Monitoring Mean Arterial Pressure (MAP) in Traumatic Brain Injury Patients during The Initial 60 Minutes of Manitol 20%

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Abstract
The effect of manitol 20% on changes in blood pressure after traumatic brain injury is unknown. The purpose of this study was to analyze the differences in blood pressure before and after the administration of 20% mannitol in traumatic brain injury patients at the Intensive Care Unit. This study was a quasi experimental research which uses a pre-post test without control one group design, a method used in observational analytic techniques. The population of this study was all traumatic brain injury patients who were given a manitol infusion of 20% 100ml. The sample was 12 respondents taken by consecutive sampling technique. With a significance threshold of p 0.05, the test was performed using the Paired T test on systolic and MAP data and the post hoc Wilcoxon test on diastolic data. Decreasing blood pressure 15 minutes after administration of 20% mannitol occurs because half live mannitol which lowers blood pressure and responds to decreased blood pressure autoregulation, at 30 minutes resulting in decreased intra-cranial pressure, improves cerebral perfusion and brain autoregulation that affects systemic blood pressure 60 changes in blood pressure may be due to diuresis effects. During the administration of mannitol there is a change in blood pressure that needs to be monitored.
INTRODUCTION

Traumatic head injury is an event that allows damage to the brain that can cause disability and even death. Direct effects of trauma to the brain include contusions, cerebral hemorrhage, and axon injuries, which can cause tissue death, as well as biochemical processes that begin with trauma or ischemia that cause cell death (Galgano et al., 2017). Contusions, cerebral hemorrhages, and axon injuries may all result in tissue death in brain trauma, as well as causing cell death through biochemical processes that begin with trauma or ischemia. Brain injury can result in an increase in intracranial pressure (ICP) which then aggravates the patient's condition (De Rosa et al., 2022). Direct effects of trauma to the brain include contusions, cerebral hemorrhage, and axon injuries, which can cause tissue death, as well as biochemical processes that begin with trauma or ischemia that cause cell death (Crupi et al., 2020). Mannitol is used to control raised intracranial pressure in two situations. The use of mannitol in the first condition, namely by administering a single dose aims to provide a short-term effect so that diagnostic procedures (CT-scans) and interventions (mass evacuation of intracranial lesions) can be performed. In both situations mannitol is used as long-term therapy in cases of increased intracranial pressure (Marchesini et al., 2023). Mannitol has been used widely and is recommended in brain injury guidelines, however, there are some adverse effects associated with mannitol administration, namely hypovolemia and hypotension (Bisri, 2013).

TBI incidence, mortality, and mechanisms in Europe. A wide range of rates of incidence and mortality were reported for all ages, all TBI severity studies, the lowest reported crude incidence rate was 47.3 per 100,000 population per year; the highest was 849 per 100,000 population per year. The reported crude mortality rates ranged from 3.3 to 28.10 per 100,000 population per year (Brazinova et al., 2021). Approximately 3,500 patients with traumatic brain injury are treated in intensive care units (ICU), with a mortality rate of 23% in severe traumatic head injuries who have been resuscitated (Bisri, 2013). Based on data from the Republic of Indonesia Health Research and Development Agency, the prevalence of traumatic brain injury in people in Indonesia is 7.5%, with the highest order of causes of injuries being falls, land traffic accidents and injuries with sharp/blunt objects. In 2013 there was an increase in the prevalence of injuries to 8.2%, with the most common causes of injury being falls 40.9%, motorcycle accidents (40.6%), injuries from sharp/blunt objects 7.3%, other land transportation 7.1% and fell 2.5% (Badan Penelitian dan Pengembangan Kesehatan, 2013).

In a study comparing 20% mannitol and 3% hypertonic saline on intracranial pressure and systemic hemodynamics, the results of both mannitol and hypertonic saline at equiosmolar concentrations in a study conducted by Yusuf Hisam & Rahardjo, (2015), there was no significant difference in changes in mean arterial pressure (TAR) for the group of subjects receiving mannitol solution, within the first 5 minutes of measurement. Although several studies have found that the use of 20% mannitol does not cause significant hemodynamic changes, the effect of 20% mannitol on changes in blood pressure after administration of 20% mannitol at 15, 30 and 60 minutes is not clearly known.

The dose of mannitol is 0.25 grams to 1 gram per kg body weight. Mannitol will cause excessive fluid diuresis resulting in fluid and electrolyte disturbances. This situation will cause hypovolemia and also hypotension which can interfere with hemodynamics thereby reducing brain perfusion which will exacerbate the condition of the traumatic brain injury itself (B. H. Batubar et al., 2016). Another complication of using mannitol is the depletion of intravascular volume, hypotension, hyperkalemia and the possibility of increased intracranial rebound (Tenny et al., 2022). High MAP blood pressure at the time of admission to the hospital can be used as an independent predictor. The greater the systolic blood pressure, the stronger the association with a poor outcome. Arterial blood pressure is the most practical sign and the most meaningful in predicting poor outcomes (Haryuni, 2017). Research conducted by (Junaedi et al., 2016) showed that hypovolemic shock with MAP <60 mmHg had greater mortality or could be used as a marker of hemodynamic changes, especially in the compensatory stage of shock and was a predictor of death.

Mannitol is an osmotic diuretic which is currently effectively used to reduce intracranial pressure (brain edema) in various conditions. Considering that mannitol has side effects and toxicity, its administration must be closely monitored for responses that arise during administration of mannitol, including changes in the patient's blood pressure. The nurse is responsible for monitoring the client's response to mannitol therapy. Based on the above background, researchers are interested in conducting research on a comparison of
blood pressure and Mean Arterial Pressure (MAP) before and after administration of 20% mannitol in traumatic brain injury patients in the Intensive Care Unit.

METHOD

The research design was experimental research using quasi-experimental research, pre-post test without control one group design, while the data collection method for this research used observational analysis techniques or analytic observation. The independent variable in this study was the administration of 20% mannitol in traumatic brain injury patients. The dependent variable in this study was MAP (Mean Arterial Pressure) after administration of 20% mannitol in traumatic brain injury patients. The sample in this study was all traumatic brain injury patients in the intensive care unit at Mardi Waluyo Regional Hospital, Blitar City, who were given 20% 100ml mannitol infusion in a 1-month data collection period. There are criteria for sample selection in this study, inclusion criteria: age 16-65 years, exclusion criteria: a) Patients with diabetes insipidus, b) Patients with impaired kidney function, c) Patients with hormonal system disorders, d) Patients on therapy inotropic, e) Patients on antihypertensive therapy, f) Patients receiving diuresis therapy, obtained a sample of 12 respondents using consecutive sampling technique. The instruments used in administering 20% mannitol were: SOP for administering 20% mannitol therapy, SOP for using an infusion pump, and a Terumo TE 331 infusion pump, while instruments for assessing blood pressure were in the form of SOP for using a bedside monitor, a bedside monitor for the brand/type of Carescap. Monitor B650, and patient observation sheet. The pre-data collection process was carried out by measuring blood pressure and then calculating MAP before being given 20% mannitol fluid, after the patient received 20% intravenous mannitol fluid with a dose of 100 ml in 15 minutes blood pressure measurement and MAP calculation were carried out, both 30 minutes and 60 minutes. The test used is the Paired T test with a degree of significance determined by p <0.05.

RESULTS

Table 1: General Data of Respondents

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>less than 30</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>30 to 40</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>41 to 50</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>51 to 60</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>More than 60</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>100</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>75</td>
</tr>
<tr>
<td>Female</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>100</td>
</tr>
<tr>
<td><strong>TBI Classifcation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>Moderate</td>
<td>4</td>
<td>33</td>
</tr>
<tr>
<td>Severe</td>
<td>5</td>
<td>42</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>12</td>
<td>100</td>
</tr>
</tbody>
</table>

Based on the table above, it is known that the age distribution is mostly over 60 years old with 4 respondents (33%). The sex distribution with the most number of respondents is male with 9 (75%) and it is known that the smallest percentage is 25% for female respondents. The highest frequency distribution is respondents with severe brain injury with a frequency of 5 respondents (42%) while the smallest percentage is respondents with mild brain injury with a percentage of 25% (3 respondents).
Table 2: Results of blood pressure and MAP before and after administration of 20% Mannitol

<table>
<thead>
<tr>
<th>Var</th>
<th>Min</th>
<th>Max</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>79</td>
<td>130</td>
<td>100.25</td>
<td>95.50</td>
<td>18.02</td>
</tr>
<tr>
<td>T1</td>
<td>72</td>
<td>122</td>
<td>92.91</td>
<td>86.50</td>
<td>18.02</td>
</tr>
<tr>
<td>T2</td>
<td>73</td>
<td>120</td>
<td>93.25</td>
<td>88.50</td>
<td>16.53</td>
</tr>
<tr>
<td>T3</td>
<td>69</td>
<td>114</td>
<td>85.50</td>
<td>81.00</td>
<td>15.76</td>
</tr>
</tbody>
</table>

The table above shows that at T0 to T1 (15 minutes after treatment) the average MAP was 92.9 mmHg. This shows that at 15 minutes after administration of 20% mannitol the blood pressure is in the normal blood pressure range.

Table 3: Statistical Test Results

<table>
<thead>
<tr>
<th>VAR</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0 - T1</td>
<td>7.33333</td>
<td>2.74138</td>
<td>0.000</td>
</tr>
<tr>
<td>T0 - T2</td>
<td>7.00000</td>
<td>2.52262</td>
<td>0.000</td>
</tr>
<tr>
<td>T0 - T3</td>
<td>14.75000</td>
<td>3.79294</td>
<td>0.000</td>
</tr>
</tbody>
</table>

The p value on the paired t test on MAP T0 with T1, T2, T3 obtained a p value <0.05.

DISCUSSION

The age distribution is mostly over 60 years old with 4 respondents (33%), age is a strong factor in influencing the prognosis of a disease, according to research conducted by Cindy & Afni, (2017) found that the risk of TBI (severe brain injury) occurred at an older age (51,.3 years). Older age is associated with a person's physiological condition which becomes a consideration in determining the efficiency of treatment, especially if the TBI patient's condition is accompanied by comorbidities, due to a lack of physiological reserves. The most common gender is male with 9 (75%) respondents. Similar to the study by Hartoyo et al. (2012), in which males made up the bulk of the patients, this study similarly revealed that men with TBI had a greater mortality rate than women. Klasiﬁkasi cedera kepala yang paling banyak adalah responden dengan cedera otak berat dengan frekuensi 5 responden (42%). The condition of patients with TBI is assessed using Glasgow Coma Scale (GCS) value of 8, where the patient's condition requires stricter monitoring, related to clinical conditions that can change quickly, GCS is also one of the instruments in scoring head trauma. Research conducted by Putra et al., (2016), showed that GCS, age and systolic blood pressure were calculated to determine the GAP score with the conclusion that there was a relationship between the GAP score and mortality in head injury patients.

In Brain Injury there are differences regarding the timing of the severity or magnitude of the autoregulation disturbance. Many experiments have been carried out but the results are not the same, the time when the autoregulation disorder occurs can take several seconds, several minutes and several hours. The severity of the autoregulation disorder depends on the severity of the Brain Injury. The finding that ICP tolerability may depend on cerebral autoregulation status, autoregulation status or individual ICP thresholds derived from autoregulation status seems to predict better outcome than fixed ICP level (Åkerlund et al., 2020).

The ability of cerebral blood arteries to regulate their lumens so that blood flow to the brain does not alter significantly even while systemic arterial blood pressure varies is referred to as autoregulation. This cerebral autoregulation capability can nevertheless maintain a systemic blood pressure of up to 50 mm Hg without disrupting local blood flow. Vasodilation and vasospasm are in equilibrium under normal conditions. An autoregulation dysfunction caused by brain injury disturbs this balance. Subarachnoid hemorrhage (SAH) is complicated by two major life-threatening complications, namely cerebral vasospasm/delayed cerebral ischemia (DCI) and early brain injury (EBI), whose prognosis does not improve over time.

The sympathetic nervous system (SN) is important for the regulation of cardiovascular function and is intimately associated with cerebral vessels and regulation of cerebral blood flow and cerebrovascular function, thus, excessive activation of the SN leads to a rapid breakdown of homeostasis in the brain. In the hyperacute phase, patients with...
SAH can develop a lethal state thought to be related to arrhythmia-associated SN (catecholamine surge) activation, neurogenic pulmonary edema, and irreversible injury to the hypothalamus and brainstem (Hasegawa et al., 2022).

Primary and secondary brain injury causes increased vascular permeability, cerebral edema and increased intracranial pressure. Traumatic brain injury is often accompanied by brain edema associated with structural damage or water and electrolyte balance disturbances induced by the primary or secondary injury. Brain edema results in an increase in intracranial pressure which will aggravate the patient's condition. A close association between various forms of cardiac arrhythmias and brainstem lesions caused due to transtentorial herniation have been identified. In a setting of brainstem ischemia or raised ICP; respiratory arrest, bradycardia and a rise in blood pressure are registered the moment ischemia reached the lower pons. Further advance of the ischemic front into the lower medulla oblongata lead to an abrupt change from bradycardia to tachycardia.

In intraoperative settings, the stimulation of the floor of the fourth ventricle during posterior fossa surgeries can result in bradyarrhythmias and the stimulation of the periventricular zone causes tachyarrhythmias and hypertension (Lionel, 2019). Intra-cranial pressure (ICP / Intra Cranial Pressure) will affect cerebral perfusion pressure (CPP / Cerebral Perfusion Pressure). CPP can be calculated as the difference between the mean arterial pressure (MAP) and ICP (CPP = MAP - ICP). If there is an increase in ICP, there will be a decrease in CPP, the body will try to compensate so that brain perfusion does not decrease by increasing MAP, if MAP rises, systolic and diastolic pressure, of course, will also increase. The increase in intracranial pressure will reduce cerebral perfusion pressure, this decrease in cerebral perfusion will activate ischemia reflexes resulting in vasoconstriction and increase arterial pressure.

In normal renal function, after a single intravenous dose, half of mannitol lives in circulating plasma for 15 minute. Cerebral perfusion is closely related to intracranial pressure and MAP. This is ensured by brain autoregulation where the ability of blood vessels in the brain to constrict or dilate to maintain a stable blood flow to cerebral perfusion. Physiologically the work of mannitol is to increase plasma osmolarity and draw normal fluid from within the brain cells with low osmolarity to the intravascular one with higher osmolarity, to reduce brain edema and reduce intracranial pressure, as well as increase cerebral perfusion. The brain will respond with autoregulation trying to make systemic blood pressure within the normal range (Suasti, 2021).

The mean systolic blood pressure at T2 (30 minutes after treatment) was 129 mmHg, the average diastolic blood pressure was 75.9, and the average MAP was 93.2 mmHg. Based on these results, the blood pressure at T2 is within the normal range. Additionally, the systolic mean and mean MAP on T2 are a little bit higher than on T1. This demonstrates that the systolic blood pressure rises after 30 minutes. Mannitol will have an osmotic effect when given. This means that the difference in osmotic gradient between the brain and blood will move fluid from the intracellular to the intravascular. This will have a real impact on cardiac output if there is an increase in vascular volume. Blood pressure may rise as a result of this increase in volume. Mannitol's primary effect on the brain is a rapid increase in plasma volume, resulting in a decrease in blood viscosity, an increase in CBF, an increase in microcirculation perfusion, and an increase in oxygen delivery to the brain. Systemic blood volume will increase as a result of the plasma volume increase, resulting in an increase in blood pressure and cardiac output. (Büyükkaragöz & Bakkaloğlu, 2023).

The traumatic brain injury patients who received 20% mannitol had the lowest average systolic blood pressure at T3, which was 115.5 mmHg, the lowest average diastolic blood pressure at T3, which was 70.5 mmHg, and the lowest average MAP at T3 was 85.5 mmHg, according to the statistical results. Based on these data, it can be concluded that the greatest reduction in blood pressure occurred at T3 (60 minutes after treatment) following administration of 20% mannitol. Within 30 to 60 minutes of administration, mannitol is eliminated through glomerular filtration. When compared to T1 and T2, this results in the greatest reduction in blood pressure and a diuresis effect after 60 minutes. According to C. A. Batubara, (2018), mannitol will cause excessive fluid diuresis, resulting in fluid and electrolyte disturbances, hypovolemia and hypotension, which can disrupt hemodynamics. These findings are consistent with these findings. At 15 minutes in this study there was a difference in blood pressure before administration of 20% mannitol. Blood pressure after administration of 20% mannitol at 15 minutes was lower than before administration of 20% mannitol.
This is because in brain injured patients blood pressure tends to be above normal. After administration of 20% mannitol there was a decrease in blood pressure because the half life of mannitol is 15 minutes which will lower blood pressure and respond to brain autoregulation. Mannitol can reduce intracranial pressure by 26% or more within 5 minutes (Laksono et al., 2017).

In the 30th minute the results of the paired t test concluded that there was a significant difference (p <0.05) in blood pressure before and after administration of 20% mannitol in the 30th minute. The dynamics of MAP after administration of 20% mannitol showed that the MAP value was labile and had a tendency to decrease, from 0 to 120 minutes in moderate brain injury patients (Patil & Gupta, 2019). Administering mannitol also reduces intracranial pressure through an osmotic mechanism that occurs more slowly (15 to 30 minutes) associated with the gradual movement of water content from the parenchyma into the blood circulation. Changes in blood pressure in the 30th minute are probably caused by the effect of mannitol which results in a decrease in intracranial pressure, improves cerebral perfusion and brain autoregulation which affects systemic blood pressure (Schizodimos et al., 2020).

To remove metabolic wastes and maintain a steady supply of oxygen and nutrients to brain tissue, autoregulation is necessary. Arterioles expand and contract rapidly in response to changes in pressure. When arterial blood pressure decreases or brain metabolism increases, cerebral vascular dilation occurs. Blood flow to the brain will be directly related to systemic blood pressure if this normal response is disrupted (Hall & Hall, 2020). At the 60th minute the test results concluded that there was a significant difference (p<0.05) in blood pressure before and after administration of 20% mannitol at 60 minutes. Changes in blood pressure occur due to the effect of osmotic diuresis where there is an increase in extravasation due to differences in osmotic pressure in the blood plasma which results in stimulation of the kidney glomeruli resulting in an increase in the amount of urine. The volume of the blood decreases when there is an increase in the amount of urine. Diminished blood volume brings about a reduction in pre-load which brings about a lessening in pulse. According to B. H. Batubara et al., (2016), the group given mannitol had 20% more urine volume than the group given hypertonic sodium lactate after one hour. Systolic blood pressure was 25.5 mm Hg, diastolic blood pressure was 11 mm Hg, and mean arterial pressure (MAP) was 14.75 mm Hg at 60 minutes after mannitol administration. decreased ICP, decreased blood pressure, and an increased amount of urine.

CONCLUSION
Patients with traumatic brain damage often had greater blood pressure before administering 20% mannitol. The highest systolic pressure was 170 mmHg, the highest diastolic pressure was 112 mmHg, and the highest MAP was 130 mmHg prior to mannitol administration.

All respondents (100%) experienced a decrease in blood pressure after receiving 20% mannitol. 60 minutes after administering mannitol, the average systolic blood pressure dropped by 115.6 mmHg, the average diastolic blood pressure dropped by 70.5 mmHg, and the average MAP blood pressure dropped by 85.5 mmHg. At 15, 30, and 60 minutes, the blood pressure before and after the administration of 20% mannitol differed significantly (p 0.05).

SUGGESTION
The effects of mannitol administration on traumatic brain injury patients' urine production, intracranial pressure, and blood plasma osmolarity can be monitored or analyzed, or additional hemodynamic variables can be added to this research.

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CONFLICTS OF INTEREST
All authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS
SA as a contributor of ideas, data analysis, preparation of manuscripts, and publications. TN, AR, and as developers of research methods carried out, data collection, data editing, and manuscript preparation. HR has the role of data collection, data editing, data analysis, and manuscript preparation.
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