

Research Article

Mannitol Usage Pattern in Hemorrhagic Stroke Patients

Siti Aisyah^{1*}, Didik Hasmono², Binti Muzayyanah³, and Firasti Agung NS¹¹Faculty of Health Sciences, Pharmacy Department, Muhammadiyah Malang University²Faculty of Pharmacy, Airlangga University³Dr.Iskak Tulungagung Regional Public Hospital**ORCID**Siti Aisyah: <https://orcid.org/0000-0002-0839-7941>**Abstract.**

Hemorrhagic stroke is a condition where one of the arteries in the brain bursts, causing bleeding in that organ. Mannitol is an osmotic diuretic drug often used to correct high intracranial pressure due to bleeding. This research aimed to determine the pattern of mannitol in hemorrhagic stroke at the Inpatient Installation of Dr. Iskak Tulungagung Regional Public Hospital. This was a retrospective observational study with the presentation of data descriptively in patients with hemorrhagic stroke who received mannitol therapy at Inpatient Installation Dr. Iskak Tulungagung Regional Public Hospital. Mannitol was only used alone with the highest dose (2x0.3g/kgBW) for 65 patients (81%). Mannitol was used in single usage with the highest dose (2x0,3g/kg BW) in 65 patients (81%). Mannitol with the most widely dose switching pattern usage is from (6x0,3g/kg BW) iv to (5x0,3g/kg BW) iv to (4x0.3g/kg BW) iv to (3x0.3g/kg BW) iv to (2x0.3g/kg BW) iv to (1x0.3g/kg BW) iv to 11 patients (14%). Mannitol was given by tapering off or decreasing the dose slowly and the duration of use of Mannitol with the highest percentage at 4-7 days in as many as 68 patients (85%).

Keywords: mannitol, hemorrhagic stroke, diuretic osmotic

Corresponding Author: Siti

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1. Introduction

According to the Ministry of Health (1) stroke is a disorder of nerve function in the brain that lasts for 24 hours suddenly and comes from non-traumatic brain blood circulation disorders. The condition occurs suddenly, quickly and can cause changes in consciousness, visual disturbances, paralysis in some parts of the body, and according to WHO (2019), clinical manifestations of stroke occur quickly, last, and can even lead to death, and have no other cause. except for vascular disease.

Stroke is the third leading cause of death in the world after coronary heart disease and cancer. According to data from American Heart Association (2) the incidence of death from stroke is about 401 people die from stroke every day. Based on the 2018 Basic Health Research, the highest prevalence of stroke in Indonesia based on a doctor's

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diagnosis at the age of 15 years by province is the highest province of East Kalimantan (14.7%). Based on the age group, the highest data was obtained, namely the age of 45-54 (45.5%) and the lowest was at the age of 25-34 (18.4%). Based on gender, stroke patients have a greater potential for men (41.0%) than women (37.8%), while the incidence of stroke based on place of residence, in urban areas, is greater (42.4%) than in rural areas (34, 1%).

Hemorrhagic strokes can be caused by various diseases that affect blood vessels, including prolonged hypertension and brain aneurysms. An aneurysm is a weak spot in the wall of an artery that swells. The presence of blood in the brain parenchyma causes mechanical stress on susceptible tissues and subsequent activation of inflammation and neurotoxins. Molecular mediators of secondary brain injury and perihematomal edema. Where is characterized by the sudden rupture of a blood vessel in the brain, which causes blood to collect rapidly in the brain tissue, ventricular system, or subarachnoid space, it is called a hematoma. Damage after hemorrhagic stroke is triggered by the rupture of red blood cells, the release of hemoglobin, and iron, and activation of coagulation, leading to permanent damage to components of the neurovascular unit, followed by blood-brain barrier disruption and lethal brain edema with cerebrum cell death (3)

Symptoms based on intracranial pressure (ICP), range from general symptoms such as headache, nausea and vomiting, decreased consciousness, and frequent seizures, to severe signs of more severe nerve damage (4)

The management of hemorrhagic stroke aims to increase cerebral blood flow and repair the occurrence of hernias. General actions can be done in the form of medication and surgery. Pharmacological therapy can be given in the form of oral anticoagulants such as warfarin, to prevent blood clots and for prolonged coagulation screening, including Rivaroxaban and Apixaban. Patients are then given iv Vitamin K along with fresh frozen plasma (FFP) to treat coagulation, antiplatelet agents to evaluate the effectiveness of platelet transfusions, hemostatic agents are used during surgical procedures to achieve hemostasis, patients are also given antihypertensive drugs for blood pressure management such as nifedipine, and given hypertonic fluids to prevent an increase in acute intracranial pressure such as mannitol or hypertonic saline (3,5)

The drug that is usually given to stroke patients when there is an increase in intracranial pressure is mannitol. Mannitol is an osmotic diuretic drug that is widely chosen as a therapy for stroke to treat high intracranial pressure. Mannitol works by creating an osmotic gradient across the blood-brain barrier that draws water into the vascular space. This effect is used to reduce intracranial pressure. Many nephrologists also

use mannitol to prevent adverse reactions when first starting patients on hemodialysis (6). Adult patients should be infused with 20% mannitol at a dose of 1-1.5 g/kg. If the intracranial pressure rises sharply without damaging the blood-brain barrier, this dose is usually given (5)

The advantage of Mannitol in lowering intracranial pressure compared to other diuretic groups is that Mannitol is given intravenously by lowering intracranial pressure within a few minutes, namely within 30 minutes by reducing hematocrit and blood viscosity which will increase oxygen supply. blood flow. Mannitol also has a free radical scavenging function with potential cytoprotection by reducing the harmful effects of free radicals during ischemic reperfusion injury(7). Among other osmotic diuretics such as Isosorbide, Glycerin, and Urea, Mannitol has the fastest half-life of 0.25 hours so it can reduce intracranial pressure rapidly (8).

2. METHOD

The research is observational, that is, by not intervening or treating the sample. The method used is a descriptive design and retrospective data collection by processing Health Medical Record data for patients with a diagnosis of hemorrhagic stroke and receiving mannitol therapy at dr.Iskak Tulungagung Hospital in the period January 1-December 31, 2020.

3. RESEARCH RESULTS

3.1. Patient Demographic Data

Total patient obtained was 80 and the domination of respondents based on gender is woman which number is 46 (58%). Based on the age classification, hemorrhagic stroke patients by age were mostly at the age of >65 years as many as 31 patients (39%). In addition, tracing the history of disease in hemorrhagic stroke patients showed that the most history of stroke was hypertension, as many as 61 patients (76%).

3.2. Mannitol Single Use Therapeutic Pattern

Table 1 shows the pattern of single-dose mannitol used by hemorrhagic stroke patients. Among them were loading doses (1x0.6g/kg BW) iv as many as 36 patients (45%), followed by doses (6x0.3g/kg BW) iv as many as 41 patients (51%), (5x0.3g/kg BW) iv

TABLE 1: Mannitol single use pattern.

No	Mannitol preparation	Dosage Regimen	Number of Patients	Percentage (%)
1	Manitol 20%	(1x0,6g/kgBW) iv	36	45
2	Manitol 20%	(6x0,3g/kgBW) iv	41	51
3	Manitol 20%	(5x0,3g/kgBW) iv	38	48
4	Manitol 20%	(4x0,3g/kgBW) iv	43	54
5	Manitol 20%	(3x0,3g/kgBW) iv	46	58
6	Manitol 20%	(2x0,3g/kgBW) iv	65	81
7	Manitol 20%	(1x0,3g/kgBW) iv	64	80
Total			333	100

* one patient may receive more than one pattern of Mannitol therapy

as 38 patients (48%), (4x0.3g/kg BW) iv as many as 43 patients (54%), (3x0.3g/kg BW) iv as many as 46 patients (58%), (1x0.3g/kg BW) iv as many as 64 patients (80%), and the highest dose was (2x0.3g/kg BW)iv as many as 65 patients (81%).

3.3. Mannitol Switching Dosage Pattern

Table 2 describes the pattern of dose switching on the use of Mannitol by tapering off or slowly decreasing the dose from the dose (1x0.6g/kg BW) iv to (2x0.3g/kg BW) iv.

3.4. Mannitol Duration of use

There are three classifications of duration of use, namely 1-3 days for as many as 5 patients (6%), >7 days for as many as 7 patients (9%), and the most frequent use is 4-7 days as many as 68 patients (85%).

3.5. Drug Therapy other than Mannitol in Ischemic stroke patients

3.6. Hospital admission and condition of patient discharge.

The distribution of the length of hospital admission obtained the highest results in 5-10 days of treatment as many as 69 patients (86%). The distribution of the condition out of the hospital was divided into 2 categories, namely recovering and improving, the most results obtained were in improving conditions as many as 78 patients (98%).

TABLE 2: Mannitol Switching Dosage Pattern.

No	Mannitol Strength	Switching Pattern	Number of patients	Percentage (%)
1	Manitol 20%	(1x0,6g/kgBW) iv → (6x0,3g/kgBW) iv → (4x0,3g/kgBW) iv → (2x0,3g/kgBW) iv → (1x0,3g/kgBW) iv	6	8
2	Manitol 20%	(1x0,6g/kgBW)iv→(5x0,3g/kgBW) iv→(4x0,3g/kg BW) iv → (2x0,3g/kgBW) iv → (1x0,3g/kgBW)iv	5	6
3	Manitol 20%	(1x0,6g/kgBW)iv → (4x0,3g/kgBW) iv → (3x0,3g/kgBW) iv → (2x0,3g/kgBW) iv → (1x0,3g/kgBW) iv	4	5
4	Manitol 20%	(1x0,6g/kgBW) iv → (3x0,3g/kgBW) iv → (2x0,3g/kgBW)iv → (1x0,3g?kgBW) iv	4	5
5	Manitol 20%	(1x0,6g/kgBW) iv → (5x0,3g/kgBW) iv → (2x0,3g/kgBW)iv → (1x0,3g/kgBW) iv	5	6
6	Manitol 20%	(1x0,6g/kgBW)iv → (6x0,3g/kgBW) iv → (3x0,3g/kgBW) iv→ (1x0,3g/kgBW) iv	4	5
7	Manitol 20%	(1x0,6g/kgBW) iv→(4x0,3g/kgBW) iv→(2x0,3g/kgBW) iv	3	4
8	Manitol 20%	(6x0,3g/kgBW) iv→ (5x0,3g/kgBW) iv → (4x0,3g/kgBW) iv→(3x0,3g/kgBW) iv → (2x0,3g/kgBW) iv→ (1x0,3g/kgBW) iv	11	14
9	Manitol 20%	(6x0,3g/kgBW)iv → iv(5x0,3g/kgBW) iv→ (3x0,3g/kgBW) iv→(2x0,3g/kgBW) iv → (1x0,3g/kgBW) iv	7	9
10	Manitol 20%	(6x0,3g/kgBW) iv → (4x0,3g/kgBW) iv → (2x0,3g/kgBW) iv → (1x0,3g/kgBW) iv	7	9
11	Manitol 20%	(6x0,3g/kgBW) iv → (3x0,3g/kgBW) iv → (2x0,3g/kgBW) iv→ (1x0,3g/kgBW) iv	2	3
12	Manitol 20%	(6x0,3g/kgBW) iv→ (5x0,3g/kgBW) iv→ (3x0,3g/kgBW) iv	2	3
Total			79	100

4. DISCUSSION

The management of hemorrhagic stroke aims to increase cerebral blood flow and repair the occurrence of hernias. General actions can be done in the form of medication and surgery. Pharmacological therapy (Table 3) can be given in the form of oral anticoagulants such as warfarin, to prevent blood clots and for prolonged coagulation screening, including Rivaroxaban and Apixaban. Patients are then given iv Vitamin K along with fresh frozen plasma (FFP) to treat coagulation, antiplatelet agents to evaluate the effectiveness of platelet transfusions, hemostatic agents are used during surgical procedures to achieve hemostasis, patients are also given antihypertensive drugs for blood pressure management such as nicardipine, and given hypertonic fluids to prevent an increase in acute intracranial pressure such as mannitol or hypertonic saline ((3,5).

TABLE 3: Drug therapy other than mannitol in ischemic stroke patients.

Class Therapy	Drug Class	Drug Regiment	Number of patients	Group percentage
Antihypertens	Calcium channel blocker	Amlodipine (1x10mg) po	63	79
		Amlodipine (2x5mg) po	5	6
		Nicardipine (1x0,5mcg /kgBB /menit) iv	55	67
		Nimodipine (3x60mg) po	4	5
		Nimodipine (3x30mg) po	2	2
		Nimodipine (3x20mg) po	4	5
	Beta-blocker	Bisoprolol(1x5mg) po	9	11
	ACE inhibitor	Captopril(1x12,5mg) po	1	1
		Captopri (1x25mg) po	6	8
	Diuretik Thiazide	Hydrochlorthiazide (1x12,5mg) po	7	9
		Hydrochlorthiazide (1x25mg) po	15	19
	Angiotensin receptor blocker	Valsartan(1x160mg) po	16	20
		Valsartan (1x80mg) po	10	13
		Candesartan (1x16mg) po	25	31
	Candesartan (1x8mg) po	3	4	
Total			225	100
Neuroprotectan		Citicoline (2x250mg) iv	40	50
		Citicoline (2x500mg) iv	32	40
Total			72	100
Antifibrinolytic		Asam Tranexamat (1x500mg) iv	22	28
Total			22	100

Based on gender, there were 46 female patients, which means 58% of the 80 samples. While male patients were 34 patients, which means 42% of the total sample. However, the incidence of stroke did not show much difference between women and men. According to Beale *et al* (9) in the case of hypertension, which is a precipitating factor for stroke, women have greater arterial elasticity, higher pulse pressure, smaller and stiffer aortic arches, and earlier wave reflection than men. depends on body size and heart rate causing pulmonary hypertension which is higher than in men.

The most widely used dose of mannitol in patients was (2x0.3g/kg BW) iv as many as 65 patients (81%). The results of the study at dr.Iskak Tulungagung Hospital is following the therapy guidelines in Indonesia contained in PERDOSSI that Mannitol 0.25-0.50 g/kg BW, for > 20 minutes, repeated every 4-6 hours with a target of 310 mOsrn/L (10). Administer mannitol intravenously as a bolus to reduce intracranial pressure. Marked intracranial decrease such as headache, vomiting, and decreased consciousness (11).

Mannitol works to reduce intracranial pressure rapidly through changes in blood fluid dynamics or rheology, namely lowering hematocrit and blood viscosity, increasing blood flow to the brain thereby reducing brain vascular diameter as a result of autoregulation. Rheological effects are best achieved by rapid bolus administration rather than continuous infusion (12). Mannitol in lowering intracranial pressure was evaluated clinically by GCS (Glasgow coma scale). Increased intracranial pressure will compress the entire brain tissue because the intracranial volume of the brain is fixed. In addition to being evaluated with GCS, other therapeutic targets are lowering blood pressure, reducing headaches, vomiting, and increasing consciousness. The target of decreasing blood pressure as seen from the pathophysiology of increased intracranial pressure is associated with an increase in blood pressure in the brain (13). Meanwhile, the pattern of dose switching on the use of Mannitol with tapering off or slowly decreasing the dose from the dose (1x0.6g/BW) iv to (2x0.3g/kgBW) iv.

In the study by Berezcki et al (14) Mannitol 20% was administered intravenously every four hours for five days. The duration of use of Mannitol in the study results obtained was associated with GCS rates and blood pressure in patients. Mannitol has a side effect of rebound phenomena, namely an increase in intracranial pressure due to a reversal of the osmotic difference if used in the long term. Mannitol can cause vasodilation depending on the dose and speed of administration. Vasodilation due to mannitol can cause an increase in cerebral blood volume and intracranial pressure simultaneously with a decrease in systemic blood pressure (15). However, the results of the research at RSUD Dr.Iskak did not find a rebound phenomenon, because its use was not long term.

The condition of leaving the hospital in stroke patients showed improved conditions or continued outpatient care with 80 (100%) patients. The patient improved with this outpatient treatment because the patient received intensive care from doctors and nurses on duty at the hospital. In addition, this condition could be because the patient had also been given the right drug for the indication, on time, on the right dose, and the right route. Patients who are improving because they have to receive further treatment by taking medication that can be done at home.

5. CONCLUSION

Mannitol was used in single usage with the highest dose (2x0,3g/kg BW) in 65 patients (81%). Mannitol with the most widely dose switching pattern usage is from (6x0,3g/kg BW) iv to (5x0,3g/kg BW) iv to (4x0.3g/kg BW) iv to (3x0.3g/kg BW) iv to (2x0.3g/kg BW) iv to (1x0.3g/kg BW) iv to 11 patients (14%). Mannitol was given by tapering off

or decreasing the dose slowly and the duration of use of Mannitol with the highest percentage at 4-7 days in as many as 68 patients (85%).

This research has been approved by the health research ethics commission of the Dr. Iskak Tulungagung Regional Public Hospital on April 21, 2021 with the number 070/365/407.206/2021

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