

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

Berdasarkan sepuluh artikel ilmiah terkait efektivitas dan efek samping deksametason pada pengobatan COVID-19 gejala berat hingga kritis dapat disimpulkan bahwa:

1. Dua artikel menunjukkan bahwa deksametason menurunkan kadar CRP, dan dua artikel lainnya menunjukkan metilprednisolon lebih efektif dibandingkan deksametason dalam menurunkan kadar CRP pada pasien COVID-19 gejala berat hingga kritis.
2. Tiga artikel menunjukkan bahwa deksametason efektif menurunkan frekuensi penggunaan ventilasi mekanis invasif dan tiga artikel lainnya melaporkan deksametason kurang efektif menurunkan kebutuhan akan ventilasi mekanis invasif pada pasien COVID-19 gejala berat hingga kritis.
3. Dua artikel melaporkan adanya kejadian efek samping hiperglikemia yang lebih tinggi pada kelompok deksametason, dan satu artikel lainnya menunjukkan tidak ada perbedaan yang signifikan pada frekuensi penggunaan insulin karena hiperglikemia.
4. Dua artikel yang melaporkan bahwa tidak ada perbedaan yang signifikan dari efek samping infeksi bakteri, dan satu artikel tidak melaporkan adanya efek samping infeksi bakteri.

5.2 Saran

1. Perlu ditambah artikel penelitian yang baru, sehingga dapat memperkuat bukti dan mendapatkan gambaran yang lebih lengkap

mengenai efektivitas dan efek samping yang ditimbulkan akibat penggunaan obat.

2. Perlu dilakukan kajian lebih lanjut mengenai dosis deksametason pada pasien COVID-19 gejala berat hingga kritis, mengingat dosis pada beberapa artikel dalam penelitian ini masih bervariasi.

DAFTAR PUSTAKA

- Abdelmannan, D., Tahboub, R., Genuth, S. and Ismail-Beigi, F. 2010, Effect of dexamethasone on oral glucose tolerance in healthy adult, *Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, **16(5)**: 770–777.
- Abdullah, S. 2015, Efficient searching strategies in pubmed, *Pakistan Oral & Dental Journal*, **35(2)**: 346-350.
- Abebe, E.C., Dejenie, T.A., Shiferaw, M.Y. and Malik, T. 2020, The newly emerged COVID-19 disease: A systemic review, *Virology Journal*, **17(1)**:1-8.
- Agarwal, K.M., Mohapatra, S., Sharma, P., Sharma, S., Bhatia, D. and Mishra, A. 2020, Study and overview of the novel coronavirus disease (COVID-19), *Sensors International*, **1**: 1-14.
- Ahmed, M.H. and Hassan, A. 2020, Dexamethasone for the treatment of Coronavirus Disease (COVID-19): a Review, *SN Comprehensive Clinical Medicine*, **2(12)**:2637-2646.
- Alessi, J., de Oliveira, G.B., Schaan, B.D. and Telo, G.H. 2020, Dexamethasone in the era of COVID-19: Friend or foe? An essay on the effects of dexamethasone and the potential risks of its inadvertent use in patients with diabetes, *Diabetology & Metabolic Syndrome*, **12(1)**: 1-11.
- Al-Harbi, N.O., Imam, F., Al-Harbi, M.M., Ansari, M.A., Zoheir, K.M., Korashy, H.M., Sayed-Ahmed, M.M., Attia, S.M., Shabanah, O.A. and Ahmad, S.F. 2016, Dexamethasone attenuates LPS-induced acute lung injury through inhibition of NF- κ B, COX-2, and pro-inflammatory mediators, *Immunological Investigations*, **45(4)**: 349-369.
- Ali, B.H. and Hamza, A.A. 2022, Effect of dexamethasone in two different doses on specific biochemical markers in patients with COVID-19, *Journal of Emergency Medicine, Trauma & Acute Care*, **4(2)**: 1-6.
- Ali, N. 2020, Elevated level of C-reactive protein may be an early marker to predict risk for severity of COVID-19, *Journal of Medical Virology*, **92(11)**: 2409-2411.

- AlQahtani, H., AlBilal, S., Mahmoud, E., Aldibasi, O., Alharbi, A., Shamas, N., Alsaedy, A., Owaidah, K., Alqahtani, F.Y., Aleanizy, F.S., Arishi, H., Baharoon, S. and Bosaeed, M. 2022, Outcomes associated with tocilizumab with or without corticosteroid versus dexamethasone for treatment of patients with severe to critical COVID-19 pneumonia, *Journal of Infection and Public Health*, **15(1)**: 36-41.
- Aslam, J., Masroor, M., Ahmad, S., Hussain, W., Mansoor, H. and Khan, L. 2021, Efficacy of methylprednisolone with dexamethasone in patients with severe covid pneumonia in term of clinical and biochemical improvement, *Pakistan Journal of Medical and Health Sciences*, **15(10)**: 2635-2636.
- Azer, S.A. 2020, COVID-19: Pathophysiology, diagnosis, complications and investigational therapeutics, *New Microbes and New Infections*, **37(C)**: 1-8.
- Azmi, N.U., Puteri, M.U. and Lukmanto, D. 2020, Cytokine storm in COVID-19: an overview, mechanism, treatment strategies, and stem cell therapy perspective, *Pharmaceutical Sciences and Research (PSR)*, **7**: 1-11.
- Badan Pengawas Obat dan Makanan. 2020, *Informatorium obat COVID-19 di Indonesia*, Jakarta: Badan Pengawas Obat dan Makanan.
- Berhandus, C., Ongkowijaya, J.A. dan Pandelaki, K. 2021, Hubungan kadar vitamin D dan kadar *C-reactive protein* dengan klinis pasien *coronavirus disease* 2019, *e-clinic*, **9(2)**: 370-378.
- Blunt, C.J. 2015, 'Hierarchies of evidence in evidence-based medicine', *Thesis*, Doctor of Philosophy, London School of Economics and Political Science, London.
- Brooks, D., Schulman-Rosenbaum, R., Griff, M., Lester, J. and Low Wang, C.C. 2022, Glucocorticoid-induced hyperglycemia including dexamethasone-associated hyperglycemia in COVID-19 infection: a systematic review, *Endocrine Practice: Official Journal of the American College of Endocrinology and the American Association of Clinical Endocrinologists*, **28(11)**: 1166–1177.
- Brosnahan, S.B., Jonkman, A.H., Kugler, M.C., Munger, J.S. and Kaufman, D.A. 2020, COVID-19 and respiratory system disorders: Current knowledge, *future clinical and translational research questions*,

- Arteriosclerosis, Thrombosis, and Vascular biology*, **40(11)**: 2586-2597.
- Brunton, L.L., Chabner, B.A. and Knollmann, B.C. (eds). 2011, *Goodman & Gilman's The Pharmacological Basic of Therapeutics* 12th Edition, MC Graw Hill, New York.
- Canese, K., and Weis, S. 2013, 'PubMed: The Bibliographic Database', in *The NCBI Handbook*, 2nd edition.
- Chisholm-Burns M.A., Schwinghammer T.L., Wells B.G., Malone P.M., Kolesar J.M. and Dipiro J.T. 2016, *Pharmacotherapy Principles and Practice*, McGraw-Hill Companies, New York.
- COVID-19 Treatment Guidelines Panel. 2021, Coronavirus Disease 2019 (COVID-19) *Treatment Guidelines*, National Institutes of Health. Diakses pada 29 September 2021, <https://www.covid19treatmentguidelines.nih.gov/>.
- Cui, Z., Merritt, Z., Assa, A., Mustehsan, H., Chung, E., Liu, S., Kumthekar, A., Ayesha, B., McCort, M., Palaiodimos, L., Baron, S., Averbukh, Y., Southern, W. and Arora, S. 2021, Early and significant reduction in c-reactive protein levels after corticosteroid therapy is associated with reduced mortality in patients with COVID-19, *Journal of Hospital Medicine*, **16(3)**: 142-148.
- Di Gennaro, F., Pizzol, D., Marotta, C., Antunes, M., Racalbuto, V., Veronese, N. and Smith, L. 2020, Coronavirus diseases (COVID-19) current status and future perspectives: A narrative review, *International Journal of Environmental Research and Public Health*, **17(8)**: 1-11.
- Erlangga, M.E., Sitanggang, R.H. dan Bisri, T. 2015, Perbandingan pemberian deksametason 10 mg dengan 15 mg intravena sebagai adjuvan analgetik terhadap skala nyeri pascabedah pada pasien yang dilakukan radikal mastektomi termodifikasi, *Jurnal Anestesi Perioperatif*, **3(3)**: 146-154.
- Fatima, S.A., Asif, M., Khan, K.A., Siddique, N. and Khan, A.Z. 2020, Comparison of efficacy of dexamethasone and methylprednisolone in moderate to severe COVID 19 disease, *Annals of Medicine and Surgery*, **60**: 413-416.

- Fatoni, A.Z. dan Rakhmatullah, R. 2021, *Acute respiratory distress syndrome (ARDS) pada pneumonia COVID-19*, *Journal of Anaesthesia and Pain*, **2(1)**: 11-24.
- Fiorini, N., Lipman, D.K. and Lu, Z. 2017, Towards PubMed 2.0, *e Life*, **6**: 1-4.
- Fitriani, N.I. 2020, Tinjauan pustaka COVID-19: virologi, patogenesis, dan manifestasi klinis, *Jurnal Medika Malahayati*, **4(3)**: 194-201.
- Goodman, L.S. and Gilman, A. 1970, *The Pharmacological Basis of Therapeutics* 4th edition, The McGraw-Hill, New York.
- Gunawan, S.G., Setiabudy, R., Nafrialdi. dan Instiaty. (eds). 2016, *Farmakologi dan Terapi Edisi 6*, Badan Penerbit FKUI, Jakarta.
- Hilberg, R.E. and Johnson, D.C. 1997, Noninvasive Ventilation, *The New England Journal of Medicine*, **337(24)**: 1746-1752.
- Horby, P., Lim, W.S., Emberson, J.R., Mafham, M., Bell, J.L., Linsell, L., Staplin, N., Brightling, C., Ustianowski, A., Elmahi, E., Prudon, B., Green, C., Felton, T., Chadwick, D., Rege, K., Fegan, C., Chappell, L. C., Faust, S.N., Jaki, T., Jeffery, K., Montgomery, A., Rowan, K., Juszczak, E., Baillie, K., Haynes, R. and Landray, M.J. 2020, Dexamethasone in hospitalized patients with Covid-19–Preliminary Report, *The New England Journal of Medicine*, **384(8)**: 693-704.
- Jamaati, H., Hashemian, S. M., Farzanegan, B., Malekmohammad, M., Tabarsi, P., Marjani, M., Moniri, A., Abtahian, Z., Haseli, S., Mortaz, E., Dastan, A., Mohamadnia, A., Vahedi, A., Monjazebi, F., Yassari, F., Fadaeizadeh, L., Saffaei, A. and Dastan, F. 2021, No clinical benefit of high dose corticosteroid administration in patients with COVID-19: A preliminary report of a randomized clinical trial, *European Journal of Pharmacology*, **(897)**: 1-5.
- Karch, A.M. 2011, *Buku Ajar Farmakologi Keperawatan Edisi 2*, Penerbit Buku Kedokteran EGC, Jakarta.
- Kementerian Kesehatan RI. 2020, *Pedoman Pencegahan dan Pengendalian Coronavirus Disease (COVID-19)*, Jakarta: Kementerian Kesehatan RI.
- Klein NC., Go CH. and Cunha BA. 2001, Infections associated with steroid use, *Infectious Disease Clinics of North America*, **15(2)**: 423-432.

- Lemke, T.L., Williams., Roche, V.F. and Zito, S.W. (eds). 2013, *Foye's Principles of Medicinal Chemistry Seventh Edition*, Baltimore : Lippincott Williams and Wilkins, Philadelphia.
- Miftakurohmah, D. 2021, 'Studi efektivitas dan efek samping terapi kombinasi oseltamivir dan klorokuin pada pasien COVID-19 di Rumah Sakit Bhayangkara Surabaya', *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.
- Montazersaheb, S., Hosseiniyan Khatibi, S. M., Hejazi, M. S., Tarhriz, V., Farjami, A., Ghasemian Sorbeni, F., Farahzadi, R. and Ghasemnejad, T. 2022, COVID-19 infection: An overview on cytokine storm and related interventions, *Virology Journal*, **19(1)**: 1-15.
- Monteverde-Fernández, N., Cristiani, F., McArthur, J. and González-Dambrasukas, S. 2019, Steroids in pediatric acute respiratory distress syndrome, *Annals of Translational Medicine*, **7(19)**: 1-11.
- Mora-Luján, J. M., Tuells, M., Montero, A., Formiga, F., Homs, N. A., Albà-Albalade, J., Corbella, X. and Rubio-Rivas, M. 2021, High-dose methylprednisolone pulses for 3 days vs. low-dose dexamethasone for 10 days in severe, non-critical COVID-19: A retrospective propensity score matched analysis, *Journal of Clinical Medicine*, **10(19)**: 1-12.
- Munch, M.W., Myatra, S.N., Vijayaraghavan, B.K.T., Saseedharan, S., Benfield, T., Wahlin, R.R., Rasmussen, B.S., Andreasen, A.S., Poulsen, L.M., Cioccarl, L., Khan, M.S., Kapadia, F., Divatia, J.V., Brøchner, A.C., Bestle, M.H., Helleberg, M., Michelsen, J., Padmanaban, A., Bose, N., ... Perner, A. 2021, Effect of 12 mg vs 6 mg of dexamethasone on the number of days alive without life support in adults with COVID-19 and severe hypoxemia: The COVID STEROID 2 randomized trial, *Journal of the American Medical Association*, **326(18)**: 1807-1817.
- Murphy, G.S., Szokol, J.W., Avram, M.J., Greenberg, S.B., Shear, T., Vender, J.S., Gray, J. and Landry, E. 2014, The effect of single low-dose dexamethasone on blood glucose concentrations in the perioperative period: a randomized, placebo-controlled investigation in gynecologic surgical patients, *Anesthesia and Analgesia*, **118(6)**: 1204-1212.
- Nasution, A. 2015, *Farmakokinetika Klinis*, USU Press, Medan.

- Oganesyan, A., Menzulín, R., Surovoy, Y., Nikiforchin, A. and Zykov, K. 2021, Target groups for a short dexamethasone course among critically ill COVID-19 patients, *Critical Care Research and Practice*, 1-10.
- Parian, A. and Ha, C. Y. 2015, Older age and steroid use are associated with increasing polypharmacy and potential medication interactions among patients with inflammatory bowel disease, *Inflammatory Bowel Diseases*, **21(6)**: 1392-1400.
- PDPI., PERKI., PAPDI., PERDATIN., IDAI. 2022, *Pedoman Tatalaksana COVID-19 Edisi 4*, Jakarta: PDPI., PERKI., PABDI., PERDATIN., IDAI.
- PERKENI. 2021, *Pedoman Pengelolaan dan Pencegahan Diabetes Melitus Tipe 2 Dewasa di Indonesia*, Jakarta: PB. PERKENI.
- Pinzón, M.A., Ortiz, S., Holguín, H., Betancur, J.F., Cardona Arango, D., Laniado, H., Arias Arias, C., Muñoz, B., Quiceno, J., Jaramillo, D. and Ramirez, Z. 2021, Dexamethasone vs methylprednisolone high dose for COVID-19 pneumonia, *PloS one*, **16(5)**: 1-13.
- Popat, B. and Jones, A.T. 2012, Invasive and non-invasive mechanical ventilation, *Medicine (Abingdon)*, **40(6)**: 298-304.
- Prasad, K. 2013, *Fundamentals of Evidence Based Medicine 2nd Edition*, Springer, India.
- Quattrocelli, M., Zelikovich, A.S., Salamone, I.M., Fischer, J. A. and McNally, E.M. 2021, Mechanisms and clinical applications of glucocorticoid steroids in muscular dystrophy, *Journal of Neuromuscular Diseases*, **8(1)**: 39-52.
- Rafiullah, M. and Siddiqui, K. 2020, Corticosteroid use in viral pneumonia: Experience so far and the dexamethasone breakthrough in coronavirus disease-2019, *Journal of Comparative Effectiveness Research*, **9(18)**: 1247-1254.
- Ranjbar, K., Moghadami, M., Mirahmadizadeh, A., Fallahi, M.J., Khaloo, V., Shahriarirad, R., Erfani, A., Khodamoradi, Z. and Gholampoor Saadi, M.H. 2021, Methylprednisolone or dexamethasone, which one is superior corticosteroid in the treatment of hospitalized COVID-19 patients: A triple-blinded randomized controlled trial, *BMC Infectious Diseases*, **21(1)**: 1-8.

- Romanou, V., Koukaki, E., Chantziara, V., Stamou, P., Kote, A., Vasileiadis, I., Koutsoukou, A. and Rovina, N. 2021, Dexamethasone in the treatment of COVID-19: Primus inter pares, *Journal of Personal Medicine*, **11(6)**: 1-25.
- Saeed, M., Mohamed, A. H. and Owaynat, A. H. 2022, Comparison between methylprednisolone infusion and dexamethasone in COVID-19 ARDS mechanically ventilated patients, *The Egyptian Journal of Internal Medicine*, **34(1)**: 1-9.
- Seo, S.J., and Priefer, R. 2020, Dexamethasone mechanism in inflammatory immune mediated disease and its application in treating 2019 coronavirus disease (COVID-19), *Medical Research Archives*, **8(12)**: 1-29.
- Sharifpour, M., Rangaraju, S., Liu, M., Alabyad, D., Nahab, F. B., Creel-Bulos, C. M., Jabaley, C. S. and Emory COVID-19 Quality & Clinical Research Collaborative. 2020, C-Reactive protein as a prognostic indicator in hospitalized patients with COVID-19, *PloS one*, **15(11)**: 1-10.
- Shereen, M.A., Khan, S., Kazmi, A., Bashir, N. and Siddique, R. 2020, COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses, *Journal of Advanced Research*, **24**: 91-98.
- Shi, Y., Wang, G., Cai, X.P., Deng, J.W., Zheng, L., Zhu, H.H., Zheng, M., Yang, B. and Chen, Z. 2020, An overview of COVID-19, *Journal of Zhejiang University Science B (Biomedicine & Biotechnology)*, **21(5)**: 343-360.
- Silva, P.L. and Rocco, P.R.M. 2018, The basics of respiratory mechanics: Ventilator-derived parameters, *Annals of Translational Medicine*, **6(19)**: 1-11.
- Smilowitz, N.R., Kunichoff, D., Garshick, M., Shah, B., Pillinger, M., Hochman, J.S. and Berger, J.S. 2021, C-reactive protein and clinical outcomes in patients with COVID-19, *European Heart Journal*, **42(23)**: 2270-2279.
- Soliman, O.M., Moeen, S.M., Abbas, Y.A. and Kamel, E.Z. 2022, The impact of dexamethasone versus methylprednisolone upon neutrophil/lymphocyte ratio in COVID-19 patients admitted to ICU and its implication upon mortality, *Egyptian Journal of Anaesthesia*, **38(1)**: 78-84.

- Sumampouw, E.L.P, Mawuntu, A.H.P. dan Tumewah, R. 2016, Efek samping terapi steroid intravena pada penderita infeksi susunan saraf pusat di Departemen Neurologi RSUP Prof. Dr. R. D. Kandou Manado periode Juli 2014 - Juni 2015, *Jurnal e-Clinic (eCl)*,**4(2)**: 1-8.
- Sweetman S.C. (eds). 2009, *Martindale* 36th Edition, Pharmaceutical Press, London.
- Tello, C.A.M., Manego, A.M.B., Etudor, C.M., Manuel, J.A., Mohsin, F., Joy, L.A., Persaud, P., Azam, A.U.F., Naz, S., Khan, M.I., Zaib, M.S. and Hanif, M. 2021, The effect of dexamethasone on outcome of patients with severe COVID-19. A retrospective cross sectional study, *Archives of Internal Medicine Research*, **4(4)**: 260-266.
- Tomazini, B. M., Maia, I. S., Cavalcanti, A. B., Berwanger, O., Rosa, R. G., Veiga, V. C., Avezum, A., Lopes, R. D., Bueno, F. R., Silva, M. V. A. O., Baldassare, F. P., Costa, E. L. V., Moura, R. A. B., Honorato, M. O., Costa, A. N., Damiani, L. P., Lisboa, T., Kawano-Dourado, L., Zampieri, F. G., Olivato, G. B., COALITION COVID-19 Brazil III Investigators. 2020, Effect of dexamethasone on days alive and ventilator-free in patients with moderate or severe acute respiratory distress syndrome and COVID-19: The CoDEX randomized clinical trial, *Journal of the American Medical Association*, **324(13)**: 1307-1316.
- Toroghi, N., Abbasian, L., Nourian, A., Davoudi-Monfared, E., Khalili, H., Hasannezhad, M., Ghiasvand, F., Jafari, S., Emadi-Kouchak, H. and Yekaninejad, M. S. 2022, Comparing efficacy and safety of different doses of dexamethasone in the treatment of COVID-19: A three-arm randomized clinical trial, *Pharmacological Reports*, **74(1)**: 229-240.
- Umar, T.P. 2021, Tatalaksana ventilasi pada pasien *coronavirus disease* 2019 (COVID-19), *Damianus Journal of Medicine*, **20(2)**: 163-171.
- Vecchié, A., Batticciotto, A., Tangianu, F., Bonaventura, A., Pennella, B., Abenante, A., Corso, R., Grazioli, S., Mumoli, N., Para, O., Maresca, A.M., Dalla Gasperina, D. and Dentali, F. 2021, High-dose dexamethasone treatment for COVID-19 severe acute respiratory distress syndrome: a retrospective study, *Internal and Emergency Medicine*, **16(7)**: 1913-1919.

- Villar, J., Ferrando, C., Martínez, D., Ambrós, A., Muñoz, T., Soler, J. A., Aguilar, G., Alba, F., González-Higueras, E., Conesa, L. A., Martín-Rodríguez, C., Díaz-Domínguez, F.J., Serna-Grande, P., Rivas, R., Ferreres, J., Belda, J., Capilla, L., Tallet, A., Añón, J.M., Fernández, R.L. and dexamethasone in ARDS network. 2020, Dexamethasone treatment for the acute respiratory distress syndrome: A multicentre, randomized controlled trial, *The Lancet Respiratory Medicine*, **8(3)**: 267-276.
- Wang, X. and Cheng, Z. 2020, Cross-sectional studies: Strengths, weaknesses, and recommendations, *Chest*, **158(1S)**: S65–S71.
- Williams D. M. 2018, Clinical pharmacology of corticosteroids, *Respiratory Care*, **63(6)**: 655–670.
- World Health Organization (WHO). 2021, Coronavirus Disease (COVID-19): Dexamethasone. Diakses pada 20 Oktober 2021, <https://www.who.int/news-room/questions-and-answers/item/coronavirus-disease-covid-19-dexamethasone>.
- World Health Organization (WHO). 2021, WHO, Coronavirus (COVID-19) Dashboard. Diakses pada 28 September 2021, <https://covid19.who.int/table>.
- Wu, H., Daouk, S., Kebbe, J., Chaudry, F., Harper, J. and Brown, B. 2022, Low-dose versus high-dose dexamethasone for hospitalized patients with COVID-19 pneumonia: A randomized clinical trial, *PloS one*, **17(10)**: 1-12.
- Wu, Y.C., Chen, C.S. and Chan, Y.J. 2020, The outbreak of COVID-19: An overview, *Journal of the Chinese Medical Association*, **83(3)**: 217-220.