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POVREMENI POST: DA LI JE KORISTAN ZA ZDRAVLJE ?

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Sažetak: Tokom evolucije životinje, uključujući ljude, su se razvijale u uslovima relativne oskudice u hrani. Prilagođavajući se takvim životnim okolnostima razvile su adaptivne promene metabolizma koje su im omogućile da dobro funkcionišu i u vremenskom periodu kada im hrana nije bila dostupna. Povremeni ili intermitentni post (PP) obuhvata obrasce ishrane u kojima pojedinci u produženom vremenskom periodu ne unose hranljive materije ili ih unose u malim količinama sa naizmeničnim periodima normalnog unosa hrane. PP je sve popularnija praksa ishrane, a njegova primena se nalazi u ljudskoj civilizaciji u različitim kulturnim, duhovnim, verskim i zdravstvenim tradicijama. Novi dokazi su pokazali da se zdravstvene prednosti PP protežu izvan ograničenja kalorija i gubitka težine. Ove prednosti uključuju metaboličke promene u proizvodnji energije i ukupno poboljšanje fizioloških markera metaboličkog zdravlja.Smatra se da PP smanjuje sistemsku upalu i da ima ulogu u prevenciji i lečenju hroničnih bolesti. U radu želimo da revijalno prikažemo dostupne rasprave i stavove o fiziološkom značaju i uticaju povremenog gladovanja na zdravlje.
Ključne reči: povremeni post, terapijska metoda, post u istoriji, post i zdravlje, metaboličke promene, ketonska tela, autofagija, glukoneogeneza, regeneracija i stres, kalorijska restrikcija, lipoliza, sirtuini, kardiometabolički efekti, ateroskleroza

UVOD

Povremeno uzdržavanje od hrane ili post se kao terapijska metoda koristi najmanje od 5. veka pre nove ere. Tada je Hipokrat preporučivao apstinenciju od hrane ili pića za pacijente koji su pokazivali određene simptome bolesti. Neki lekari su i kasnije prepoznavalili instinkt posta (kod pacijenata koji u određenim bolesnim stanjima prirodno doživljavaju gubitak apetita) i smatrali su da je davanje hrane tokom takvih stanja nepotrebno, a možda čak i štetno, verujući da je post važan prirodni deo procesa oporavka. Razumevanje fizioloških efekata posta počelo je da se razvija u drugoj polovini 19. veka, kada su neke od prvih organizovanih studija posta sprovedene na životinjama i ljudima. U 20. veku, kako se sve više znalo o ishrani i nutritivnim potrebama ljudskog tela, metode posta su postajale sve sofisticiranije i pojavljuje se širok spektar načina primene ovog načina ishrane.Pod terminom post pravoslavni hrišćani podrazumevaju odricanjeod određene vrste hrane, prvenstveno od mesa, mlečnih proizvoda i jaja, a u nekim periodima posta izbegava se i riba, ulje i alkoholna pića. U ovom radu ćemo postom označavati povremeni prekidunosa bilo koje vrste hrane (ili uzimanje hrane i kaloričnih napitaka u minimalnim količinama) u periodima koji se obično kreću od 12-36 sati. PP se može primenjivati svakog dana, naizmenično svakog drugog dana, dva puta nedeljno ili jednom nedeljno. Post se može praktikovati iz religijskih ali i iz zdravstvenih pobuda. Pripadnici pojedinih verskih zajednica tradicionalno poste određenim danima u nedelji ili kalendarskoj godini. U mnogim zdravstvenim ustanovama pacijenti pod kontrolom lekara imaju režim posta ili restrikcije kalorija radi kontrole telesne težine, prevencije ili lečenja bolesti. Post se razlikuje od kalorijske restrikcije (KR) u kojoj se dnevni unos kalorija hronično smanjuje za 20–40%, ali se zadržava učestalost obroka. Za razliku od posta i KR, gladovanje je hronična nutritivna insuficijencija koja se često koristi kao zamena za reč post, ali se takođe koristi i za definisanje ekstremnih oblika posta (npr. izgladnjivanje), koji mogu dovesti do degeneracije i smrti. Istraživanja na animalnim modelima, ali i studije na ljudima, pokazuju da post dovodi do ketogeneze, promoviše snažne promene u metaboličkim putevima i ćelijskim procesima kao što su otpornost na stres, lipoliza i autofagija, i može imati medicinsku primenu [1].

Povremeni post tehnički nije samo plan ishrane, već način ishrane koji se koncentriše na vreme, a ne na vrstu hrane. Studije na

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INTERMITTENT FASTING: IS IT BENEFICIAL FOR HEALTH?

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Summary: During evolution, animals, including humans, developed in conditions of relative food scarcity. Adapting to such life circumstances, they developed adaptive metabolic changes that allowed them to function well even during periods when food was not available. Intermittent fasting (IF) encompasses eating patterns in which individuals refrain from consuming nutrients for extended periods or consume them in small quantities with alternating periods of normal food intake. IF has become an increasingly popular dietary practice, and its application can be found in various cultural, spiritual, religious, and health traditions throughout human civilization. New evidence has shown that the health benefits of IF extend beyond caloric restriction and weight loss. These benefits include metabolic changes in energy production and overall improvement in physiological markers of metabolic health. It is believed that IF reduces systemic inflammation and plays a role in the prevention and treatment of chronic diseases. In this paper, we aim to review available discussions on the physiological significance and impact of intermittent fasting on health.

Key words: intermittent fasting, therapeutic method, fasting in history, fasting and health, metabolic changes, ketone bodies, autophagy, gluconeogenesis, regeneration and stress, caloric restriction, lipolysis, sirtuins, cardiometabolic effects, atherosclerosis

INTRODUCTION

Intermittent fasting or fasting as a therapeutic method has been used at least since the 5th century BC. At that time, Hippocrates recommended abstinence from food or drink for patients exhibiting certain disease symptoms. Some doctors later recognized the instinct of fasting (in patients who, in certain diseased states, naturally experience a loss of appetite) and believed that providing food during such conditions was unnecessary and possibly even harmful, believing that fasting was an important natural part of the recovery process. The understanding of the physiological effects of fasting began to develop in the second half of the 19th century when some of the first organized fasting studies were conducted on animals and humans. In the 20th century, as knowledge of nutrition and the nutritional needs of the human body grew, fasting methods became more sophisticated, and a wide range of ways to apply this form of eating emerged.

The term fasting for Orthodox Christians refers to the abstention from certain types of food, primarily meat, dairy products, and eggs, and in some fasting periods, even fish, oil, and alcoholic beverages are avoided. In this paper, fasting will refer to the occasional interruption of the intake of any type of food (or the consumption of food and caloric drinks in minimal quantities) during periods typically ranging from 12-36 hours. Intermittent fasting (IF) can be practiced daily, alternating every other day, twice a week, or once a week. Fasting can be practiced for religious reasons as well as for health purposes. Members of certain religious communities traditionally fast on specific days of the week or calendar year. In many healthcare institutions, patients under medical supervision follow a fasting regimen or calorie restriction to control body weight, prevent, or treat diseases.

Fasting differs from caloric restriction (CR), where daily caloric intake is chronically reduced by 20-40%, but meal frequency is maintained. Unlike fasting and CR, starvation is chronic nutritional insufficiency often used as a substitute for the word fasting, but it is also used to define extreme forms of fasting (e.g., starvation), which can lead to degeneration and death. Research on animal models, as well as studies on humans, shows that fasting leads to ketogenesis, promotes strong changes in metabolic pathways and cellular processes such as stress resistance, lipolysis, and autophagy, and can have medical applications [1].

životinjama i ljudima su pokazale da mnoge zdravstvene prednosti povremenog posta nisu samo rezultat smanjene proizvodnje slobodnih radikala ili gubitka težine. Umesto toga, povremeni post izaziva evolutivno očuvane, adaptivne ćelijske odgovore koji poboljšava regulaciju glukoze, povećavaju otpornost na stres i potiskuju upalu. Tokom posta, ćelije aktiviraju puteve koji pojačavaju odbranu od oksidativnog i metaboličkog stresa i one koji uklanjaju ili popravljaju oštećene molekule [2]. Izuzetni efekti tipične KR od 20–40% na starenje i bolesti kod miševa i pacova se često posmatraju kao reakcije sisara tokom evolucije da se prilagode periodima ograničene dostupnosti hrane. Međutim, ćelijski i molekularni mehanizmi odgovorni za zaštitne efekte KR verovatno su evoluirali milijardama godina ranije kod prokariota koje su pokušavale da prežive u okruženju koje je u velikoj meri ili potpuno lišeno izvora energije [3]. Na primer, bakterija E. coli prebačena sa podloge bogate hranljivim materijama na medijum bez kalorija preživljava 4 puta duže, što je efekat obrnut dodavanju različitih hranljivih materija, ali ne i acetata, izvora ugljenika koji je povezan sa uslovima gladovanja [4]. Skraćenje dužine života bakterije u uslovima bogatog medijuma, ali ne i acetata upućuje na to da izvor ugljenika nalik na ketonsko telo, kao što je acetat, može biti deo „alternativnog metaboličkog programa" koji je evoluirao pre više milijardi godina u mikroorganizmima i koji sada omogućava sisarima da prežive tokom perioda nedostatka hrane dobijanjem većeg dela energije katabolizmom masnih kiselina i ketonskih tela uključujući acetoacetat i β-hidroksibutirat [5]. Kod pivskog kvasca (*Saccharomyces cerevisiae*), prebacivanje ćelija sa standardnog medijuma za rast, na vodu takođe uzrokuje konzistentno dvostruko hronološko produženje životnog veka, kao i značajno povećanje otpornosti na višestruke stresove [6]. Još jedan model organizma u kome post produžava životni vek je nematoda *Caenorhabditis elegans*. Uslovi nedostatka hrane postignuti hranjenjem crva sa malo ili bez bakterija, dovode do značajnog produženja životnog veka [1]. Kod vinske mušice, većina studija ukazuje da povremeni nedostatak hrane ne utiče na životni vek. Međutim, dosledno se pokazalo da smanjenje ili razblaživanje hrane produžavaju dugovečnost Drosophile što sugeriše da mušice mogu imati koristi od ograničenja u ishrani, ali mogu biti osetljive čak i na kratke periode gladovanja. Zajedno, ovi rezultati ukazuju na to da nedostatak hrane može dovesti do efekata produžetka života kod širokog spektra organizama, ali takođe naglašavaju da različiti organizmi imaju različite odgovore na post [1].

Metaboličke promene u postu

Kod većine sisara, jetra služi kao glavni rezervoar glukoze, koja se skladišti u obliku glikogena. Kod ljudi, u zavisnosti od nivoa njihove fizičke aktivnosti, posle 12 do 24 sata gladovanja dolazi do snižavanja nivoa glukoze u serumu za 20 ili više procenata. Rezerve glikogena u jetri se iscrpljuju. Prelazi se na metabolički režim u kojem jetra i bubreg proizvode glukozu iz neugljenohidratnih izvora, iz glikogenih aminokiselina mišića (izoleucin, fenilalanin, tirozin, triptofan), glicerola iz masti i mlečne kiseline a zatim dolazi do lipolize u masnom tkivu pri čemu se oslobađaju slobodne masne kiseline i glicerol koje telo koristi kao energiju. Dok većina tkiva može da koristi masne kiseline za energiju, tokom produženih perioda posta, mozak se pored glukoze oslanja na ketonska tela β-hidroksibutirat i acetoacetat za potrošnju energije. Ketonska tela se proizvode u hepatocitima iz acetil-CoA nastalog β oksidacijom masnih kiselina koje adipociti oslobađaju u krvotok, a takođe i konverzijom ketogenih amino kiselina (leucin i lizin). Nakon 3-5 dana gladovanja jetra u procesu ketogeneze iz masnih kiselina proizvodi ketonska tela (beta-hidroksibutirat i acetoacetat), koja postaju glavni izvor energije za mozak i mišiće. Istovremeno korišćenje proteina kao izvora energije se smanjuje. Posle 5 dana bez hrane mozak se skoro u potpunosti prebacuje na ketonska tela kao izvor energije, čime se štiti mišićna masa. I dalje postoji minimalna glukoneogeneza, od približno 80 grama dnevno, pri čemu se glukoza proizvodi samo u količinama neophodnim za ćelije koje ne mogu koristiti ketonska tela (npr. eritrociti i neki delovi mozga) [7]. U zavisnosti od telesne težine i sastava, ketonska tela, slobodne masne kiseline i glukoneogeneza omogućavaju većini ljudi da prežive 30 ili više dana u uslovima nedostatka hrane i dozvoljavaju određenim vrstama, kao što su kraljevski pingvini, da prežive bez hrane više od 5 meseci [8].

Metaboličke adaptacije na povremeni post

Kod ljudi, tri najviše proučavana režima intermitentnog gladovanja su naizmenično

Intermittent fasting is technically not just a diet plan but a way of eating that focuses on timing rather than the type of food. Studies on animals and humans have shown that many health benefits of intermittent fasting are not solely a result of reduced free radical production or weight loss. Instead, intermittent fasting triggers evolutionarily preserved, adaptive cellular responses that improve glucose regulation, increase stress resistance, and suppress inflammation. During fasting, cells activate pathways that enhance defense against oxidative and metabolic stress and those that remove or repair damaged molecules [2]. The remarkable effects of typical CR (20-40%) on aging and diseases in mice and rats are often seen as mammalian responses during evolution to adapt to periods of limited food availability. However, the cellular and molecular mechanisms responsible for the protective effects of CR likely evolved billions of years earlier in prokaryotes attempting to survive in environments that were largely or completely devoid of energy sources [3]. For example, the bacterium E. coli, transferred from a nutrient-rich medium to a calorie-free medium, survives four times longer, an effect reversed by adding various nutrients, but not acetate, a carbon source associated with starvation conditions [4]. The shortening of the bacterium's lifespan in a rich medium, but not acetate, suggests that a ketone-body-like carbon source such as acetate could be part of an "alternative metabolic program" that evolved over billions of years in microorganisms, now allowing mammals to survive periods of food scarcity by obtaining most of their energy through fatty acid and ketone body catabolism, including acetoacetate and β-hydroxybutyrate [5]. In Saccharomyces cerevisiae (brewer's yeast), transferring cells from a standard growth medium to water also causes consistent double chronological lifespan extension, as well as a significant increase in resistance to multiple stressors [6]. Another organism model where fasting extends lifespan is the nematode Caenorhabditis elegans. Food deprivation conditions achieved by feeding the worms with little or no bacteria lead to significant lifespan extension [1]. In the fruit fly, most studies suggest that intermittent food deprivation does not affect lifespan. However, it has consistently been shown that reducing or diluting food extends the longevity of Drosophila, suggesting that flies may benefit from dietary restriction but may be sensitive even to short periods of starvation. Taken together, these results indicate that food deprivation can lead to lifespan-extending effects across a wide range of organisms but also emphasize that different organisms have different responses to fasting [1]..

Metabolic Changes During Fasting

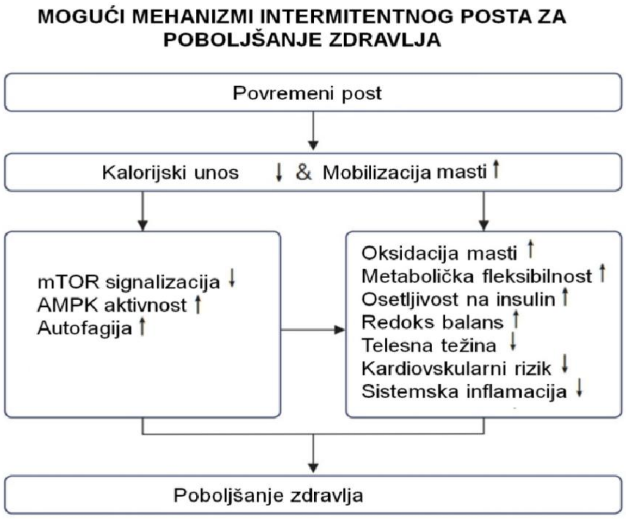
In most mammals, the liver serves as the main reservoir for glucose, which is stored in the form of glycogen. In humans, depending on the level of physical activity, after 12 to 24 hours of fasting, the glucose levels in the serum drop by 20% or more. The glycogen reserves in the liver become depleted. The body shifts to a metabolic state in which the liver and kidneys produce glucose from non-carbohydrate sources, such as glycogenic amino acids from muscles (isoleucine, phenylalanine, tyrosine, tryptophan), glycerol from fats, and lactic acid, followed by lipolysis in adipose tissue, releasing free fatty acids and glycerol, which the body uses as energy. While most tissues can use fatty acids for energy, during extended fasting periods, the brain, in addition to glucose, relies on ketone bodies β-hydroxybutyrate and acetoacetate for energy consumption. Ketone bodies are produced in hepatocytes from acetyl-CoA formed through β-oxidation of fatty acids released into the bloodstream by adipocytes, and also through the conversion of ketogenic amino acids (leucine and lysine). After 3-5 days of fasting, the liver produces ketone bodies (beta-hydroxybutyrate and acetoacetate) from fatty acids through ketogenesis, which become the main energy source for the brain and muscles. At the same time, the use of protein as an energy source decreases. After 5 days without food, the brain almost completely switches to ketone bodies as an energy source, thus protecting muscle mass. Minimal gluconeogenesis still occurs, approximately 80 grams daily, with glucose being produced only in amounts necessary for cells that cannot use ketone bodies (e.g., erythrocytes and some parts of the brain) [7]. Depending on body weight and composition, ketone bodies, free fatty acids, and gluconeogenesis allow most people to survive for 30 or more days in conditions of food scarcity, and allow certain species, such as royal penguins, to survive without food for more than 5 months [8].

gladovanje (jedan dan bez hrane, drugi dan ishrana ad libitum), 5:2 intermitentno gladovanje (post 2 dana svake nedelje) i dnevno hranjenje sa vremenskim ograničenjem. Dijete koje značajno smanjuju unos kalorija za 1 dan ili više svake nedelje (npr. smanjenje na 500 do 700 kalorija dnevno) dovodi do povišenih nivoa ketonskih tela tih dana [9,10].

Metabolički prelazak sa upotrebe glukoze kao izvora goriva na upotrebu masnih kiselina i ketonskih tela („metabolički prekidač") rezultuje smanjenim odnosom disajne razmene (odnos proizvedenog ugljen-dioksida i utrošenog kiseonika), što ukazuje na veću metaboličku fleksibilnost i efikasnost proizvodnje energije iz masnih kiselina i ketonskih tela [11].

Ketonska tela nisu samo gorivo koje se koristi tokom perioda posta; oni su moćni signalni molekuli sa velikim uticajem na funkcije ćelija i organa. Ketonska tela deluju kao metabolički signali koji regulišu epigenetiku preko beta-hidroksibutirata (BHB) koji inhibira histonsku deacetilazu (HDAC). Ova inhibicija zatim rezultuje antioksidativnim odgovorom i produženjem životnog veka. Povećavaju aktivnost sirtuina (posebno SIRT1 i SIRT3) čime se smanjuje oksidativni stres. Ketoni takođe modulišu upalne i antioksidativne puteve podstičući aktivaciju Nrf2 (Nuclear factor erythroid 2-related factor 2) koji je glavni regulatora antioksidativnog odgovora i smanjujući aktivnost NF-κB (Nuclear Factor kappa-light-chain-enhancer of activated B cells), ključnog faktora za upalne procese. Pored toga, ketoni povećavaju otpornost na stres i promovišu autofagiju pomoću AMPK (AMP-activated protein kinase) koja stimuliše autofagiju i mitohondrijalnu biogenezu, što doprinosi ćelijskom zdravlju i otpornosti na stres. Ketonska tela indirektno inhibiraju aktivnost mTORC1 (kompleks mTOR-a- Mammalian/Mechanistic Target of Rapamycin), glavnog regulatora ćelijskog rasta i sinteze proteina. Mehanicistički gledano, ključni regulator autofagije i ćelijskog metabolizma kod sisara je mTOR. Smanjenje aktivnosti mTOR preusmerava ćelijske resurse od neesencijalnih anaboličkih reakcija ka kataboličkim procesima, uključujući aktivaciju kompleksa bitnih za autofagiju. Smanjena aktivnost mTOR povezana je sa produženim životnim vekom i zaštitom od bolesti povezanih sa starenjem [12]. Utičući na ove glavne ćelijske puteve, ketonska tela proizvedena tokom posta imaju duboke efekte na sistemski metabolizam. Štaviše, ketonska tela stimulišu ekspresiju gena za neurotrofični faktor koji potiče iz mozga, sa implikacijama na zdravlje mozga i psihijatrijske i neurodegenerativne poremećaje [13]. Mnoge studije su pokazale da su neke od prednosti povremenog posta odvojene od njegovih efekata na gubitak težine. Ove prednosti uključuju: poboljšanja regulacije nivoa glukoze, regulisanje krvnog pritiska i sniženje broja otkucaja srca, efikasnost treninga izdržljivosti i gubitak abdominalne masti [14].

Slika 1. Mogući mehanizmi PP za poboljšanje zdravlja
Preuzeto 25.02.2025 sa: *Song DK, Kim YW. Beneficial effects of intermittent fasting: a narrative review. J Yeungnam Med Sci. 2023 Jan;40(1):4-11.https://pmc.ncbi.nlm.nih.gov/articles/PMC9946909/*



Metabolic Adaptations to Intermittent Fasting

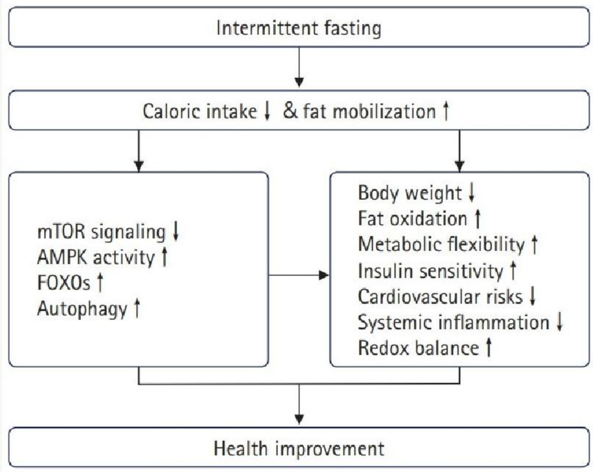
In humans, the three most studied intermittent fasting regimens are alternate-day fasting (one day without food, the next day food ad libitum), 5:2 intermittent fasting (fasting for 2 days each week), and daily time-restricted feeding. Diets that significantly reduce caloric intake for 1 day or more each week (e.g., reducing to 500–700 calories per day) lead to increased levels of ketone bodies on those days [9, 10].

The metabolic shift from using glucose as a fuel source to using fatty acids and ketone bodies ("metabolic switch") results in a decreased respiratory quotient (the ratio of carbon dioxide produced to oxygen consumed), indicating greater metabolic flexibility and efficiency in energy production from fatty acids and ketone bodies [11].

Ketone bodies are not only fuels used during fasting periods; they are powerful signaling molecules with significant effects on cellular and organ functions. Ketone bodies act as metabolic signals that regulate epigenetics through beta-hydroxybutyrate (BHB), which inhibits histone deacetylase (HDAC). This inhibition then results in an antioxidant response and lifespan extension. They increase the activity of sirtuins (especially SIRT1 and SIRT3), which reduces oxidative stress. Ketones also modulate inflammatory and antioxidant pathways by promoting the activation of Nrf2 (Nuclear factor erythroid 2-related factor 2), the primary regulator of the antioxidant response, and by reducing the activity of NF-κB (Nuclear Factor kappa-light-chain-enhancer of activated B cells), a key factor in inflammatory processes. Additionally, ketones increase stress resistance and promote autophagy through AMPK (AMP-activated protein kinase), which stimulates autophagy and mitochondrial biogenesis, contributing to cellular health and stress resilience. Ketone bodies indirectly inhibit mTORC1 activity (the mechanistic/mammalian target of rapamycin complex), the major regulator of cellular growth and protein synthesis. Mechanistically, mTOR is a key regulator of autophagy and cellular metabolism in mammals. Reduced mTOR activity shifts cellular resources from non-essential anabolic reactions toward catabolic processes, including activation of complexes important for autophagy. Reduced mTOR activity is linked to extended lifespan and protection from age-related diseases [12].

By affecting these key cellular pathways, ketone bodies produced during fasting have profound effects on systemic metabolism. Furthermore, ketone bodies stimulate the expression of genes for brain-derived neurotrophic factor, with implications for brain health and psychiatric and neurodegenerative disorders [13]. Many studies have shown that some of the benefits of intermittent fasting are separate from its effects on weight loss. These benefits include: improvements in glucose regulation, regulation of blood pressure, reduction in heart rate, increased endurance training efficiency, and loss of abdominal fat [14].].

Picture 1. POSSIBLE MECHANISMS OF INTERMITTENT FASTING ON HEALTH IMPROVEMENT
Source (25.02.2025): *Song DK, Kim YW. Beneficial effects of intermittent fasting: a narrative review. J Yeungnam Med Sci. 2023 Jan;40(1):4-11.* *https://pmc.ncbi.nlm.nih.gov/articles/PMC9946909/*



Efekti povremenog posta na zdravlje i starenje

Posle skoro jednog veka istraživanja o ograničenju kalorija na amimalnom modelu, opšti zaključak je bio da smanjeni unos hrane značajno produžava životni vek ispitivanih životinja. U jednoj od najranijih studija o povremenom postu, Goodrick i saradnici su pokazali da se prosečan životni vek pacova produžava do 80% kada se održavaju na režimu naizmeničnog hranjenja, započetom kada su mladi odrasli. Međutim, veličina efekata ograničenja kalorija na zdravstveni vek i životni vek varira i na njega mogu uticati pol, ishrana, starost i genetski faktori [2]. Meta-analiza podataka dostupnih od 1934. do 2012. godine pokazala je da se kalorijskom restrikcijom kod pacova srednji životni vek produžava za 14 do 45%, ali za samo 4 do 27% kod miševa [15].

Nepodudarni rezultati dve značajne studije na majmunima doveli su u pitanje vezu između poboljšanja zdravstvenog stanja i produženja životnog veka sa ograničenjem kalorija. Jedna studija, na rezus majmunima je pokazala pozitivan efekat ograničenja kalorija i na zdravlje i na dužinu preživljavanja [16], dok druga studija, takođe kod rezus majmuna nije pokazala značajno smanjenje mortaliteta pri kalorijskoj restrikciji, uprkos jasnim poboljšanjima ukupnog zdravlja [17]. Naknadna studija je pokazala da razlike u dnevnom unosu kalorija, početku intervencije, sastavu hrane, protokolima hranjenja, polu i genetskoj pozadini mogu da objasne različite efekte kalorijskog ograničenja kod ispitivanih životinja na dužinu životnog veka u prethodne dve studije [18].

Intermitentni post kod ljudi ublažava gojaznost, insulinsku rezistenciju, dislipidemiju, hipertenziju i upalu. Čini se da povremeni post donosi zdravstvene koristi u većoj meri nego što se može pripisati samo smanjenju kalorijskog unosa. U jednom ispitivanju, 16 zdravih učesnika podvrgnuto je režimu gladovanja naizmeničnih dana tokom 22 dana izgubilo je 2,5% svoje početne težine i 4% masne mase, uz smanjenje nivoa insulina natašte za 57% [19]. U dva druga ispitivanja, otprilike 100 žena sa prekomernom težinom u svakom ispitivanju su podeljene u dve grupe režima: povremenog gladovanja 5:2, ili smanjenju od 25% kalorija u dnevnom unosu. Ispitanice obe grupe su izgubile istu telesnu težinu u istom obimu tokom perioda od 6 meseci, ali one u grupi kojoj je dodeljen intermitentni post 5:2 imale su veći porast osetljivosti na insulin i veće smanjenje obima struka [20].

Prednosti PP za staru i bolesnu vaskulaturu

Vaskularno starenje uključuje krutost arterija i formiranje fibrolipidnih lezija u arterijskom zidu, što dovodi do ateroskleroze. Glavne kliničke manifestacije ateroskleroze uključuju ishemijsku bolest srca, ishemijski moždani udar i bolest perifernih arterija, koje su uzrokovane hiperlipoproteinemijom (lipoproteinom niske gustine LDL holesterolom), zapaljenjem, vaskularnim remodelovanjem i formiranjem plaka [21]. PP je povezan sa sniženjem nivoa LDL holesterola [22]. Kod pacova u odsustvuali i u prisustvu različitih stresora (npr. plivanje) povremeni post smanjuje krvni pritisak u mirovanju i broj otkucaja srca. Smanjenje krvnog pritiska moglo bi da bude delimično posledica pojačane vazodilatacije zavisne od endotelnih ćelija [23,24].

Štaviše, PP aktivira parasimpatički nervni sistem stimulacijom moždanih ćelija. Tokom posta se oslobađa neurotrofični faktor i sekretuje acetilholin, koji putem vagusnog nerva, dovode do smanjenja srčane frekvencije i krvnog pritiska [25].

Rizici PP za staro i bolesno srce i vaskulaturu

Uprkos brojnim zdravstvenim prednostima privremenog posta neki rizici su ipak prijavljeni u različitim modelima kardiovaskularnih bolesti. Na primer, pacovi koji su bili podvrgnuti alternativnom dnevnom gladovanju tokom 6 meseci pokazali su smanjenu dijastolnu komplijansu leve komore i smanjenu srčanu rezervu [26].

Efikasnost aktiviranja autofagije u senescentnim ćelijama je predmet tekuće debate jer je takođe prijavljeno da autofagija promoviše ćelijsko starenje olakšavanjem sinteze proteina povezanih sa starenjem. Štaviše, prekomerna [illegible]acija autofagije može da izazove nekoliko patoloških ishoda, uključujući inhibiciju angiogeneze [27]. Stoga, smanjeni regenerativni kapacitet endotela i akumulacija senescentnih ćelija kod starijih osoba bi potencijalno mogla ograničiti korisne efekte povremenog posta na zdravlje krvnih sudova.

Kod starijih osoba, posebno onih sa hipertenzijom ili drugim kardiovaskularnim bolestima, potencijalne fluktuacije krvnog pritiska tokom perioda PP mogu izazvati zabrinutost u smislu kardiovaskularnih rizika,

The Effects of Intermittent Fasting on Health and Aging

After nearly a century of research on caloric restriction in animal models, the general conclusion was that reduced food intake significantly extends the lifespan of the animals studied. In one of the earliest studies on intermittent fasting, Goodrick and colleagues showed that the average lifespan of rats was extended by up to 80% when maintained on an alternate day feeding regimen, starting when they were young adults. However, the magnitude of the effects of caloric restriction on healthspan and lifespan varies and can be influenced by gender, diet, age, and genetic factors [2]. A meta-analysis of data available from 1934 to 2012 showed that caloric restriction in rats extended the average lifespan by 14 to 45%, but only by 4 to 27% in mice [15].

Conflicting results from two significant studies on monkeys raised doubts about the relationship between improved health status and extended lifespan through caloric restriction. One study on rhesus monkeys showed a positive effect of caloric restriction on both health and survival [16], while another study, also on rhesus monkeys, did not show a significant reduction in mortality with caloric restriction, despite clear improvements in overall health [17]. A subsequent study showed that differences in daily caloric intake, the timing of the intervention, food composition, feeding protocols, gender, and genetic background could explain the varying effects of caloric restriction on lifespan in the two previous studies [18].

Intermittent fasting in humans alleviates obesity, insulin resistance, dyslipidemia, hypertension, and inflammation. It seems that intermittent fasting provides more health benefits than can be attributed solely to a reduction in caloric intake. In one study, 16 healthy participants who underwent an alternate-day fasting regimen for 22 days lost 2.5% of their initial body weight and 4% of body fat, along with a 57% reduction in fasting insulin levels [19]. In two other studies, approximately 100 overweight women in each study were divided into two groups: one following a 5:2 intermittent fasting regimen, and the other reducing their daily caloric intake by 25%. Participants in both groups lost the same amount of weight during the 6-month period, but those in the 5:2 intermittent fasting group had a greater increase in insulin sensitivity and a larger reduction in waist circumference [20].

Benefits of Intermittent Fasting for the Aged and Diseased Vasculature

Vascular aging involves arterial stiffness and the formation of fibrolipid lesions in the arterial wall, leading to atherosclerosis. The main clinical manifestations of atherosclerosis include coronary artery disease, ischemic stroke, and peripheral artery disease, which are caused by hyperlipoproteinemia (low-density lipoprotein LDL cholesterol), inflammation, vascular remodeling, and plaque formation [21]. Intermittent fasting (IF) is associated with a reduction in LDL cholesterol levels [22]. In rats, both in the absence and presence of various stressors (e.g., swimming), intermittent fasting reduces resting blood pressure and heart rate. The reduction in blood pressure may be partially due to enhanced endothelial cell-dependent vasodilation [23,24].

Furthermore, intermittent fasting activates the parasympathetic nervous system by stimulating brain cells. During fasting, neurotrophic factors are released, and acetylcholine is secreted, which, via the vagus nerve, leads to a decrease in heart rate and blood pressure [25].

Risks of Intermittent Fasting for the Aged and Diseased Heart and Vasculature

Despite the numerous health benefits of intermittent fasting (IF), some risks have been reported in various models of cardiovascular diseases. For example, rats subjected to alternate-day fasting for 6 months showed reduced diastolic compliance of the left ventricle and diminished cardiac reserve [26].

The efficacy of activating autophagy in senescent cells remains a subject of ongoing debate, as autophagy has also been reported to promote cellular aging by facilitating the synthesis of aging-associated proteins. Furthermore, excessive stimulation of autophagy can lead to several pathological outcomes, including inhibition of angiogenesis [27]. Therefore, reduced regenerative capacity of the endothelium and the accumulation of senescent cells in older individuals may ortostaze i povreda od pada [28]. Još jedan rizik koji je povezan sa PP proizilazi iz metaboličkih promena, kao što su neravnoteža elektrolita ili aktivacija simpatičkog nervnog sistema, što može kod starijih osoba predisponirati dehidraciju i srčane aritmije, posebno u prisustvu već postojeće srčane patologije.

Ukratko, usled nedostatka podataka, primena PP kod starijih osoba ili pacijenata sa kardiovaskularnim oboljenjima zahteva oprezno razmatranje zbog potencijalnih rizika, koji zavise od režima PP, srčanog stanja, komorbiditeta, pola i starosti [29].

Efekat PP na kardiometaboličko zdravlje

Gubitak telesne težine izazvan PP prvenstveno se pripisuje smanjenju mase masnog tkiva. Studije su dokumentovale smanjenje potkožnog i visceralnog masnog tkiva, pri čemu je ovo poslednje posebno korisno zbog povezanosti sa metaboličkom disregulacijom i povećanim kardiovaskularnim rizikom [30].

Obim struka, ključni antropometrijski marker kardiovaskularnog rizika, koji se koristi za procenu abdominalne adipoznosti snažno je povezan sa smrtnošću od svih uzroka i kardiovaskularnim mortalitetom. Pokazano je da se obim struka značajno smanjuje kod osoba koje primenjuju PP. Ovo smanjenje obima struka je u direktnoj korelaciji sa nižim rizikom od bolesti koronarnih arterija i drugih kardiovaskularnih patologija [31].

Osim toga, PP poboljšava nekoliko kardiovaskularnih faktora rizika, uključujući redukciju krvnog pritiska, poboljšanje lipidnog profila, sniženje srčane frekvence u mirovanju, sniženje nivoa glukoze i insulina i smanjuje insulinsku rezistenciju. Štaviše, PP može ublažiti hroničnu infalamicija intimalnog sloja krvnih sudova povezanu sa životnom dobi smanjenjem sistemskih inflamatornih markera i oksidativnog stresa koji su povezani sa aterosklerozom kod ljudi [29].

Starenje je kritičan faktor u patogenezi i progresiji srčane insuficijencije (SI), povećavajući incidencu i težinu SI. Nekoliko studija je sugerisalo da PP može poboljšati faktore rizika povezane sa razvojem SI kod zdravih osoba i onih sa gojaznošću i ishemijskom bolešću srca [32].

Na primer, u jednoj studiji su učesnici, koji su i sami prijavili da praktikuju rutinski PP jednom mesečno najmanje 5 godina, doživeli smanjenje rizika od SI za 71% u poređenju sa onima koji nisu postili [33]. Druga prospektivna opservaciona studija je otkrila da su kasniji periodi prvog i poslednjeg obroka bili povezani sa većim rizikom od kardiovaskularnih događaja, što je u skladu sa randomizovanim studijama koje izveštavaju da kasniji večernji obroci mogu da pojačaju kardiovaskularne faktore rizika [34]. Ova nedosledna zapažanja zahtevaju dalje istraživanje odnosa između PP i SI kroz velika randomizovana kontrolisana ispitivanja na efekat posta u različito doba dana.

Efekat povremenog posta na zdravlje mišića je predmet debate jer je nepoznato da li PP čuva mišiće tokom gubitka telesne težine ili pogoršava razgradnju mišićnih proteina i neto katabolizam. Iako su neke prethodne studije sugerisale smanjenje mišićne mase dijetom, opšti konsenzus je da PP nema štetan uticaj na nemasnu masu, čak i sa gubitkom telesne mase kod inače zdravih osoba, kao i kod pacijenata sa dijabetesom lečenih insulinom [35].

Fizički i kognitivni efekti intermitentnog posta

Kod životinja i ljudi, fizička funkcija se poboljšava povremenim postom. Na primer, uprkos sličnoj telesnoj težini, miševi koji se održavaju na naizmeničnom postu imaju bolju izdržljivost u trčanju od miševa koji imaju neograničen pristup hrani [2]. Ravnoteža i koordinacija su takođe poboljšani kod životinja na dnevnom vremenski ograničenom hranjenju ili režimima gladovanja naizmeničnih dana [36]. Mladići koji poste dnevno 16 sati gube masnoću dok održavaju mišićnu masu tokom 2 meseca napornog treninga [37]. Studije na životinjama pokazuju da povremeni post poboljšava kogniciju u više domena, uključujući prostornu memoriju, asocijativnu memoriju i radnu memoriju [38]. Naizmenični post i dnevno ograničenje kalorija poništavaju štetne efekte gojaznosti, dijabetesa i neuroinflamacije na prostorno učenje i pamćenje. U kliničkom ispitivanju, starije odrasle osobe na kratkotrajnom režimu restrikcije kalorija imale su poboljšanu verbalnu memoriju. U studiji koja je uključivala odrasle sa prekomernom težinom sa blagim kognitivnim oštećenjem, 12 meseci ograničenja unosa kalorija doveli su do poboljšanja verbalne memorije, izvršne funkcije i globalne kognicije [39,40]. Veliko, multicentrično, randomizovano kliničko ispitivanje je pokazalo da je 2 godine dnevnog ograničenja kalorija dovelo do značajnog poboljšanja radne memorije [41]. Svakako potentially limit the beneficial effects of intermittent fasting on vascular health.

In older adults, particularly those with hypertension or other cardiovascular diseases, potential fluctuations in blood pressure during intermittent fasting periods may raise concerns regarding cardiovascular risks, orthostasis, and fall-related injuries [28]. Another risk associated with intermittent fasting arises from metabolic changes, such as electrolyte imbalances or activation of the sympathetic nervous system, which can predispose older individuals to dehydration and cardiac arrhythmias, especially in the presence of pre-existing heart conditions.

In summary, due to the lack of data, the implementation of intermittent fasting in older individuals or patients with cardiovascular diseases requires careful consideration due to potential risks, which depend on the specific fasting regimen, cardiac condition, comorbidities, gender, and age [29].

Effect of Intermittent Fasting on Cardiometabolic Health

The weight loss induced by intermittent fasting is primarily attributed to a reduction in fat mass. Studies have documented reductions in subcutaneous and visceral fat, with the latter being particularly beneficial due to its association with metabolic dysregulation and increased cardiovascular risk [30].

Waist circumference, a key anthropometric marker of cardiovascular risk used to assess abdominal adiposity, is strongly associated with all-cause mortality and cardiovascular mortality. It has been shown that waist circumference significantly decreases in individuals practicing intermittent fasting. This reduction in waist circumference is directly correlated with a lower risk of coronary artery disease and other cardiovascular pathologies [31].

Moreover, intermittent fasting improves several cardiovascular risk factors, including blood pressure, lipid profile, resting pulse, glucose and insulin levels, and insulin resistance. Furthermore, intermittent fasting can alleviate chronic inflammation associated with aging by reducing systemic inflammatory markers and oxidative stress linked to atherosclerosis in humans [29].

Aging is a critical factor in the pathogenesis and progression of heart failure (HF), increasing the incidence and severity of HF. Several studies have suggested that intermittent fasting may improve risk factors associated with the development of HF in both healthy individuals and those with obesity and ischemic heart disease [32].

For instance, in one study, participants who reported routinely practicing intermittent fasting at least once a month for a minimum of 5 years experienced a 71% reduction in the risk of heart failure compared to those who did not fast [33]. Another prospective observational study found that later periods of the first and last meals were associated with a greater risk of cardiovascular events, consistent with randomized studies reporting that late evening meals may exacerbate cardiovascular risk factors [34]. These inconsistent findings require further research into the relationship between intermittent fasting and heart failure through large randomized controlled trials investigating the effect of fasting at different times of the day.

The effect of intermittent fasting on muscle health is a topic of debate as it remains unclear whether intermittent fasting preserves lean muscle mass during weight loss or exacerbates the breakdown of muscle proteins and net catabolism. While some earlier studies suggested a reduction in lean mass with dieting, the general consensus is that intermittent fasting does not have a detrimental effect on lean mass, even with weight loss in otherwise healthy individuals, as well as in insulin-treated diabetic patients [35].

Physical and Cognitive Effects of Intermittent Fasting

In both animals and humans, physical function improves with intermittent fasting. For example, despite having similar body weights, mice maintained on an intermittent fasting regimen exhibit better running endurance than mice with unlimited access to food [2]. Balance and coordination are also improved in animals following time-restricted daily feeding or alternate-day fasting regimens [36]. Juveniles who fast for 16 hours daily lose fat while maintaining muscle mass over 2 months of intense training [37]. Animal studies show that intermittent fasting improves cognition across various domains, including spatial memory, associative memory, and working memory [38]. Alternate-day fasting and daily caloric restriction counteract the harmful effects of obesity, diabetes, and neuroinflammation on postoji potreba da se preduzmu dalja istraživanja veze intermitentnog gladovanja i kognicije kod starijih ljudi, posebno imajući u vidu odsustvo bilo kakvih farmakoloških terapija koje utiču na starenje mozga i progresiju neurodegenerativnih bolesti.

DISKUSIJA

Sve veći broj dokaza podržava PP u svim njegovim varijantama kao potencijalno bezbednu i izvodljivu dijetnu intervenciju za poboljšanje ljudskog zdravlja. PP može poboljšati fiziološke i molekularne markere starenja i pružiti koristi za kardiovaskularno i metaboličko zdravlje kod pacijenata sa gojaznošću, dijabetesom melitusom tipa 2, metaboličkim sindromom i SI [29]. Sa značajnim gubitkom telesne težine i drugim zdravstvenim prednostima bile su povezane dve vrste povremenog posta: modifikovani post naizmenični dan (naizmenično jednog dana dnevno unošenje hrane kao i obično a drugog dana konzumiranjem hrane do 600 kalorija) i "dijeta 5:2" (2 dana u nedelji bez kalorija) [42].

Iako su dostupni klinički dokazi uglavnom istraživačke prirode, ove studije pružaju solidno obrazloženje za ispitivanje efikasnosti PP u poboljšanju kardiovaskularnog zdravlja i u starijoj populaciji u riziku od ili sa kardiovaskularnim oboljenjima. U budućnosti će biti neophodna randomizovana ispitivanja većih obima i dugog trajanja da bi se ispitali dugoročni rezultati, pridržavanje i bezbednost PP, posebno kod starijih učesnika.

Uprkos dokazima o zdravstvenim prednostima povremenog posta i njegovoj primenjivosti na mnoge bolesti, postoje prepreke za široko usvajanje ovih obrazaca ishrane u zajednici i od strane pacijenata. Prvo, ishrana od tri obroka sa grickalicama svaki dan je toliko ukorenjena u našoj kulturi da pacijenti ili lekari retko razmišljaju o promeni ovog obrasca ishrane. Obilje hrane i opsežan marketing u razvijenim zemljama su takođe velike prepreke koje treba prevazići. Drugo, prilikom prelaska na režim povremenog posta, mnogi ljudi će osetiti glad, razdražljivost i smanjenu sposobnost koncentracije tokom perioda ograničenja u ishrani. Međutim, ovi početni neželjeni efekti obično nestaju u roku od meseca dana i pacijente treba obavestiti o ovoj činjenici [2].

Uz ograničenja i rizike navedene napred treba upozoriti pacijente da obrasci ishrane u kojima ne konzumiraju kalorije tokom dužeg vremenskog perioda mogu predstavljati opasnost za ljude sa dijabetesom koji koriste insulin ili su na drugi način skloni hipoglikemiji [42]. Takođe se preporučuje edukacija lekara da pacijentima sa nizom hroničnih stanja ili u riziku od takvih stanja, posebno onih stanja povezana sa prejedanjem i sedentarnim načinom života daju uputstva za povremeni post za prevenciju ili u sklopu ranog lečenja tih stanja.

Još jedan važan aspekt koji treba uzeti u obzir je da PP menja gastrointestinalni mikrobiom [43]. Čini se da režimi posta imaju pozitivan uticaj na mikrobiotu creva. Buduće studije koje karakterišu zdravstvene uticaje režima gladovanja na ljudsku mikrobiotu imaju potencijal da daju važan doprinos ovoj oblasti. Stoga će, takođe, biti važno ispitati promene u metabolitima koje proizvode crevne bakterije, fokusirajući se na molekularne mehanizme koji leže u osnovi efekata PP na ćelijsko starenje.

ZAKLJUČAK

Intermitentni post zavisi od koncepta označenog kao „metabolički prekidač", koji uključuje promenu sa metabolizma zavisnog od glukoze tokom tipične ishrane, na ketone dobijene iz masnih ćelija tokom posta. "Metabolički prekidač" može poboljšati regulaciju nivoa glukoze i smanjiti upalu. Stresno stanje posta takođe povećava autofagiju, koja uklanja oštećene molekule. S obzirom na ove fiziološke promene, povremeni post može doneti značajne dugoročne zdravstvene koristi. Eksperimentalni modeli PP na životinjama pokazuju da ovaj način ishrane poboljšava zdravlje ispitivanih životinja tokom čitavog životnog veka. Kliničke studije na humanim modelima su takođe pokazale značajne zdravstvene prednosti, iako su uglavnom uključivale relativno kratkoročne intervencije, tokom perioda od nekoliko meseci. Pretkliničke studije i klinička ispitivanja su pokazala da povremeni post ima širok spektar prednosti za mnoga zdravstvena stanja, kao što su gojaznost, dijabetes, kardiovaskularne bolesti, neka maligna stanja i neurološki poremećaji. Veliki broj studija sugeriše da režimi povremenog posta mogu biti obećavajući pristup za gubitak težine i poboljšanje metaboličkog zdravlja za ljude koji mogu da tolerišu intervale bez hrane, ili jedu vrlo malo, u određenim časovima u danu ili danima u nedelji. Kod zdravih, normalne težine, ili gojaznih odraslih, malo je dokaza da su spatial learning and memory. In a clinical trial, older adults on a short-term caloric restriction regimen experienced improved verbal memory. In a study involving overweight adults with mild cognitive impairment, 12 months of caloric restriction led to improvements in verbal memory, executive function, and global cognition [39, 40]. A large, multicenter, randomized clinical trial demonstrated that 2 years of daily caloric restriction resulted in significant improvements in working memory [41]. Further research is needed to explore the relationship between intermittent fasting and cognition in older adults, especially considering the absence of pharmacological therapies affecting brain aging and the progression of neurodegenerative diseases.

DISCUSSION

An increasing body of evidence supports intermittent fasting (IF) in all its variations as a potentially safe and feasible dietary intervention for improving human health. IF can improve physiological and molecular markers of aging and provide benefits for cardiovascular and metabolic health in patients with obesity, type 2 diabetes, metabolic syndrome, and heart failure [29]. Significant weight loss and other health benefits have been associated with two types of intermittent fasting: modified alternate-day fasting (alternating between a day of normal food intake and a day consuming up to 600 calories) and the "5:2 diet" (2 days of no caloric intake per week) [42].

While clinical evidence is mostly of a research nature, these studies provide a solid rationale for investigating the efficacy of IF in improving cardiovascular health, particularly in the elderly population at risk for or already experiencing cardiovascular diseases. Future randomized trials with larger sample sizes and longer durations will be necessary to assess the long-term outcomes, adherence, and safety of IF, especially in older participants.

Despite the health benefits of intermittent fasting and its applicability to many diseases, there are barriers to widespread adoption of these dietary patterns in the community and by patients. First, the traditional three-meal-a-day pattern with snacks is so ingrained in our culture that patients or physicians rarely consider changing this eating pattern. The abundance of food and extensive marketing in developed countries also pose significant barriers that must be overcome. Second, when transitioning to an intermittent fasting regimen, many people experience hunger, irritability, and reduced concentration during periods of food restriction. However, these initial side effects usually subside within a month, and patients should be informed of this [2].

Given the limitations and risks outlined above, patients should be cautioned that eating patterns involving extended periods without food could pose risks for people with diabetes who are on insulin or otherwise prone to hypoglycemia [42]. Physician education is also recommended for patients with a range of chronic conditions or at risk of such conditions, particularly those associated with overeating and a sedentary lifestyle, on how to implement intermittent fasting for prevention or as part of early treatment for these conditions.

Another important aspect to consider is that intermittent fasting alters the gastrointestinal microbiome [43]. Fasting regimens appear to have a positive impact on gut microbiota. Future studies characterizing the health effects of fasting regimens on the human microbiome have the potential to make an important contribution to this field. Therefore, it will also be crucial to investigate changes in metabolites produced by gut bacteria, focusing on the molecular mechanisms underlying the effects of intermittent fasting on cellular aging.

CONCLUSION

Intermittent fasting relies on the concept of a "metabolic switch," which involves a shift from glucose-dependent metabolism during a typical diet to ketones derived from fat cells during fasting. This "metabolic switch" may improve glucose regulation and reduce inflammation. The stress of fasting also increases autophagy, which removes damaged molecules. Given these physiological changes, intermittent fasting can offer significant long-term health benefits. Animal models of intermittent fasting show that this dietary pattern improves the health of the animals throughout their lifespan. Clinical studies in human models have also demonstrated significant health benefits, although these studies have mostly involved relatively short-term interventions lasting several months. Preclinical studies and clinical trials have shown režimi povremenih postova štetni fizički ili mentalno. Buduće studije treba da utvrde da li bi prednosti koje se vide na životinjskim modelima bile održive i pri dugogodišnjem povremenom postu kod ljudi različite starosne dobi i zdravstvenog statusa. Daljnjim razumevanjem procesa koji povezuju povremeni post sa mnogim zdravstvenim prednostima, možda ćemo moći da razvijemo ciljane farmakološke terapije, uključujući i delovanje na mikrobiotu creva, koje oponašaju efekte povremenog posta bez potrebe da se suštinski menjaju navike u ishrani.

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that intermittent fasting offers a broad range of advantages for many health conditions, such as obesity, diabetes, cardiovascular diseases, certain cancers, and neurological disorders. Numerous studies suggest that intermittent fasting regimens may be a promising approach for weight loss and improving metabolic health in people who can tolerate periods without food or consume very little at certain times of the day or on specific days of the week. For healthy, normal-weight, or obese adults, there is little evidence that intermittent fasting regimens are harmful physically or mentally. Future studies should determine whether the benefits observed in animal models can be sustained over long-term intermittent fasting in humans of various ages and health statuses. Further understanding of the processes linking intermittent fasting to many health benefits may allow us to develop targeted pharmacological therapies, including interventions on the gut microbiome, that mimic the effects of intermittent fasting without requiring fundamental changes to eating habits.

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