e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2023; 15(11); 236-240

Original Research Article

An Observational Study on Role of Oral Glycerol in Patients with Moderate Head Injury

Sushil Bhojraj Machhale[1], Ranjeet Kamble[2]

[1]Junior Resident, Department of General Surgery, Lokmanya Tilak Municipal General Hospital, Mumbai, Maharashtra, India.

[2]Associate Professor, Department of General Surgery, Lokmanya Tilak Municipal General Hospital, Mumbai, Maharashtra, India

Received: 02-07-2023 Revised: 16-08-2023 / Accepted: 22-09-2023

Corresponding author: Dr. Sushil Bhojraj Machhale

Conflict of interest: Nil

Abstract

Background: This study was conducted to evaluate the benefits of oral glycerol in moderate head injury patients and assess the outcome in terms of GCS (Glasgow Coma Scale).

Methods: This was a hospital based prospective, observational study conducted among 200 patients with moderate head injuries at the Department of General Surgery, LTMMC and LTMGH, Sion, Mumbai-400022, over a period of 18 months after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Results: We compared the GCS score over a follow-up period of 15 days in group A. We observed statistically significant improvement in the GCS scores. (The value of the F-ratio was 316.11148. The p-value was<0.00001. At $p < 0.05$, the outcome was significant). We compared the GCS score over a follow-up period of 15 days in group B. We observed statistically significant improvement in the GCS scores. (The F-ratio value was 147.45626. The p-value was < 0.00001. At $p < 0.05$, the result was significant).

Conclusion: Mannitol 10% plus 10% glycerol is better than mannitol 20% because it keeps the mannitol dose the same and offers better CNS bioregulation without causing neurodeficiency.

Keywords: Oral Glycerol, Moderate, Head Injury.

Introduction

Degradation of membrane phospholipids is a result of traumatic brain damage, subsequent brain injury, cerebral ischemia, and elevated intracranial pressure (ICP). They could cause cell death and interfere with how the cell membrane works. One of the byproducts of phospholipid breakdown in the brain is glycerol, which has the potential to be a useful indicator of cell damage in people with traumatic brain injury. [1,2]

In patients with TBI (Traumatic Brain Injuries) and infections of the central nervous system, raised ICP has repeatedly been demonstrated to be a significant predictor of prognosis. A common aftereffect of a CVA (Cerebro Vascular Accident), a head injury, a convulsive condition, or an infection or toxic brain involvement is cerebral oedema. [3] Injured blood vessels leak, damaged cells enlarge, and blocked absorption routes all contribute to the complicated aetiology of cerebral oedema, which forces fluid into the brain tissues. An injury cascade occurs when glutamate is released into the extracellular space, opening calcium and sodium entry channels on cell membranes, which causes cellular and blood vessel damage. One calcium ion is released by the membrane ATPase pump in exchange for three sodium ions, which forms an osmotic gradient that encourages more water to enter cells and leads to malfunction but may not always result in long-term harm. Hypoxia eventually exhausts the energy reserves of the cells and inhibits the sodium-potassium ATPase, which reduces calcium exchange. [4-5]

When calcium builds up inside the cell, it starts intracellular cytotoxic processes. When the energy-dependent sodium pump in the cellular membrane stops working, sodium and water build up inside the cell to maintain the osmotic gradient. The synthesis of genes like c-foc and c-jun, as well as cytokines and other intermediate molecules, initiates the inflammatory response. When microglial cells are activated, they emit free radicals and proteases that target capillaries and cell membranes, making cell recovery difficult. [6]

In addition, people who experience the dreaded sequel of hypertension, namely CVA, which causes unconsciousness, convulsions, paralysis, and coma, suffer from improper or negligent restrictions, investigations, health care counselling, and education. These complications change the course of the disease and raise mortality. In addition to lowering ICP, management with elevated ICP aims to maximise CPP and oxygen delivery to the brain. Postural adjustments, temperature control, hyperventilation, sedation, cerebro-spinal fluid drainage, surgical decompression, and osmotherapy—the most popular technique—are all ways to lower ICP. [7-9]

Utilising pharmacologically inert chemicals to raise plasma's osmotic pressure and encourage water transfer from interstitial to vascular space is known as osmotherapy. Mannitol, urea, sorbitol, glycerol, and hypertonic saline are examples of osmotic agents. Despite the fact that these substances primarily work by lowering ICP via an osmotic gradient, they may also have other advantageous effects including lowering blood viscosity, which improves circulation, and causing vasoconstriction, which lowers cerebral blood volume. Glycerol (1, 2, 3-propanetriol) is a trivalent alcohol. It has proved particularly effective both by intravenous and oral route. At convenient doses, glycerol promotes diuresis. Glycerol increases plasmatic concentration. Its mechanism of action, therefore, would be to draw liquids from the tissues, particularly those that are more hydrated. The most frequently recommended immediate treatment for brain oedema is still oxygen inhalation and intravenous mannitol. Typically, oral glycerol is another option for treating brain oedema. [10]

The present study was conducted at a tertiary healthcare center to assess the benefits of oral glycerol in moderate-head injury patients and, hence, the outcome in terms of GCS.

Aims and Objectives

1. To observe the benefits of oral glycerol in moderate head injury patients.
2. To assess the outcome in terms of the Glassgow Coma Scale.

Material and Methods

This was a hospital-based prospective, observational study conducted among 200 patients with moderate-head injuries at the Department of General Surgery, LTMMC and LTMGH, Sion, Mumbai-400022, over a period of 18 months after obtaining clearance from the institutional ethics committee and written informed consent from the study participants.

Inclusion Criteria

- Age group more than 18 years
- Isolated head injury
- Head injuries with a GCS score of 9 to 12 (moderate head injury)
- Any mode of injury
- Patients with no history of any neurosurgery.
- Intoxicated patients (GCS after resuscitation).

Exclusion Criteria

- Patients treated on an OPD basis.
- Patient with an allergy to oral glycerol
- Patients not willing to get enrolled in the study.

Study Procedure

This was a prospective observational study and was conducted at LTMMC and LTMGH, SION, Mumbai**.** Approval was obtained from the Institutional Ethics Committee for the study. Patients admitted to the emergency and surgery wards through the emergency unit were observed in terms of the parameters mentioned in the case record form. Patients with moderate head injuries (GCS 9-12) were included in this study. All the patients who received the first 5 days of mannitol therapy were observed, out of which those patients who received oral glycerol (240 ml/day) for 2 weeks were taken as a test group (Group A) and those who had not received oral glycerol were taken as a control group (Group B). Daily GCS charting for both groups of patients was done and follow-up was taken for both groups. All these data were collected and recorded in a semi-structured, pre-validated, standard case record form for each patient.

The following categories are used by the Extended Glassgow Outcome Scale (GOS-E) to classify a patient's recovery after a traumatic brain injury:

1. Death

2. Prolonged vegetative state, which leaves a person mute and unresponsive

3. Severe disability (lower): Requires daily assistance from someone who must spend the most of each day at home.

4. Severe disability (upper): Can be left alone for more than eight hours a day but is unable to travel or shop without help.

5. Moderate disability (lower): Unable to work or restricted to a sheltered workshop.

6. Moderate disability (upper): Reduced employment capability; continuing social and recreational activities at a level that is only 50% higher than before the injury.

7. Good recovery (lower): Minor issues that interfere with day-to-day activities; returns to more than 50% of pre-injury levels of social and recreational activities.

8. Good healing (upper): No ongoing issues with the brain damage that interfere with normal living.

Statistical Methods: Data was entered in MS Excel and analysed using SPSS software. Results were presented as tables.

Results

Table 1: Demographic Distribution

Age Distribution	Group A (Cases)		Group B (Controls)	
	Number of Subjects	Percentage	Number of Subjects	Percentage
Less than 30 years	7	7	14	14
31 to 40 years	43	43	34	34
41 to 50 years	36	36	36	36
51 o 60 years	14	14	16	16
Total	100	100	100	100
Mean age	39.89 ± 7.96 years		39.31 ± 8.9 years	
Age Distribution				
Gender Distribution	**Group A (Cases)**		**Group B (Controls)**	
	Number of Subjects	**Percentage**	**Number of Subjects**	**Percentage**
Males	78	78	83	83
Females	22	22	17	17
Total	100	100	100	100
Sex Distribution				

In the current study, we evaluated how old the study participants were. According to our observations, the majority of the participants were between the ages of 31 and 40 (43% and 34% in groups A and B, respectively), followed by those between 41 and 50 (36% in each group A and B). The mean age of the study subjects was 39.89 ± 7.96 years in group A and 39.31 ± 8.9 years in group B.

In the current study, we evaluated the gender distribution of the research participants. In groups A and B, respectively, 78% and 83% of the participants were men.

Table 2: Glasgow Coma Scale: Group A

Group A	Day 0	Day 5	Day 10	Day 15
3 to 8	0	0	0	0
9 to 12	100	97	68	33
13 to 15	0	3	32	67
Mean	10.87	11.08	11.97	12.91
Significance	The F-ratio value was 316.11148. The p-value was < .00001. The result was significant at p < .05.			

In the present study, we compared the Glasgow Coma Scale score over a follow-up period of 15 days in group A. We observed statistically significant improvement in the GCS scores. (The F-ratio value was 316.11148. The p-value was < 0.00001. The result was significant at p < 0.05.)

Table 3: Glasgow Coma Scale: Group B

Group B	Day 0	Day 5	Day 10	Day 15
3 to 8	0	0	0	0
9 to 12	100	97	77	41
13 to 15	0	3	23	59
Mean	10.9	11	11.61	12.64
Significance	The F-ratio value was 147.45626. The p-value was < .00001. The result was significant at p < .05.			

In the present study, we compared the Glasgow Coma Scale score over a follow-up period of 15 days in group B. We observed statistically significant improvement in the GCS scores. (The F-ratio value was 147.45626. The p-value was < 0.00001. The result was significant at p < 0.05.)

Table 4: Comparison of the Improvement in GCS Scores over a Follow-Up Duration

Study Groups	F-Value	P-Value
Group A (Cases)	316.11	<0.0001
Group B (Controls)	147.45	<0.0001

In the present study, we compared the improvement in GCS scores using a repeated measure ANOVA test. We observed that the F-value of cases (316.11) was higher as compared to controls (147.45). The

improvement in GCS scores was more significant in case groups as compared to control groups.

Discussion

When the CNS is hurt or doesn't get enough blood flow, compounds like glutamate, free fatty acids, or high extracellular potassium are made or set off. These chemicals cause swelling and nerve cell death. In addition, recognised mediators of cerebral oedema include histamine, arachidonic acid, and free radicals, including nitrous oxide.

After ischemic brain damage, concussive brain injury, traumatic spinal cord injury, and a cold lesion, bradykinin may be implicated. In a stroke, cerebral ischemia results in the loss of membrane ionic pumps and cell swelling, while the production of free radicals and proteases damages cell membranes irreversibly.

According to the Monro-Kellie theory, when one of the three contents of the skull—the brain, which contains 1400 ml, the cerebral spinal fluid (CSF), which contains 150 mL, and the blood, which contains 150 ml—changes volume, the other two do as well. On the other hand, basic blood flow issues can also cause brain oedema.

The following can be used to explain why mannitol 10% with glycerol 10% is superior to mannitol 20%: Sorbitol has an isomer called mannitol. . When administered intravenously, it is only able to reach the extracellular space, where the kidney quickly eliminates it after minimal metabolism. In 3 hours, around 80% of a 100g dosage is excreted in the urine. The medication is not released by tubular cells and is readily filtered by the glomeruli with only <10% tube reabsorption. It causes diuresis by increasing the osmolarity of the glomerular filtrate. Mannitol is used to lower acutely elevated intracranial pressure (ICP) until more conclusive therapy, such as following head trauma, can be given.

Such treatments are successful in reducing ICP as well as enhancing cerebral blood flow and metabolism. Glycerol has additional impacts on brain metabolism in addition to being a powerful osmotic dehydrating agent. Glycerol lowers ICP in a variety of illness situations in dosages of 0.25–2.0 g/kg; however, in extreme cases of increased ICP, intravenous doses of 1-2 g/kg every two hours can be safely used.

Hence, the current study was conducted at a tertiary healthcare center to observe the benefits of oral glycerol in moderate-head injury patients and hence to assess the outcome in terms of the Glasgow Coma Scale.

Demographic Characteristics

In the current study, we evaluated how old the study participants were. According to our observations, the majority of the participants were between the ages of 31 and 40 (43% and 34% in groups A and B, respectively), then those between 41 and 50 (36% in each group A and B). The mean age of the study subjects was 39.89 ± 7.96 years in group A and 39.31 ± 8.9 years in group B. In the current study, we evaluated the gender distribution of the research participants. In groups A and B, respectively, 78% and 83% of the participants were men. [11]

In a study by Avinash Shankar et al., they found that of the 1,171 patients with cerebral oedema who were hospitalised, 797 (68%) and 374 (32%), respectively, were men and women. The majority of the patients were over 50 years old, however, 14 instances were children between the ages of 10 and 15 years. [12]

Comorbidities

We evaluated the comorbidities among the study participants in the current study. In groups A and B, respectively, 78% and 83% of the participants were men.

In their study, Avinash Shankar et al. found that 77.2% of people had hypertension, 9.3% of whom had malignant hypertension (average >160); 75.5% were diabetic, out of which 10.7% had random blood sugar >400 mg%.

Clinical Presentation

In the current study, we evaluated the study individuals' clinical presentations were. We observed that unconsciousness (26%, and 21%), convulsions (29% and 26%), and hemiplegia were observed among 32% and 29% of subjects, respectively, in the study groups.

In their study, Avinash Shankar et al. noted that all hospitalised individuals were unconscious, 36.9% had convulsions, and 53.8% had hemiplegia.

Glasgow Coma Scale

In the present study, we assessed the GCS score at day 0. In groups A and B, 100% of subjects had a moderate GCS score. In the present study, we assessed the GCS score at the end of 15 days. In groups A and B, 97% of subjects had a moderate GCS score. In the present study, we assessed the GCS score at the end of 15 days. In group A, 32% of subjects had a mild score, while in group B, 23% of subjects had a mild score. In the present study, we assessed the GCS score at the end of 15 days. In group A, 67% of subjects had a mild score, while in group B, 59% of subjects had a mild score.

In the present study, we compared the Glasgow Coma Scale score over a follow-up period of 15 days in group A. We observed statistically

significant improvement in the GCS scores. (The F-ratio value was 316.11148. The p-value was < .00001. The result was significant at $p < .05$.). In the present study, we compared the Glasgow Coma Scale score over a follow-up period of 15 days in group B. We observed statistically significant improvement in the GCS scores. (The value of the F-ratio was 147.45626. The p-value was <.00001. At $p < .05$, the outcome was significant.)

Comparison of the Improvement in GCS Scores over a Follow-Up Duration

In the present study, we compared the improvement in GCS scores using a repeated measure ANOVA test. We observed that the F-value of cases (316.11) was higher as compared to controls (147.45). The improvement in GCS scores was more significant in case groups as compared to control groups.

As a result, the mannitol dosage is reduced when combined with glycerol. As a result, adverse effects including asthenia and diuresis are diminished.

Glycerol also aids in brain recovery and the prolonged reduction of cerebral oedema, guaranteeing quick CNS function recovery without a change in intelligence or residual paresis.

Restrepo Lucas et al. (2000) performed a study entitled "Role of Glycerol in Cerebrovascular Disease." They showed that glycerol can be used safely to decrease the brain oedema associated with ischemic stroke. [12]

Conclusion

Mannitol 10% plus 10% glycerol is better than mannitol 20% because it keeps the mannitol dose the same and offers better CNS bioregulation without causing neurodeficiency.

References

1. Li AL, Zhi DS, Wang Q, Huang HL. Extracellular glycerol in patients with severe traumatic brain injury. Chinese Journal of Traumatology. 2008;11(02):84-8.
2. Frykholm P, Hillered L, Langstrom B, Persson L, Valtysson J, Watanabe Y, et al. Increase of interstitial glycerol reflects the degree of ischaemic brain damage: a PET and microdialysis study in a middle cerebral artery occlusion-reperfusion primate model. J Neurol Neurosurg Psychiatry. 2001; 71(4): 455-61.
3. Gwer S, Gatakaa H, Mwai L, Idro R, Newton CR. The role for osmotic agents in children with acute encephalopathies: a systematic review. BMC Pediatrics. 2010; 10:23.
4. Newton CR, Crawley J, Sowumni A, Waruiru C, Mwangi I, English M, et al. Intracranial hypertension in Africans with cerebral malaria. Arch Dis Child. 1997;76(3):219-26.
5. Papo I, Caruselli G, Luongo A. Intracranial pressure in children and adolescents with severe head injuries. J Neurosurg Sci. 1982; 26(3):193-8.
6. Lindvall P, Ahlm C, Ericsson M, Gothefors L, Naredi S, Koskinen LO: Reducing intracranial pressure may increase survival among patients with bacterial meningitis. Clin Infect Dis. 2004; 38(3):384-90.
7. Nara I, Shiogai T, Hara M, Saito I. Comparative effects of hypothermia, barbiturate, and osmotherapy for cerebral oxygen metabolism, intracranial pressure, and cerebral perfusion pressure in patients with severe head injury. Acta Neurochir Suppl 1998; 71:22-6.
8. Rutigliano D, Egnor MR, Priebe CJ, McCormack JE, Strong N, Scriven RJ, et al. Decompressive craniectomy in pediatric patients with traumatic brain injury with intractable elevated intracranial pressure. J Pediatr Surg. 2006;41(1):83-7.
9. Oertel M, Kelly DF, Lee JH, McArthur DL, Glenn TC, Vespa P, et al. Efficacy of hyperventilation, blood pressure elevation, and metabolic suppression therapy in controlling intracranial pressure after head injury. J Neurosurg 2002;97(5):1045-53.
10. Zornow MH, Oh YS, Scheller MS. A comparison of the cerebral and effects of mannitol and hypertonic saline in an animal model of brain injury. Acta Neurochir Suppl (Wien) 1990; 51:324-5.
11. Shankar A. Clinical efficacy of mannitol (10%) with glycerine (10%) versus mannitol (20%) in cerebral oedema. J Neurol Stroke 2019; 00209(4):222-7.
12. Restrepo L, Silverman IE. Osmotherapy: a call to arms. Stroke 2001;32(3):811-2.