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# Antihypertensive and Increased Intracranial Pressure Therapy in Patient with Intracerebral Haemorrhage Stroke and Life Expectancy of Patients during Hospitalization

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**Research Article**

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**Abstract**

**Background and Objectives** --- Intracerebral hemorrhage (ICH) stroke is a type of stroke with the highest mortality rate, with only about 38% of patients who survived for the first year after stroke. Antihypertensive treatment and therapy for increased intracranial pressure is still the main therapy for reduce the mortality rate in ICH. The objective for this research is to study the effect of early antihypertensive treatment and therapy for increased intracranial pressure on life expectancy of patient with ICH stroke during hospitalization in Dr. Sardjito Hospital.

**Methods** --- 165 patients with ICH stroke who meet the inclusion and exclusion criteria divided into 2 major group for case control study. There were 81 patients in case and 84 patients in control groups. Data collection conducted retrospectively through patient medical record.

**Results** --- There were 8 (9,88%) patients in case group and 19 (22,63%) patients in control group which didn't get early antihypertensive therapy. Furosemide, nimodipine and valsartan is the most commonly used antihypertensive for ICH patients during hospitalization. Odds ratio for early antihypertensive therapy is 2,67 (95% CI 1,09 – 6,50; *P* 0,027). Patients which didn't get therapy for increased intracranial pressure as much as 35 (43,21%) patient in case group and 36 (42,86%) patient in control group. Mannitol is one and the only agent used to treat increased intracranial pressure for ICH patient during hospitalization. Odds ratio for used of mannitol is 0,986 (95% CI 0,532 – 1,826; *P* 0,371).

**Conclusions** --- Early use of antihypertensive therapy may increase life expectancy of ICH stroke patient during hospitalization. The relationship between the use of increased intracranial pressure therapy mannitol in ICH stroke patient during hospitalization and life expectancy of patients has not been established clearly.

***Keywords:*** stroke, intracerebral hemorrhage, ntihypertension, intracranial pressure therapy, life expectancy

## Introduction

Intracerebral hemorrhage stroke is a type of stroke with the highest mortality rate, with only about 38% of patients who can survived for the first year after a stroke[1]. Hypertension and increased intracranial pressure is commonly found in patients with intracerebral hemorrhage stroke. Hypertension is the most common cause of intracerebral hemorrhage. High blood pressure can lead to further widening of the hematoma. The hematoma can trigger the occurrence of edema, which can interfere with and suppress the brain tissue then can cause increased intracranial pressure and potentially fatal herniation syndrome[2,3,4].

Morgenstern et al.[5] developed a therapy guidelines for intracerebral hemorrhage stroke patients which is evidence based, one of the focus is the blood pressure therapy. With a focus on treatment of increased blood pressure, expected levels of mortality in patients can be declined. Therapy for the increased intracranial pressure are also expected to reduce mortality and morbidity in patients with intracerebral hemorrhage stroke[2,5].

Research on the use of mannitol and hypertonic saline as a therapy for the increased intracranial pressure and antihypertensive therapy continue to be developed in order to determine the optimal therapy for the treatment of increased intracranial pressure and

hypertension in patients with intracerebral hemorrhage stroke.

The existence of therapy guidelines for intracerebral hemorrhage stroke patients can be used as a reference for health workers to provide treatment to his patients, but did not rule out the existence of other agents can also be used to handle the increased intracranial pressure and the condition of hypertension in patients with intracerebral hemorrhage stroke[6]. It was necessary to do research to find out what therapies are provided to handle the increased intracranial pressure and hypertension conditions experienced by patients with intracerebral hemorrhage stroke during hospitalization at the hospital and its effect on patient life expectancy during hospitalization at the hospital.**Comparison of**

## Methodology

Research was conducted in Dr. Sardjito general hospital at Yogyakarta. This study used a case control design which is an observational study. The study The cases in this study were intracerebral hemorrhage stroke patients who survive after undergoing inpatient in hospital, while controls were patients who died because intracerebral hemorrhage stroke during their inpatient hospital. Patient age must be 40 year old or above and the onset of attack is must be less than 24 hours. Patient with recurrent stroke, patient who had intracerebral hemorrhage because of head injury, patient who is a referral patient and/or has been hospitalized before in another hospital for the intracerebral hemorrhage diagnose and patient who have past history of illness have had transient ischemic attack or ischemic stroke were excluded from this study. Patient's data taken retrospectively using their medical record.

Data were taken from the patient's medical records including age, gender, previous history of illness, glasgow coma scale, onset of attack, blood pressure, temperature, history of present illness, major complaint, diagnose from the doctors, head CT scan, previous history of drug use, antihypertensive therapy, increased intracranial therapy and progress note of patients. Both groups then compared for the antihypertensive treatment and therapy for increase intracranial pressure that they were receive during hospitalization, and seeing the therapy effect on life expectancy of patients during hospitalization.

### Data analyses

Dependent variables measured in this study are the life expectancy of patients during hospitalization use a nominal scale. Independent variables are antihypertensive use and increased intracranial pressure therapy use. Based on data obtained odds ratio will be calculated for each exposure were studied. Statistical analysis to see whether there are differences between the two groups for each treatment using the Statistical Product and Service Solutions (SPSS) version 16. Statistical analysis performed with Chi-Square test and Mann-Whitney test to determine whether there were differences between case group and control group due to the influence of exposure therapy of the use of antihypertensive drugs and therapies for the increased intracranial pressure using 95% level of confidence.

## Results and Discussion

This study is a retrospective study, data taken from patient medical records with a diagnosis of intracerebral haemorrhagic stroke and being treated at Dr. Sardjito hospital during year 2008, 2009 and 2010, patients can be treated in stroke units or neurological inpatient installation. Patients should meet the study inclusion and exclusion criteria. Total patients who become research subjects were 165 patients who are divided into groups of cases for 81 people and a control group of 84 people. Summary of patient demographic data can be seen in Table 1.

**TABLE 1.** Summary of demography data of research subjects patients based on medical record data of RSUP Dr. Sardjito Yogyakarta year 2008 - 2010

| | CONTROL (%) | CASE (%) | TOTAL (%) | P |
|---|---|---|---|---|
| **Sex** | | | | |
| **1. Male** | 56 | 53,1 | 54,5 | 0,712 |
| **2. Female** | 44 | 46,9 | 45,5 | |
| **Age** | | | | |
| **1. 40 to 65 years old** | 58,3 | 71,6 | 64,8 | 0,173 |
| **2. 66 to 75 years old** | 29,8 | 22,2 | 26,1 | |
| **3. 76 to 85 years old** | 11,9 | 6,2 | 9,1 | |
| **History of previous illness** | 78,6 | 76,5 | 77,6 | 0,755 |
| **1. Hypertension** | 16,7 | 9,9 | 13,3 | 0,200 |
| **2. Diabetes Mellitus** | 6 | 3,7 | 4,8 | 0,501 |
| **3. Dislipidemia** | | | | |
| **Onset of attack** | | | | |
| **1. Less than 3 hours** | 25 | 49,4 | 37 | 0,007 |
| **2. 3 to 6 hours** | 34,5 | 17,3 | 26,1 | |
| **3. > 6 to 12 hours** | 17,9 | 12,3 | 15,2 | |
| **4. > 12 to 24 hours** | 22,6 | 21 | 21,8 | |
| **Initial *Glasgow Coma Scale* (GCS)** | 6 | 35,8 | 20,6 | 0,000 |
| **1. 15** | 34,5 | 30,9 | 32,7 | |
| **2. 9 s.d 14** | 59,5 | 33,3 | 46,7 | |
| **3. < 9** | | | | |
| **Body temperature at admission on hospital** | | | | |
| **1. Afebris** | 89,3 | 95,1 | 92,1 | 0,169 |
| **2. Febris** | 10,7 | 4,9 | 7,9 | |

Chi-square statistical test using SPSS 16 carried out to see the distribution of patient demographic data in the case group and control group. Data for gender, age, previous disease history, blood pressure when admitted to hospital and the temperature at admission to the hospital did not show significant differences in distribution between case group and control group, which is the P value for those variables are > 0.05. Significant differences occurred in the distribution of

patient onset attack and the value of GCS, where the P value obtained for both data are < 0.05.

Figure 1 shows systolic blood pressure of patients at admission on Dr. Sardjito hospital, both in the case group and control group. Although there are differences in the percentage of patients for each group of systolic blood pressure between case and control groups, there is no significant difference between the distribution of systolic blood pressure patients in the case and control groups (P = 0.168> 0.05).

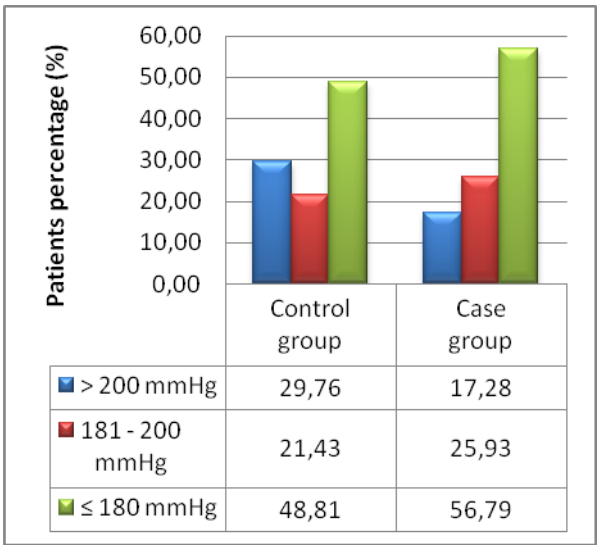


**FIGURE 1.** Systolic blood pressure in cases and controls groups at the admission on RSUP Dr. Sardjito Yogyakarta based on medical record data of RSUP Dr. Sardjito Yogyakarta year 2008 – 2010

**Antihypertensive and increased intracranial pressure therapy**

**a. Antihypertensive drug**

Types of antihypertensive drugs given to patients with intracerebral hemorrhage stroke at Dr. Sardjito hospital Yogyakarta is quite diverse. In figure 2 be seen that the early antihypertensive medications obtained by the patients during hospitalization at the hospital. Management of increased blood pressure in patients with intracerebral hemorrhage stroke at Dr. Sardjito hospital using 12 different types of antihypertensive drugs, either used as single agent or in combination. There are differences between the choice of antihypertensive drug therapy between of AHA guidelines[2,5] and the kind of drug that patient obtained for the first time hospitalized at Dr. Sardjito hospital. Of the 12 types of antihypertensive drugs used in Dr. Sardjito hospital, there is only one agent in accordance with AHA recommendations, which is nicardipine incoming class of calcium channel blockers.

Recommendation selection of antihypertensive drugs was using an antihypertensive drug with rapid onset of effects and the dose is easy to titrate. With the rapid onset, patient high blood pressure can be quickly controlled. While easily titrated doses intended to make adjustments dose can be done more easily and flexibly[2,5,7].

**b. Therapy for increased intracranial pressure**

Therapy for increase intracranial pressure in patients with intracerebral hemorrhage stroke in Dr. Sardjito hospital using osmotic agent mannitol in accordance with the recommendations of the AHA[2,5]. Table 2 shows the percentage use of the mannitol in the control and cases groups. The use of mannitol starts on the first day of treatment in the control group 39.29% and 43.21% in the case group is more common while compared to the use of the mannitol that began on the second day of treatment on wards.

**TABLE 2.** Mannitol use in patients with intracerebral hemorrhage stroke during hospitalization in hospital based on medical record data of RSUP Dr. Sardjito Yogyakarta year 2008 - 2010

| Mannitol | Control group n (%) | Cases group n (%) | Total n (%) |
|---|---|---|---|
| **Without mannitol therapy** | 36 (42,86) | 35 (43,21) | 71 (43,03) |
| **Start at day 1** | 33 (39,29) | 35 (43,21) | 68 (41,21) |
| **Start at day 2** | 9 (10,71) | 8 (9,88) | 17 (10,30) |
| **Start at day 3** | 2 (2,38) | 1 (1,23) | 3 (1,82) |
| **Start at day 4 onward** | 4 (4,76) | 2 (2,47) | 6 (3,64) |
| **TOTAL** | 84 | 81 | 165 |

**Analysis of the influence of drug therapy on patients life expectancy during hospitalization at the hospital**

**a. Effect of antihypertensive therapy**

Table 3 shows the number of patients in the case group and control group who have early antihypertensive therapy in the hospital. Odds ratio of early antihypertensive therapy was 2.67 (95% Confidence Interval (CI) 1.09 to 6.50). Values of the odds ratios showed that patients with intracerebral hemorrhage stroke who received early antihypertensive therapy in the hospital has a life expectancy of 2.67 times greater than patients with intracerebral hemorrhage stroke who did not receive early antihypertensive therapy in the hospital.

Analysis results use of antihypertensive therapy in intracerebral hemorrhage patient in this study was supported by current research. Meyer and Baurer[8] demonstrated the improvement in mortality in patient with intracerebral hemorrhage who were treated with antihypertensive medication even if the result of this study were limited by the fact that the treated group had less severe symptomps. Dandapani et al.[9] have shown reduction in mortality and morbidity with the reduction of blood pressure within 2 – 6 hours after intracerebral hemorrhage, but this study did not consider variables like ICH volume, ventricular blood and initial GCS.

**TABLE 3.** Odds ratio for early antihypertensive therapy that obtained by the patients with intracerebral hemoorhage stroke based on medical record data of RSUP Dr. Sardjito Yogyakarta year 2008 - 2010

| | Cases | Control |
|---|---|---|
| **Antihypertensive** | 73 | 65 |
| **Without antihypertensive** | 8 | 19 |
| **Odds rasio = (74 x 19) : (65 x 8) = 2,67**<br>**95% Confidence Interval = 1,09 – 6,50** | | |

**TABLE 4.** Results of statistical tests for the early use of antihypertensive medication in patient with intracerebral hemorrhage stroke based on medical record data of RSUP Dr. Sardjito Yogyakarta year 2008 - 2010

| Antihypertensive therapy | Control group | Cases group | *P* |
|---|---|---|---|
| **Antihypertensive therapy** | | | |
| **With antihypertensive therapy** | 65 | 73 | 0,027 |
| **Without antihypertensive therapy** | 19 | 8 | |
| **The combination of antihypertension** | | | |
| **Single agent** | 48 | 47 | 0,175 |
| **Combination of 2 agent** | 15 | 19 | |
| **Combination ≥ 3 agent** | 2 | 7 | |

Statistical test results showed that there were significant differences of live expectancy between case and control groups due to the effect of antihypertensive therapy (P = 0.027). The statistical test showed that there is no significant differences of live expectancy between the use of a single antihypertensive with the use of antihypertensive combination in the case and control groups (P = 0.175> 0.05). This is can be caused by the distribution of patients with a history of hypertension and diabetes mellitus evenly between the control group and groups of cases, other than that there was no significant difference to patients' blood pressure when admitted to hospital between case group and control group.

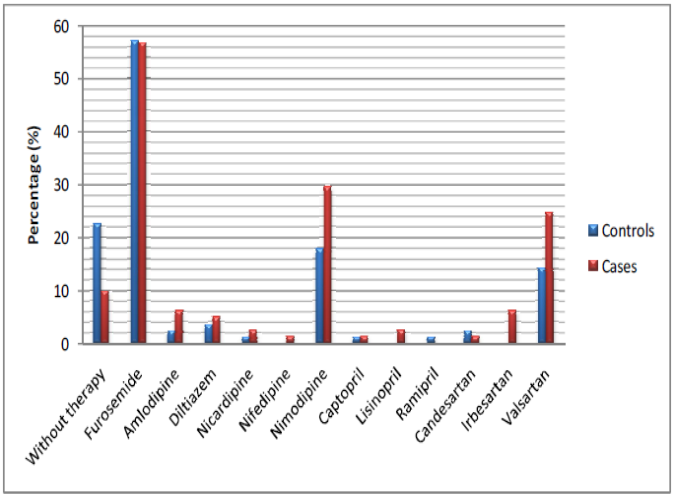


**FIGURE 2.** Type of early antihypertensive therapy on intracerebral hemorrhage stroke patient based on Dr. Sardjito Hospital medical record of 2008 -2010

**b. Effect of mannitol therapy**

Table 5 shows the calculation of odds ratios using mannitol as a therapy to treat increased intracranial pressure in patients with intracerebral hemorrhage stroke. Odds ratio is the use of mannitol as a whole is 0.986 (95% CI 0.532 to 1.826). Value odds ratio approached a value of 1 and range level of 95% cover value of 1, this shows that the relationship between the use of mannitol during hospitalization and life expectancy of patients during hospitalization cannot be clearly demonstrated in this study. Then when therapy with mannitol is divided based on usage within ≤ 48 hours after hospitalization and use of more than 48 hours after admission is considered not get the therapy mannitol as shown in table 5 the second row, the odds ratio value obtained was 1.132 (95 % CI 0.614 to 2.085). This means that although mannitol is given within the first 48 hours after the patient entered the hospital also has not been established clearly whether mannitol administration will have an influence on life expectancy of patients during hospitalization at the hospital.

**TABLE 5.** Odds rasio and result of statistical test for the use of mannitol in patients with intracerebral hemorrhage stroke based on medical record data of RSUP Dr. Sardjito Yogyakarta year 2008 - 2010

| Mannitol | Control group | Cases group | OR (95% CI) | *P* |
|---|---|---|---|---|
| **Mannitol use during hospitalization** | | | | |
| • **Mannitol** | 48 | 46 | 0,986 (0,532 – 1,826) | 0,371 |
| • **Without Mannitol** | 36 | 35 | | |
| **Mannitol use within 48 hours** | | | | |
| • **Mannitol ≤ 48 hours** | 42 | 43 | 1,13 (0,614-2,09) | 0,693 |
| • **Without Mannitol** | 42 | 38 | | |

Statistical test for the use of mannitol during hospitalization showed that there was no significant difference in the effect of mannitol during hospitalization of the case group and control group (P = 0.371> 0.05), whereas the use of mannitol in the statistical test within first 48 hours after admission also showed no significant difference between the effect of mannitol within the first 48 hours of hospital care with the use of mannitol over 48 hours after admission or without use of mannitol (P = 0.693> 0.05). It means giving mannitol on intracerebral haemorrhagic stroke patients do not have a different effect on the outcome of therapy in this study is the life expectancy for patients undergoing inpatient at the hospital.

Review of 3 researches on the use of mannitol in stroke cases by Bereczki et al.[10], one study is about the use of mannitol in ischemic stroke cases and two studies on the use of mannitol in cases of intracerebral hemorrhagic stroke showed that clinical improvement no higher after treatment with mannitol. Not found and no adverse events were reported in the study. Based on this 3 small study, it can not prove the existence of a beneficial effect or harm from use of the mannitol. Although nort found statistically significant differences between groups that obtain mannitol therapy and control groups, but the calculation of confidence

intervals for therapeutic effects including wide, encompassing the possibility of clinical benefit significant as well as the possibility of significant harm.

## Conclusion

Result of this study showed that the use of early antihypertensive drug can increase the live expectancy of patient with odd ratio 2,67. Research result for mannitol showed that the relationship between the use of mannitol during hospitalization and the patient's life expectancy cannot be clearly established. However, it is need to considering the effect of confounding factor. Gender, age, previous history of illness, blood pressure and temperature at admission is the confounding which can be controlled in this study. Onset of attack and GCS is the confounding factor which is cannot be controlled. The statistical result showed that there is a significant difference between cases group and control group for onset of attack and GCS value of patients. A well designed, prospective, cohort or randomized controlled trial is urgently needed to confirm our results.

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## AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

## PEER REVIEW

Not commissioned; externally peer reviewed

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests