

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

Penelitian dilakukan pada bulan November 2021 hingga Agustus 2022. Dari hasil kajian pustaka yang dilakukan pada 9 artikel tentang efektivitas dan efek samping lamotrigine pada pasien epilepsi dapat disimpulkan sebagai berikut:

1. Dari 9 artikel mengenai parameter efektivitas dapat ditarik kesimpulan sebagai berikut:
 - a. Terdapat 3 artikel yang menjelaskan lamotrigine monoterapi memberikan *seizure free* yang lebih baik, terapi kombinasi lamotrigine dan asam valproat memberikan *seizure free* yang lebih baik dibandingkan carbamazepin-CR monoterapi, 3 artikel menjelaskan bahwa lamotrigine memberikan *time to first seizure* yang lebih lama.
 - b. Terdapat 6 artikel yang menjelaskan mengenai efek *withdrawal* pada pasien epilepsi dan semuanya menunjukkan hasil yang lebih baik dari obat pembandingnya, 1 artikel yang menjelaskan bahwa pasien yang diberikan terapi lamotrigine menunjukkan perbaikan kualitas hidup dibuktikan dengan peningkatan skor QOLIE-31.
2. Efek samping yang sering terjadi di dalam penelitian yakni ruam namun tidak sampai menyebabkan *steven johnson syndrome* kemudian efek samping lain seperti gangguan kognitif, insomnia, dan *ataxia* juga terjadi namun secara statistik tidak signifikan sedangkan efek samping tremor, aggression, dan kelelahan terjadi secara signifikan.

5.2 Saran

Berdasarkan hasil kajian pustaka dan kesimpulan yang telah diuraikan maka dapat dikemukakan beberapa saran sebagai berikut:

1. Perlu dilakukan penelitian lebih lanjut terkait pengaruh lamotrigine terhadap kualitas hidup pasien karena penelitian terkait hal tersebut masih terbatas.
2. Perlu dilakukan penelitian lebih lanjut tentang efektivitas dan efek samping lamotrigine pada pasien epilepsi apabila terdapat penyakit penyerta.
3. Perlu dilaksanakan kajian pustaka mengenai efektivitas dan efek samping lamotrigine pada pasien epilepsi yang ada di Indonesia.

DAFTAR PUSTAKA

- Abdel-Kareem, A., Kabbash, I., Saied, S., and Al-Deeb, A. 2019, Knowledge, Practices and Attitudes of Physicians Towards Evidence-based Medicine in Egypt, *Eastern Mediterranean Health Journal*, **25(2)**: 82-89.
- Alsfouk, B. A., Alsfouk, A. A., Chen, Z., Kwan, P., and Brodie, M. J. 2019, Pharmacological Outcomes in Teenagers with Newly Diagnosed Epilepsy: A 30-year Cohort Study, *Epilepsia*, **60(6)**: 1-8.
- Bakta, I.M., Wibawa, I.D., N., Suastika, K., Putra, T.R., Parwati, K.T., Rai, IB.N., Widiana, G.R., Kuswardani, T., dan Rina, K. (eds). 2018, *Pendidikan Kedokteran Berkelanjutan XXVI Imu Penyakit Dalam Fakultas Kedokteran Universitas Negeri Udayana/Rumah Sakit Umum Pusat Sanglah*, Controversies in Internal Medicine, Proceeding Book, Udayana University Press, Denpasar.
- Bresnahan, R., Panebianco, M., and Marson, A.G. 2020, Lamotrigine add-on Therapy for Drug Resistant Generalized Tonic-Clonic Seizures, *Cochrane Database of Systematic Reviews*, **7(7)**: 1-32.
- Brodie, M. J. 2015, Lamotrigine Versus Other Antiepileptic Drugs: A Star Rating System Is Born, *Epilepsia*, **35(5)**: S41-S46.
- Chisholm-Burns, M.A., Schwinghammer, T.L., Wells, B.G., Malone, P.M., Kolesar, J.M., and Dipiro, J.T. (eds). 2016, *Pharmacotherapy Principles and Practice 4th Edition*, Mc Graw Hill Education, New York.
- Dipiro, J.T., Yee, G.C., Posey, M., Haines, S.T., Nolin, T.D., and Ellingrod, V. (eds). 2020, *Pharmacotherapy a Pathophysiologic Approach*, 11th Edition, Mc Graw Hill, New York.
- Ebrahimi, H.A. and Ebrahimi, F. 2012, The Effect of Lamotrigine on Epilepsy, *Iranian Journal of Neurology*, **11(4)**: 162-163.
- Eun, S.-H., Eun, B.-L., Lee, J.S., Hwang, Y.S., Kim, K.J., Lee, Y.-M., Lee, I.G., Lee, M., Ko, T.-S., Kim, J.T., Eom, S., and Kim, H.D. 2012, Effects of Lamotrigine on Cognition and Behavior Compared Carbamazepine as Monotherapy for Children with Partial Epilepsy, *Brain and Development*, **34(10)**: 818-823.

- Egunsola, O., Choonara, I., and Sammons, H.M. 2015, Safety of Lamotrigine in Paediatrics: A Systematic Review, *British Medical Journal Open*, **5(6)**: 1-9.
- Ferranti, S., Rossetti, A., Cerrone, C., Grande, E., and Grosso, S. 2017, Antiepileptic Drug-Related Ataxia in Children, *Journal of Neurology and Translational Neuroscience*, **5(2)**: 1-4.
- Fowler, T., Bansal, A.S., and Lozsadi, D. 2019, Risk and Management of Antiepileptic Drug Induced Skin Reactions in the Adult Out-Patient Setting, *Seizure: European Journal of Epilepsy*, **72(8)**: 61-70.
- Girsang, E.F., Bintoro, A.C., dan Pudjonarko, D. 2018, Hubungan Kadar Vitamin D Serum dengan Kualitas Hidup pada Pasien Epilepsi, *Majalah Kedokteran Neurosains Perhimpunan Dokter Spesialis Saraf Indonesia*, **35(4)**: 272-278.
- Gurbani, S., Chayasirisobhon, S., Gurbani, A., Tovar, S., Pietzsach, E., and Spurgeon, B. 2020, Effectiveness at 24 Months Single-Source Generic Carbazepine, Lamotrigine, or Levetiracetam in Newly Diagnosed Focal Epilepsy, *The Permanente Press*, **25(20)**: 1-6.
- Gunawan, S.G., Nafrialdi, R.S., dan Elysabeth. (eds). 2012, *Farmakologi dan Terapi Edisi 5 (cetakan ulang dengan tambahan)*, Departemen Farmakologi dan Terapeutik, Badan Penerbit Fakultas Kedokteran Universitas Indonesia, Jakarta.
- Glauser, T.A., Cnaan, A., Shinnar, S., Hirtz, D.G., Dlugos, D., Masur, D., Clark, P.O., Adamson, P.C., and for the Childhood Absence Epilepsy Study Team. 2013, Ethosuximide, Valproic acid, and Lamotrigine in Childhood Absence Epilepsy: Initial Monotherapy Outcomes at 12 months, *Epilepsia*, **54(1)**: 141-155.
- Ismael, S., Pusponegoro, H.D., Widodo, D.P., Mangunatmadja, I., dan Handryastuti S. (eds). 2016, *Rekomendasi Tatalaksana Status Epileptikus*, Unit Kerja Koordinasi Neurologi Ikatan Dokter Anak Indonesia, Badan Penerbit Ikatan Dokter Anak Indonesia, Jakarta.
- Keputusan Menteri Kesehatan Republik Indonesia. 2017, *Pedoman Nasional Pelayanan Kedokteran Tatalaksana Epilepsi pada Anak*, Jakarta.
- Kim, H., Kim, D.W., Lee, S.T., Byun, J. I., Seo, J.G., No, Y.J., Kang, K.W., kim, D., Kim, K.T., Cho, Y.W., and Yang, K.I. 2020, Antiepileptic Drug Selection According to Seizure Type in Adult Patients with Epilepsy, *Korean Neurological Association*, **16(4)**: 547-555.

- Kurniawan, M., Suharjanti, I., Pinzon, R.T. (eds). 2016, *Pedoman Tatalaksana Epilepsi*, Perhimpunan Dokter Spesialis Saraf Indonesia, Airlangga University Press, Surabaya.
- Kusumawati, K., Gunadharma, S., Kustiowati, S. (eds). 2014, *Pedoman Tatalaksana Epilepsi*, Edisi Kelima, Perhimpunan Dokter Spesialis Saraf Indonesia, Airlangga University Press, Surabaya.
- Lee, B.I., No, S.K., Yi, S-D., Lee, H.W., Kim, O.J., Kim, S.H., Kim, M.K., Kim, S.E., Kim, Y.K., Kim, J.M., Leek, S-J., Shin, D.J., Park, S.P., Kim, Y.I., Heo, K., Cho, Y.M., Cho, Y-J., and Kim, Y.N. 2017, Unblinded, Randomized Multicenter Trial Comparing Lamotrigine and Valproate Combination with Controlled-Release Carbamazepine Monotherapy as Initial Drug Regimen in Untreated Epilepsy, *British Epilepsy Association*, **55(3)**: 17-24.
- Leen, B., Bell, M., and McQuillan, P. 2014, *Evidence-based Practice: a Practice Manual*, Evidence-based Practice Group South East, Health Service Executive, Kilkenny.
- Lee, S-A., Kim, M.J., Lee, H-W., Heo, H., Shin, D-J., Song, H-K., Kim, O-K., Kim, S-O., and Lee, B. I. 2015, The Effect Of Recurrent Seizures on Cognitive, Behavioral, and Quality-of-Life Outcomes After 12 Months of Monotherapy in Adults with Newly Diagnosed or Previously Untreated Partial Epilepsy, *Epilepsy and Behavior*, **53(4)**: 202-208.
- Liguori, C., Toledo, M., and Kothare, S. 2021, Effects of Anti-Seizure Medications on Sleep Architecture and Daytime Sleepiness in Patients with Epilepsy: A literature review, *Sleep Medicine Reviews*, **60(10)**: 1-12.
- Lukas, A., Harsono, dan Astuti. 2016, Gangguan Kognitif pada Epilepsi, *Berkala Ilmiah Kedokteran Duta Wacana*, **1(2)**: 144-152.
- Macedo, P.J.O.M., Oliveira, P.S., Foldvary-Schaefer, N., and Gomes, M.M. 2017, Insomnia in People with Epilepsy: A review of Insomnia Prevalence, Risk Factors and Associations with Epilepsy-related Factors, *Epilepsy Research*, **135(5)**: 158-167.
- Machado, R.A., Garcia, V.F., Astencio, A.G., and Cuartas, V.B. 2013, Efficacy and Tolerability of Lamotrigine in Juvenile Myoclonic Epilepsy in Adults: A Prospective, Unblinded Randomized Controlled Trial, *British Epilepsy Association*, **22(10)**: 846-855.

- Mani, R., Monteleone, C., Schalock, P.C., Truong, T., Zhang, X.B., and Wagner, M.L. 2019, Rashes and Other Hypersensitivity Reactions Associated with Antiepileptic Drugs: A Review of Current Literature, *Seizure: European Journal of Epilepsy*, **71(7)**: 270-278.
- Marson, A., Burnside, G., Appleton, R., Smith, D., Leach, J.P., Sills, G., Tudur-Smith, C., Plumpton, C., Hughes, D.A., Williamson, P., Baker, G.A., Balabanova, S., Taylor, C., Brown, R., Hindley, D., Howell, S., Maguire, M., Mohanraj, R., Smith, P.E., and kolaborator SANAD II. 2021, The SANAD II Study of the Effectiveness and Cost-Effectiveness of Levetiracetam, Zonisamide, or Lamotrigine for Newly Diagnosed Focal Epilepsy: An Open-Label Non-Inferiority Multicentre, Phase 4, Randomised Controlled Trial, *Lancet*, **397(10282)**: 1363-1374.
- Mazurkiewicz-Beldzinska, M., Szmuda, M., and Matheisel, A. 2010, Long-Term Efficacy Of Valproate Versus Lamotrigine In Treatment Of Idiopathic Generalized Epilepsies In Children And Adolescents, *Seizure*, **19(3)**: 195-197.
- Minardi, C., Minacapelli, R., Valastro, P., Vasile, F., Pitino, S., Pavone, P., Astuto, M., and Murabito, P. 2019, Epilepsy in Children: From Diagnosis to Treatment with Focus on Emergency, *Journal of Clinical Medicine*, **8(39)**: 1-10.
- Murad, M.H., Asi, N., Alsawas, M., and Alahdab, F. 2016, New Evidence Pyramid, *Evidence-based Medicine*, **21(4)**: 1-3.
- Nesbitt, D.A., Leschziner, G.D., and Peatfield, R.C. 2014, Headache, Drugs and Sleep, International Headache Society, *Cephalgia*, **34(10)**: 1-11.
- Nice Institute for Health and Care Excellence. 2021, Epilepsies: Diagnosis and Management.
- Novianae, L. dan Sumarno. 2020, Ligan SV2A sebagai Terapi Epilepsi, *Jurnal Farmasi Udayana*, **9(1)**: 01-12.
- O'Gorman, K. dan MacIntosh. 2015, *Research Methods for Business and Management: A Guide to Writing Your Dissertation*, Goodfellow Publishers Limited, London.
- Panebianco, M., Bresnahan, R., Ramaratnam, S., and Marson, A.G. 2020, Lamotrigine add-on Therapy for Drug-Resistant Focal Epilepsy (Review), *Cochrane Database of Systematic Reviews*, **3(3)**: 1-50.

- Preveen, A., Aqil M., Imam, S. S., Ahad, A., Moolakkadath T., and Ahmad, F. J. 2018, Lamotrigine Encapsulated Intra-Nasal Nanoliposome Formulation for Epilepsy Treatment: Formulation Design, Characterization and Nasal Toxicity Study, *Colloids and Surface Biointerfaces*, **174(11)**: 553-562.
- Quigg, M., Gharai, S., Ruland, J., Shroeder, C., Hodges, M., Ingersoll, K.S., Thorndike, F.P., Yan, G., and Ritterband, L.M. 2016, Insomnia in Epilepsy is Associated with Continuing Seizure and Worse Quality of Life, *Epilepsy Research*, **122(9)**: 1-23.
- Rahayu, T., Syafril, S., Wekke, I.S. dan Erlinda, R. 2019, Teknik Menulis Review dalam Sebuah Artikel Ilmiah. Diakses pada 10 November 2021, <https://osf.io/preprints/inarxiv/z6m2y/>
- Retnawati, H., Apino, E., Katianom., Djidu, H., dan Anazia, R.D. 2018, *Pengantar Analisis Meta*, Parama Publishing, Yogyakarta.
- Rosenow, F., Brittinger, C.S., Burchardi, N., Bauer, S., Klein, K.M., Weber, Y., Lerche, H., Evers, S., Kovac, S., Hallmeyer-Elgner, S., Winkler, G., Springub, J., Niedhammer, M., Roth, E., Eisensehr, I., Berrouschat, J., Arnold, S., Schro-der, M., Beige, A., Oertel, W.H., Strzelczyk, A., Haag, A., Reif, P.S., Hamer, H.M., and for the LaLiMo Study Group. 2012, The LaLiMo Trial: Lamotrigine Compared with Levetiracetam in The Initial 26 Weeks of Monotherapy for Focal and Generalized Epilepsy-An Open-Label Prospective, Randomised Controlled Multicenter Study, *Journal Neurol Neurosurg Psychiatry*, **8(11)**: 1-6.
- Rugg, F.J. dan Sapley, H.N. (eds). 2017, *Epilepsy 2017 from Bench to Bedside: A Pratical Guide to Epilepsy*, International League Against Epilepsy, University College London.
- Samad, F., Saeed, Z., Hasan, Z., and Fahim, M.F. 2018, Evidence Based Medicine; Evidence Based Medicine Perceptions of Undergraduate Medical Students in Karachi, *The Professional Medical Journal*, **25(6)**: 896-902.
- Seiden, L., G. and Connor, G., S. 2022, The Importance of Drug Titration in the Management of Patients with Epilepsy, *Epilepsy and Behavior*, **128(10)**: 1-6.
- Sudira, P.G. 2016, *Basic Clinical Skill Semester 1 Panduan Pencarian Literatur Medis*, Program Studi Pendidikan Dokter, Fakultas Kedokteran Universitas Udayana.

- Sarva, H. and Shanker, V. L. 2014, Treatment Options in Degenerative Cerebellar Ataxia: A Systematic Review, *International Parkinson and Movement Disorder Society*, **1(4)**: 291-298.
- Scheffer, I.E., Berkovic, S., Capovilla, G., Conolly, M.B., French, J., Guilhoto, L., Hirsch, E., Jain, S., Mathern, G.W., Moshe, S.L., Nordli, D.R., Perucca, E., Tomson, T., Wiebe, S., Zhang, Y., and Zuberi, S.M. 2017, International League Against Epilepsy Classification of the Epilepsies: Position paper of the International League Against Epilepsy Commission for Classification and Terminology, *Epilepsia* **58(4)**: 512-521.
- Snyder, H. 2019, Literature Review As A Research Methodology: An Overview and Guidelines, *Journal of Business Research*, **104(11)**: 333-339.
- Tebala, G.D. 2018, The Emperors New Clothes: a Critical Appraisal of Evidence-based Medicine, *International Journal of Medical Sciences*, **15(12)**: 1397-1405.
- Tuttle, J. 2018, Helping To Achieve Safe Medication Use, *Medication Safety In Seconds*, **15(4)**: 1-5.
- Triandini, E., Jayanatha, S., Indrawan, A., Putra, G.W. Iswara, B. 2019, Metode Systematic Literature Review untuk Identifikasi Platform dan Metode Pengembangan Sistem Informasi di Indonesia, *Indonesian Journal of Information*, **1(2)**: 63-77.
- Triono, A., Herini, E.S., dan Mangunatmadja, I. 2019, Luaran Klinis Anak dengan Epilepsi yang Mengalami Relaps Setelah Penghentian Obat Antiepilepsi, *Sari Pediatri*, **20(6)**: 335-341.
- Warshawsky, A., Eilam, A., and Gilad, R. 2016, Lamotrigine as Monotherapy in Clinical Practice: Efficacy of Various Dosages in Epilepsy, *Brain and Behavior*, **6(3)**: 2-4.
- World Health Organization. 2019, Epilepsy, World Health Organization, Diakses 15 Oktober 2021, <https://www.who.int/news-room/fact-sheets/detail/epilepsy>
- Yasam, V.R., Jakki, S.V., Senthil, V., Eswaramoorthy, M., Shanmuganathan, S., Arjunan, K., and Nanjan, M. J. 2016, A Pharmacological Overview of Lamotrigine for The Treatment of epilepsy, *Expert Review of Clinical Pharmacology*, **9(12)**: 1533-1546.

- Zeng, Q-Yi, Fan, T-Tian, Zhu, P., He, R-Qian, Bao, Y-Xin, Zheng, R-Yuan., and Xu, H-Qin. 2015, Comparative Long-Term Effectiveness of a Monotherapy with Five Antiepileptic Drug for focal Epilepsy in Adult Patients: A Prospective Cohort Study, *Public Library of Science*, **10(7)**: 1-16.
- Zhang, D., Qiu, L., Zhang, Y., Sang, Y., Zheng, N. and Liu, X. 2020, Efficacy and Safety of Sodium Valproat plus Lamotrigine in Children with Refractory Epilepsy, *Experimental and Therapeutic Medicine*, **20(3)**: 2698-2704.
- Zhao, W. and Meng, H. 2022, Effects of Geneic Polymorphism of Drug-Metabolizing Enzymes on the Plasma Concentrations of Antiepileptic Drug in Chinese Population, *Bioengineered*, **13(3)**: 7709-7745.
- Zhu, F., Lang, S-Yang, Wang, X-Qing, Ma, Y-Feng, Shi, X-Bing, Chen, Y-Nan, and Zhang, J-Tang. 2015, Long-term Effectiveness of Antiepileptic Drug Monotherapy in Partial Epileptic Patients: A 7-year Study in an Epilepsy Center in China, *Chinese Medical Journal*, **128(22)**: 3015-3022.