

Effect of intravenous administration of 20% Mannitol on the Optic Nerve Sheath Diameter (ONSD) in patients with raised intracranial



pressure.

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1. Proposal Title:

Effect of intravenous administration of 20% Mannitol on the Optic Nerve Sheath Diameter (ONSD) in patients with raised intracranial pressure.

2. Project summary:

This is a prospective observational cross-sectional study which will determine the extent of change brought in the optic nerve sheath diameter by the intravenous administration of 20% Mannitol in patients with raised intracranial pressure. The studied patient will be those above the age of 18 years with traumatic brain injury, acute stroke or intracranial hemorrhage, with the features of elevated intracranial pressure as diagnosed by clinical findings, ONSD value > 5 mm and under 20% Mannitol osmotherapy, admitted in the intensive care unit of our institution. Written informed consent will be taken and after the eligibility criteria are met, epidemiological data including age, sex, weight, BMI at the time of admission will be recorded. Measured baseline observational values including optic nerve sheath diameter, mean arterial pressure will also be recorded. Observational variables will be measured after 30 minutes, 60 minutes and 120 minutes following the intravenous administration of 20% Mannitol. The data will be tabulated and analysis performed with SPSS software. The primary outcome will be the change in optic nerve sheath diameter, while the correlation between these variables will also be interpreted.

3. Introduction

Raised intracranial pressure is a common incidence and complication in critically ill patients. There have been intense studies and research for understanding the underlying patho-physiology and treatment. Much of our understanding of the intracranial pressure is based on the Monro-Kellie hypothesis which states that the sum of intracranial volumes of blood, brain, CSF and other components is constant, and that an increase in any one of these must be offset by an equal decrease in another or else the pressure increases.¹ The normal ICP is defined as 5 to 15 mmHg (7.5-20 cmH₂O). Under normal conditions the brain is able to auto-regulate its blood flow. Cerebral perfusion pressure (CPP) defined by the equation $CPP = MAP - ICP$, is the single-most important determinant of this auto-regulation. Within a CPP ranging from 50-150 mmHg, the auto-regulation is intact. However during any insult/injury this ability of the brain may be impaired or absent thus leading to an unregulated change in ICP. Trauma, intracranial hemorrhage, intracranial tumors and ischemic stroke are the major causes of such insult and raised intracranial pressure.² Prompt diagnosis and treatment of elevated intracranial pressure is the cornerstone of management in TBI, intracranial hemorrhages and acute stroke and has been associated with poor outcomes. Care based on ICP monitoring has been proved to be associated with frequency of good recovery and favorable outcome.³ Such monitoring can be invasive or non-invasive. Currently, invasive ICP monitoring is the gold standard. External ventricular drainage and micro-transducer ICP monitoring devices are the commonly used modes for ICP monitoring. However there are various hazards (infection and hemorrhage) of such invasive procedures and few studies have shown no such difference in outcomes with or without invasive monitoring.^{4, 5}

There have been various validated modes of non-invasive ICP monitoring. Trans-cranial Doppler ultrasonography (TCD), optic nerve sheath diameter (ONSD), tympanic membrane displacement and fundoscopic examinations have been proposed as being surrogates to invasive ICP monitoring.^{3,4} There have been many studies comparing the use of invasive against the use of non-invasive modes of ICP monitoring. Among these Optic nerve sheath diameter (ONSD) can be taken as the simplest mode with high positive and negative predictive values on detecting rise in intracranial pressure.⁶ It's correlation with invasively measured intracranial pressure and imaging findings has also been validated⁷ and used extensively in diagnosing episodes of raised intracranial pressure in emergency departments, intensive and neurosurgical units.⁸

The optic nerve is part of the central nervous system and therefore surrounded by the dural sheath. Between the sheath and the white matter is a small 0.1-0.2 mm subarachnoid space which communicates with the intracranial subarachnoid space. In cases with raised intracranial pressure the pressure is also transmitted into this sheath and expansion occurs. This expansion is appreciable via various imaging modalities like CT scans, MRI and ultrasonographic imaging. The feasibility and simplicity of this measurement by ultrasonography has made it a efficient tool in diagnosing and monitoring in acute care setup. The major drawbacks are the inter-observer variation in measurement and conditions that may confound the finding such as tumors, inflammation, grave's disease and sarcoidosis. Change in ONSD measurements performed before and after interventions including hyperventilation, drainage of CSF, administration of Mannitol, tracheal manipulation and lumbar puncture appear to correlate well with the induced change in ICP.^{6,7}

The incidence of elevated ICP is more than 50% in patients with ICP ranging as high as 80% in patients with traumatic brain injury.^{10, 11} The fundamental goal of management in TBI is based on managing ICP, maintaining adequate CPP and is based upon the Monro-Kellie doctrine and cerebral autoregulation.¹¹ Similarly incidence of raised intracranial pressure in patient with intracranial hemorrhage ranges from 36% to 80%.¹² Malignant cerebral edema leading to raised intra-cranial pressure is a major cause of adverse outcome in patients with acute ischemic stroke with an incidence of 10-20%. Use of osmotic therapy in such patients has been recommended in both ENLS guidelines for management of intra-cerebral hemorrhage and AHA/ASA guidelines.¹³

Mannitol, is a polyol (sugar and alcohol) a hyper-osmolar agent that has been used for osmotherapy in neurosurgical patients since many years. The proposed mechanism of its action are transient hypervolemia thus decreasing blood viscosity, increase in CBF and the microvascular circulation leading to autoregulatory vasoconstriction and thus reducing cerebral blood volume.¹⁴ However there is controversy regarding its mechanism of effect when given as single bolus dose. Its effect in red blood cell rheology and improved oxygen delivery/circulation has also been hypothesized for explaining its immediate effect in decreasing ICP¹⁴. Another hypothesis argues about the ability of Mannitol to lower intracranial pressure by reducing brain water content (diuretic effect)⁹ and decreasing CSF production.

Pharmacokinetics of Mannitol:

Onset of action: 15 minutes

Half life: 100 minutes

Osmolarity: 1100 for 20% Mannitol

Duration of action: 3-6 hours

Excretion: Urine (80%)

Time of peak action: 30- 100 minutes

Literature review:

Launey et. al,¹⁵ performed a study to determine the rate of ONSD variation after Mannitol administration for increased ICP episodes. They included thirteen patients in their study comparing and correlating the changes in ONSD, pulsatility index and invasively monitored ICP. The ONSD significantly decreased after Mannitol infusion from 6.3 to 5.56mm (p=0.0007). Concomitantly the intracranial pressure also decreased for 35(32-41) to 25(22-29)mmHg (p=0.001) and the CPP increased from 47 to 69 (p=0.003). The study concluded that the variations of ONSD appear to be an interesting and effective parameter to evaluate the efficacy of osmotherapy for elevated ICP episodes in patients with acute brain injury/SAH.

A study by Li-juan Wang et al¹⁶ which included 60 patients who underwent measurement of ONSD prior to lumbar puncture on admission and during follow up, concluded that ICP was strongly correlated with ONSD(r=0.758, p<0.001) and this association was independent of all other factors like age, sex, BMI, mean arterial pressure and diastolic blood pressure. It also states that ultrasonographic ONSD measurements provide a potential noninvasive method to quantify ICP that can be conducted at the bedside.

Another study performed in the Indian population by Shirodkar et. al¹⁷ evaluated the efficacy of ONSD by ultrasonography as a non-invasive method for detecting raised intracranial pressure in intensive care unit to compare with CT/MRI findings of raised ICP and to prognosticate ONSD value with treatment. The results showed a sensitivity of detecting raised ICP by ONSD to be 84.6% and a specificity approaching around 99%.

A study by Joushua E Nash et al¹⁸ uses ONSD to diagnose raised ICP along with correlation with CT findings. It also reviews the literature from the past and concludes that <0.50 cm ONSD ensured normal pressure (95% CI 0.469-0.540, p<0.001). The study also quantifies the inter-observer variability in ONSD measurement (0.001-0.002cm). The study also determines the expertise required for measuring ONSD to be around 10-25 case examinations and this has been supported by various other studies.

In a prospective convenience sample study, Shushrutha Hedna MD, and colleagues¹⁹ enrolled 86 patients with stroke from a tertiary care center. They measured ONSD on the day of admission and subsequent day, taking longitudinal and transverse measurements of both eyes of each patient. Compared with patients who survived, those who died had increased ONSD in both ischemic stroke categories (0.582 vs. 0.533; P=.0092) and the intracerebral hemorrhage category (0.623 vs. 0.572; P=.0187). With each ONSD increase of 0.1 cm, the odds of mortality increased 4.239 times among patients with ischemic stroke (95% CI, 1.317-13.642; P=.0155) and 6.222 times among patients with intracerebral hemorrhage (95% CI, 1.160-33.382; P=.0329).

Rajajee et al.²⁰ performed a prospective blinded observational study on 65 patients in the ICU. All patients in the study had either had an EVD or intra-parenchymal ICP monitor in situ. The authors used individual as well as mean ONSD values to account for possible fluctuation in the ICP during ONSD measurement. For the individual ONSD measurements the median was 0.53 cm for ICP > 20 mmHg, and was 0.4 cm for ICP < 20 mmHg (p < 0.0001). An ONSD of 0.48 cm demonstrated a sensitivity of 96% and specificity of 94% for predicting ICP > 20 mmHg.

Using a described ONSD cut-off of 5 mm, Tayal et al.²¹ performed a prospective blinded observational study in the emergency department on 59 adult patients with a mean age of 38 years, suspected of having raised ICP. The mean ONSD in patients with CT evidence of raised ICP was 6.37 mm, and in the group without evidence of raised ICP, the mean ONSD was 4.94 mm. Using 5 mm as a cut-off point, the study described a sensitivity of 100%, and specificity of 63% for predicting raised ICP.

The use of ONSD measurement specifically in the acute phase (within 6 hours) to detect intracranial haemorrhage (ICH), was investigated by Skoloudik and colleagues²². This study included 31 patients with ICH, comparing them to 31 control patients. Sonographic ONSD measurements were performed at 3 and 12 mm behind the globe. Relative ONSD enlargement of > 0.66 mm (> 21%) demonstrated an accuracy of 90.3% for predicting an ICH volume > 2.5cm³. The authors then used an ONSD value of > 5mm, demonstrating a sensitivity of 0.708 (95% CI 0.620 – 0.708), specificity of 1.000 (0.697 – 1.000), positive predictive value of 1.000 (95% CI 0.875 – 1.000) and a negative predictive value of 0.500(0.348 – 0.652), concluding that enlargement of the ONSD may be detectable in the hyperacute stage of increased ICP. The use of ONSD to evaluate the clinical evolution of ICH beyond the acute stage was also later confirmed.

A study by Jun IJ and friends²³ aimed at studying the effect of mannitol on ONSD as a surrogate for intracranial pressure during robot assisted laparoscopic prostatectomy with pneumo-peritoneum and the Trendelenburg position. Mannitol (0.5 g/kg) was administered after pneumoperitoneum establishment and shifting to the Trendelenburg position. ONSDs were measured at six predetermined time points: 10 minutes after anesthesia induction (T0); 5 minutes after pneumoperitoneum and the Trendelenburg position before Mannitol administration (T1); 30 minutes (T2), 60 minutes (T3), and 90 minutes (T4) after completion of Mannitol administration during pneumoperitoneum and the Trendelenburg position; and at skin closure in the supine position (T5). Results showed that ONSDs were significantly lower at T2, T3, and T4 than at T1 (all $p < 0.001$), with the greatest decrease observed at T4 compared with T1 (4.46 ± 0.2 mm vs 4.81 ± 0.3 mm, $p < 0.001$) while mean arterial blood pressure and heart rate were also significantly different. However regional cerebral oxygen saturation, cardiac output, corrected flow time, peak velocity, body temperature, arterial CO₂ partial pressure, peak airway pressure, plateau airway pressure, dynamic compliance, and static compliance were not significantly different during pneumoperitoneum and the Trendelenburg position.

4. Rationale and Justification of Study

Optic nerve sheath diameter measurement is a common acute care sonographic procedure. Since the change in intracranial pressure is a continuum of event, sonographic monitoring of such an event is possible through optic nerve sheath diameter monitoring. Mannitol is a common drug used in patients/subjects with raised intracranial pressure either due to trauma, subarachnoid haemorrhage or stroke. Its effects on intracranial pressure reduction are well known though the mechanism is not properly understood yet. My study/research aims at studying the pattern and extent of change in the optic nerve sheath diameter after osmotherapy with intravenous 20% Mannitol within its time of peak effect. Monitoring such changes can help tailor the treatment modality and tier according to efficacy. In absence of invasive monitoring in a limited setup like ours and in light of the various complications associated with invasive monitoring, noninvasive monitoring can help us in improving the outcomes in such neurosurgical or neurological cases.

5. Objectives

General:

To study the effect of intravenous administration of 20% Mannitol on the optic nerve sheath diameter in patients with raised intracranial pressure.

Specific:

- To compare the changes in optic nerve sheath diameter brought about by administration of Mannitol within the time of its peak effect.
- To correlate and compare the extent of change in ONSD (Δ ONSD) at 30, 60 and 120 minutes in relation with dose of mannitol administered and change in Mean Arterial Pressure (Δ MAP).
- To correlate the changes in ONSD in relation with PIP and PEEP in patients on Mechanical ventilation.

6. Research Questions/Hypothesis:

Null Hypothesis (H_0): Serial Optic nerve sheath diameter monitoring with a cut-off value of 5.0 mm can reflect changes due to IV administration of 20% Mannitol in patients with raised ICP.

Alternate Hypothesis (H_1): Serial Optic nerve sheath diameter monitoring with a cut-off value of 5.0 mm cannot reflect changes due to IV administration of 20% Mannitol in patients with raised ICP.

Expected outcome: $H_0 \neq H_1$

7. Research Design and Methodology

7.1. Research Method

Quantitative

7.2 Types of study

Prospective, observational, cross-sectional

7.3 Study Population:

All adults in the intensive care unit admitted with the diagnosis of Traumatic brain injury, SAH and acute stroke under treatment with IV 20% Mannitol.

7.4 Study site and its justification: Intensive care unit of TUTH, IOM.

Optic nerve sheath diameter has been used for the evaluation of patients with neurological lesion or injuries and in acute care settings. However no studies have been performed on its usefulness in our institute. It can be used to guide the treatment of acute episodes of raised intracranial pressure in the intensive care units and to quantify the efficacy of measures taken to reduce raised intracranial pressure. The examination is easy and is non-interventional, so examination can be made mandatory in such cases.

7.5 Sampling Method

Probability sampling

7.6 Sample size

Basis and method of determination including power of the study, level of significance etc.

Power of study: 80% ($1-\beta = 0.84$)

Level of significance: 95% ($\alpha = 0.05$)

Assuming mean difference and standard deviation of differences (σ) of 0.24 and 0.49 respectively, effect size (Δ) was 0.49 as derived from previous study²³,

Using the formula

$$N = \frac{(z_{1-\alpha/2} + z_{1-\beta})^2}{\Delta^2} + \frac{z_{1-\alpha/2}^2}{2},$$

The sample size required would be 35.

Assuming a dropout of 10%, the required sample size would be 40.

7.7 Inclusion and Exclusion Criteria

Inclusion criteria:

- Age > 18 yrs
- Gender: any
- H/o traumatic brain injury/ subarachnoid hemorrhage/ acute stroke
- Mean optic nerve sheath diameter > 5mm (0.5cm)
- Under osmotherapy with 20% Mannitol.

Exclusion criteria:

- Baseline ocular pathology like tumors, Grave's disease and Sarcoidosis
- Previous ocular surgery
- Decompressive cranial surgery

7.8 Study Variables:

Epidemiological variables:

- Age
- Gender
- Weight
- BMI

Measured base line variables:

- GCS score
- Mean arterial pressure
- Optic nerve sheath diameter, T₁ (mean of 3 measurements in each eye)
- Ventilator parameters (PIP and PEEP) in patients on mechanical ventilation.

Measured variables after infusion of 20% Mannitol:

- Dose of 20% mannitol administered
- Mean arterial pressure
- Optic nerve sheath diameter (mean of 3 measurements in each eye) after 30mins(T₂), 60 mins(T₃) and 120 mins(T₄).

7.9 Primary outcomes:

Change in the optic nerve sheath diameter (Δ ONSD) at T₂, T₃ and T₄.

7.10 Secondary outcomes:

- Change in the mean arterial pressure before and after mannitol administration.
- Comparison and correlation between the extent of change in ONSD (Δ ONSD) with dose of mannitol and change in MAP(Δ MAP).
- Correlation between Δ ONSD with PIP and PEEP in mechanically ventilated patients

7.10 Expected Duration of the Study: 6 months

7.11 Tools and techniques for data collection:

Tools:

- 6-10 Hz linear array USG probe (Sonosite M-Turbo)
- Ultrasound coupling jelly
- Transparent dressing (Tegaderm)
- Cleaning gauze pieces
- Proforma
- Arterial blood pressure monitor (invasive or non-invasive)

Methodology:

- Included patients will be those above 18 years, admitted in the ICU of TUTH, Maharajgunj, with the diagnosis of traumatic brain injury, acute stroke or intracranial hemorrhage and under osmotherapy with 20% Mannitol.
- Written informed consent will be taken from the patient or patient's responsible guardian. Conscious patients will be explained about the procedure.
- The patient's diagnosis, epidemiological variables and baseline variables will be recorded.
- Baseline ventilator parameters will be noted and the ICU staffs instructed not to change those variables over the study period until deemed necessary by the treating physician.
- Positioning of the patient will be done: supine, 30° head elevated.
- Mean arterial blood pressure will be noted from arterial line readings or NIBP reading as appropriate or available.
- A protective transparent dressing will be placed over the closed eyelid in sedated or ventilated patients as an additional measure to prevent any irritation of the conjunctiva.
- For ONSD measurement, generous amount of coupling gel will be applied over the closed upper eyelid.
- The probe will be held with a pincer grasp between the thumb and index finger, using the remaining fingers for stability by resting them on the maxilla or supraorbital ridge.
- The depth will be adjusted to optimize the visualization of the intended structures, i.e. the optic nerve, the surrounding CSF space and the ONS. The gain will be adjusted to create a hypoechoic posterior chamber.
- The mechanical index will be adjusted as per the recommended values for the eye, in order to limit the amount of energy absorbed by the eye.
- Values will be noted 0.3 cm posterior to the retinal surface after optimal visualization of the entry of optic nerve in the orbit.

- Mean will be obtained after taking 3 readings in each eye. Only patients with mean ONSD > 0.5cm will be included and the baseline value designated as T₁.
- Intravenous 20% Mannitol as prescribed will be administered via a dedicated IV line over 20 minutes.
- Mean arterial pressure and Optic nerve sheath diameter readings will be performed as previously described and noted at 30(T₂), 60(T₃) and 120(T₄) minutes after completion of IV administration.
- The coupling gel will be removed gently after each measurement and the protective adhesive dressing will be removed at the end of the study.

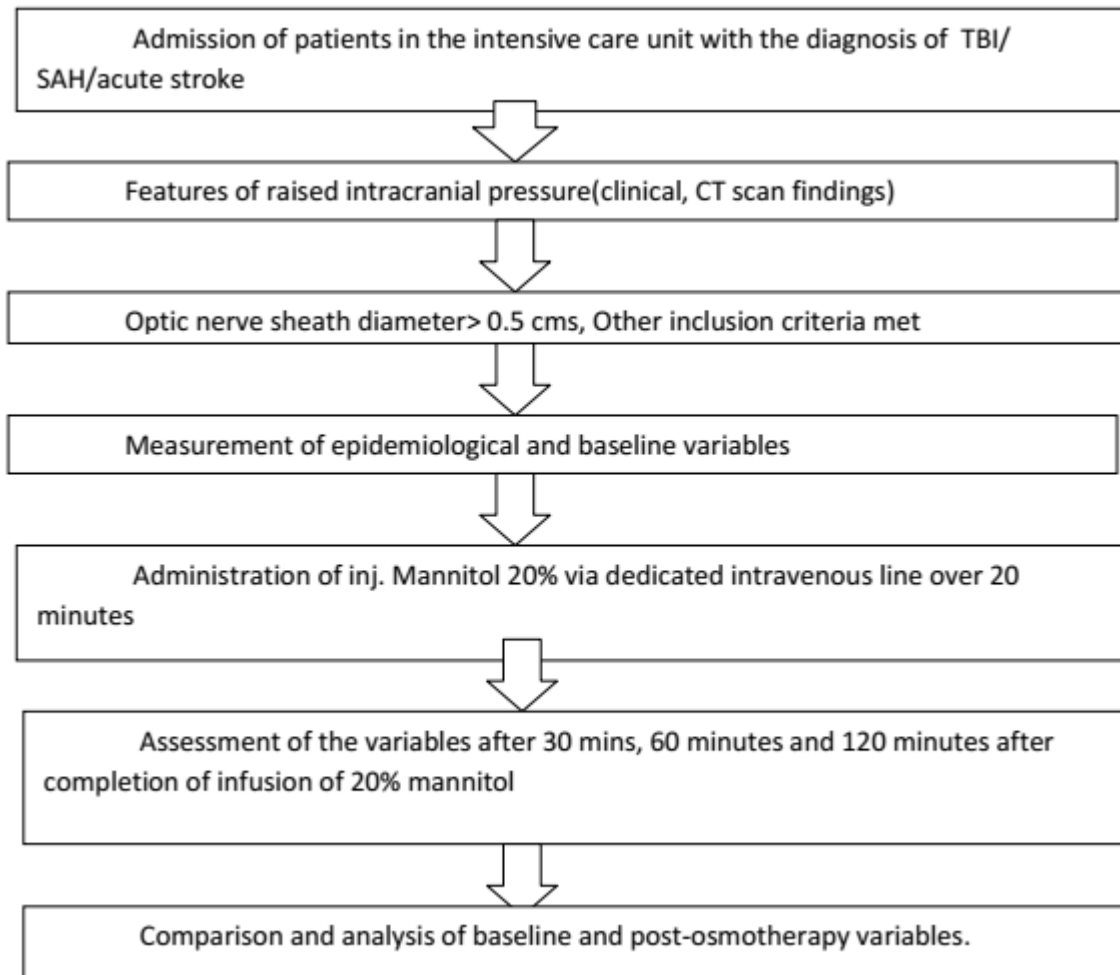
7.12 Management protocol of patients/participants if applicable:

All patients will be managed according to the current ICU protocol abiding with the ENLS and Brain Trauma Foundation guidelines for TBI and intra-cerebral hemorrhage and AHA/ASA guidelines for acute ischemic stroke. In subjects with persistently elevated intracranial pressure and ONSD findings above 5.0 mm despite the administration of 20% Mannitol, decision for further treatment will rest upon the treating physician.

7.13 Plan for Data Management and Statistical Analysis

- Data will be entered by the investigator and resident on duty in the intensive care unit and will be destroyed after the completion of the study, however the results and conclusions will be stored without hampering the subject/ patient's privacy or rights.
- Power of the study is based on the primary outcome which is the change in ONSD following infusion of 20% Mannitol.
- Paired t test, chi square test will be used for data analysis.
- Data will be analysed by using SPSS 20 software version
- The value of $p < 0.05$ will be considered as statistically significant.

7.14 A graphic outline of the study design and procedures using a flow diagram including the timing of assessments.



8. Biases:

Data collection by on duty MD anesthesiology Resident or DM Critical Care Residents will reduce observer and performance bias.

9. Limitation of the study:

- Single centered
- Open label
- No control group

10. Safety considerations:

Regarding the safety concerns during the measurement of optic nerve sheath diameter subjects with ocular injury, glaucoma are being excluded. The acoustic energy used for diagnostic purposes has no described adverse effects. The recent bioeffects and safety report by the American Institute of Ultrasound in Medicine (AIUM) makes no specific mention of the eye. The United States Food and Drug Administration Center for Devices and Radiological Health (US FDA/CDRH) describes an output intensity limit for all eye exposure of 50 mW/cm², recommending the use of a mechanical index (MI) < 0.23, and a thermal index (TI) < 1. The definition of an experienced operator differs, but studies have defined an experienced operator as having performed more than 25 prior transorbital ultrasound examinations.

11. Plan for Supervision and Monitoring:

The research will be continuously supervised by the co-guides Dr. Pramesh Sundar Shrestha and Dr. Arjun Gurung and will be conducted under the guidance of Dr. Subhash P. Acharya.

12. Expected outcome of the Research:

Optic nerve sheath diameter changes are expected to be associated with the administration of 20% Mannitol in patients with raised intracranial pressure. Such an outcome would have various benefits in terms of usefulness of the optic nerve sheath diameter monitoring.

13. Plan for Dissemination of Research:

Research results will be submitted to the Department of Anaesthesiology and Research department, IOM.

Research results will also be submitted for publication in national and international journals of repute.

14. Plan for Utilization of the Research Findings:

The research results would help us in the care of patients in the neurosurgical and neurological intensive care units with non-invasive monitoring.

15. Work Plan

S.N	Activities	2018 AD		2019 AD			
		Nov	Dec	Jan	Feb	Mar	Apr
1	Problem identification						
2	Literature review						
3	Topic selection						
4	Writing thesis proposal						
5	Presentation to sub committee						
6	Review thesis proposal						
7	Submission to IRB						
8	Approval from IRB						
9	Data collection						
10	Data analysis						
11	Final thesis writing						
12	Final correction and submission						

16. Ethical Consideration

Research is based on human optic nerve sheath diameter.

Approval by IRB.

Verbal consent from patients relatives and/or legal guardian would suffice as the study is non-interventional and non-invasive with no effect on patients safety.

Confidentiality will be maintained.

17. Obtaining the Consent

Patients legal guardian will be well counseled and no information will be withheld.

18. Budget

The expenditure during the study will be made by the principal investigator.

Transparent dressing (Tegaderm): 50 pcs: Rs. 2400

Data statistician: Rs. 8000

Stationary: Rs. 4000

Photocopies of proforma and information sheet: Rs.2000

Binding: Rs. 4000

Total: Rs 20400

19. Annexes:

INFORMED CONSENT

Department of Anaesthesiology

Tribhuvan University, Institute of Medicine, Kathmandu, Nepal,

Study Title: Effect of intravenous administration of Mannitol 20% on the Optic nerve sheath diameter(ONSD) in patients with raised intracranial pressure

Study Number: _____

Subject's Initials: _____

Subject's Name: _____

Date of Birth / Age: _____

(i) I confirm that I have read and understood the information sheet and consent form dated for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the researchers and the IRB and other regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)

(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legal Guardian:

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Signatory's Name: _____

Signature of the Investigator:

Date: ____/____/____

Study Investigator's Name: _____

Date: ____/____/____

Signature of the Witness:

Name of the Witness: _____

Date: ____/____/____

सुसूचित मन्जुरीनामा

म _____ (उमेर _____ वर्ष) ले 'Study on the effect of intravenous administration of 20% Mannitol on the Optic nerve sheath diameter(ONSD) in patients with raised intracranial pressure' शिर्षकको अनुसन्धान सम्बन्धी संलग्न मिति २०७ / / को 'जानकारी पत्र/पुस्तिका' सुनेर/पढेर र प्रश्नोत्तर समेत गरेर यो अध्ययन-अनुसन्धान सम्बन्धमा जानकारी प्राप्त भयो। यो अनुसन्धान कार्यमा मेरो सहभागिता मेरो व्यक्तिगत इच्छामा भर पर्ने र मैले चाहेको खण्डमा कुनै पनि बेला यो अनुसन्धान प्रक्रियाबाट बाहिरिन पाउने भन्ने कुरा मैले बुझेको छु। यसको लागि मैले कुनै कारण दिनु नपर्ने र त्यसबाट मैले पाउने सेवा र मेरो कानुनी अधिकारमा असर नपर्ने समेत मलाई बुझाईएको छ। यस अनुसन्धानको प्रतिवेदन वा सम्बन्धित प्रकाशित कृतिहरूमा मेरो कुनै व्यक्तिगत परिचय खुल्ने जानकारी प्रकाशित हुने छैन भन्ने कुरा मैले बुझेको छु।

सहभागीको बुढीआँलाको ल्याप्चे

दायाँ	बायाँ

यी सबै कुराहरू जानी-बुझी, म यस अध्ययन-अनुसन्धानमा सहभागी हुन स्वेच्छाले राजी भई यो सुसूचित मन्जुरीनामामा सहिछाप गरेको छु।

सहभागीको सही _____

सहभागीको नाम थर _____

मिति २०७ / /

साक्षीको सही _____

साक्षीको नाम थर _____

Proforma

“Study on the effect of intravenous administration of 20% Mannitol on the Optic nerve sheath diameter (ONSD) in patients with episodes of raised intracranial pressure.”

Participant serial no.: IP no.: Date:

Name: Age/sex: Weight:

Height: BMI:

Diagnosis: Admission date:

Ventilator parameters at time of baseline measurement

PIP: cmH₂O
PEEP: cmH₂O

Time of 20% Mannitol administration:
Dose of 20% Mannitol administered:
Time of measurement: 30 minutes:
60 minutes:
120 minutes:

MEASURED VARIABLES:

VARIABLES	BASELINE (T ₁)	POST-MANNITOL (30MINUTES: T ₂)	60 MINUTE (T ₃)	120 MINUTES (T ₄)
MEAN ARTERIAL PRESSURE	mmHg	mmHg	mmHg	mmHg
OPTIC NERVE SHEATH DIAMETER	RIGHT: mm	RIGHT: mm	RIGHT: mm	RIGHT: mm
	LEFT: mm	LEFT: mm	LEFT: mm	LEFT: mm
	MEAN: mm	MEAN: mm	MEAN: mm	MEAN: mm
GLASGOW COMA SCALE	E:	E:	E:	E:
	V:	V:	V:	V:
	M:	M:	M:	M:

List of Abbreviations:

ICP	Intracranial pressure
TBI	Traumatic brain injury
SAH	Subarachnoid hemorrhage
ONSD	Optic nerve sheath diameter
CPP	Cerebral perfusion pressure
CBF	Cerebral Blood Flow
MAP	Mean arterial pressure
GCS	Glasgow Coma Scale
USG	Ultrasonography
ICU	Intensive care unit
IOM	Institute of medicine
TUTH	Tribhuvan University Teaching Hospital
IV	Intravenous
BMI	Body Mass Index
ASA/AHA	American Heart Association/American Stroke Association
SPSS	Statistical Package for the Social Sciences
TCD	Transcranial Doppler
cmH₂O	Centimeter of water
COR	Class of recommendation
LOE	Level of evidence
MI	Mechanical index
TI	Thermal index
US FDA/CDRH	United States Food and Drug Administration/ Center for Devices and Radiological Health
AIUM	American Institute Of Ultrasound In Medicine
ENLS	Emergency Neurological Life Support
CI	Confidence Interval
PIP	Peak Inspiratory Pressure
PEEP	Positive End Expiratory Pressure

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