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Clinical efficacy of mannitol (10%) with glycerine (10%) versus mannitol (20%) in cerebral oedema

Abstract

Cerebral oedema is a common cause of unconsciousness and various manifestation in Cerebrovascular accident, head injury**,** convulsive disorder and encephalitis either due to infection or toxin due to failure of energy dependant Sodium Potassium ATPase pump resulting accumulation of sodium and water in addition release of free radicals and proteases due to activation of microglial cells disrupts cell membrane and capillaries.

Objective of the study: Comparative assessment of clinical efficacy of Mannitol 10% with Glycerol 10% versus Mannitol 20% in cerebral oedema of varied origin.

Material & method: In this study 1171 patients of cerebral oedema of various aetiology attending Medical Emergency of RA Hospital & Research Centre, Warisaliganj (Nawada) Bihar been selected for comparative evaluation of Mannitol (10%) with Glycerol (10%) versus Mannitol (20%) intravenously to adjudge the clinical efficacy and safety profile.

Result: Patients of Group A taking Mannitol (10%) with Glycerol (10%) had grade I clinical response in % 9584/586) without any adversity, residual neurological deficit or mortality and morbidity while patients of Group B on Mannitol (20%) only % (108/585) with 92 mortality and morbidity in 279 cases.

Keywords: cerebral oedema, cerebrovascular accident, sodium potassium ATPase pump, free radicals, proteases, mortality, morbidity

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Introduction

Cerebral oedema is a common sequel of cerebro vascular accident (CVA), Head injury, convulsive disorder and infective or toxic involvement of brain. Cerebral oedema pathogenesis at cellular level is complex as - damaged cells swell, injured blood vessels leak and blocked absorption pathways force fluid to enter brain tissues. Cellular and blood vessel damage activate an injury cascade i.e.- release of glutamate into the extracellular space opens Calcium and sodium entry channels on cell membranes. Membrane ATPase pumps releases one calcium ion in exchange for 3 sodium ions which create an osmotic gradient promoting increase water entry to cells and causes dysfunction but not necessarily permanent damage. Ultimately hypoxia depletes the cells' energy stores and disables the sodium – potassium ATPase reducing calcium exchange.[1–3]

Failure of the energy-dependent sodium pump in the cellular membrane causes accumulation of Sodium and water to the intracellular space to maintain osmotic gradient while accumulation of Calcium inside the cell activate intracellular cytotoxic processes. Formation of genes like *c-foc* and *c-jun* and cytokines and other intermediary substances initiate inflammatory response. Activation of Microglial cells releases free radicals and proteases attacks on cell membranes and capillaries which results in the cells recovery impossible.[4–7]

In addition negligent and lack of proper restriction, investigation and health care counselling and education, people suffer with dreaded sequel of hypertension i.e.- Cerebrovascular accident results in unconscious, convulsion, paralysis and coma which modify the outcome of the disease and increases the mortality. To overcome the brain oedema, the commonly prescribed urgent measure remains intravenous mannitol and oxygen inhalation. Usually Oral glycerol remains the choice to relieve brain oedema. Considering the clinical effect of oral glycerol and availability of Mannitol 10% with Glycerol 10%, a clinical study was conducted to evaluate the clinical effect and safety profile of 10% glycerol with 10% mannitol versus Mannitol 20% in management of cerebral oedema of either origin.

Objective of study

To adjudge the clinical efficacy of Mannitol 10% with Glycerol 10% versus Mannitol 20% in management of cerebral oedema of varied origin.

Design of study

Comparative clinical study

Material & method

Material

Patients of cerebral oedema of either origin attending at RA. Hospital & Research Centre Emergency were selected for evaluation of Mannitol (10%) with Glycerol (10%) versus conventional Mannitol 20% therapy.

Methods

Parent or attendants of the admitted patients were thoroughly interrogated for the presenting feature onset, its duration, treatment taken and their outcome, any history of such attacks in past. All the patients were examined for their blood pressure, temperature, any marks of injury over the head, blood sugar, and sample collected for other vital parameters assessment. Patients were classified in to two groups comprising equal number of patients i.e.-

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Clinical status	Group A	Group B
Head injury	54	54
Cerebro vascular accident	315	315
Toxemia		
Febrile convulsion	5	5
Convulsive disorder	181	180
Convulsive disorder	26	26

All the patients irrespective of their cause of unconsciousness Or cerebral oedema were advocated

a. Oxygen inhalation.
b. Specific treatment (Anti hypertensive measure for hypertension, anti diabetic measure for diabetes mellitus,)
c. IV nutrition.
d. IV chemoprophylaxis.
e. Other desired measures as per need (anti convulsant for convulsion).
f. Diazepam administration is duly restricted.

While group a patients were given Mannitol 10% and glycerol 10% (Glycerol is a potent osmotic dehydrating agent with additional effects on brain metabolism. In doses of 0.25-2.0g/kg glycerol) Intravenous and group B Mannitol 20%. (Mannitol in a dose of 1.5g/kg body weight was infused over a period of 15minutes, followed by 0.5g/kg body weight every 8hours until the patient regained consciousness or for a maximum period of 72hours.)

Patients were assessed as per following index of assessment i.e.

Index of assessment

a. Recovery time from unconsciousness
b. Status of paralysis
c. Neural recovery
d. Status of alertness
e. Status of speech
f. Mental capability
g. Motor power and tone
h. Effect on various bio parameters

Post therapy sequel

i. Polyuria
j. Polydipsia
k. Irritability
l. Pulmonary congestion
m. Fluid and electrolyte imbalance
n. Acidosis
o. Electrolyte loss
p. Dryness of mouth, thirst
q. Marked diuresis
r. Urinary retention
s. Oedema,
t. Headache
u. Blurred vision
v. Convulsions
w. Nausea
x. Vomiting
y. Hypotension
z. Tachycardia

To assess the safety profile of the administered drug the basic bio parameters i.e. haematological, hepatic and renal profile are repeated. On the basis of clinical achievement clinical response was graded as

Grade I: Complete recovery from unconsciousness within 6hrs no convulsion, recovery from paralysis (motor power and Tone) without any adversity and residual neuropsychiatric presentation or change in bio parameters.

Grade II: Complete recovery from unconsciousness within 12hours no convulsion, recovery from paralysis (motor power and tone) without any adversity and residual neuropsychiatric presentation or change in bio parameters

Grade III: Improvement in unconsciousness, complete recovery in >48hrs, Occasional convulsion, improvement in power and tone, presence of adversity like polyuria, polydipsia, hypotension, tachycardia, blurred vision, post therapy urinary retention, marked change in bio parameters.

Observation

Among the admitted 1171 patients of cerebral oedema 797 (68%) and 374(32%) respectively were of male and female respectively. Majority patients ( ) were of age >50years though 14 cases were of age 10-15years (Table 1 & Figure 1).

Table 1 Number of patients of cerebral oedema

Age group (In yrs)	Number of patients		
	Male	Female	Total %
10-15	09	05	14
15-20	11	07	18
20-25	28	13	41
25-30	64	34	98
30-35	58	26	84
35-40	87	29	116
40-45	54	24	78
45-50	58	30	88
50-55	110	54	164

Citation: Shankar A. Clinical efficacy of mannitol (10%) with glycerine (10%) versus mannitol (20%) in cerebral oedema. *J Neurol Stroke.* 2019;9(4):222–227. DOI: 10.15406/jnsk.2019.09.00380

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Table Continued

Age group (In yrs)	Number of patients		
	Male	Female	Total %
55-60	130	70	200
>60	188	82	270
Total	797	374	1171
	(68%)	(32%)	

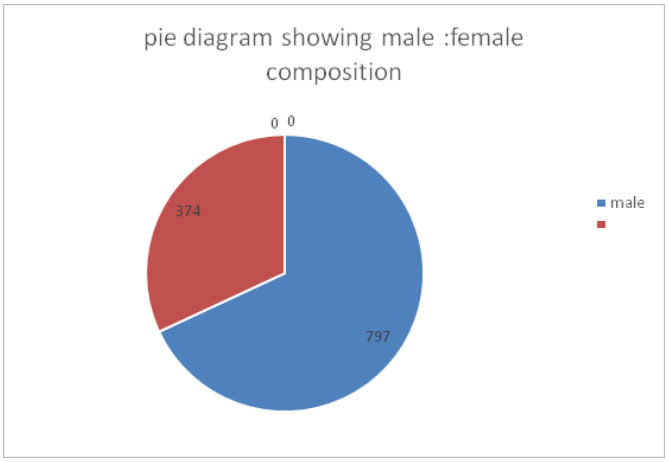

Figure 1 Pie diagram showing sex wise composition of patients.

Out of all majority 630 (53.8%) were of CVA, 361 (30.8%) were of convulsive disorder while 108(9.2% were of head injury (Table 2). Among the selected patients 77.2% were hypertensive out of which 9.3% were with malignant hypertension (average >160) (T-3) and 75.5% were diabetic out of which 11.1% were with random blood sugar >400mg% (T-4). All admitted cases were unconscious, 36.9% were presenting with convulsion and 53.8% with hemiplegia (T-5). 67.3% patients been admitted within 24hrs of incident while rest after 24hrs (Figure 2) among the patients 704 known hypertensive and 590 known diabetic were not taking any drug while no history been elucidated in 287 cases (T-6). Among the selected patients 183 were addict to all types of narcotics while 355 were having no history of any personal habits (T-7), 865 were pure vegetarian while rest were non vegetarian (Figure 3).

Table 2 Shows distribution of patients as per causes of Cerebral Oedema

Causative factors	Causative factors
Head injury	108
Cerebro vascular accident	630
Toxemia	10
Febrile convulsion	10
Convulsive disorder	361
Encephlitis	52

Patients of group A had complete recovery from unconsciousness by 4hrs while group B patients taken >12hrs and 92 patients fails to revive and succumb. Out of all 536 patients of group A achieved normal CNS function without any residual paralysis, improved general condition and normal life status grade I response in 534 without any adversity or alteration in bio parameters while in group B only 212 patients regained power and tone, improved general condition in 108, normal life status 112, altered CNS function in 132 with residual paralysis in 147grade I clinical response in only 108 with altered bio parameters in 24 cases (Tables 3–8) (Figure 4).

Table 3 Distribution of patients as per average blood pressure recorded on admission

Average blood pressure (in mmHg)	Number of patients			
	Male	Female	Total	Percent
<120	152	115	267	
130-135	74	46	120	
135-140	74	39	113	
140-145	91	38	129	
145-150	95	40	135	
150-155	101	57	158	
155-160	100	40	140	
>160	80	29	109	
Total	767	404	1171	

Table 4 Distribution of patients as per random blood sugar status

Random blood pressure (in mg)	Number of patients			
	Male	Female	Total	%
<200	200	87	287	26.8
200-250	54	40	94	
250-300	166	84	250	22.5
300-350	89	45	124	
350-400	223	68	291	
>400	75	50	125	11.1

Table 5 Distribution of patients as per clinical presentation

Clinical presentation	Number of patients	Percent
Unconscious	1171	100%
Hemiplegia	630	53.8
Right side	139	22.06
Left side	491	77.94
Convulsion	433	36.9

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Table 6 Distribution of patients as per previous history of illness

History of previous illness	Number of patients
Hypertensive taking AHT	296
Hypertensive never taken any drug	701
Known diabetic taking drugs	294
Known diabetic not taking any drug	590
Unknown	287

Table 7 Distribution of patients as per their personal habits

History of previous illness	Number of patients
Alcoholic	302
Smoker	254
Tabacco chewer	567
Cannabis smoker	165
Gutka	214
All types of narcotics	183
Non addicts	355

Table 8 Out com of the study

Particulars	Number of patients	
	Group A	Group A
Consciousness recovery time	4hrs	>12hrs
Regain in power and tone	All	212
Improved general condition	All	108
Quality of life		
Normal	586	112
Mortality	None	92
CNS function		
Normal	586	214
Altered	None	132
Residual paralysis	None	147
Safety profile		
Renal profile		
Blood urea		
< 26mg	586	472
>26mg	-	21

Table Continued

Particulars	Number of patients	
	Group A	Group A
Serum Creatinin		
<1.5mg	586	473
>1.5mg	-	20
Urine albumin		
Positive	None	24
Urine RBC		
Present	None	120
Hepatic profile		
Serum bilirubin		
<1mg	586	493
SGOT		
<35 IU	586	493
SGPT		
<35 IU	586	493
Clinical grade		
Grade I	584	108
Grade II	2	106
Grade III	-	279

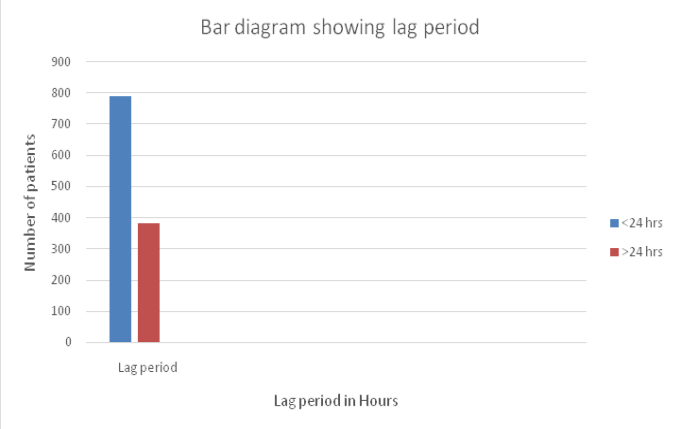

Figure 2 Bar diagram showing lag period.

Result

584/586 Patients of Cerebral oedema on Mannitol 10% with Glycerol 10% intravenously had early regain of consciousness and recovery of power, tone, memory and IQ without any adversity or residual neuro deficit than Mannitol 20% which had grade I clinical response in only 108/585 morbidity in 279585 mortality 92/585 with altered neurological function.

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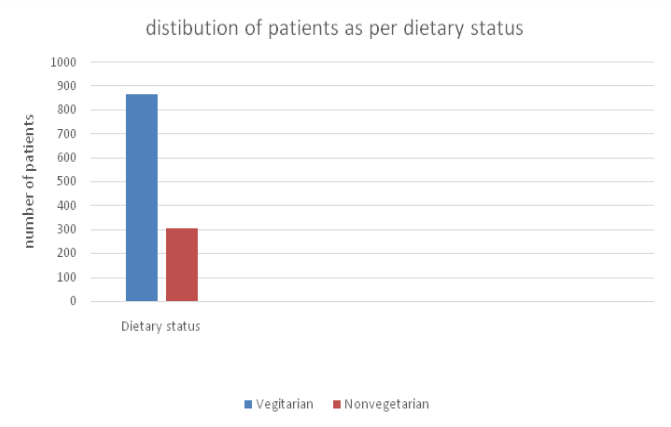

Figure 3 Bar diagram showing dietary status.

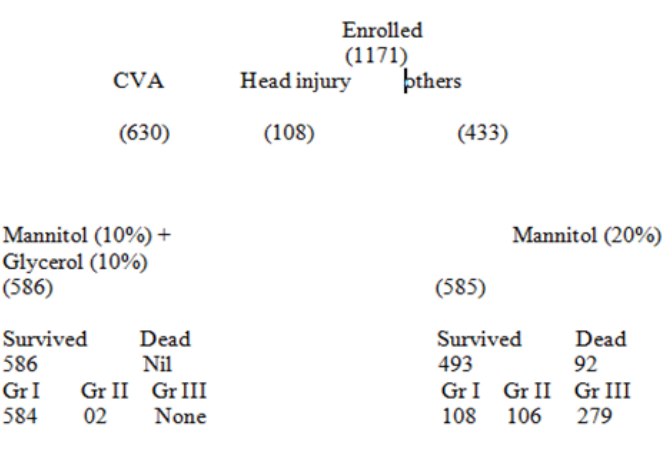

Figure 4 Showing schematic presentation of outcome.

Discussion

On injury or ischemia of Central nervous system CNS mediators like Glutamate, free fatty acid or high extracellular potassium compounds are released or activated resulting in swelling and damage of nerve cells. In addition substances like histamine, arachidonic acid and free radicals including nitrous oxide are also known mediators causing cerbral oedema. Bradykinin may be involved after cold lesion, concussive brain injury, traumatic spinal cord and ischemic brain injury.[8,9]

In stroke cerebral ischaemia causes loss of membrane ionic pumps and cell swelling while irreversible cell membrane damage is caused by generation of free radicals and proteases. As per Monro-Kelie hypothesis, change in the volume of any of the three content of skull (inside the skull) i.e. brain – 1400ml, cerebral spinal fluid (CSF) 150 ml and blood 150ml change the volume of other Conversely, primary blood flow disturbances also lead to brain oedema.[10–12]

Significant supremacy of Mannitol 0% with Glycerol 10% as compared to Mannitol 20% can be explained as -Mannitol is an isomer of sorbitol, administered intravenously confined to the extracellular space, only slightly metabolized and rapidly excreted by the kidney. Approximately 80% of a 100 g dose appears in the urine in 3hours. The drug is freely filtered by the glomeruli with less than 10% tubular re absorption; it is not secreted by tubular cells and induces diuresis by elevating the osmolarity of the glomerular filtrate.[13–15] Mannitol is used to reduce acutely raised intracranial pressure until more definitive treatment can be applied, e.g., after head trauma.[16,17]

Such solutions are effective not only in lowering the intracranial pressure, but also in improving the cerebral blood flow and metabolism. Glycerol is a potent osmotic dehydrating agent with additional effects on brain metabolism. In doses of 0.25-2.0g/kg glycerol decreases intracranial pressure in various disease state however, intravenous doses of 1–2g/kg every 2hr can be administered safely in severe cases of elevated ICP. Thus combination of Mannitol and Glycerol decreases the dose of mannitol thus its side effects like diuresis and asthenia in addition Glycerol helps in neural recovery and sustained resolution of cerebral oedema thus ensure prompt recovery of CNS function without alteration in mental capability and IQ Or residual paresis.[18–22]

Conclusion

Mannitol 10% with Glycerol 10% proves better than Mannitol 20% as it spares dose of mannitol and protect from mannitol overdose adversity with better CNS bio regulation without any residual neurodificit.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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None.

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