

## Pharmacy

**KEYWORDS:** Neuropathic  
Diabetic, Quality of Life,  
Gabapentin, Pain Intensity.

**EFFECTIVENESS USING GABAPENTIN TOWARD  
PAIN INTENSITY DECREASED & LIFE QUALITY  
OF DIABETIC NEUROPATHY PATIENTS AT  
NEUROLOGY UNIT – REGIONAL PUBLIC  
HOSPITAL, WEST NUSA TENGGARA PROVINCE**



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**ABSTRACT**

Diabetic neuropathy pain is one of the microvascular complications due to prolonged hyperglycemia which results in disruption of peripheral blood flow. Because chronic pain often makes patients frustrated causing the quality of life of patients to decrease so that a drug is needed that can improve the quality of life of patients. This study aims to determine the effectiveness of the use of gabapentin to reduce pain intensity and the quality of life of neuropathic diabetic patients in neurology at the NTB Provincial Hospital in 2018. This study used a quasi-experimental research design. Data collection was conducted by interviewing and filling in the backer faces pain rating scale to see the intensity of pain before and after using gabapentin and questionnaires for EQ-5D-3L and EQ-VAS to see the quality of life of patients before and after gabapentin use. During 1 month, 12 patients were willing to participate in this study. Obtained pain intensity before and after gabapentin use decreased  $p = 0.000$  ( $p = 0.05$ ) differed significantly while using quizoner EQ-5D-3L Increased level of quality of life before and after gabapentin use increased both in walking / moving ability, self care, activities what is usually done, feeling of pain / not and feeling anxious / depressed and there is a significant improvement in EQ-VAS measurements with a value of  $p = 0.002$  ( $p < 0.05$ ).

**BACKGROUND**

Neuropathy pain is one of pain which come from ribs or central Nerves disorder system or peripheral nerves where this pain can caused by degenerative disease, diabetes mellitus, shingles or zoster herpes, AIDS, surgery and stroke. Population increased trend in neuropathy pain intervention like the effect of health costs, daily activity disorder, emotional health until patient productivity decreased (Harden & Raja, 2005). Based on epidemiology research, neuropathy peripheral pain found at 16 % diabetes mellitus patients.

Neuropathy pain is one of microvascular diabetic caused by acute hyperglycemia and creates peripheral blood stream disorder (Baughman, 2000). So it needs medicine to control blood sugar level as profilaksis therapy and using drugs to relieve pain (Snedecor, 2014).

Antidepressant and antiepilepsy drugs are the first line drugs used to relieve neuropathy pain (Cahyaningsih, 2013). Antiepilepsy drugs showed efficacy toward many types of neuropathy pain. At march 2000, gabapentin as first drug which registered in British as therapy drugs for all neuropathy pain. This phenomenon based on many evidence from randomized trials for neuropathy pain like diabetic neuropathy and postherpetic neuropathy (Serpell, 2002).

Gabapentin as antiepilepsy drugs which proven has analgesic

effect. Gabapentin has been accepted by Food and Drug Administration (FDA) as one of additional therapy for partial epilepsy and postherpetic neuralgia management (VHA, 2004). There are many research which study the effect of comparison between gabapentin therapy and amitriptylin at post stroke with neuropathy pain (Utami, 2013). It showed that there is no differentiation therapy effect at herniated nucleus pulposus. The result of those research have the same result so its possible to create differentiation if gabapentin used for diabetic neuropathy patients.

This research aims to know the effectiveness using gabapentin toward pain intensity decreased and life quality for diabetic neuropathy patients at neurology unit in Regional Publik Hospital - West Nusa Tenggara Province

**METHODS**

This research used quasi experimental method which taken patients data prospectively by using Wong Backer Faces Pain Rating Scale (WBFPRS) to measure pain intensity decreased and EQ-SD-3L and EQ-VAS questionnaires, measure patients life quality level. This research done in neurology unit, Regional Public Hospital -West Nusa Tenggara Province from june until july 2018.

Sample taken in this research were all diabetes mellitus atients which suffered neuropathy pain and got 300 mg therapy, it consumed twice a day in neurology unit, Regional Public Hospital - West Nusa Tenggara Province from june until july 2018, twelve patients which classified into inclusion & exclusion criterias.

The effectiveness of therapy used Wong Backer Faces Pain Rating Scale (WBFPRS) which used to measure pain intensity decreased, EQ-SD-3L & EQ-VAS questionnaires which used to measure patients life quality level.

EQ-SD-3L Questionnaires consist of 5 dimensions such as mobility, self treatment, activity, pain or uncomfortable, depression and every dimension has level of problem such as there is no problem, many problems, and extrem problem. The level of problems feel by patients give thick at every dimension and give code 1 at first column, second column give code 2, and third column give code 3. Note that the first column = there is no problem at mobility, self treatment, pain or uncomfortable feeling and depression.

EQ VAS questionnaires used to assess patient health condition, score 100 give for the best health condition which can imagined and score 0 for worst health condition. Questionnaires gave for patients before therapy and after four weeks therapy.

**RESULTS AND DISCUSSION**

This research about the effectiveness using gabapentin 300 mg toward pain intensity decreased and neuropathy diabetic patients life quality at neurology unit of Regional Public Hospital -West Nusa Tenggara Province which held from june until july 2018. Population in this research were 12 patients which have been fulfilled inclusion

and exclusion criterias used Wong Backer Faces Pain Rating Scale (WBFPRS).

The results of this data are presented based on the characteristics of the study subjects grouped by gender, age and level of education.

**A. Characteristics of pain patients Diabetic neuropathy**

A total of 12 people were sampled in the study that met the inclusion and exclusion criteria. All research subjects had signed an informed consent. Characteristics of research subjects include gender, age and education. Characteristics of research subjects based on gender, age and education can be seen in the table below:

**1. Gender**

**Table 1. Characteristic of patient based on gender**

No	Gender	n	%
1.	Male	7	56%
2.	Female	5	42%
Total	12	100%	

Based on the table above it is known that the respondents of diabetic neuropathy pain with female gender as much as 5 (42%), while the male sex as many as 7 (56%). Some studies have shown varying results in gender distribution. men and women have the same opportunity to suffer from diabetic neuropathy pain. This research is in line with research (Wheeler et al., 2007) in the case of San Luis Valley control in Type 2 diabetes mellitus patients in Colorado, namely Peripheral Diabetic Pain was more common in men (54.4%) than women (45.6%).

**2. Age**

Research data on patient age is categorized into 2 levels, namely age > 50 and ≤50 years. In the results of the study there were 8 people aged > 50 years and 3 people aged ≤50. Data is presented in table 2 below: Table 2. Characteristic of patient based on ages

**Table 2. Characteristic of patient based on ages**

No	Usia	n	%
1.	>50 tahun	9	75%
2.	≥50 tahun	3	25%
Total	12	100%	

Based on the picture above the characteristics of respondents based on the age of the respondent. It is known that the respondent of diabetic neuropathic pain based on respondents age > 50 years is 75% and ≤50 years as much as 25%. This shows that this research is in line with research (Trisnawati, 2014) with peripheral diabetic pain (NDP) results in patients aged 26-39 years, 71 were 44.6%, patients aged 40-54 years were 49.9%, patients aged 55-69 years by 50.6%, and patients over the age of 70 by 66.5%. So this shows DM patients aged over 50 years have a 2.94 times risk of suffering from NDP compared with DM patients under 50 years of age. Pain response besides being influenced by gender factors can also be influenced by age, age in someone who responds to pain perception is not yet widely known (Smaltzer & Bara, 2006).

**3. Education**

In the research results obtained the characteristics of the last level of education of respondents in this study were divided into 2 categories, namely: ASMA and > SMA. In the respondent category, the level of ASMA obtained as many as 10 respondents and > high school, namely 2 people. Percentages can be seen in the table below:

**Table 3. Characteristic of patient based on education**

No	Education	n	%
1.	>Senior High School	2	20%

2.	≤Senior High School	10	80%
Total	12	100%	

Based on the table above the characteristics of respondents based on education it is known that diabetic neuropathic pain respondents are categorized as respondents > SMA 20% as much and ≤SMA as much as 80%. dominated by patients with education levels below high school, because the level of education influences the response to everything that comes from outside, where in someone with higher education will provide a more rational response than those with secondary or low education (Asri, 2006). This is consistent with the results of research that shows that when viewed from the last level of education, respondents with a ≤SMA level were more than 80% compared to the level of > SMA, which was 20%.

**4. Pain intensity**

In this study the measurement of pain intensity using Wong Backer Face Pain Rating Scale (WBFPRC) which was assisted by SPSS 16.0. The resulting data is obtained normally in the normality test after that Paired Simple t-Test is analyzed to see the significance before and after the use of gabapentin, the test results can be seen in the table below:

**Table 4. Pain intensity before and after gabapentin use**

Groups	Mean±SD	P
Before	6,00±1,47	0.000*
After	3,50±1,50	

Exp: mean= average; SD=deviation standart; \* : Significant. Based on the table above can be seen the average initial value of pain intensity of patients before taking the drug as a whole obtained 6.00 ± 1.47 after getting gabapentin therapy for 2 weeks and then measured again obtained 3.50 ± 1.50 systematically there was a decrease which is then strengthened with the result of p-value 0,000 (p <0,05) which means statistically different (significant). In this study showed that the use of gabapentin 300 mg a day 2 times for 2 weeks had the effectiveness of reducing pain intensity. The results of this study are in line with previous studies which say that gabapentin is effective in reducing pain intensias in neuropathic diabetic patients (Yuniarti, 2017) and in the study (Kusumo, 2017) gabapentin showed significant results in reducing pain in patients with Painful diabetic neuropathic.

Gabapentin has indeed been used as a treatment for neuropathic pain for the first time starting in 1990. Originally planned as a spasmolytic and ultimately proven to be more effective as an antiseizure drug, gabapentin has also been shown to be effective in the treatment of neuropathic pain. General use has until now been used as a treatment for seizures and neuropathic pain. The use of Gabapentin in dealing with pain has been almost 18 years, especially believed in treating chronic pain such as neuropathic pain which is very difficult to overcome. Gabapentin has been approved for administration of neuropathic pain in adults (> 18 years of age). Although there are many modalities to overcome them, such as tricyclic antidepressants, opioids, but all of them have adverse side effects. Gabapentin provides a new approach in dealing with this pain with minimal side effects (Kusumo, 2017).

**5. Quality of life**

In this study using the EQ-5D questionnaire for knowing the level of quality of life of respondents by looking at the total questionnaire. The EQ-5D questionnaire consists of 2 types of questionnaires, namely:

**a. EQ-5D-3L**

The EQ-5D-3L questionnaire has 5 dimensions, namely the ability to walk / move, self care, activities that are commonly done, feeling of pain / discomfort, anxiety / depression and having 3 levels of

problems faced by the patient, ie there are no problems, some problems, extreme problems occur. The results of research conducted using questionnaires EQ-5D-3L can be seen in table 4.5 below:

**Table 5. The data of EQ-5D-3L before and after based on respondent's answer**

Dimention	Before treatment						After Treatment					
	TB		BS		BB		TB		BS		BB	
	N	%	N	%	N	%	N	%	N	%	N	%
Ability to walk	1	8,3%	10	83%	1	8,3%	6	50%	6	50%	0	0
Self care	5	42%	6	50%	1	8,3%	8	67%	4	33%	0	0
Usual activities	1	8,3%	10	83%	1	8,3%	2	17%	10	83%	0	0
Pain or discomfort	2	17%	1	8,3%	9	75%	2	17%	10	83%	0	0
Anxious or depressed	4	33%	5	41%	3	25%	8	67%	4	33%	0	0

Exp : N= number of patient; TB= No problem; BS= Medium; BB= very problematic.

In the table above can be seen the results of the level of quality of life using the questionnaire EQ-5D-3L which has 5 dimensions and 3 levels of problems. Based on the table shows the average respondent before being treated by Gabapentin has several perceived problems. The highest problem felt was in pain / discomfort that was 75% followed by anxiety / depression by 25%, usual activities, as much self-care and ability to walk / move 8.3%. For moderate problems the highest level is found in walking / moving ability as much as 83% and usual activities are 83%, self-care as much as 50%, anxiety / depression 41% and feeling of pain / discomfort 8.3%. Then for the highest level of problems there is 42% self-care, anxiety is 33%, pain is 17% and the ability to walk and move is 8.3%. This shows that even though the patient is suffering from pain, he can still treat himself.

After the use of gabapentin 300 mg 2 times a day for 2 weeks the level of quality of life of patients at severe problematic levels of pain / discomfort initially as much as 75% then followed by anxiety / depression as much as 25%, usual activities, self-care and ability to walk / move as much as 8.3% to 0%. Then the problem is the highest level is found in walking / moving ability as much as 83% and the usual activities are 83%, followed by self-care as much as 50%, anxiety / depression 41% and feeling of pain / discomfort 8.3% to be 50%, 83%, 83%, 33%, 25%. Finally, the highest level of quality of life is not problematic, there are 67% of self-care and anxiety / depression, which is initially 42% and 33%, followed by 50% walking / moving ability which is initially 8.3%, the last level of activity usually done and 17% feeling of pain / discomfort which was initially 8.3% and 17%. This shows that the results of each patient's response based on the EQ-5D-3L questionnaire after gabapentin use were an improvement in the quality of life of neuropathic diabetic patients. Where this shows that gabapentin has the effectiveness of reducing nerve damage continuously which causes pain and ultimately causes hyperalgesia and allodynia (Kusumo, 2017). The results of this study are also strengthened by previous studies in which gabapentin is quite effective in improving quality of life pain Neuropathy caused by post-stroke neuropathy pain and gabapentin can be used as a therapy for various types of neuropathy according to the ability of Gabapentin which can enter the cell to interact with the A2β receptor which is a subunit of Ca2 + - channel (Nicholson, 2006).

This research is in line with the research (Saputri, 2017) using an EQ-5D-3L questionnaire which proves that after using gabapentin

patients experience an improvement in the quality of life about health conditions that can be imagined. Aspects that are used as indicators of quality of life include the ability to walk / move, self-care, usual activities carried out, a sense of pain / discomfort and anxiety or depression.

**a. EQVAS**

EQVAS is a scale to assess respondents 'health on a vertical 20cm visual analogue scale with the endpoint having a score of 100 labeled' the best health you can imagine 'and a score of 0 labeled' the worst health you can imagine (Andriana Sari, 2017). The data generated is then inputted by SPSS 16.0. The data produced normally in the normality test after that were analyzed Paired Simple t-Test to see the significance before and after the use of gabapentin. The results of research conducted using the EQ-VAS questionnaire can be seen in table 4 below:

**Table 6 Quality of life before and after gabapentin used**

Groups	Mean±SD	P
Before	48,33±7,17	0.002*
After	54,16±1,50	

Exp : mean= average; SD=deviation standart; \* = significant (P <0.05 ).Based on the table above can be seen the average initial value of quality of life of patients before taking the drug as a whole obtained 48.33 ± 7.17 kemdian after gabapentin therapy for 2 weeks then measured again obtained 54.16 ± 1.50 systematically found the increase is then strengthened by the p-value of 0.002 (p <0.05) which means that it is statistically different (significant). This proves that after using gabapentin 300 mg 2 times a day for 2 weeks shows an improvement in quality of life based on health imagined in neuropathic diabetic patients.

This study is in line with previous studies which stated that there was an increase in the quality of life of patients using EQ-VAS after treatment with gabapentin (Saputri, 2017) and in the study (Utami, 2013) which said the use of gabapentin and amitriptyline for 4 weeks also showed a decrease in quality of life. which is measured by the Brief Pain Inventory (BPI) where the questionnaire is able to describe: general activity, mood, ability to walk, work, relationships with others and how to enjoy life. This questionnaire has a score where the lowest score has a better quality of life. Then get data on the use of gabapentin 300 mg 2 times a day obtained 2.70 ± 1.34 systematically there is a decrease of 1.67 strengthened by the paired sample t-test obtained p -value 0.00 (p <0.05) which means statistically different (significant), this proves the effectiveness of gabapentin for pain therapy can be felt after 1-2 weeks of initial use of gabapentin but can be longer for patients who experience more severe pain but some patients also experience beneficial effects immediately after using gabapentin. For the period of use if it is felt gabapentin helps reduce pain, it is used at least 2-3 months (Anonim, 2010).

**CONCLUSION**

From the results of research conducted in NTB Provincial Hospital can be concluded: The intensity of pain before and after the use of gabapentin has a significant decrease with p = 0.000 (p <0.05) and an increase in the level of quality of life before and after gabapentin use has improved in the ability to walk / move, self care, activities that are usually done, feeling of pain / not and feeling anxious / depressed and there is a significant improvement in EQ-VAS measurements with a value of p = 0.002 (p <0.05).

**REFERENCES**

1. mellitus. Diabetes Care. 2003;27(Suppl 1):S5-S10.
2. Anonim. 2010. FAQs about Gabapentin for Pain Relief, Cambridge University Hospitals NHS Foundation Trust.
3. Annisa, 2013, Penilaian Kualitas Hidup pada Usia Lanjut Dengan Eq-5d Di Klub Jantung Sehat Kelurahan Pondok Kelapa Dan FaktorFaktor Yang Mempengaruhi, Tesis, Fakultas Kedokteran Universitas Indonesia, Jakarta.
4. A.Kukkar, A.Bali, N. Singh, AS. Jaggi, 2013, Implications and Mechanism of Action Gabapentin in Neuropathic pain, Pubmed, Abstract.
5. Anggreta Ocky F.H. 2012. Kadar Glukosa darah pada Diabetes Melitus.

- Universitas Muhammadiyah. Semarang.
6. Argoff C, B. M. (2006). Consensus guidelines ; breatment and planing option; diabetic neuropathic Pain. Mayo Clin proc, 81 (suppl), S12-S25.
  7. Asri, Suryaniati. (2006). Perbedaan pengaruh pemberian anestesi spinal dengan anestesi umum terhadap kadar gula darah. Karya tulis ilmiah, Universitas Diponegoro
  8. Baughman, D.C. (2000). Keperawatan. Jakarta: EGC.
  10. Backonja M , Beydoun A, Edwards KL.1998. Gabapentin for the symptomatic treatment of painful neuropathy in patients with diabetes mellitus : a randomized controlled trial. JAMA 1998;280:211-4.
  11. Black, Joyce, Hawks, Jane Hokanson.(2009). Medical Surgical Nursing : Clinical Management for Positive Outcomes. (8th ed.). Vol.1. St. Louis : Elsevier
  12. Cahyaningsih, I. (2013). Perbandingan penggunaan gabapentin dan amitriptilin sebagai terapi nyeri terhadap efek terapi pada pasien Herniated Nucleus Pulposus Rawat Jalan di Poli saraf Rumah Sakit Jogja. Yogyakarta: Universitas Gajah Mada Yogyakarta.
  13. Cohen, A.D. 2002. Spirituality in Palliative Care, Geriatric Times November/Desember 2002. Volt III
  14. Darmojo, R.B. 2011. Buku Ajar Geriatri Ilmu Kesehatan Usia Lanj, Jakarta: Fakultas Ilmu Kedokteran Universitas Indonesia.
  15. Demura, S, Sato, S, 2003. Relationship between depressions, lifestyle and quality of life in community dwelling elderly :A comparison between gender and age grup, j of psychol Antropol Appl Hum scil, 22(3):159-166.
  16. EQ-5D-3L User Guide, 2015. Basic information on how user the EQ-5D-3L Instrument. Di akses dari [http://www.euroqol.org/fileadmin/user\\_upload/documenten/PDF/Folders Flyers/EQ-5D-3L UserGuide 2015.pdf](http://www.euroqol.org/fileadmin/user_upload/documenten/PDF/Folders Flyers/EQ-5D-3L UserGuide 2015.pdf).
  17. Faisal S Hutapea, d. (2016). Gambaran klinis neuropati pada pasien diabetes mellitus di Poli klinik Neurologi RSUD Prof. Dr. R. D. Kandou periode Juli 2014 – Juni 2015. Jurnal e-Clinic (eC) Volume 4 Nomor 1, 2.
  18. Harden, R.N., 2005, Chronic Neuropathic Pain – Mechanisms, Diagnosis, and Treatment, The Neurologist, Vol. 11, No.2.
  19. Hartono. J.M. 2004. Metodologi Penelitian Bisnis; Salah Kaprah Dan Pengalaman-Pengalaman, 120, 123-129.
  20. International Diabetes Federation (IDF). 2011. Global diabetes plan, from <http://www.idf.org/global-diabetes-plan>.
  21. Karlsten, R., dan Gordh, T., 1997, How do drugs relieve neurogenic pain?, Drug Aging, Vol 11. 398-412 : NICE, 2010, Neuropathic Pain: The Pharmacological Management of Neuropathic Pain in Adults in Non-Specialist Settings, National Insititute for Health and Clinical Excellence: London.
  22. Karlsten, R., dan Gordh, T., 1997, How do drugs relieve neurogenic pain?, Drugs Aging, Vol 11. 398-412.
  23. Kementerian Kesehatan Republik Indonesia (KEMENKES RI). 2014. Situasi dan Analisis Diabetes Mellitus. <http://www.depkes.go.id/download.php?file=download/pusdatin/infodatin/infodatin-diabetes.pdf> [3 Nopember 2016].
  24. Kesehatan RI, D. B. (2015). Pharmaceutical care untuk penyakit Diabetes Mellitus. Jakarta: DEPARTEMEN KESEHATAN RI.
  25. Kusumo, D. D. (2017). perbedaan efektivitas gabapentin dengan gabapentin dan methylcobalamin terhadap perbaikan rasa nyeri pada pasien Painful Diabetic Neuropathy di RSUD Dr.Moewardi Surakarta. Surakarta: PPSD I ILMU PENYAKIT SARAF LAB/SMF ILMU PENYAKIT SARAF RSUD DR.MOEWARDI SURAKARTA.
  26. Miller KE, H. M. (2011). Glutamate Pharmacology and metabolism in peripheral primury afferent\_Physiological and pathophysiological meehanisme. Pharmacol Ther., 130(3):283-309.
  27. Morello, C.M., Susan, G.L., Carol, P.S., David, F.M., Gregory, A.S., 1999. Randomized Double-blind Study Comparing the Efficacy of Gabapentin with Amitriptyline on Diabetic Peripheral Neuropathy Pain, Arch Intern Med, Vol 159, 1931-1937.
  28. Najwa. (2016). Studi Penggunaan Obat Analgesik pada Pasien Diabetik Neuropatik di Rumah Sakit Universitas Airlangga (RSUA) Surabaya. Surabaya: Uneversitas Airlangga Surabaya.
  29. NICE, 2010, Neuropathic Pain: The Pharmacological Management of Neuropathic Pain in Adults in Non-Specialist Settings, National Insititute for Health and Clinical Excellence: London.
  30. Nicholson, B. (2006). Differential Diagnosis : Nociceptive and Neuropathic Pain. The American Journal of Managed Care, p256-61.
  31. Nopitasari, B. L. (2016). Perbandingan Outcome Nyeri Pada Pasien Nyeri Neuropatik yang di Terapi dengan Amitriptilin dan Gabapentin di Klinik Syaraf RSUD dr. Mohammad Soewandhie Surabaya. Surabaya: Universitas Surabaya.
  32. Notoadmodjo, S. 2012. Metodologi Kesehatan , Jakarta; Rineka Cipta.
  33. Palaian S, Chheri, A.K., M. Rajan, S.R., and Shankar, P.R., 2005, Role of Pharmacist in Counseling Diabetes Patient, The Internet J. Pharmacol, 4, 1.
  34. Pandelaki, K. 2009. Retinopati Diabetik. Jakarta: Interna Publishing.
  35. Pappagallo, M., 2003, Newer Antiepileptic Drugs: Possible Uses in The Treatment of Neuropathic Pain and Migraine, Clinical Therapeutics, Vol. 25, 2506-2538.
  36. Perkumpulan Endokrinologi Indonesia (PERKENI). 2006. Konsensus Pengelolaan dan Pencegahan Diabetes Mellitus Tipe 2 di Indonesia. Jakarta: perkeni.
  37. Pickar SA, neary, m.pand cella D. 2007. Healt And Quality of Life Outcomes Open Acces Research Estimation of minimally important differences in EQ-5D utility and VAS scores in cencer Center For Pharmacoeconomic, Research, Department of Farmacy Praticce, Collage of Pharma Health And Quality of Life Outcumes 2007;5:70 doi:10.1186/1477-7525-5-70.
  38. Price A.Sylvia. 2005. Patofisiologi : Konsep Klinis Proses-Proses Penyakit. EGC : Kedokteran. Jakarta.
  39. Price, S. A. dan Wilson, L. M. (2006). Patofisiologi : Konsep Klinis Proses-Proses Penyakit, Edisi 6, Volume 1. Jakarta: EGC.
  40. .
  41. Raylene M respond. 2008. Penilaian Nyeri alih bahasa. D.Lyrawatihall 141-152 Centers for Disease Control and Prevention (CDC). National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2015. Atlanta, Georgia: U.S. Department of Health and Human Services; 2015.
  42. Romanoff, M. (2006). In: Ramamurthy S, Alanmanou E, Rogers JN. Decision Making in Pain Management. 2nd ed. Philadelphia: Mosby, p86-89.
  43. Rubin, RR & Peyrot, M. 1999. Quality of Life and Diabetes, Diabetes Metabolism Research And Review. 15, 205.
  44. Saputri, C. (2017). Efektifitas penggunaan Gabapentin terhadap penunjang perbaikan kualitas hidup pasien neuropatik diabetik di Poli Klinik Syaraf RSUD Provinsi NTB Tahun 2017. Mataram: Universitas Muhammadiyah Mataram.
  45. Sari, A., Lestari, N.Y., Perwitasari, D.A., 2015, Validasi StEuropean Quality Of Life-5Dimensions (Eq-5d) Versi Indonesia Pada Pasien Hipertensi Di Puskesmas Kotagede II Yogyakarta, Jurnal Ilmiah Nasional Tidak Terakreditasi "Pharma Ciana", Vol. 5 No. 2 November 2015, ISSN: 2088-4559.
  46. Serpell, M.G., 2002, Gabapentin in Neuropathic Pain Syndromes: A Randomised, Double-Blind, Placebo-Controlled Trial, Pain, Vol 99, 557-566.
  47. Setiati, S., Harimurti, K., Dewiasty E, Istanti R., 2010. Predictors and Scoring System for Healthrelated Quality of Life in an Indonesian Community -Dwelling Elderly Population. Department of Internal Medicine, Faculty of Medicine, University of Indonesia, Jl. Diponegoro No. 71 Jakarta 10430, Indonesia. Acta Med Indones-Indones J Intern Med.
  48. Schatzberg, A.F, dan Nemeroff, C.B., 2009. Textbook of Psychopharmacology, The American Psychiatric Publishing, Arlington.
  49. Sjahrir, I. (2006). Diabetic Neuropathy: The Pathoneurobiology dan Treatment Update. Medan: USU Press.
  50. Smeltzer & Bare . (2008). Textbook of Medical Surgical Nursing Vol.2. Philadelphia: Lippincott William & Wilkins.
  51. Smeltzer & Bara. 2013. buku ajar keperawatan medical bedah. Ed 8. Jakarta: EGC
  52. Smeltzer, S.C., Bare, B.G., Hinkle, J.L., & Cheever, K.H. 2010. Brunner & suddarth's textbook of medical-surgical nursing (12th ed.). Philadelphia: Wolters Kluwer Health; Lippincott Williams & Wilkins.
  53. Snedecor SJ, d. (2014). Systematic Review and meta-analysis of pharmacological therapies for painful diabetic peripheral neuropathy. Pain Pract, 167-184.
  54. Soewondo. 2006. Hidup Sehat Bebas Diabetes. Yogyakarta: Araska
  55. Subekti, I. 2009. Apa itu Diabetes : Patofisiologi, Gejala dan Tanda/ Dalam: Penatalaksanaan Diabetes Mellitus Terpadu Edisi 2. Balai Penerbit FKUI, Jakarta.
  56. Testa M.A & Simonson D.C. 1996. Assesment of Life Outcuome, New England Journal of Medicine. 334:835-39.
  57. Treede RD, J.T. (2008). Neuropathic pain redefinition and a grading system for clinical and research purposes. Neurology, 70(18):1630-5.
  58. Tjokropawiro, A. (2011). Hidup sehat bersama diabetes Edisi 2. Jakarta: Gramedia Pustaka Utama.
  59. Utami, P. (2013). Perbandingan Penggunaan Gabapentin dan Amitriptilin Terhadap Efek Terapi dan Kualitas Hidup pada Pasien Stroke dengan Nyeri Neuropati di Rumah Sakit Jogja. Yogyakarta: Universitas Gajah Mada Yogyakarta.
  60. VHA, 2004, Guidance on the Use of Gabapentin, diakses pada 14 Februari 2013, <http://www.pbm.va.gov/Clinical%20Guidance/Clinical%20Recommendations/Gabapentin%20Clinical%20Recommendations.pdf>.
  61. Wheeler, S., Singh, N., Boyko, E.J. 2007. The Epidemiology of Diabetic Neuropathy. In: Veves, A., Malik, R.A, editors. Diabetic Neuropathy Clinical Management, 2nd ed, New Jersey: Human Press. pp 7-30.
  62. Whyne, D. K., Does the correspondence between EQ-5D health state description and VAS score vary by medical condition? Whyne Health and Quality of Life Outcomes 2013, 11:155.
  63. Widiastuti. A., Nurachmah, E., & Besral. 2012. Efektifitas Edukasi Terstruktur Berbasis Teori Perilaku Terencana Terhadap Pemberdayaan dan Kualitas Hidup Pasien Penyakit Jantung Koroner Di Rumah Sakit Pondok Indah Jakarta. Tesis FIKUI.
  64. WHO Expert Committee on Diabetes Mellitus: Second report. World Health Organ Tech Rep Ser 1980:646:1-80.
  65. WHO Study Group. Diabetes mellitus: Report of a WHO Study Group. World Health Organ Tech Rep Ser 1985:727:1-113.
  66. Yuniarti, M. (2017). Analisis Efektifitas Gabapentin Terhadap Penurunan Intensitas Nyeri Pada Pasien Neuroptik Diabetik di Klinik Syaraf RSUD PROVINSI NTB periode Mei – Juli 2017. Mataram: Universitas Muhammadiyah Mataram.
  67. Zhun, M. (2002). Glutamate receptors and persistent pain\_ tergering forehain NR2B subunits. Drug Discov Today, 7(4):259-67.