

Gabapentin and Amitriptilin Treatment toward Living Quality of Post Ischemic Stroke Patients with Neurophaty Pain

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ABSTRACT

Stroke becomes a significant problem for developing countries. In Indonesia the data show its incidences 234 per 100.000 people, and around 2 - 8 % stroke patients experiencing cerebrovascular session will get neurophaty pain. It happens because of sensoric deviation after stroke, so the brain does not completely send information to the body correctly. Patients experiencing neurophaty pain are able to face decreasing living quality as the effect of long term painful disturbance. Therefore, it is important to maintain the patients' living quality. The aim of the study is to investigate the comparison of using gabapentin and amitriptilin toward living quality of ischemic stroke patients with neurophaty pain in the hospitals in Jogja. The method used in this study was *quasi experimental* with *consequtive sampling*. The study was conducted on 22nd of April-31st of Juli 2013 by involving 23 patients in gabapentin group and 18 patients in amitriptilin group that would be evaluated during 1 month. Living quality was assessed by *Brief Pain Inventory* (BPI) in week 0 and week 4. The result of the study showed that the use of gabapentin and amitriptilin in 4 weeks showed the increase of living quality represented by decreasing the score based on BPI questioner 1.67 ± 0.78 and 1.37 ± 0.80 with $p\text{-value} > 0.05$ meaning that there was no significant difference. It can be concluded the comparison of using gabapentin and amitriptilin in post ischemic stroke patient with neuropathy pain not significantly increase the quality of in the hospitals in Jogja.

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1. INTRODUCTION

Stroke becomes a problem in developing countries. According to WHO, there are 15 million populations get stroke attack every year in the whole of the world, and the most common patients are elderlies with death rate every 10 years between 55 and 85 year old [1].

Based on a survey in Bogor, the data in the developing countries like Indonesia showed its incidences of 234 per 100.000 people. According to the data of Riskesdas Depkes RI (2007) in its national report, it was mentioned that the main death cause for all ages was stroke (15,4%), TB (7,5%), and hipertension (6,8%) [2].

Medical treatment for post stroke pain in Indonesia has been started to use medicine from the group of tricyclic anti-depresant like amiriptilin and from the group of anti-convulsanlike gabapentin. Patients' response that used both medicines was good enough. Here they are some *Evidence Based Medicine* (EBM) studies of amiriptilin and gabapentin medicine used as pain relief medicine:

1. The research conducted by Lamphlet *al* (2002) showed the result in placebo group having pain level 21% and 17% in profilaksis group with amitriptilin in 1 year after the diagnosis of *post stroke pain* [3].
2. A research done by Ter Ong *et al* (2003) mentioned that between 1998 and 2001 with 684 patients, in which 52 of them were in the main age of 58 years old, participated in two stages reserach. The first stage, tehreseracher examined the patients without any special treatment for parestesia. The patients were only given antiplatelet orantikoagulan medicine during 6 month. During the second stage, the patients (44 patients) got amitriptilinthraphy, and the result showed that 14 patients (31.8%) reported that they did not experience parestesia. The data shows that amitriptilin can be used in *post stroke paresthesia management* [4].
3. A research done by Attal N *et al* (1998) mentioned that the effect of gabapentin with low dose, and if it was increased frequently until its maximum 2.400 mg/ day showing that gabapentin had the effect of antiallodiniaandantihiperalgesia. Although there was side effect, it was only the light one. And it does not disturb the patients' daily activities [5].

The explanation above shows that gabapentin andamitriptilincould be used as pain killer for neurophaty pain although both of the medicines were not mentioned in the medicine indication on the medicine leaphlet. The patients having post stroke neurophaty pain can cause the decrease of patients' living quality because they experienced long term pain disturbance, so it had significant effect to the patients' mood condition, sleeping quality, and daily activities. Thus, it is important to measure the intencity, pain quality, and abnormal sensation. The measurement of living quality becomes a significant factor in the outcome of stroke therapy because based on jaracz & kozubski (2003), It is shown the research result that the change of living quality is clearly seen to the patients after getting stroke [6], but there are still very few researches which focus on living quality of the patients especially the pain of post stroke and on both medicines. Therefore, measurement is needed whether both medicines can give significant influence of the patients' living quality after stroke, so there should be fuether research investigating the patients' living quality after stroke the period before and after using both medicines.

Choosing a hospital in Jogja was significant because this hospital was one of the government hospitals type B which had some facilities such as neuro outpatient department with patients visit aroud 800-1000 patients per month. Stroke patients visitation was in the first highest rate in 1 month. Jogja Hospital was an educational hospital supporting the research, so it was easier for the researcher to take the data there.

2. RESEARCH METHOD

The research is an experimental study with *QuasyEksperimental Design* framework conducted to ischemic stroke patients having *post stroke pain* coming to neuro-pily in the hospitals in Jogja during 22nd of April-31st of July 2013.

2.1. Material

The research uses primary data in the form of questioner as the media to collect the data. Questioner used was in the form of *Brief Pain Inventory* in English translated to Bahasa Indonesia. The questioner had been tested for its validity and reliability.

2.2. Research Process

The research was conducted within these following steps:

1. Preparation step

This step includes finishing *etichal clearance*of the research and permission from the hospitals as the places for the research as well as the preparation of report sheets of the patients' medical record and questioners.

2. Research Steps

The research was conducted in several forms of activities, such as:

- a. The patients who were diagnosed by the doctors clinically having post ischemic stroke in the Hospital in Jogja were given *informed consent*. Initial examination was given single amitriptilin treatment and single gabapentin, and the patients' living quality was assessed by using *Brief Pain Inventory* questioner. In the end, the patients got 1 month treatment, and ther living quality was re-assessed again.
- b. *Questioner filling* was guided directly by the researcher, so the resepondents could ask some questions if they did not understand the materials. After that, the researcher rechecked after the questioners were returned by the respondents. In the questioner of BPI, there were 1-10 scales in which score 1 was used for the definition not to disturb, and score 10 for disturbing definition, so the questioner has the lowest score having the best living quality.

3. Data Processing and Data Analysis

The data from the patients and the data from the questioners were processed and analyzed based on its analysis method used.

2.3. Data Processing and Analysis

Research data were processed within these following steps as follow:

1. Descriptive analysis from the characteristic of research subject (based on gender).
2. The Test analysis of Brief Pain Inventory questioner significance was conducted by using a statistical method namely *student t-test* with the rate of trust 95.

3. RESULTS AND ANALYSIS

The research was conducted on 22nd of April until 31st of July 2013 by using *consecutive sampling*. The patients were patients of ischemic post stroke 57 patients. The patients were allocated into 2 groups: gabapentin group (n=31) and amitriptilin group (n=26). During the research, there were 16 patients who did not continue/stopped from the research consisting of 8 patients from gabapentin and 8 patients from amitriptilin because of double therapy, side effect of the medicine and the unclear address and phone number, so it was difficult to reach them. Here they were the patients' characteristics following the research until the end of the process that is shown in Table 1.

Table 1. The Characteristic of Patients Demographic Following the Research in the Hospitals in Jogja.

Respondent Characteristic	Gabapentin		Amitriptilin		Value
	N	%	N	%	
<u>Gender</u>					
• Male	16	69.6	8	44.4	0.105
• Female	7	30.4	10	55.6	
<u>Age</u>					
• < 40 years old	0	0	1	5.6	0.436
• 40 years old – 60 years old	10	43.5	9	50	
• >60 years old	13	42.5	8	44.4	
<u>Education</u>					
• Elementary School	7	30.4	9	50	0.283
• Junior High School	4	17.4	5	27.8	
• Senior High School	9	39.1	3	16.6	
• Diploma	3	13.1	1	5.6	
<u>Job</u>					
• Unemployment	17	74	12	66.7	0.151
• Entrepreneur	3	13	6	33.3	
• Private Sector	3	13	0	0	

The characteristic of the research subject was grouped into several categories such as gender, age, education background, and job. The result of statistical analysis using *chi square* test got the result respectively *p* value >0.05 they were 0.105; 0.436; 0.283; 0.151. It shows that there was no significant difference in every characteristic of the research subject, so it could be concluded that the subjects of the research were homogenous.

Neuropathic pain can cause the decrease of living quality to the patients, so it is significant to have a research to investigate the image of patients' living quality after stroke syndrome. It is similar to what was written by NICE (2010) mentioning that living quality needs to be measured because neuropathic pain can have significant effect to people's living quality [7]. This research used Brief Pain Inventory questioner, in which questioner was able to represent: general activities, mood situation, walking capability, usual chores, relationship with other people, and the way to enjoy life. This questioner has lowest score which means to have the best living quality. The processing data of the questioner result score used *t-test* with trust rate 95% by comparing the mean rate of patients' living quality.

Measurement of living quality value used score with 0-10 scales in which score 0 meaning that it did not disturb, and score 10 was very disturbing, so the less the score, the better living quality the patients have. The result of this research also shows that both gabapentin group and amitriptilin group show living quality decrease if it was compared before and after the therapy. The result of the analysis is presented in Table 2.

Table 2. Mean Score of Living Quality of Patients with *PostNyeriPain* in the Initial Condition

Description	Gabapentin Group (mean±SD)			Amitriptilin Group (mean±SD)		
	Week 0	Week 4	p-value	Week 0	Week 4	p-value
Daily Activities	4.83±2.19	3.00±1.76	*0.00	4.50±1.98	2.94±1.69	0.00
Mood Situation	3.91±1.99	2.35±1.27	0.00	4.22±2.24	2.44±1.19	*0.00
Walking Ability	5.22±2.09	3.17±1.59	0.00	3.11±2.35	2.00±1.41	0.00
Daily Chores	4.78±2.11	3.13±1.71	0.00	4.22±1.96	2.89±1.75	*0.00
Relationship with Others	4.43±2.15	2.91±1.62	*0.00	3.06±1.79	1.89±0.83	0.00
Sleeping Quality	3.30±2.64	1.83±1.80	0.00	3.33±2.47	2.06±1.66	0.00
Enjoying Life	4.13±1.91	2.52±1.41	*0.00	3.50±2.04	2.17±1.25	*0.00
Whole Living Quality	26.49±11.08	16.39±8.14	*0.00	22.44±9.85	14.22±6.98	*0.00
Mean Value of Living Quality	4.37±1.82	2.70±1.34	*0.00	3.71±1.64	2.34±1.14	*0.00

*independent test result of *t-test*

Based on the Table 2, it can be known that the mean score of initial whole living quality in gabapentin group got 4.37±1.82. After getting 1 month therapy, they were re-measured, and the result was 2.70±1.34. Systematically there was decrease 1.67 strengthening by *paired sample t-test* which got *p-value* 0.00 ($p < 0.05$) meaning that it was statistically different (significant), while amitriptilin group got 3.71±1.64. After getting the therapy for 1, the patients were re-examined, and the result got was 2.34±1.14. Systematically, there was decrease 1.37 strengthening by *paired sample t-test* (normal data distributed) getting *p-value* 0.00 ($p < 0.05$). It means that it was statistically different (significant).

The explanation above shows that the use of gabapentin and amitriptilin can increase the patients' living quality shown by the decrease of BPI score. There is also the examination of pain intensity, and there was decrease of pain scale by using VAS scale 2.87±1.33 for gabapentin group, and 2.44±0.78 for amitriptilin group in 1 month. Pain intensity could also affect the patients' living quality because the patients do not experience long term pain disturbance, so the patients would feel more comfortable to the disease they had. The idea is similar to Smith (2012) mentioning that patients with neuropathic pain can increase their living quality if they have good living management [8]. Connor (2009) also mentions that the repairment of living quality is strongly correlated to the increase of living quality [9].

In addition, the comparison of using amitriptilin and gabapentin as a neuropathic pain therapy of post stroke is not included in the list of medicine leaphet, so the use still becomes off label use because there were not enough researches that supported the effectivity of both medicines in pain management of post stroke neuropathic. So far there are two Randomized Control Trial investigating the comparison of the therapy effect of gabapentin and amitriptilin; those are Diabetic Peripheral Neuropathic Pain (DPN) (Morello et. al., 1999) and Spinal Cord Injury (Rintala et. al., 2007) [10], [11]. The result of Morello's research (1999) reported that 52% (11 of 21) patients got gabapentin cure (daily dosage 1.565 mg) and 67% (14 of 21) with amitriptilin (daily dosage 59 mg). The research shows that the cure of both medicines can decrease pain intensity, but it could not reflect the comparison effectivity between gabapentin and amitriptilin.

In this research, the investigation was seen from the difference of the initial and the end mean score of the patients' living quality, and those two groups were compared. The objective was to see from which group that was able to repair the patients' living quality after stroke. Based on the table 3 it can be known that the whole living quality of the patients got Mean result±SD. Systematically, gabapentin group was better than amitriptilin group. However, after they were tested by using independent *t-test* sample (normal distribution), significance score was $p > 0,05$ meaning that in this research the change of living quality of gabapentin group and amitriptilin group was not significantly different statistically (not significant). The result of the analysis is presented in Table 3.

Table 3. Mean Score of Living Quality Difference of Post Stroke Pain Patients

Explanation	Gabapentin Group (mean±SD)	Amitriptilin Group (mean±SD)	p-value
Daily Activities	1.83±1.23	1.56±0.98	0.53
Mood Condition	1.57±1.16	1.78±1.35	0.71
Walking Ability	2.04±1.43	1.11±1.23	0.03
Usual Chore	1.65±1.07	1.33±0.97	0.34
Relationship with Other People	1.52±1.08	1.17±1.25	0.18
Sleeping Quality	1.48±1.38	1.28±1.23	0.66
Enjoying Life	1.61±0.89	1.33±1.09	0.15
Whole Living Quality*	10.87±4.90	8.22±4.81	0.22
Mean Value of Difference Living Quality	1.67±0.78	1.37±0.80	0.22

Stroke patients experienced brain sensoric damage, stiff joint/paralyse which can cause pain and strange sensation that is usually called as *central stroke pain or central pain syndrome (CPS)*. CPS was caused by the damage of the area in the thalamus. The pain was the mixture of the feeling of hot, cold, burnt, painful, and numb. That kind of feeling can influence the patients' living quality. Some of the patients complained that the feeling would get worse with the movement difference and cold temperature (before the dawn and twilight). From the research result, there was difference after conducting 1 month therapy both from gabapentin group and from amitriptilin. The patients were capable to do their daily activities better, having more comfortable mood feeling, better walking activity, able to have outdoor activities, so their relationship with other people could be maintained. They were able to have better sleep and enjoy their life better. The reference of researches about living quality of post stroke patients using gabapentin and amitriptilin medicines as pain therapy is very limited. This research is similar to Nurwahyuni research (1999) entitled *Living Quality of Post Stroke Patients Based on Lesi and Stroke Kind*. In this research, 39.13 patients could have good living quality by assessing their answer using Euro Qol questioner [12].

In this research, the researcher also investigated the side effect of using gabapentin and amitriptilin. In gabapentin group, the highest rate of the side effect is sleepiness (16.1%), while for amitriptilin the highest rate was sleepiness (19.2%), weak (11.5%), and dry mouth (7.7%). The result is similar to a previous research by Backonja et. al. (1998) reporting that the main side effect of using gabapentin was headache (24%) and sleepiness (23%) [13], while the side effect that is often reported in the use of amitriptilin is sleepiness and anticholinergic effect (dry mouth and constipation). Gabapentin group and amitriptilin group had the same number of the patients 11 patients getting the side effect of the medicine, but after it was divided with the total patients in the group, there was 42.2% to the group of amitriptilin and 35.3% in the group of gabapentin. From the explanation above, gabapentin had good, secure tolerability, and less interacted with other medicines compared to the other painkillers [14].

Based on the investigation and research data got from gabapentin and amitriptilin group, it could be concluded that those medicines have similar influence to the patients' living quality, so it is expected that both medicines can be re-included as the List and Plafon of Medicine Price as neuron therapy, or in 2014, all Indonesian people can get health insurance, so both medicines can be included in insurance medicine list. It is not only for patients with *Diabetic Peripheral Neuropathy* and *Post Herpetic Neuralgia*. Besides, living quality should become a main consideration in the aspect of cost and side effect. From the aspect of cost, amitriptilin was cheaper than gabapentin, but the efficacy and side effect should be considered too. In the literature, the side effect of amitriptilin medicine can be avoided to the elderly, but based on the demographic data patients with >60 were quite high. In the literature, the side effect of amitriptilin is avoided in elderly, which is based on Morello's research (1999), and Lacy et. al. (2002) reported that it has side effect risk on cardiovascular system and extrapyramidal system [10],[15], however from the demographic data that could be achieved, patients with the age >60 was quite high.

4. CONCLUSION

Both using gabapentin and amitriptilin treatment during 4 weeks showed increasing of living quality in every group, but the comparison of them was not significantly different. That means the comparison of using gabapentin and amitriptilin in post ischemic stroke patient with neuropathy pain not significantly increase the quality of in the hospitals in Jogja.

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