Evaluation of the Use of Antihypertensive Agents in Ischemic Stroke Patients Hospitalized in West Nusa Tenggara Hospital, Indonesia

Evaluasi penggunaan obat antihipertensi pada pasien stroke iskemik rawat inap di Rumah Sakit Umum Daerah Provisi NTB

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ABSTRACT

Antihypertensive agents are one of the drugs recommended on ischemic stroke patients as a secondary therapy for prevention of occurrence repeated stroke and reduce the risk of brain edema. If the management of hypertension is incorrect on ischemic stroke patient can worsen the patient’s condition and affect mortality. The use of antihypertensive drugs must be evaluated accordingly with rational use of drugs. This study aims to examine the accuracy of the use of antihypertensive drugs in ischemic stroke patients which includes right indication, right patient, right medicine, right dose and right frequency. This research is a cross sectional descriptive study using medical record data of 19 ischemic stroke patients. The inclusion criteria of the study were all ischemic stroke hospitalization patients and receiving antihypertensive drugs therapy. The evaluation of accuracy was done descriptively by comparing research data to the literature which includes JNC VII & VIII, PERDOSSI 2011, PIONAS 2015, FORNAS and Revised RSUDP Formulary 6th. The results showed the accuracy of use antihypertensive agents is 100% that is 100% precise indication; 100% right patient; 100% right dose; and 95% right frequency. The type of inaccuracy encountered is frequency imprecision drug administration, therefore the role of a pharmacist in hospital are needed as part of efforts to improve the accuracy of the use of drugs in ischemic stroke patients.

Keywords: antihypertension, ischemic stroke, rational evaluation of drug use

ABSTRAK

Obat antihipertensi merupakan salah satu obat yang direkomendasikan pada pasien stroke iskemik sebagai terapi sekunder untuk pencegahan terhadap terjadinya stroke ulang dan menurunkan resiko edema otak. Apabila penatalaksana hipertensi yang tidak...
tepat pada pasien stroke iskemik maka dapat memperburuk keadaan pasien dan mempengaruhi mortalitas. Penggunaan obat antihipertensi harus dievaluasi sesuai dengan penggunaan obat yang rasional. Penelitian ini bertujuan untuk mengkaji ketepatan penggunaan obat antihipertensi pada pasien stroke iskemik yang meliputi tepat indikasi, tepat pasien, tepat obat, tepat dosis dan tepat frekuensi. Penelitian ini merupakan penelitian deskriptif cross sectional dengan menggunakan data rekam medis 19 pasien stroke iskemik. Kriteria inklusi pada penelitian yaitu semua pasien stroke iskemik rawat inap dan menerima terapi obat antihipertensi. Evaluasi ketepatan dilakukan secara deskriptif dengan membandingkan data penelitian terhadap literature yang meliputi JNC VII & VIII, PERDOSSI 2011, PIONAS 2015, FORNAS dan Formularium RSUDP revisi ke-6. Hasil penelitian menunjukkan ketepatan penggunaan obat yaitu 100%, tepat indikasi; 100%, tepat pasien; 100%, tepat dosis; 100% dan tepat frekuensi; 95%. Jenis ketidak tepatan yang ditemui adalah ketidak tepatan frekuensi pemberian obat, oleh karena itu dibutuhkan peran seorang farmasi di rumah sakit sebagai bagian dari upaya peningkatan ketepatan penggunaan obat pada pasien stroke iskemik.

Kata kunci: antihipertensi, evaluasi penggunaan obat yang rasional, stroke iskemik

Introduction
Stroke is a focal or sometimes global neurological disorder with a sudden onset and occurs more than 24 hours or leads to death, which is estimated to come from blood vessels (WHO, 2006). The cause of stroke is divided into two, namely the presence of ischemia (blockage), which results in disruption of blood flow to the brain and hemorrhagic (bleeding), where blood vessels rupture and blood flow to the brain and extravascular area between the cranium [skull]. Ischemic strokes are strokes that arise as a result of thrombosis or embolysis that occurs in the cerebral blood vessels and causes obstruction of cerebral blood flow to one or more blood vessels of the brain (Saseen et al., 2008).

Stroke is the second death cause in the world after heart disease; the prevalence of stroke patients is approximately 200 per 100,000 population in the world (Padiastuti, 2011). Based on diagnosis in people aged ≥ 15 years, stroke disease in Indonesia has increased from 7,0% per 1.000 population to 10,9% per 1.000 population (Anonym, 2018).

Hypertension or high blood pressure is a major modifiable risk factor for stroke. High blood pressure causes loss of function of the vascular system, leading to a build-up of plaque (crust) or a blockage in the arteries supplying oxygen- rich blood to the brain. Plaque can rupture, causing embolism and the formation of blood clot fragments, which can cause blockage of brain vessels, resulting in decreased blood flow to the brain, which can lead to ischemic stroke (Gorgui et al., 2014).

Handling hypertension is essential for stroke patients to prevent recurrent strokes and other vascular complications. Antihypertensive therapy in stroke patients is recommended as a
secondary therapy to prevent recurrent strokes, reduce the risk of cerebral edema, and hemorrhagic risk, as well as prevent damage-vascular disease (Muir, 2013). Therefore, the selection and use of drugs must be rational, in order for treatment to achieve maximum therapeutic effects with minimum side effects (Munaf, 2004).

Evaluation of the use of antihypertensive drugs in ischemic stroke patients has an essential role in the pharmacy clinical services of hospitals in order to achieve a rational use of antihypertensive medicines in ischemic stroke patients. The number of ischemic strokes in the General Hospital of NTB Province was included in the top 10 diseases to be hospitalized, which ranked 6th in 2018, the number of ischemic stroke cases in January - December 2018 was 518 patients. Previous research on the same topic has never been conducted at the General Hospital of NTB Province. It was the reason for the researchers to be interested in conducting the research related to the evaluation of the use of antihypertensive drugs in ischemic stroke patients at the Inpatient Unit in the General Hospital of NTB Province.

**Results and Discussion**

**Patients' Characteristics**

Based on Table 1, in terms of the gender characteristics, that the ischemic stroke patients who were hospitalized and received therapy with antihypertensive drugs at the NTB General Hospital consisted of 9 males (47.37%) and 10 females (52.63%). These results indicated that female ischemic stroke patients who used antihypertensive medicines were higher in number compared to male patients. This is because there were more female patients who met the inclusion criteria to be included as the sample of the study compared to male patients. According to Appelros research (2009), women after...
menopause have the same risk of stroke as men. The American Heart Association/AHA say that stroke attacks are more common in men than women. This condition is thought to be related to lifestyle and is associated with other risk factors, such as smoking, alcohol consumption, and dyslipidemia (AHA, 2006). Meanwhile, the small number of strokes in women is due to the influence of estrogen, which plays a role in increasing the levels of High-Density Lipoprotein (HDL). High levels of HDL cholesterol can be a protective factor in preventing atherosclerosis in women (Saseen JJ et al, 2008).

In terms of the age characteristics, as shown in the table above the majority (16 of 19) of the hospitalized patients with ischemic stroke patients (84.21%) fell in the age range of 40-65 years, and only 3 patients (15.79%) aged ≥ 65 years. According to research done by Puspita and Putro (2008), they stated that the risk of stroke at the age of ≥ 55 years is 3.64 times compared to the age group of ≤ 55 years. The incidence of stroke increases, along with the aging process. In fact, the results of the study showed that there were 13 patients whose age was ≥ 55 years (68.42%), and 6 patients who were ≤ 55 years (31.57%). Age is one of the risk factors that cannot be modified, PERDOSSI (2011) suggests that stroke attacks productive age (15-65 years) and elderly (≥ 60 years). This is related to the degeneration process (aging) that occurs naturally, especially in the elderly, causing the blood vessels to be stiffer due to plaque or atherosclerosis (Goldstein, 2006).

The most common characteristic of comorbidities in ischemic stroke is hypertension, i.e., 10 cases (52.63%). Hypertension is a blood vessel disorder characterized by a persistent enhancement in blood pressure.

Table 1. Demographic and clinical characteristics of ischemic stroke patients at RSUDP NTB in May-April 2019

<table>
<thead>
<tr>
<th>Patients' characteristics</th>
<th>Parameter</th>
<th>Number of patients (n=19)</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>9</td>
<td>47.37</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>10</td>
<td>52.63</td>
</tr>
<tr>
<td>Age</td>
<td>42-65 years old</td>
<td>16</td>
<td>84.21</td>
</tr>
<tr>
<td></td>
<td>&gt; 65 years old</td>
<td>3</td>
<td>15.79</td>
</tr>
<tr>
<td>Comorbid clinical conditions</td>
<td>Stroke + hypertension</td>
<td>10</td>
<td>52.63</td>
</tr>
<tr>
<td></td>
<td>Stroke + hypertension + DM</td>
<td>1</td>
<td>5.2</td>
</tr>
<tr>
<td></td>
<td>Stroke + hypertension + hyperlipidemia</td>
<td>4</td>
<td>21.05</td>
</tr>
<tr>
<td></td>
<td>Stroke + hypertension + hyperlipidemia + DM</td>
<td>2</td>
<td>10.53</td>
</tr>
<tr>
<td></td>
<td>Stroke + hypertension + cardio heart failure (CHF)</td>
<td>2</td>
<td>10.53</td>
</tr>
</tbody>
</table>
Hypertension is the most critical risk factor for stroke, both strokes caused by an obstruction and one caused by bleeding (PERDOSSI, 2011). A person with hypertension has a 3-4 times higher risk of having a stroke than someone who does not have a history of hypertension. This is because hypertension is able to change the structure of the arteries, so they are damaged or injured, thus leading to plaque formation. Plaque that is in the blood vessels will cause a thrombus, causing reduced oxygen supply to the brain. An unstable thrombus will release and clog small blood vessels, causing oxygen supply to be diminished and tissue death to occur (Kirshner, 2009).

The Pattern of Using Antihypertensive Drugs for Ischemic Stroke Patients at NTB General Hospital for the period May-April 2019

Table 2 shows the pattern of antihypertensive drug use at NTB General Hospital for the period of May-April 2019. The most common use of antihypertensive drugs in ischemic stroke patients in combination therapy, namely the CCB and ARB drug classes, is Amlodipine and Candesartan (42.11%) and in single therapy, is Amlodipine (36.84%) (JNC VIII, 2014). PERDOSSI (2011) recommends specific treatment for stroke patients. The recommended options are angiotensin receptor blockers (ARB) or angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCB) or diuretics. The target blood pressure that must be achieved is <140/90 mmHg (James et al, 2014). The use of antihypertensive drugs in ischemic stroke patients of the research referred to the PERDOSSI literature (2011).

Table 2. Patterns of using antihypertensive drugs for ischemic stroke patients at RSUDP NTB for the period May-April 2019

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Drug type</th>
<th>Total</th>
<th>Percentage (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCB</td>
<td>Amlodipine</td>
<td>7</td>
<td>36,84 %</td>
</tr>
<tr>
<td>ARB</td>
<td>Candesartan</td>
<td>1</td>
<td>5,26 %</td>
</tr>
<tr>
<td>β1-Adrenergic receptor inhibitor</td>
<td>Bisoprolol</td>
<td>1</td>
<td>5,26 %</td>
</tr>
<tr>
<td><strong>2-drug Combination Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CCB + ARB</td>
<td>Amlodipine + candesartan</td>
<td>8</td>
<td>42,11 %</td>
</tr>
<tr>
<td>ARB + β1-Adrenergic receptor inhibitor</td>
<td>Candesartan + bisoprolol</td>
<td>1</td>
<td>5,26 %</td>
</tr>
<tr>
<td><strong>3-drug Combination Therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretic + β1-Adrenergic receptor inhibitor + ARB</td>
<td>Furosemide + bisoprolol + candesartan</td>
<td>1</td>
<td>5,26 %</td>
</tr>
</tbody>
</table>
Rational Use of Antihypertensive Drugs in Ischemic Stroke Patients

For the proper indication aspect, this study obtained 19 cases with a percentage of 100%. Antihypertensive therapy is the recommended therapy for all ischemic stroke patients. The benefits of antihypertensive agents as secondary stroke prevention therapy are to reduce the risk of cerebral edema, and risk of bleeding, as well as to prevent damage to blood vessels (Gofir, 2011).

Right indication refers to the fact that each drug has a specific therapeutic spectrum for a disease or based on the symptoms experienced by the patient (The Ministry of Health of the Republic of Indonesia, 2011). The patient's accuracy of the study was 19 cases with 100% accuracy. The evaluation of the patient's accuracy in applying antihypertensives was done by comparing antihypertensive drugs given at RSUDP NTB with PERDOSSI 2011 and JNC 7, where PERDOSSI recommended antihypertensive agents in ischemic stroke patients with diabetes comorbidities, including CCB or ARB. In this study, all patients with diabetes comorbidities were given the right drug according to the recommended drug class.

When diagnosis made, is incorrect, then the drug given will not properly treat the indications as it should (The Ministry of Health of the Republic of Indonesia, 2011). In terms of the right dose, there were 19 cases from 19 patients with 100% accuracy of the dose of antihypertensive therapy. There was no dose inaccuracy in the analysis, while a previous study found 98% of incorrect dose (Ayu, 2019). Incorrect dosage, namely the administration of excessive doses, especially with a narrow therapeutic index, has a high risk of side effects. In contrast, the administration of drugs with insufficient doses results in an ineffective of drug therapy (The Ministry of Health of the Republic of Indonesia, 2011; the 2017 National Formulary; and the 2019 NTB Provincial Hospital Formulary the 6th revision).

In terms of right frequency, there were 19 cases with 100% accuracy. In the frequency accuracy analysis, there was no inaccuracy of frequency. In fact, is called as incorrect frequency if the use of drugs is not in accordance with the specified frequency of administration. The inaccurate frequency, results in an inaccurate therapeutic dose given. The recommended frequency of using furosemide is divided into 1 daily dose of 20-40 mg in the morning and can be increased by 80 mg in edema (PIONAS, 2015). Patient No. 11 used combination of furosemide at a dose of 40 mg once a day. This case, was said to be given the right frequency, because it followed the criteria or standards set by PIONAS (2015) and the 6th Revised Hospital Formulary (2019).

Conclusion

Based on the analysis, the results of the evaluation of the use of antihypertensive drugs in ischemic stroke patients hospitalized at the General Hospital of West Nusa Tenggara...
Province for the period of May-April 2019, are as follows; the use of antihypertensive medications is 100% of right indication; 100% of right patient; 100% of right medicine; 100% right dosage, and 100% right frequency. There are two patterns of antihypertensive drugs mostly given, namely combination therapy, CCB and ARB, as well as amlodipine and candesartan (42.11%), and a single therapy, i.e., amlodipine (36.84%).

Reference


