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Research Article

The Use of Azithromycin and Paracetamol Therapy is Most Important for Faster Recovery of Patients with Coronavirus Disease (COVID-19)

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Abstract

In this research we analyzed the influence of using of azithromycin and paracetamol therapy for the recovery of patients with Coronavirus disease (COVID-19). 392 patients (male, 55.1%; mean, 64.2 years old) who had positive the chain reaction genetic test real-time with reverse transcriptase (rRT-PCR test) and who had at least three symptoms characteristic of patients with COVID-19 we were allocated in two groups. For eight days, investigated group of patients (patients who had pneumonia and at least two more symptoms characteristic of patients with COVID-19), 196 patients used azithromycin and paracetamol like a therapy for COVID-19. Control group of patients (patients who had fever like one of symptoms characteristic of patients with COVID-19 and at least two symptoms more), 196 patients took only paracetamol. After eight days of therapy, the rRT-PCR test was performed again on the ninth day for all patients from both of investigated groups. In our research exist statistically significant correlation between COVID-19 and using of azythromycin and paracetamol like a therapy for COVID-19 (x^2=2.312; p>0.05).

Keywords: *Coronavirus; Pneumonia; The Chain Reaction Genetic Test Real-Time With Reverse Transcriptase (Rrt-PCR Test); Therapy With Azithromycin And Paracetamol*

Introduction

Coronavirus disease (COVID-19) is new pandemic disease caused by severe Coronavirus acute respiratory syndrome (SARS-CoV-2). COVID-19 appeared in Hubei Province, in China, so is December 31, 2019 World Health the organization was the first to report cases of pneumonia of unknown origin in the city of Wuhan in humans which were associated with the use of products from the local animal and seafood markets. Infection soon followed spread to the whole world, so on March 11, 2020, it was proclaimed pandemic.

SARS-CoV-2 is a new, previously unknown strain of the virus a single, positive, unsegmented chain ribonucleic acid (RNK) which forms part of the helix nucleocapsids, size 30 thousand nucleotide pairs (kb). This virus is taxonomically classified into the SARS species related viruses (SARS-CoV), subgenus Sarbecovirus, genus Betacoronavirus, a subfamily of Orthocoronavirinae, family Coronaviridae, order Nidovirales [1]. it's over it is certain that SARS-CoV-2, as well as other similar viruses, of animal origin, but it is not yet clear which one it is type of primary source, whether and to what extent it occurred recombination of genetic material by passage through others animal species as well as how the virus transmitted to man. SARS-CoV-2 shows the highest degree of homology genetic sequences with one of the coronavirus blind mice and many consider this type of mammal to be primary tank. However, the mutual homology of these two viruses precisely in the sequence that determines the part of the protein that is binding to the receptor on human cells is significantly lower than expected. That is why some species of snakes and mammals proposed as probable intermediate hosts [2,3]. Pangolin coronavirus, a mam-

mal from the group of shellfish, Pangolin-CoV, in 91.02% of the sequence is completely homologous to in 5 amino acid sequences of a key part of the receptor identical to the SARS-CoV-2 virus, which is why this species most likely candidate for a transitional host [4]. Despite the fact that phylogenetic analyzes show that SARS-CoV-2 is genetic different from severe acute respiratory coronavirus syndrome (SARS-CoV) and respiratory coronavirus Middle East syndrome (MERS-CoV), which were previously were the cause of two epidemic waves in the world, comparative analyzes are necessary for better insight into biological ones characteristics and epidemiological and clinical aspects of new infection strain, primarily due to significant mutual similarities. A modeling study showed that these viruses have similar parts of receptors to which they bind to angiotensin converting enzyme 2 (ACE2) (SARS-CoV / SARS-CoV-2) or CD26 (MERS / SARS-CoV-2) [5,6].

Coronavirus disease (COVID-19) is caused by RNA virus of severe acute respiratory syndrome 2 (SARS-CoV-2) which is extremely contagious to humans,significantly more than SARS-CoV and MERS-CoV viruses. SARS-CoV-2 virus explain his far greater, pandemic potential. Estimated reproductive number (R0)), which indicates the number of healthy people who become infected from of one carrier SARS-CoV-2, is 2–2.5 [7].

The primary receptor for the virus is angiotensin-converting enzyme 2 (ACE2). The mean incubation time is 5.2 days, ranging 1-14 days. The most common symptoms are: fever, dry cough, malaise, productive sputum and dyspnea, followed, sore throat, headache, myalgia, arthralgia, fever and dizziness and, occasionally, confusion, rhinorrhea, nasal congestion, gastrointestinal symptoms, hemoptysis and conjunctival congestion [8-18].

The chain reaction genetic test real-time with reverse transcriptase (rRT-PCR) is “gold”diagnostic standard but specificity and sensitivity have not been definitely established.

The entry of SARS-CoV-2 into human cells is a complex process, which requires receptor interaction. Primary the receptor for the virus in humans is most likely ACE2, for when binds a special spike (S) protein of the viral envelope. This protein has two parts, S1 which determines the propensity of the virus to bind to receptors and cells of certain species and the S2 part that mediates the fusion of virions and target cell membranes. SARS-CoV-2 S glycoprotein before binding to ACE2 is degraded by human action of the proteolytic enzyme furin at the boundary between S1 and S2 subunits, by which this virus differs from SARS-CoV virus [9-12]. Functional consequence of proteolytic Degradation of the S protein SARS-CoV-2 is not known, but is considers it important in terms of increased portability and pathogenicity of this virus [23]. High density ACE2 exists in the lungs, heart, esophagus, kidneys, bladder, and distal part of the small intestine due to which it can be assumed that there is a tendency for the virus to bind to these organs [24]. Spike protein of SARS-CoV-2 virus has a special site for N- and O-linked glycosylation and its S part can affect the CD26 antigen human cells, which may further enhance virulence (8). Differences in genetic sequence and molecular pathways of infection of human cells with SARS-CoV-2 virus in compared to other related viruses, they are most likely biological basis of different epidemiological characteristics and clinical manifestations of COVID-19 relative to other related diseases such as severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS).

The most common complication is acute respiratory distress syndrome which occurs in15–29% of patients with COVID-19, and other complications were: acute liver damage (14–53%), acute damage heart (7–19.7%), arrhythmias (16%), secondary infections (6.1–10%), acute respiratory failure (8%), acute renal impairment (3–7%), sepsis and / or septic shock (2–8%), pneumothorax (2%), disseminated intravascular coagulation (1%), acute cardiac insufficiency (1%) and individual cases of rhabdomyolysis and thrombosis associated with the presence of antiphospholipids antibodies [25-35].

Disease duration varies and in hospitalized patients it is estimated to be 16-26 days (interquartile range 12-29 days), while the global mortality rate is still unknown with certainty. Drugs against SARS-CoV-2 prescribed by empirical protocols (off-label use) are lopinavir/ritonavir, chloroquine and hydroxychloroquine, nitazoxanide, umifenovir, ribavirin, inhaled interferon alpha while the new drugs of clinical trial stages are remdesivir, nafamostat and favipiravir. Proven drug prophylaxis of COVID-19 does not yet exist. Seven vaccines against SARS-CoV-2 were developed and their administration started two months ago.

Methods

In our study, we analyzed the effect of therapy on 392 patients with Corona virus (COVID-19) who had positive rRT-PCR test and who had at least three symptoms characteristic of patients with COVID-19: fever, dry cough, malaise, sputum expectoration, dyspnea, sore throat, headache, myalgia and arthralgia, fever, dizziness, confusion, rhinorrhea, nasal congestion, gastrointestinal symptoms such as nausea, vomiting and diarrhea, haemoptysis or conjunctival congestion. Our patients we investigated at the Department of General Surgery in Belgrade in the period from 1st April 2020 to 31st December 2020. Every patient took his therapy in period of eight days at home. We organized our research like a prospective study. Investigated patients were divided in two groups. In first group were patients who had positive rRT-PCR test and who had pneumonia (diagnosis of pneumonia was made by computed tomography of the lungs-CT) and at least two more symptoms characteristic of COVID -19 patients. In that group 196 patients like a therapy took azithromycin and paracetamol. They took one 500 mg of athromycin twice a day on the first day, then one tablet each day. During the study, patients from this group also took one 500 mg tablet of paracetamol each day. Second grou p is a control group of 196 patients who had positive rRT-PCR test and who had fever and at least two more sympto ms characteristic of COVID-19 patients. They used only one 500 mg tablet of paracetamol every day. In all patients, after eight days of therapy, the rRT-PCR test w as performed again on the ninth day. In our investigation stati stical sample size is determined by the statistical methodology to meet the basic principle of representativeness. In our study, results are presented in graphics. For statisti cal analysis in our paper we used parametric tests (Student's t-te st) and nonparametric Chi-square test. In statistical an alysis we took the software package SPSS 14.0, and the imagin g table and a Microsoft Office Word 2007.

Results

Of the 392 patients examined, 196 took azithromycin and paracetamol like a therapy for COVID-19 or 50.0% and 196 patients took only paracetamol like a therapy for COVID-19. In our study ex ist statistically significant correlation between COVID-19 and using of azithromycin and paracetamol like a therapy for COVID-19 ($x^2 = 2.312$; $p > 0.05$). 2 patients or 1.1% from all patients who took azithromycin and paracetamol and eight days after that therapy had positive rRT-PCR test. 194 patients with azithromycin and paracetamol the rapy did not have positive rRT-PCR test after eight days of th erapy or 98.9% patients. 178 patients who took only paracetamol, had positive rRT-PCR test and eight days after t herapy with paracetamol every evening in eight days or 90.8% patients and 18 patients with paracetamol therapy d id not have positive rRT-PCR test on the ninth day after therapy or 9.2% patients (Figure 1).

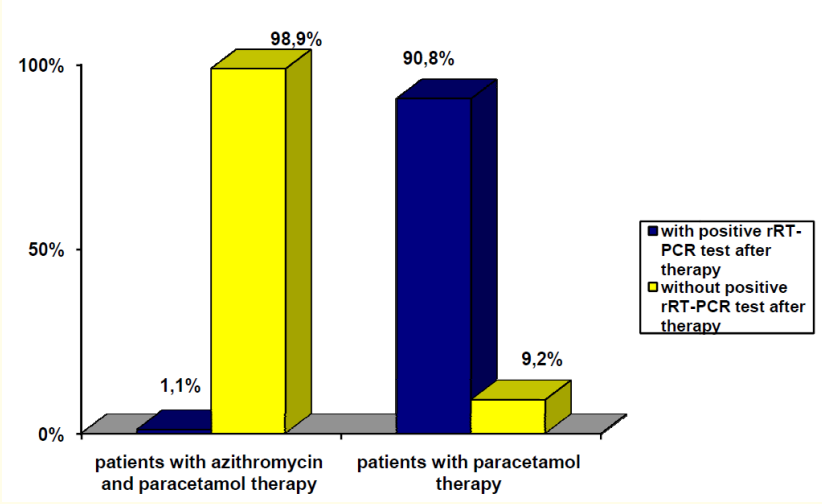

Figure 1: The impact of using of azithromycin and paracetamol therapy on the faster recovery of patients with Coronavirus disease (COVID-19).

Discussion

Coronavirus disease (COVID-19) is a respiratory infection, primarily transmitted by droplets and close contact with a diseased person.

The most common symptoms of COVID-19 are elevated body temperature (in 83 - 95% of patients), dry cough (57 - 82%), malaise (29 - 69%), expectoration of sputum (26 - 33%), dyspnea (18 - 55%), sore throat (5 - 17%), heada che (13.6%), myalgia and arthralgia (14.8%), fever (11.4%), dizziness (9 - 12%), confusion (9%), rhinorrhea (4 - 5%), nasal congestion (4.8%), gastrointestinal symptoms such as nausea, vomiting and diarrhea (1 - 10%), hemo ptysis (1- 5%) and conjunctival congestion (0.8%) [8-18]. Fever can occur after a pattern of continuous or intermittent flow, with fever or without it, the cough is usually unproductive, chest pain may suggest the presence of pneumonia while gastrointestinal symptoms may precede a day or two fever and dyspnoea. In our study we had 361(92.1%) patients with elevated body temperature, 265 (67.6%) patients with dry cough, 127 (32.4%) patients with expectoration of sputum, 172 (43.9%) patients with dyspnea and 43 (14.3%) patients with sore throat. Comparing the percentages of symptoms onset in the examined patients in the previously mentioned world studies with the percentages of onset of symptoms in patients in our prospective study, we conclude that the results are very similar.

Leather manifestations have not been sufficiently investigated, but in one group patients with erythematous rash (15.9%), generalized urticaria (3.4%) and vesicular rash (1.1%) [36].

In our study exist statistically significant correlation between COVID-19 and using of azithromycin and paracetamol like a therapy for COVID-19 (x^2=2.312; p>0.05). 194 (98.9%) patients from group of 196 investigated patients with azithromycin and paracetamol therapy did not have positive rRT-PCR test after eight days of therapy.

Azithromycin is an antibiotic medication used for the treatment of a number of bacterial infections. This includes middle ear infections, strep throat, pneumonia, traveler's diarrhea, and certain other intestinal infections.

Azithromycin has relatively broad but shallow antibacterial activity. It inhibits some Gram-positive bacteria, some

Gram-negative bacteria, and many atypical bacteria.

Paracetamol, also known as acetaminophen, is a medication used to treat pain and fever.

Very common complications are secondary infections that occur in 6.1-10% of patients with COVID'-19 [25-35]. After azithromycin and paracetamol therapy in our research 98.9% patients did not have positive rRT-PCR test after eight days of therapy which is much more than 10% of patients who develop a secondary infections as reported by the aforementioned world studies.

The mechanism of action has not been fully elucidated, but the use of azithromycin and paracetamol therapy is definitely very important for faster recovery of patients with corona virus (COVID-19).

Conclusion

Our research has shown that the use of azithromycin and paracetamol therapy can affect the faster recovery of patients with coronavirus disease (COVID-19). Azithromycin and paracetamol therapy is a simple and inexpensive treatment.

The spread of COVAID-19 infection throughout the world has begun numerous re-examinations, not only from the aspect of medical science and practice, but also from the socio-cultural and all other aspects. New knowledge from our research and experience gained in our practice should be a basic guide for the future.

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