Dijagnostika i lečenje COVID–19 u primarnoj zdravstvenoj zaštit

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Sažetak

Pandemija COVID–19 izazvana je virusom SARS-Cov-2 i najpre se pojavila u gradu Vuhan, u Kini, u decembru 2019. U Domu zdravlja, Kruševac Ambulanta za respiratorne infekcije osnovana je 24. marta 2020. U njoj je do sada obavljeni blizu 100.000 pregleda.

Među ljudima se virus prenosi kapljičnim putem ili, rede, prljavim rukama i ulazno mesto su sluznice nosa, usta, očiju.

Infekcija se odvija u dva stadijuma. Prvi, u gornjem respiratornom traktu (GRT) i traje 5-7 dana i drugi, kada se virus spušta na pluća i zatim daje sistemsku upalu, pre svega krvnih sudova.

Dijagnoza se postavlja na osnovu anamneze, kliničke slike, fizikalnog pregleda, specifičnih virusnih testova, laboratorijskih analiza i eventualno, rendgen snimanja pluća.

Terapija je uglavnom simptomatska, a od marta 2021. godine dostupan nam je antivirotik favipiravir, dok se u januaru 2022. pojavio i molnupiravir. Kod pojave upale pluća oralni kortikosteroidi su dali dobre rezultate.

Primarna zdravstvena zaštita je, i ovog puta, bila brana ka sekundarnom i tercijarnom nivou zdravstvene zaštite. Kao i naše kolege u svetu, učili smo u hodu i taj proces traje i dalje. Prokužavanje većeg broja ljudi bilo je prilikom zaražavanja, ili vakcinacijom vremenom će dovesti do završetka pandemije, koja će verovatno postati sezonska infekcija, ali sa mnogo blžom kliničkom slikom.

Ključne reči: COVID-19, primarna zdravstvena zaštita, lečenje

Diagnosis and treatment of COVID–19 in primary healthcare

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Abstract

COVID-19 pandemic is caused by the SARS-Cov-2 virus and it was first isolated in Wuhan, China, in December 2019. In Primary Healthcare Center (PHC), Kruševac, the outpatient clinic for respiratory infections was formed on March 24th, 2020. Nearly 100,000 medical exams were performed there, up till now.

The virus transmission is carried out by airborne droplets, or rarely using contaminated hands. The entrance site of the infection is nose, mouth, or eye mucose.

The infection develops in two stages. The first happens in the upper respiratory tract (URT) and lasts 5-7 days, and the second, when the virus descends to the lungs, and from there causes systemic inflammation, primarily of the blood vessels.

The diagnosis is based on the personal history, clinical presentation, physical exam, specific viral tests, lab analysis, and eventually, chest X-ray.

Therapy is mainly symptomatic, and since March 2021 we got antiviral favipiravir, and in January 2022 another antiviral, molnupiravir, became available. Oral corticosteroids showed promising results in patients with viral pneumonia.

Primary healthcare was a dam against the secondary and tertiary healthcare this time, too. As our colleagues worldwide, we were learning in stride, and the process is ongoing. The more people get exposed to the virus, either naturally or by vaccination, the sooner the pandemic will end but not entirely and probably stay with us as a seasonal infection with easier clinical presentation.

Keywords: COVID-19, primary healthcare, treatment
Introduction

COVID-19 pandemic is caused by the SARS-CoV-2 virus. It was first isolated in Wuhan, China, in December 2019 and it spread worldwide. World Health Organization (WHO) proclaimed the pandemic on March 11th, 2020. This is a tragedy of epic proportions and it’s still causing huge health, social, and economic problems all over the world. The WHO, as a cover world advisory organization endeavors continuously to coordinate the fight against the virus. In practice, different countries have different measures in their fight against the virus. The only measures that proved to be effective are isolation, face masks, and keeping physical distance. The emergence of the vaccines, at the end of 2020, gave hope in the fight against the virus but the new mutant variants partially weakened their efficacy.

In PHC, Krusevac the Outpatient Clinic for Respiratory Infections was founded on March 24th, 2020. Over 100.000 medical exams were performed there. The clinic also has its lab, X-ray, and its own ambulance. The number of health workers working there varies, depending on the epidemiological situation (max numbers, 16 physicians and 25 nurses). The staff is provided by the Department of General Medicine, which also provides the personnel for the vaccination against COVID-19, and treats non-COVID patients, as well.

Method

Review of the current literature and the data obtained from the electronic health records on antibiotic prescription in Outpatient Clinic for Respiratory Infections, Krusevac, from 01.01.2020. to 31.01.2022.

Epidemiology

There’s still no solid evidence on how the virus became anthropoanosis from zoonosis. The virus is spread among people by inhaling viral droplets and the entrance sites are the nose, mouth, and eye mucosae. The incubation period lasts from 1-14 days (most commonly 2-5 days). A patient is contagious 2-3 days before the onset of the symptoms and approximately 10 days after the onset. These characteristics are changing, depending on the virus strain. Patients at risk for the severe forms of the disease are obese, diabetics, cardiovascular patients, as well as, patients with comorbidities, unvaccinated, older persons.

Pathogenesis

The infection develops in two stages. The first is in the upper respiratory tract - URT and it lasts 5-7 days and the second is when the virus descends to the lungs and then
rusa. Aktiviranje urođenog imuniteta je signal za aktivaciju stečenog imuniteta (CD4, CD8, memorijske B čelije) koji je odgovoran za održavanje donjeg respiratornog traka. Dok je replikacija virusa u GRT brza, razvoj pneumonije nije i ona se javlja tek nakon 7-14 dana (objašnjenje za efikasnu zaštitu od teže bolesti i hospitalizacije kod vakcinisanih pacijenata). Veoma je važno poznavati patogenesu virusa zbog tumačenja simptoma, odlučivanja za odgovarajuće laboratorijske i dijagnostičke postupke, kao i određivanje terapije.

Klinička slika

*Rani simptomi* – Većina pacijenata se žali na subfebrilne temperature (rede visoka febrilnost), jezu, drhtavac, malakalost, glavobolju, mijalgie, gusobolju, zapušen nos, naražajni kašalj, gastrointestinalne tegebe (rede kod odraslih, češće kod dece). Jedan broj pacijenata se žali i na gubitak ili izmjenjeno čulo ukusa i / ili mirisa, što se u pogledu ozbiljnosti kliničke slike pokazalo kao dobar prognoistički znak. Pacijenti sa anosijom su značajno rede hospitalizovani i završavali u jedinicama intenzivne nege u poređenju sa pacijentima kod kojih su ova čula bila očuvana tokom COVID-19 infekcije.

*Kasni simptomi* – JVlaljuju se kada se bolest spusti na pluća. Manifestuju se nastavkom febrilnosti, kašljem koji je praćen gušenjem, osećanjem nedostatka vazduha, zamaranjem, gubitkom apetita. Kod ovih pacijenata se razvija upala pluća koja neretko progredira u ARDS (akutni respiratorni distres sindrom).

Dijagnoza

Anamneza i klinička slika – COVID-19 u početnom stadijuju liči na većinu drugih respiratornih infekcija. Teško ga je razlikovati bez dodatne dijagnostike. Pacijenti obično imaju subfebrilne temperature, malakalosti su, žale se na glavobolju, mijalgie. U epidemiološkoj anamnezi često navode kontakt sa zaraženom osobom.

Fizikalni pregled – grlo je obično blaže hiperemično, podvilične žlezde nisu bolne, niti uvećane, nos je često zapušten. Ako je razlikovan iz čulo ukusa i / ili mirisa, što se u pogledu ozbiljnosti kliničke slike pokazalo kao dobar prognoistički znak. Pacijenti sa anosijom su značajno rede hospitalizovani i završavali u jedinicama intenzivne nege u poređenju sa pacijentima kod kojih su ova čula bila očuvana tokom COVID-19 infekcije.

Fiziološka slika i dijagnostika

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Virusni testovi:

RT-PCR (Reverse Transcription Polymerase Chain Reaction) – visokosenzitivan i specifičan test. Registruje jedan ili više virusnih RNK gena i ukazuje na trenutnu ili nedavnu infekciju. Duže vreme detektuje prисусство čestica virusa i nije dokaz da je osoba trenutno zaražena. Treba ih tumačiti u sklopu kliničke slike.

Brzi antigenski test – Registruje specifičan virusni antigen. Manje je senzitivan nego PCR, ali je praktičan za brzu dijagnostiku. Treba ga uraditi u odgovarajućem vremenskom razmaku (između 1.-7. dana od početka bolesti, po uputstvu proizvođača, ali su se u praksi pokazali najpouzdaniji između 2.-5. dana).

Serološki testovi – nemaju svrhu u dijagnostici akutne bolesti. Prva IgM antitela se javljaju tek nakon 7 dana od početka bolesti1.

Laboratorijska dijagnostika: U ambulantnim uslovima dostupni su nam krvna slika (KS) sa leukocitarnom formuloj, CRP i glikemija (glukometar). Krvna slika je neretko nespecifična, ali se sreću i nalazi limfopenija (može biti prediktor ozbiljnije bolesti), neutrofilija sa limfocitopenijom, trombocitopenija, smanjen PCT (procent zapremine trombocita u krvi). CRP (C-reaktivni protein) je produkt jetre koji nastaje kao odgovor organizma na bilo koji oblik infekcije. U COVID ambulantama pokazao se kao koristan parametar za praćenje stanja pacijentana. Njegove vrednosti treba pratiti u kontekstu kliničke slike i pogodan je za odlučivanje o uvođenju odgovarajuće terapije. Dostupno nam je i merenje glikemije na glucometerima. Pogoršanje glukokontrole pokazalo se kao loš prognozički znak kod COVID-a.

Rendgen dijagnostika – Neproporčujuće se zadiagnostikovanje COVID-a. Naročito je ne treba raditi prvih dana bolesti, jer se virus tek nakon 5-7 dana spušta na pluća. Radiografski nalazi kod COVID-a nisu specifični (mogu ličiti na druge respiratorne bolesti) i treba ih tumačiti u sklopu kliničke slike.

Terapija

Do sada je u Republici Srbiji izdato 13 protokola o lečenju COVID-19 infekcije koji su se menjali kako su se sticala nova znanja u lečenju bolesti. Deo protokola koji se odnosi na lečenje u PZZ od terapije nije preporučivao ništa drugo osim vitamina (vit C, vit D) i antioksidansa (alfalipoinska kiselina). Budući da se radi o virusnoj infekciji za koju ne postoji specifično lečenje, ovakav pristup je opravdan, ali je u praksi to izgledalo drugačije. Mnogo je pacijenata kod kojih dođo do pojave upale pluća i pogoršanja saturacije (i po protokolima bi ih trebalo uputiti na bolničko lečenje), ali zbog preopterećenosti zdravstvenog sustava to nije bilo uvek moguće. anemia, cold fingers, nail polish, and comorbidities). The COVID 19 treatment protocol recommendations suggest that patients with saturation of less than 94% and pneumonia or comorbidities should be sent to a hospital. But, in practice, it’s often impossible, mostly due to the overwhelmed hospital capacities. Every patient should be evaluated individually. If it was necessary, we also measured arterial tension and performed ECGs.

Viral tests:

RT-PCR (Reverse Transcription Polymerase Chain Reaction) test – is a highly sensitive and specific test. It registers one or more viral RNK genes and signifies current or recent infection. It detects viral particles for a longer period of time and is not necessarily a proof of current infection. It should be interpreted in the current clinical setting.

Rapid antigen test – It registers specific viral antigens. It is less sensitive than PCR but practical for rapid diagnosing. It should be performed at the right moment (between 1.-7. day since the disease onset, as advised by the producer, but in practice, they proved to be the most sensitive between 2.-5. day).

Serological tests – are of no use in diagnosing acute illness. First IgM antibodies appear mostly after 7 days from the disease onset1.

Lab results: In our outpatient clinic we had CBC (complete blood count) with leukocyte formula, CRP, and glycemia (measured by glucometer). CBC is often non-specific but lymphopenia can be present3 (may be a predictor of the severe illness), neutrophilia with lymphocytopenia, thrombocytopenia, lower PCT (percentage of platelets volume). CRP (C-reactive protein) is emerging as a body’s response to any form of inflammation. In the COVID outpatient clinics, it proved as a very useful parameter in following the patient’s condition. Its values should be interpreted in line with clinical presentation and it’s useful for therapy decision making. We also had glucometers. Worsening of glucose control proved to be a bad prognostic sign in COVID.

Chest X-ray – is not recommended for COVID diagnosis3. It shouldn’t be performed in the early days of the disease since the virus descends to the lungs only after 5-7 days. Radiologic findings in COVID are not specific (they may resemble any other respiratory disease findings) and should be interpreted in the current clinical setting.

Therapy

There were 13 COVID-19 treatment protocols in Serbia and they changed as new information on the disease treatment occurred. A part of the protocol referring to primary health-
Ovaj rad pisan je dok je na snazi bio 12. protokol za lečenje COVID-19 infekcije u Republici Srbiji.

Lečenje COVID-19 infekcije u PZZ podrazumeva:

**Odmor, dovoljan unos tečnosti** – mnogi pacijenti ne uzimaju za ozbiljno ove preporuke, a one su od esencijalne važnosti u borbi organizma sa virusom. Cesto smo svedoci kolabiranja pacijenata zbog dehidracije (febrilitet, nedovoljan unos tečnosti).

**Vitaminska terapija** – protokoli preporučuju veći unos vitamina **D** (minimum 2000 i.j./dan), vitamin C 1g/dan. Alfalipoinska kiselina je preporučivana u prvim protokolima zbog svojih antioksidativnih dejstava i eventualnog lečenja anomije, ali nije dala željene rezultate i izbačena je iz protokola. Voditi računa kod doziranja vitaminske terapije zbog nezneljenih dejstava u vidu mučnine, dijareje.

**Favipiravir** – antivirak koji je primarno korišćen u lečenju ozbiljnijih oblika gripa. Prema studijama dovodi do smanjenja virusnog prouzroka nakon upotrebe. Od mart 2021. dostupan je u COVID ambulantama. Preporučuje se za testom potvrđene COVID pacijente, koji imaju simptome i kod kojih postoji rizik od komplikacije bolesti. Preporuka je da se uvede u terapiju do petog dana od početka simptoma. Doziranje 1.600 mg/12h prvog dana, a zatim 600 mg/12h još 4 dana.

**Molnupiravir** – takođe antivirak novije generacije, specifičan za lečenje COVID-a. Funkcionisuje po principu izazivanja grešaka u genetskom kodu virusa i na taj način sprečava njegovu dalju reprodukciju. Preporučuje se pacijentima kod kojih je potvrđena infekcija i imaju rizik za teži oblik bolesti. Takođe se preporučuje davanje do 5. dana od početka simptoma. Tablete su od 200mg i preporučeno doziranje je 800 mg/12h.

**Antibiotici** – nemaju ulogu u lečenju COVID-a, osim ako ne dođe do bakterijske superinfekcije. Po nekim dosadašnjim saznanjima to je u PZZ nešto u oko 7%-8% pacijenata. Zubanu je uvela preporuka za azitromicin u prvom protokoluma (zajedno sa hidroksihlorokinom), ali je ideja za preporuku bilo njegovo imunomodulorno dejstvo. Nažalost, u praksi nije dao željene efekte, te je ubrzo isključen iz protokola. Statistika u našoj ambulanti početkom 2020 govori da je oko 50% pacijenata sa potvrđenom dijagnozom COVID-19 dobijala antibiotik, a 50% simptomatsku terapiju. U oktobru 2021, antibiotik je dobijalo 65%, antivirike 9%, a simptomatsku terapiju 26%. Početkom 2022. propisivanja antibiotika i dalje ostaje visoko 64%, antivirike dobi ja 21%, a simptomatsku terapiju 15%. U PZZ nemamo mogućnost određivanja prokalcitonina (ukazuje na postojanje bakterijske infekcije), te se eventualno uvođenje antibiotika zasniva na proceni kliničke slike, Le formule i CRP-a.

The COVID-19 treatment in PCP includes:

**Rest, fluid intake** – many patients don’t take these recommendations seriously and they are of essential importance in a body’s fight against the virus. We often witnessed patients fainting due to dehydration (febrility, insufficient fluid intake).

**Vitamin therapy** – protocols recommend a higher intake of vitamin D (minimum 2000 I.U./day), vitamin C 1g/day. Alpha-lipoic acid was recommended in the first protocols for its antioxidant characteristics and as a possible anosmia treatment but it failed to be effective so it was removed from the protocol. Vitamins should be given with precaution due to their side effects in the form of nausea, diarrhea, etc.

**Favipiravir** – is an antiviral, primarily used in the treatment of severe forms of flu. According to studies, it leads to a decrease in the viral load. Since March 2021 it was available in the COVID outpatient clinics. It’s recommended for COVID positive symptomatic patients who are expected to develop a severe form of the disease with complications. The recommendation is to introduce it until the fifth day from the symptom onset. Dosing as follows: 1,600 mg/12h, on the first day, and then 600 mg/12h for 4 more days.

**Molnupiravir** – is also an antiviral of the new generation, a COVID specific treatment. It works by causing mistakes in the viral genetic code and thus prevents its replication. It’s recommended for patients with confirmed infection and at higher risk for the severe forms of the disease. It should also be taken within 5 days from the symptom onset. Tablets are 200mg and the recommended dosing is 800 mg/12h.

**Antibiotics** – play no role in COVID treatment, unless there is a bacterial superinfection. As far as we know now, it’s around 7%-8% in PHC patients. The confusion appeared with azithromycin in the treatment recommendations, at first (together with hydroxychloroquine) but the whole idea for its use was his immunomodulatory effect. Unfortunately, it didn’t produce a desirable effect in practice, so it was soon discontinued from the protocol. The statistics from our clinic show that at the beginning of 2020 about 50% of patients with the confirmed diagnosis of COVID got an antibiotic and 50% got symptomatic therapy. In October 2021, an antibiotic was prescribed to 65%, an antiviral to 9%, and symptomatic
Kortikosteroidi – u protokolima nisu predviđeni za lečenje u PZZ (tek od 13. protokola) ali nas je aktuelna situacija i preopterećenost bolnica naterala da ih i mi koristimo kod lečenja virusnih pneumonija, što je dalo odlične terapijske odgovore kod većine pacijenata. Treba naći pravo vreme za njihovo uvođenje (ne na početku bolesti da se ne suprimira imunološki odgovor, ali svakako u kasnijem stadiju kada se razvije pneumonija i dođe do pada saturacije)⁹. U praksi najčešće koristimo prednizon, jer preporučene doze deksametazona zahtevaju unos mnogo tableta (kod nas na tržištu su u dozi od 0.5 mg). Davati ih u jutarnjoj dozi, uz obaveznu gastroprotekciju. Polako smanjivati dozu ali ne prerano jer može doći do ponovnog skoka citokinima.

Simptomatska terapija – imamo mogućnost primene infuzione terapije, vitamina parenteralno, oksigenoterapije.

Zaključak

Primarna zdravstvena zaštita je dala veliki doprinos u lečenju pandemije i bila je brana ka sekundarnom i tercijar nom nivou zdravstvene zaštite. Kao i naše kolege u svetu, učili smo u hodu i taj proces traje i dalje. Čitav zdravstveni sistem i sada je izdržao pre svega zahvaljujući natčovečan skim naporima zdravstvenih radnika. Vakcinacija je spasila živote mnogih pacijenata, koji bez nje inače ne bi imali šansu. Ono što se može videti u COVID ambulantama je da vakcinisani pacijenti, čak i ako se zaraze, prodaju sa mnogo blažim kliničkim slikama i prežive. Prokužavanje većeg broja ljudi, bilo prirodnim zaražavanjem, bilo vakcinacijom, vremenom će dovesti do završetka pandemije, koja će verovatno postati sezonska infekcija, ali sa mnogo blažom kliničkom slikom.

therapy to 26% of patients. At the beginning of 2022 antibiotic prescription still remained at a high level of 64%, antivirals were given to 21%, and symptomatic therapy to 15% of patients. In the PHC setting we can’t order procalcitonin (informs of the possibility of the bacterial infection), so the prescription of an antibiotic is based on the clinical judgment, Le formula, and CRP value.

Corticosteroids – were not recommended for the treatment in the PHC (only since the 13th protocol) but the current situation and hospital overload made us use them, as well, in the treatment of viral pneumonia, which gave excellent results in the majority of patients. The timing for their introduction should be right (not at the beginning, in order not to suppress an immune response but surely later with the appearance of pneumonia and the drop in saturation)⁹. We mainly used prednisone because the recommended doses of dexamethasone require intake of a lot of tablets (in our market there is only a dose of 0.5 mg). They should be given in a single, morning dose, with gastroprotection. The dose should be tapered down slowly because there is a danger of a repeated cytokine increase.

Symptomatic therapy – we were able to give infusion therapy, parenteral vitamins, oxygen.

Conclusion

Primary healthcare made huge effort in the fight against pandemic and was a dam against the secondary and tertiary healthcare system. As our colleagues worldwide, we were learning in stride, and the process is ongoing. The entire health system is still standing, primarily thanks to the extreme effort of all health workers. Vaccination surely saved many patients’ lives, who would have no chance without it otherwise. We witnessed, in our clinic, that vaccinated patients, even if they got infected, had milder symptoms and they survived. The more people get exposed to the virus, either naturally or by vaccination, the sooner the pandemic will end but not entirely and probably stay with us as a seasonal infection with easier clinical presentation.
Reference/ Literatura

1. Grifoni A, Weiskopf D, Ramirez SI, Mateus J, Dan JM, Moderbacher CR, et al. Targets of T Cell Responses to SARS-CoV-2 Coronavirus in Humans with COVID-19 Disease and Unexposed Individuals. Cell [Internet]. 2020 Jun 25 [cited 2022 Jan 24];181(7):1489-1501.e15. Available from: https://pubmed.ncbi.nlm.nih.gov/32473127

2. Foster KJ, Jauregui E, Tajudeen B, Bishehsari F, Mahdavinia M. Smell loss is a prognostic factor for lower severity of coronavirus disease 2019. Ann Allergy, Asthma Immunol [Internet]. 2020 Oct 1 [cited 2022 Jan 24];125(4):481. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7305732/

3. Overview of Testing for SARS-CoV-2, the virus that causes COVID-19 | CDC [Internet]. [cited 2022 Jan 24]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing-overview.html

4. Tavakolpour S, Rakhshandehroo T, Wei EX, Rashidian M. Lymphopenia during the COVID-19 infection: What it shows and what can be learned. ImmunoLett [Internet]. 2020 Sep 1 [cited 2022 Jan 24];225:31. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7305732/

5. ACR Recommendations for the use of Chest Radiography and Computed Tomography (CT) for Suspected COVID-19 Infection | American College of Radiology [Internet]. [cited 2022 Jan 24]. Available from https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Recommendations-for-Chest-Radiography-and-CT-for-Suspected-COVID19-Infection

6. Manabe T, Kambayashi D, Akatsu H, Kudo K. Favipiravir for the treatment of patients with COVID-19: a systematic review and meta-analysis. BMC Infect Dis [Internet]. 2021 Dec 1 [cited 2022 Jan 24];21(1):1–13. Available from: https://bmcinfectdis.biomedcentral.com/articles/10.1186/s12879-021-06164-x

7. Molnupiravir dosing, indications, interactions, adverse effects, and more [Internet]. [cited 2022 Jan 24]. Available from: https://reference.medscape.com/drug/molnupiravir-4000252

8. COVID-19 & Antibiotic Resistance | CDC [Internet]. [cited 2022 Jan 27]. Available from:https://www.cdc.gov/drugresistance/covid19.html

9. Corticosteroids | COVID-19 Treatment Guidelines [Internet]. [cited 2022 Jan 24]. Available from:https://www.covid19treatmentguidelines.nih.gov/therapies/immunomodulators/corticosteroids/

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