

The Role of Hypertonic Saline in Managing Malignant Cerebral Edema Due to Large Vessel Occlusion Stroke: A Case Report

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Received: March 24, 2024; Accepted: April 23, 2024; Available online: July 10, 2024

ABSTRACT

Background: Malignant cerebral edema (MCE) is a complication of large vessel occlusion stroke mainly treated by decompressive craniectomy. The aim of this case report is to demonstrate the efficacy of providing hypertonic saline (3% NaCl) as an alternative treatment for reducing intracranial pressure (ICP) in an MCE patient who refuses surgery.

Case Presentation: A 66-year-old man went to the emergency department with unconsciousness, right-sided hemiplegia, and global aphasia for 4.5 hours before admission. His National Institutes of Health Stroke Scale (NIHSS) score was 12. The patient's brain magnetic resonance imaging (MRI) revealed a large infarction on the left frontotemporoparietal lobe which caused a subfalcine herniation 1.4cm to the right side. He also suffered hyponatremia (115mmol/L). The family refused decompressive craniectomy. The patient received 200ml of 3% NaCl drip intravenous as an initial dose over 20 minutes every 6 hours. Subsequent administration is gradually reduced every 25ml with a distance adjusted to the patient's condition up to 50ml as the last dose. The patient's 90-day modified Rankin Scale (mRS) score was 4.

Results: The patient with MCE in this case who was administered 3% NaCl as conservative therapy had satisfactory outcomes, as demonstrated by the improvement of the clinical neurological condition.

Conclusion: In patients who decline surgery, 3% NaCl might be given as a conservative treatment option to reduce ICP while maintaining serum sodium levels under control. This case revealed a positive clinical result without complications.

Keywords: Hypertonic saline, large vessel occlusion stroke, malignant cerebral edema

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Cite this as:

Zairinal RA, Malufti CN (2024). Indones J Med. The Role of Hypertonic Saline in Managing Malignant Cerebral Edema Due to Large Vessel Occlusion Stroke: A Case Report. 09(03): 382-387. <https://doi.org/10.26911/theijmed.2024.09.03.12>.



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BACKGROUND

Stroke cases remain a major public health issue to this day. According to the Global Burden of Disease (GBD) in 2019, stroke is the world's second leading cause of death, with over 12.2 million new stroke cases reported each year (Feigin et al., 2022;

World Stroke Organization, 2022). Ischemic stroke accounted for 62.4% of all new cases reported in 2019 (Feigin et al., 2021).

Ischemic stroke due to large vessel occlusion (large vessel occlusion/LVO) can cause extensive infarction which carries the risk of further complications in the form of

malignant cerebral edema (MCE) (Miao et al., 2020; Berger et al., 2023). MCE is a complication with a mortality rate up to 78% (Wu et al., 2018). This occurs due to swelling of the brain parenchyma and progressive herniation which is directly related to increased intracranial pressure (ICP) (Wu et al., 2018; Chugh, Sunshine, et al., 2021; Dalby et al., 2021). Decompressive craniectomy has been proven to reduce the 30-day mortality rate by up to 24.3%, so surgery is recommended as a treatment for MCE patients (Raffiq et al., 2014; Thorén et al., 2017; Beez et al., 2019).

In patients who do not undergo surgery, no alternative therapy has been proven to be as effective as operative management for lowering ICP. Hypersaline therapy has been used for decades to reduce cerebral edema and ICP, but the role of continuous hypertonic infusion in patients with large ischemic infarction remains controversial. The data supporting its use over intermittent bolus dosing are limited, no studies have demonstrated a sustained reduction in cerebral edema or improvement in neurologic outcome in patients with ischemic infarction of the large vessel region (Chugh, Maynard, et al., 2021; Chugh, Sunshine, et al., 2021).

Recently published guidelines from the Neurocritical Care Society highlight the lack of evidence regarding the use of hypertonic saline for the management of cerebral edema in ischemic stroke. Additionally, most studies involved comparisons of mannitol versus hypertonic saline with the primary outcome is ICP control, without optimally matched cohort groups. Most of these studies show that transient use of hypertonic saline results in effective control of ICP even in cases of mannitol failure (Cook et al., 2020). One study by Chugh et al., stated that short-term use of hypertonic saline showed a decrease in ICP, but there was no significant difference in neurological,

functional, or overall death outcome (Cook et al., 2020; Chugh, Maynard, et al., 2021; Chugh, Sunshine, et al., 2021). The aim of this case report is to demonstrate the case of administering 3% NaCl to an MCE patient who refused surgery with improvement of the neurological condition.

CASE PRESENTATION

A 66 year old man went to the emergency department with unconsciousness, weakness on the right side of the body, and unable to speak since 4.5 hours before admission. The patient had no history of previous disease. On examination of vital signs, blood pressure was found to be 163/76 mmHg, heart rate 89 times/minute, respiratory rate 20 times/minute, and oxygen saturation 98% (room air). General physical examination was within normal limits. On neurological examination, the Glasgow coma scale score (GCS) E3M5V2, round pupils isochore diameter 3mm/3mm reactive bilaterally, and neck stiffness is negative. There was a right-sided VII central nerve paresis, the impression of right-sided hemiplegia with a negative Babinski reflex, and the sensory examination could not be evaluated. Score of National Institutes of Health Stroke Scale (NIHSS) patient's was 12.

Laboratory results showed hyponatremia (115mmol/L). On the examination of non-contrast brain magnetic resonance imaging (MRI) revealed a large acute infarction of the left frontotemporoparietal lobe which caused a subfalcine herniation 1.4 cm to the right (Figure 1). Based on clinical and supporting data, the patient was diagnosed with malignant cerebral edema due to ischemic stroke in left middle cerebral artery (MCA) with brain herniation, hypertension, and hyponatremia. We planned a decompressive craniectomy on the patient, but the patient's family refused.

We gave conservative therapy to patient using hypertonic saline (NaCl 3%) with an initial dose of 200ml NaCl 3% intravenous for 20 minutes every 6 hours. After the first 24 hours, the patient's serum sodium level began to rise to 118mmol/L and 3% NaCl administration was continued (Figure 2). On day 3 of treatment, the patient's serum sodium rise to 127mmol/L. The dose of 3% NaCl was reduced gradually by 25ml every 12 hours. The serum sodium level remained at 127mmol/L on day 4, so the 3% NaCl dose was maintained at 150 ml 4 times a day. The dose of hypertonic saline

was reduced again gradually by 25ml every 12 hours on day 5 and 6. The patient's clinical condition tended to improve and stabilize since being admitted to the hospital. Adequate patient contact and GCS score E4M5Vaphasia with persistent right hemiplegia. On day 7, the patient's serum sodium level remained at 127mmol/L so administration was stopped after one dose of 50ml of 3% NaCl. The patient was allowed to discharged after 1 week of treatment. For patient's 90-day *Modified Rankin Scale* (mRS) score was 4.

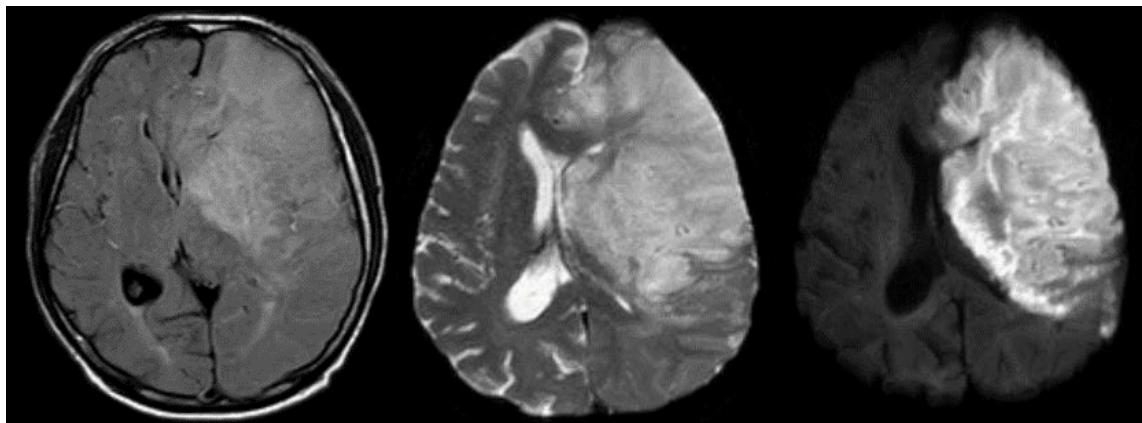


Figure 1. Patient's Brain MRI (Personal Documentation)
A large infarction in the left frontotemporoparietal lobe compressed the left lateral ventricle and third ventricle, causing a midline shift.

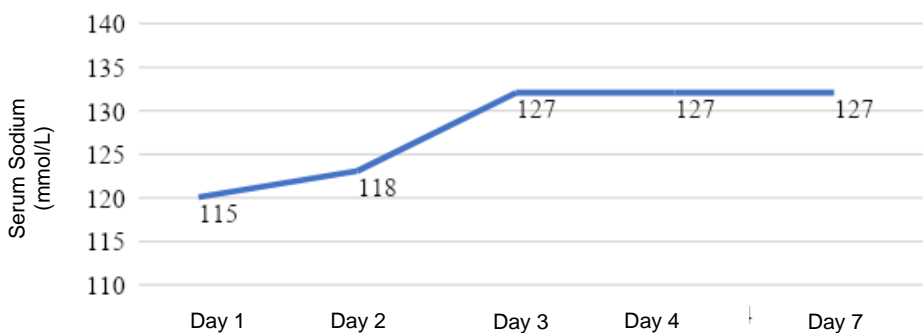


Figure 2. Patient's Serum Sodium Level during Treatment

DISCUSSION

The evolution of cerebral edema occurs within hours to days in acute ischemic stroke. This condition depends on many factors including the severity of the stroke and the size of the lesion. The severity of stroke is measured through the NIHSS score which is generally higher in MCE patients (Miao et al., 2020; Foroushani et al., 2022). For our patient with a clinical manifestation and an NIHSS score of 12, MCE occurred due to the large size of the lesion resulting in midline shift and cerebral herniation on the MRI image. The MRI results also showed the fronto-temporoparietal lobe as the location of a large infarction, where the large MCA blood vessels supply blood to those area (Baehr and Frotscher, 2018). Extensive infarction of the MCA is the most feared complication of ischemic stroke in the anterior circulation because it can cause MCE (Chugh, Sunshine, et al., 2021; Berger et al., 2023).

For our 66 year old patient who is already experiencing the aging process, this condition causes brain atrophy. Aging is characterized by a progressive reduction in brain volume of approximately 5% per decade after the age of 40 years. The morphological changes that occur are: gray matter, white matter, cerebral atrophy, ventricular enlargement, and sulcus widening. The volume of the frontal lobe can decrease by up to 9% but there is no significant change in the occipital and parietal lobes. A study in the UK found that the prefrontal cortex is most affected in the aging process (Peters, 2006; Markov et al., 2017; Lee and Kim, 2022).

Several studies have found that brain atrophy can prevent increased ICP and cerebral herniation in patients with large cerebral infarction by providing additional intracranial space as compensation. This condition can prevent in worsening the

outcome by reducing the mass effect in large cerebral infarctions. This can also illustrate that cerebral infarction is more at risk of causing MCE in younger patients due to brain atrophy in elderly patients (Beck et al., 2014; Kwon et al., 2018; Wu et al., 2018).

Regarding the condition of MCE patients who refuse surgery, as happened to our patient, until now there has been no other therapy that has been proven to be an alternative therapy (Cook et al., 2020; Chugh, Maynard, et al., 2021; Chugh, Sunshine, et al., 2021) The choice of hypertonic saline in this case is adjusted to the hyponatremia condition experienced by the patient. Administration of such hypertonic fluids has been used for decades to reduce cerebral edema and ICP (Cook et al., 2020; Chugh, Maynard, et al., 2021). So in our case, apart from correcting hyponatremia, administration of 3% NaCl can be used as an alternative therapy to reduce ICP in MCE patients who refuse surgery. Although no other studies have demonstrated a significant improvement in clinical outcomes and no delay in the evolution of cerebral edema with continuous hypertonic saline administration (Chugh, Maynard, et al., 2021; Chugh, Sunshine, et al., 2021), our case illustrates the occurrence of clinical neurological improvement in the patient without any complications.

In conclusions, 3% NaCl can be administered as an additional conservative therapeutic option in MCE patients who refuse surgery to reducing ICP while keeping serum sodium levels under control. This instance demonstrated a good clinical outcome without complication. Nevertheless, this case report can serve as a resource for future research regarding the current insufficiency data on the use of 3% NaCl to lower ICP and cerebral edema.

AUTHOR CONTRIBUTION

Ramdinal Aviesena Zairinal is the main author, an expert who concept and review the paper. Chandrika Najwa Malutfi for literature, editing, and reviewing.

FINANCIAL SUPPORT AND SPONSORSHIP

None.

ACKNOWLEDGEMENT

There is no acknowledgement declared by the authors.

CONFLICT OF INTEREST

There are no conflict of interest.

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