjom na malapsorpciju žučnih kiselina korisni su **sekvestranti žučnih kiselina (holestiramin)**.

Rifaksimino, neapsorptivni antibiotik, efikasan je u redukciji nadimanja i globalnih simptoma; efekat može biti prolazan i terapija se može ponoviti kod relapsa.

Kod teških i refraktornih oblika mogu se primeniti **5-HT₃ antagonisti (alosetron, ondansetron, ramosetron)**, koji smanjuju bol, urgentnost i učestalost stolica. Njihova primena zavisi od regulatornih ograničenja zbog retkog rizika od ishemijskog kolitisa.

Antispazmodici (mebeverin, pinaverin, alverin, ulje peperminta) ublažavaju bol delovanjem na glatku muskulaturu.

Uloga neuromodulatora Centralni neuromodulatori (SSRI, SNRI, TCA) danas se definišu kao „modulatori osovine crevo-mozak“. Koriste se u nižim dozama nego u psihijatriji i imaju za cilj smanjenje visceralne hipersenzitivnosti i modulaciju centralne obrade bola. Meta-analize pokazuju da neuromodulatori dovode do poboljšanja simptoma kod približno jednog od četiri do pet pacijenata. TCA su pokazale najveću efikasnost u redukciji abdominalnog bola.

Terapija IBS-M (mešoviti tip)

IBS-M karakteriše smenjivanje dijareje i konstipacije, što zahteva fleksibilan pristup. Terapija se prilagođava dominantnom simptomu u datom periodu, uz izbegavanje preterane farmakološke intervencije koja može dovesti do oscilacija u tranzitu.

Antispazmodici i neuromodulatori imaju centralnu ulogu, jer bol i nadimanje predstavljaju zajednički imenitelj različitih faza bolesti. Neuromodulatori utiču na visceralnu

senzitivnost i vreme tranzita: TCA produžavaju tranzit, SSRI ga skraćuju, dok SNRI deluju pretežno analgetski.

Probiotici (posebno bifidobakterije) mogu smanjiti nadimanje i bol. Meta-analize potvrđuju globalno poboljšanje simptoma kod približno jednog od tri lečena pacijenta.

Terapija IBS-U (neklasifikovani tip)

Kod pacijenata koji ne ispunjavaju kriterijume za jasnu klasifikaciju, terapija je simptomatska i individualizovana. Fokus je na kontroli bola, nadimanja i regulaciji stolice, uz naglašenu ulogu dijetetskih i psiholoških intervencija.

Zaključne osnove farmakološkog terapijskog pristupa:

- Lečenje IBS zahteva stepenasti pristup;
- Edukacija i dijetetske mere
- Terapija prema dominantnom simptomu
- Uvođenje sekretornih modulatora ili selektivnih lekova kod perzistentnih simptoma
- Neuromodulatori kod izraženog bola i hipersenzitivnosti
- Psihološke intervencije kod refraktornih oblika [1]

Nefarmakološko lečenje sindroma iritabilnog creva

S obzirom na centralnu ulogu osovine crevo-mozak u patogenezi sindroma iritabilnog creva (IBS), psihološke intervencije predstavljaju važan terapijski modalitet, naročito kod pacijenata sa izraženom visceralnom hipersenzitivnošću, anksioznošću, depresivnim simptomima ili hroničnim stresom. Njihova primena zasniva se na dokazima o centralnoj modulaciji bola i uticaju stresa na motilitet, permeabilnost i imunološku aktivaciju creva.

Psihološke terapije obuhvataju kognitivno-bihejvioralnu terapiju (KBT), hipnoterapiju usmerenu na creva, relaksacione tehnike, programe upravljanja stresom i druge strukturisane intervencije. Meta-analize pokazuju da psihološki tretman značajno smanjuje rizik perzistencije simptoma.

Kognitivno-bihejvioralna terapija je najopsežnije proučena metoda. Usmerena je na prepoznavanje i modifikaciju maladaptivnih misli i ponašanja koji pojačavaju percepciju bola i održavaju začarani krug anksioznosti i visceralne hipersenzitivnosti. Randomizovane studije potvrđuju njenu superiornost u odnosu na kontrolne intervencije.

general population, with higher frequency in women and individuals younger than 50 years. Genetic and familial factors contribute to susceptibility, while acute gastroenteritis and post-infectious forms represent important etiological triggers. Epidemiological data suggest a relatively stable prevalence over time, with spontaneous remission occurring in a subset of patients. IBS does not increase mortality but is associated with reduced quality of life and increased healthcare utilization.

Biopsychosocial Model and Clinical Significance

Modern understanding of IBS shifts the focus from purely gastrointestinal symptoms toward a broader concept of brain-gut axis dysregulation. Interactions between the enteric nervous system, autonomic regulation, microbiota, immune responses, and psychological factors shape the individual disease phenotype. This explains why uniform therapeutic approaches often yield limited results and highlights the importance of personalized treatment strategies. Although IBS does not lead to structural intestinal damage or increased mortality, it represents a significant public health burden due to frequent medical consultations, diagnostic procedures, reduced productivity, and impaired quality of life. Psychological distress, stigma, and the chronic nature of symptoms further contribute to disease burden. IBS should therefore not be viewed as a single disease entity, but rather as a heterogeneous clinical syndrome with varying dominant mechanisms, allowing for more precise diagnostic and therapeutic approaches.

Epidemiology

IBS is one of the most common gastrointestinal disorders in the general population. Population-based studies estimate a prevalence of 10–15% and an annual incidence of 1–2%.

Prevalence varies significantly across countries, ranging from 1.1% in France to 35.5% in Mexico, while a pooled prevalence of 7.1% has been reported in the USA, Europe, Australia, and New Zealand. Approximately 50% of patients report symptom onset before the age of 35.

IBS is more common in young adult women; in Western countries, women are 2–3 times more likely to be affected than men, whereas in some regions (e.g., the Indian subcontinent), men may predominate among diagnosed cases.

The syndrome is most frequently diagnosed in individuals under 50 years of age. Familial aggregation suggests a genetic contribution,

although shared environmental factors also play a significant role. Post-infectious IBS is an important subtype, developing after acute gastroenteritis and involving low-grade inflammation, altered permeability, and microbiota changes.

Psychosocial factors such as chronic stress and early-life trauma significantly influence both risk and symptom severity. The natural course is variable, with symptom remission in 10–40% of patients, while mortality is not increased.

Etiopathogenesis

The etiopathogenesis of IBS is not fully understood, but it is considered the result of complex interactions among genetic, neurobiological, immunological, microbiological, and psychosocial factors. The biopsychosocial model explains IBS as a disorder of regulation rather than structure.

Visceral hypersensitivity is a key mechanism, present in approximately 60% of patients, involving both peripheral sensitization and altered central pain processing. Neuroimaging studies show increased activation of the anterior cingulate cortex and amygdala, with reduced prefrontal modulation.

Low-grade immune activation is particularly relevant in post-infectious IBS, with increased mast cells and T lymphocytes contributing to neural sensitization. Serotonergic dysregulation affects motility and secretion, while bile acid malabsorption contributes to diarrhea in IBS-D. Alterations in gut microbiota (dysbiosis) influence immune activation, serotonin metabolism, and epithelial barrier integrity. Increased intestinal permeability may allow antigen translocation and immune activation.

Psychological factors, including chronic stress and early-life trauma, modulate symptoms via the hypothalamic-pituitary-adrenal (HPA) axis, leading to altered motility, secretion, and visceral sensitivity.

Genetic studies suggest heritability, with involvement of genes related to ion channels, smooth muscle function, and autonomic regulation.

Diagnosis

The modern diagnostic approach is based on a positive diagnosis using Rome IV criteria, rather than exclusion alone. IBS is defined by recurrent abdominal pain occurring at least 1 day per week over the past 3 months, associated with at least two of the following: relation to defecation,

Hipnoterapija usmerena na gastrointestinalni trakt deluje putem centralnih mehanizama modulacije visceralne percepcije. Studije pokazuju klinički značajno poboljšanje simptoma nakon 6–12 nedelja terapije. Relaksacione tehnike mogu poboljšati kvalitet života, iako je njihov efekat na osnovne simptome IBS-a manje konzistentan.

Zbog hroničnog toka bolesti, mnogi pacijenti pribegavaju **komplementarnoj medicini**. **Akupunktura**, prema dostupnim analizama, verovatno nije superiorna u odnosu na placebo. Dokazi za **lečenje biljem** su ograničeni, iako pojedina istraživanja ukazuju na moguću korist individualizovanih pristupa.

Terapija IBS-a mora biti personalizovana.

Osnovu čine edukacija pacijenta, racionalna dijetetska intervencija i ciljana farmakoterapija. Kod izražene centralne senzibilizacije i psiholoških komorbiditeta, kombinacija neuromodulatora i psiholoških intervencija često daje najbolje rezultate. Individualizovan i kombinovani pristup odražava savremeno razumevanje IBS-a kao heterogenog poremećaja regulacije osovine crevo-mozak i omogućava optimalnu kontrolu simptoma uz minimalno terapijsko opterećenje pacijenta. [1]

Prikaz terapijskog pristupa kod IBS-C i IBS-D je pokazan na slici 3.

Terapija IBS-C sa dominantnom konstipacijom	Terapija IBS-D sa dominantnom dijarejom
TERAPIJA PRVE LINIJE • Psilijum • PEG • Mg mineralne vode	TERAPIJA • Loperamid • Eluksadolin • Rifaximin
TERAPIJA DRUGE LINIJE • Linaklotid ili plekanatid • Lubiproston • Prukaloprid	Bol ili nadimanje • Antispazmodici • Triciklični antidepresivi (TCA) • Eluksadolin • Rifaximin • Low-FODMAP dijeta • Probiotici • Psihološke intervencije
Bol ili nadimanje • Antispazmodici • SSRI • Linaklotid • Psihološke terapije	

Slika 3. Terapija IBS sa dominantnom konstipacijom i sa dominantnom dijarejom

Zaključak

Sindrom iritabilnog creva predstavlja čest i hroničan funkcionalni poremećaj koji značajno narušava kvalitet života pacijenata. Kod bolesnika koji ispunjavaju Roma IV dijagnostičke kriterijume i nemaju alarmne znake, dijagnoza se može postaviti na osnovu pažljivo uzete anamneze, analize tipičnih kliničkih simptoma i fizikalnog pregleda, bez potrebe za opsežnom dijagnostikom. Nasuprot tome, prisustvo alarmnih simptoma, pojava tegoba nakon pedesete godine života, pozitivna porodična anamneza na kolorektalni karcinom, kao i sumnja na celijakiju ili hroničnu inflamatornu bolest creva, zahtevaju dodatnu laboratorijsku, slikovnu i endoskopsku obradu.

Lečenje IBS-a započinje detaljnim objašnjenjem prirode poremećaja i uveravanjem

pacijenta da se ne radi o malignoj ili životno ugrožavajućoj bolesti. Terapija je dugoročna i individualizovana, usmerena na dominantne simptome i njihov intenzitet. Osnov lečenja čine edukacija, dijetetske mere i ciljana farmakoterapija, dok kod pacijenata sa izraženom visceralnom hipersenzitivnošću i psihološkim komorbiditetima značajnu ulogu imaju neuromodulatori i psihološke intervencije. Uspešno lečenje zahteva kontinuiranu i konstruktivnu saradnju između pacijenta i lekara, uz po potrebi uključivanje drugih specijalista. Multidisciplinarni i personalizovani pristup odražava savremeno razumevanje IBS-a kao poremećaja regulacije osovine crevo-mozak i omogućava optimalnu kontrolu simptoma uz očuvanje kvaliteta života.

change in stool frequency, or change in stool form.

Alarm features (weight loss, bleeding, anemia, nocturnal symptoms, family history of colorectal cancer/IBD, or onset after age 50) require further investigation.

Basic evaluation includes blood tests (CBC, CRP/ESR), celiac serology, and fecal calprotectin. Endoscopy is not routinely required in young patients without alarm features.

IBS is classified into IBS-C, IBS-D, IBS-M, and IBS-U based on stool patterns (Bristol Stool Scale).

Psychosocial assessment is an important part of diagnosis, as anxiety, depression, and stress significantly influence symptom severity.

Treatment

Treatment is individualized and based on symptom predominance.

General principles

Education is essential, emphasizing the benign but chronic nature of IBS and the role of the brain-gut axis. Dietary and lifestyle modifications include physical activity, sleep regulation, and stress management.

A low-FODMAP diet may improve symptoms in approximately 20% of patients. Excessively restrictive diets should be avoided.

IBS-C (Constipation-predominant)

First-line therapy includes dietary fiber (psyllium, methylcellulose). Osmotic laxatives (PEG) improve stool consistency. Secretagogues and prokinetics include lubiprostone, plecanatide, tenapanor, tegaserod, and prucalopride.

Antidepressants (SSRIs, SNRIs, TCAs) may be used for pain and visceral hypersensitivity.

IBS-D (Diarrhea-predominant)

Loperamide is first-line therapy. Eluxadoline reduces diarrhea and pain but is contraindicated in patients without a gallbladder.

Rifaximin improves bloating and global symptoms. Bile acid sequestrants are used in suspected bile acid malabsorption.

5-HT₃ antagonists (alosetron, ondansetron, ramosetron) are used in refractory cases.

Antispasmodics and neuromodulators are also effective for pain.

IBS-M and IBS-U

Treatment is symptom-driven and flexible. Neuromodulators and antispasmodics play a central role. Probiotics (especially *Bifidobacterium* strains) may improve symptoms in a subset of patients.

Neuromodulators and Psychological Therapy

Neuromodulators (TCAs, SSRIs, SNRIs) act on the brain-gut axis and reduce visceral hypersensitivity.

Psychological therapies include cognitive-behavioral therapy (CBT), gut-directed hypnotherapy, relaxation techniques, and stress management programs. CBT is the most extensively studied and has demonstrated significant efficacy in reducing symptom severity and improving quality of life.

Gut-directed hypnotherapy acts through central mechanisms of modulation of visceral perception. Studies demonstrate clinically significant improvement in symptoms after 6–12 weeks of therapy. Relaxation techniques may improve quality of life, although their effect on core IBS symptoms is less consistent.

Due to the chronic course of the disease, many patients turn to complementary medicine. Acupuncture, according to available analyses, is likely not superior to placebo. Evidence for herbal treatments is limited, although some studies suggest potential benefit from individualized approaches.

IBS treatment must be personalized. The foundation consists of patient education, rational dietary intervention, and targeted pharmacotherapy. In cases of pronounced central sensitization and psychological comorbidities, the combination of neuromodulators and psychological interventions often yields the best results. This individualized and combined approach reflects the modern understanding of IBS as a heterogeneous disorder of brain-gut axis regulation and enables optimal symptom control with minimal therapeutic burden for the patient [1].

A schematic overview of the therapeutic approach for IBS-C and IBS-D is shown in Figure 3.

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Boi ili nadimanje • Antispazmodici • SSRI • Linaklotid • Psihološke terapije	

Slika 3. Terapija IBS sa dominantnom konstipacijom i sa dominantnom dijarejom

Conclusion Irritable bowel syndrome (IBS) is a common and chronic functional gastrointestinal disorder that significantly impairs patients' quality of life. In patients who fulfill the Rome IV diagnostic criteria and do not present alarm features, the diagnosis can be established based on a carefully obtained medical history, analysis of typical clinical symptoms, and physical examination, without the need for extensive diagnostic testing. In contrast, the presence of alarm symptoms, onset after the age of 50, a positive family history of colorectal cancer, or suspicion of celiac disease or chronic inflammatory bowel disease requires additional laboratory, imaging, and endoscopic evaluation. Management of IBS begins with a clear explanation of the nature of the disorder and reassurance that it is not a malignant or life-

threatening condition. Treatment is long-term and individualized, targeting predominant symptoms and their severity. The foundation of therapy includes patient education, dietary measures, and targeted pharmacotherapy, while neuromodulators and psychological interventions play an important role in patients with pronounced visceral hypersensitivity and psychological comorbidities. Successful management requires continuous and constructive collaboration between the patient and the physician, with involvement of other specialists when necessary. A multidisciplinary and personalized approach reflects the modern understanding of IBS as a disorder of brain-gut axis regulation and enables optimal symptom control while preserving quality of life..

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