IAI SPECIAL EDITION

RESEARCH ARTICLE



Drug therapy for COVID-19 inpatients in West Nusa Tenggara hospital

Mahacita Andanalusia, Shah Iqbal Ikraman Akbar, Anna Pradiningsih Faculty of Health Science, Universitas Muhammadiyah Mataram, West Nusa Tenggara, Indonesia

Keywords COVID-19 Hospital

Hospital Inpatient Therapy

Correspondence

Anna Pradiningsih Department of Clinical and Community Pharmacy Faculty of Health Science Universitas Muhammadiyah Mataram West Nusa Tenggara Indonesia annapradiningsih@gmail.com

Abstract

Background: COVID-19 represents an unprecedented challenge to the world. Various attempts have been made to overcome COVID-19, including employing multiple drug therapies. Objective: This study was conducted to describe the drug therapy of COVID-19 inpatients at the West Nusa Tenggara Hospital in 2020. Methods: Observation of 102 patients was conducted retrospectively. Data collection was performed by analysing medical records. Results: A total of 62 out of the 102 patients (60.8%) were hospitalised more than four weeks. 57 patients (55.9%) received antivirus therapy with Oseltamivir and 47 patients (46.1%) recieved azithromycin as adjuvant antibiotic therapy. Most of the patients (63.7%) received vitamin C as an immunomodulator. A small number of patients received other supportive therapies recommended to decrease the symptoms of COVID-19. The most frequent administered therapies for COVID-19 patients hospitalised at the West Nusa Tenggara Hospital are antivirals, antibiotics, and immunomodulators. Conclusion: The findings provide an overview of therapy use for COVID-19 inpatients in West Nusa Tenggara Hospital. There is a need to assess the effectiveness of the therapy to promote safe and effective use of drugs for COVID-19 patients in the future.

Introduction

The World Health Organization (WHO) explained that the global prevalence of COVID-19 in August 2021 had exceeded 209 million people. In Indonesia, COVID-19 cases had reached almost four million (WHO, 2021). More than 24,000 cases in Indonesia came from West Nusa Tenggara (Diskominfotik NTB, 2021).

Vaccination is one of the preventive actions for stopping virus transmission. In Indonesia, the COVID-19 vaccination programme began gradually from January 2021. Whilst the vaccination programme is still in progress, therapeutic interventions have been provided to COVID-19 patients. Even today, however, there is still no specific drug specifically for treating COVID-19. Pharmacology therapies employed consist of antivirals and adjuvant therapy, such as antibiotics, anticoagulants, bronchodilators, analgesics, mucolytic, corticosteroids, immunomodulators, and NSAIDs (BPOM, 2020; Smith *et al.*, 2020). There is no drug interaction found among the recommendations. The

objective of this study is to provide an overview of the therapies used on COVID-19 patients at West Nusa Tenggara hospital in 2020.

Methods

This study was conducted by obtaining data from the electronic medical records (SIRS) of COVID-19 patients hospitalised in West Nusa Tenggara Hospital in 2020. A total of 102 patients from a total sample size of 838 patients were randomly selected. All patients who were diagnosed with COVID-19 and hospitalised in West Nusa Tenggara Hospital were included in the study. Patients employing herbal therapies and passing away were excluded from this study. This research has received ethical approval from the Research Ethics Committee in West Nusa Tenggara Hospital (No. 070.1/15/KEP/2021). Patient therapy data is categorised into antivirals, antibiotics, immunomodulators, anticoagulants, bronchodilators,

analgesics, mucolytics, corticosteroids, and Non-steroidal anti-inflammatory drugs (NSAIDs).

Result

The characteristics of the patients are displayed in Table I. Of the 102 patients, 56.9% were men, 42.2% were in productive age (22-45 years), and 60.8% were hospitalised for more than 4 weeks. Table II presents the drug therapy description employed during hospitalisation. Commonly used therapies were antivirals, antibiotics, and immunomodulators. 55.9% of patients were administered oseltamivir as an antiviral, 46.1% of patients were given azithromycin as an antibiotic, and 63.7% of patients were administered vitamin C as an immunomodulator. The remaining therapies utilised for COVID-19 patients, aside from antivirals, antibiotics, and immunomodulators, consisted of mucolytics, analgesics, corticosteroids, bronchodilators, NSAIDs, and anticoagulants. Out of all the patients, 36.3% of patients had received acetylcysteine, 22.5% were given paracetamol, 6.9% were administered methylprednisolone, 3.9% were given ketorolac, 3.9% were given MDI (salbutamol and ipratropium bromide), and 2.9% were treated with enoxaparin sodium.

Table I: Patients' characteristics

Characteristics n (%)		n (%)
Sex		
	Male	58 (56.9%)
	Female	44 (43.1%)
Age		
	0-4	1 (1.0%)
	5-11	2 (2.0%)
	12-25	24 (23.5 %)
	25-45	43 (42.2%)
	>45	32 (31.4%)
Lengt	h of stay	
	0-7 days	14 (13.7%)
	8-14 days	19 (18.6%)
	15-21 days	4 (3.9%)
	22-28 days	3 (2.9%)
	>28 days	62 (60.8%)

Therapy	n (%)
Antivirals	
None	39 (38.2%)
Oseltamivir	57 (55.9%)
Chloroquin	1 (1.0%)
Oseltamivir + Chloroquin	4 (3.9%)
Remdesivir	1 (1.0%)
Antibiotics	
None	39 (38.2%)
Azithromycin	47 (46.1%)
Levofloxacin	10 (9.8%)
Meropenem + Levofloxacin	1 (1.0 %)

herapy	n (%)
Azithromycin + Levofloxacin	3 (2.9%)
Azithromycin + Levofloxacin +	2 (2.0%)
Meropenem	
nmunomodulators	
None	27 (26.5%)
Vitamin C	65 (63.7%)
Vitamin B Complex	3 (2.9%)
Vitamin C + Vitamin B Complex	5 (4.9%)
Vitamin C + Vitamin B12	1 (1.0%)
Vitamin C + B Complex + D	1 (1.0%)
lucolytics	. ,
None	64 (62.7%)
Acetylcysteine	37 (36.3%)
Ambroxol	1 (1.0%)
nalgesics-antipyretics	= (=:570)
None	79 (77.5%)
Paracetamol	23 (22.5%)
orticosteroids	(22.370)
None	89 (87.3%)
Hydrocortison	1 (1.0%)
Methyl prednisolone	7 (6.9%)
Dexamethasone	2 (2.0%)
Dexamethasone + Budenisone	2 (2.0%) 1 (1.0%)
Dexamethasone + Methyl	1 (1.0%)
prednisolone	1 (1.0%)
Dexoximethasone + Methyl	I (I.U/0)
prednisolone	
SAIDs	
None	91 (89.2%)
Ketorolac	4 (3.9%)
Mitamizole	3 (2.9%)
Aspirin	1 (1.0%)
Ketorolac + Metamizole	1 (1.0%)
Ketoprofen + Metamizole	1 (1.0%)
Mefenamin acid + Ketorolac +	1 (1.0%)
Ibuprofen + Metamizole	± (1.070)
onchodilators	
None	94 (92.2%)
Salbutamol	3 (2.9%)
Salbutamol+Ipratropium	4 (3.9%)
Bromide	4 (3.9%) 1 (1.0%)
Terbutaline	I (I.U/0)
nticoagulants	
None	95 (93.1%)
Enoxaparin Sodium	3 (2.9%)
Enoxaparin Sodium Enoxaparin Sodium + Heparin	3 (2.9%) 2 (2.0%)
Heparin Heparin	. ,
перанн	1 (1.0%)
Fondaparinux + Enoxaparin	1 (1.0%)

Discussions

The study discovered that the patients were overwhelmingly men. It is likely because the immune response in men is genetically lower than in women (Pivonello *et al.*, 2020). Besides, age is also an essential factor in the infection of COVID-19 . Most elderly patients possess a greater risk of infection (Bonanad *et al.*, 2020). However, in this study, COVID-19 cases were more common at productive age. This happens because the mobility of people in this age is higher; thus, the risk of physical contact with others is also greater. The length of hospitalisation for the majority of patients might be caused by comorbidities, as it can be the factor prolonging the length of hospitalisation (Id *et al.*, 2020).

The results presented most patients received oseltamivir as the antiviral. Oseltamivir is originally a treatment and therapy for influenza types A and B (Zhang & Yap, 2004). The administration of oseltamivir was considered effective in fighting against COVID-19 infection, although this therapy has limited evidence for SARS-CoV-2. In its development, oseltamivir is considered unable to treat SARS-CoV-2 (Tan *et al.*, 2020). However, one study showed that the use of oseltamivir, if combined with hydroxychloroquine, was the most effective antiviral based on the duration of treatment (Ramatillah & Isnaini, 2021). Currently, there is a study conducted to assess the effectiveness of all potential antiviral that has been registered in ClinicalTrials.gov (NCT04303299).

Azithromycin is a therapy used to treat upper respiratory pathogenic bacteria possessing the potential to provide secondary infections. In most patients with suspected or confirmed COVID-19 infection, lung damage is associated with the severity of viral infections. Hence, this therapy is extensively employed for patients with COVID-19 (Donsu & Hasmono, 2020). Although the WHO does not include azithromycin as the main therapy in the treatment of COVID-19, several hospitals still administer this antibiotic due to some of the benefits, such as the low arrhythmogenic potential compared to other macrolide groups (Sultana *et al.*, 2020).

Previous studies on COVID-19 immunomodulators revealed that high doses of vitamin C reduce the levels of the proinflammatory cytokine (Mira *et al.*, 2021). As a result, the symptoms of infection are decreased. For this reason, vitamin C was extensively used for COVID-19 patients in this study. However, another study has shown inconsistent results for the efficacy of vitamin C as an immunomodulator. A study by Thomas and colleagues showed that there was no significant improvement in symptoms duration among COVID-19 patients with vitamin C (Thomas *et al.*, 2021).

Furthermore, there were some other additional therapies recommended to reduce symptoms caused by COVID-19 (BPOM, 2020). Paracetamol and acetyl-cysteine were recommended by the Indonesian National Agency of Drug and Food Control (BPOM) to reduce the symptoms of analgesic-antipyretic and mucolytic, respectively. The use of methylprednisolone is supported by previous studies, in which it has been shown to shorten the hospitalisation time of COVID-19 patients with severe pneumonia (Pinzón *et al.*, 2021). The administration of ketorolac was in line with a previous study presenting beneficence in COVID-19

infection (Maruta & He, 2020). The previous publication explained that the use of MDI as bronchodilators is more likeable to treat COVID-19 patients with asthma and COPD since it is able to decrease viral transmission (Smith *et al.*, 2020). The use of enoxaparin sodium was supported by another study, where the administration of heparin to COVID-19 inpatients was required since COVID-19 has a high risk of thrombosis (Susen *et al.*, 2020).

The main limitation of this study is the use of retrospective data to describe the drug therapy profile when there was some missing data, such as comorbidities and therapy regimens. Thus, the findings could not be used to detect the presence of drug-related problems. Nonetheless, the findings can suggest the need to improve the practice. Future research should be directed toward the assessment of COVID-19 therapy effectiveness.

Conclusions

The findings provide an overview of therapy used for COVID-19 inpatients in West Nusa Tenggara Hospital. The most common administered therapies for COVID-19 inpatients in West Nusa Tenggara Hospitals were antivirals, antibiotics, and immunomodulators. Assessment of the effectiveness of the antivirals, antibiotics, and immunomodulators as COVID-19 therapy is needed to promote safe and effective drugs in the future.

Acknowledgement

The authors would like to thank the Research Institute and Community Service of Universitas Muhammadiyah Mataram for the funding research and also to West Nusa Tenggara Hospital for technical assistance.

References

Bonanad, C., García-blas, S., Tarazona-santabalbina, F., Sanchis, J., Bertomeu-gonzález, V., Fácila, L., Ariza, A., Núñez, J., & Cordero, A. (2020). The Effect of Age on Mortality in Patients With COVID-19 : A Meta-Analysis With 611 , 583 Subjects. *Journal of the American Medical Directors Association*, **21**(7), 915–918. https://doi.org/10.1016/j.jamda.2020.05.045

DISKOMINFOTIK NTB. (2021). Data COVID-19 NTB (online). Available from: https://corona.ntbprov.go.id/

Donsu, Y.C., & Hasmono, D. (2020). Tinjauan Azitromisin Pada Penyakit Virus Korona 2019 (COVID-19) Review of Azithromycin for Coronavirus Disease 2019 (COVID-19). PHARMACON Jurnal Ilmiah Farmasi, **17(**2), 133–147

Id, S. W., Xue, L., Legido-quigley, H., Khan, M., & Wu, H. (2020). Understanding factors influencing the length of hospital stay among non-severe COVID-19 patients : A retrospective cohort study in a Fangcang shelter hospital. 1– 14. https://doi.org/10.1371/journal.pone.0240959

Maruta, H., & He, H. (2020). PAK1-blockers: Potential Therapeutics against COVID-19. *Medicine in Drug Discovery*, **6**, 100039. https://doi.org/10.1016/j.medidd.2020.100039

Mira, A., Dewi, C., Dagradi, E.M., & Wibowo, P. (2021). The effect of high dose vitamin c (ascorbic acid) on proinflammatory cytokines in COVID-19, **5**(01), 46–50.

Pinzón, M.A., Ortiz, S., Holguín, H., Betancur, J.F., Arango, D.C., Laniado, H., Arias, C.A., Munõz, B., Quiceno, J., Jaramillo, D., & Ramirez, Z. (2021). Dexamethasone vs methylprednisolone high dose for Covid-19 pneumonia. *PLoS ONE*, **16**(5 May), 1–13. https://doi.org/10.1371/journal.pone.0252057

Pivonello, R., Auriemma, S., & Pivonello, C. (2020). Sex Disparities in COVID-19 Severity and Outcome : Are Men Weaker or Women Stronger ? *Neuroendocrinology*, 1–20. https://doi.org/10.1159/000513346

Ramatillah, D.L. & Isnaini, S. (2021) Treatment profiles and clinical outcomes of COVID-19 patients at private hospital in Jakarta, *PLoS ONE*, **16**(4 April), 1–11. https://doi.org/10.1371/journal.pone.0250147

Smith, T., Bushek, J., & Prosser, T. (2020). COVID-19 Drug Therapy Highlights : Antimicrobials with potential activity against SARS-CoV-2 : Clinical Drug Information, Cdc, 1–21 Sultana, J., Maria, P., Salvatore, C., Gabriele, C., Gaetano, P., & Trifirò, G. (2020). Azithromycin in COVID - 19 Patients : Pharmacological Mechanism , Clinical Evidence and Prescribing Guidelines. *Drug Safety*, https://doi.org/10.1007/s40264-020-00976-7

Susen, S., Susen, S., Tacquard, C.A., Godon, A., Mansour, A., Garrigue, D., Nguyen, P., Godier, A., Testa, S., Levy, J.H., Albaladejo, P., & Gruel, Y. (2020). Prevention of thrombotic risk in hospitalised patients with COVID-19 and hemostasis monitoring. *Critical Care*, **24**(1), 1–8. https://doi.org/10.1186/s13054-020-03000-7

Tan, Q., Duan, L., Ma, Y., Wu, F., Huang, Q., Mao, K., Xiao, W., Xia, H., Zhang, S., Zhou, E., Ma, P., Song, S., Li, Y., Zhao, Z., Sun, Y., Li, Z., & Geng, W. (2020). Is oseltamivir suitable for fighting against COVID-19 : In silico assessment, in vitro and retrospective study. *Bioorganic Chemistry*, **104**(104257)

Thomas, S., Patel, D., Bittel, B., Wolski, K., Wang, Q., Kumar, A., Il'Giovine, Z.J., Mehra, R., McWilliams, C., Nissen, S.E., & Desai, M.Y. (2021). Effect of High-Dose Zinc and Ascorbic Acid Supplementation vs Usual Care on Symptom Length and Reduction among Ambulatory Patients with SARS-CoV-2 Infection: The COVID A to Z Randomized Clinical Trial. *JAMA Network Open*, **4**(2), 1–10. https://doi.org/10.1001/jamanetworkopen.2021.0369

WHO (World Health Organization) (2021). WHO Coronavirus Disease (COVID-19) Dashboard (online). Available at: COVID-19 .who.int

Zhang, X.W., & Yap, Y. L. (2004). The 3D structure analysis of SARS-CoV S1 protein reveals a link to influenza virus neuraminidase and implications for drug and antibody discovery. *Journal of Molecular Structure (Theochem)*, **681**, 137–141. https://doi.org/10.1016/j.theochem.2004.04.065