Original Article

Post Traumatic Cerebral Oedema in Severe Head Injury is Related to Intracranial Pressure and Cerebral Perfusion Pressure but not to Cerebral Compliance

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This was a prospective cohort study, carried out in the Neuro Intensive Care Unit, Department of Neurosciences, Hospital Universiti Sains Malaysia, Kubang Kerian Kelantan. The study was approved by the local ethics committee and was conducted between November 2005 and September 2007 with a total of 30 patients included in the study. In our study, univariate analysis showed a statistically significant relationship between mean intracranial pressure (ICP) as well as cerebral perfusion pressure (CPP) with both states of basal cistern and the degree of diffuse injury and oedema based on the Marshall classification system. The ICP was higher while CPP and compliance were lower whenever the basal cisterns were effaced in cases of cerebral oedema with Marshall III and IV. In comparison, the study revealed lower ICP, higher mean CPP and better mean cerebral compliance if the basal cisterns were opened or the post operative CT brain scan showed Marshall I and II. These findings suggested the surgical evacuation of clots to reduce the mass volume and restoration of brain anatomy may reduce vascular engorgement and cerebral oedema, therefore preventing intracranial hypertension, and improving cerebral perfusion pressure and cerebral compliance. Nevertheless the study did not find any significant relationship between midline shifts and mean ICP, CPP or cerebral compliance even though lower ICP, higher CPP and compliance were frequently observed when the midline shift was less than 0.5 cm. As the majority of our patients had multiple and diffuse brain injuries, the absence of midline shift did not necessarily mean lower ICP as the pathology was bilateral and even when after excluding the multiple lesions, the result remained insignificant. We assumed that the CT brain scan obtained after evacuation of the mass lesion to assess the state basal cistern and classify the diffuse oedema may prognosticate the intracranial pressure and cerebral perfusion pressure thus assisting in the acute post operative management of severely head injured patients. Hence post operative CT brain scans may be done to verify the ICP and CPP readings postoperatively. Subsequently, withdrawal of sedation for neurological assessment after surgery could be done if the CT brain scan showed an opened basal cistern and Marshall I and II coupled with ICP of less than 20 mmHg. [*Asian J Surg* 2009;32(3):157–62]

Key Words: cerebral oedema, severe head injury, intracranial pressure, cerebral perfusion pressure, cerebral compliance

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Introduction

Cerebral oedema following severe head injury is common and leads to secondary brain damage. Immediate evacuation of a mass lesion restores the anatomy and minimises further secondary insults resulting from a vicious cycle that causes cerebral oedema. Midline shift and effacement of the basal cistern on computed tomography (CT) directly determine the degree of cerebral oedema and are predictors of developing intracranial hypertension, lowering the cerebral perfusion pressure and cerebral compliance and eventually the outcome of severely head injured patients.[1] In this study we aimed to relate the state of cerebral oedema as evidence on postoperative CT after evacuation of surgical mass lesion with intracranial pressure, cerebral perfusion pressure and brain compliance in severe head injury patients.

Clinical Material and Methods

Study protocol

This is a prospective cohort study of 30 patients who were enrolled after consent and approval of the local ethics committee between the end of 2005 until September 2007 carried out in Hospital Universiti Sains Malaysia. Severely head injured patients classified based on the Glasgow Coma Score[2,3] were enrolled. Patients aged between 10 to 65 years and who had abnormal CT scans which necessitated surgical evacuation were included in the study. Patients with bilaterally fixed and dilated pupils, bleeding diathesis, devastating injuries meaning they were not expected to survive for more than 24 hours and significant brain stem involvement were excluded. All patients had an immediate craniotomy or craniectomy but not decompressive craniectomy to evacuate the mass lesion. A double lumen intraventricular Spiegelberg catheter (GmbH & Co. KG, Hamburg, Germany) with an air pouch mounted on the tip was inserted into the frontal horn of the lateral ventricle following evacuation of mass lesion and connected to the Spiegelberg Brain-Pressure monitor and compliance-monitor; GmbH&CO. The Speigelberg compliance monitor calculates intracranial compliance ($C = \Delta V/\Delta P$) from a moving average of small intracranial pressure (ICP) perturbations (ΔP) resulting from a sequence of up to 200 pulses of added volume ($\Delta V = 0.1$ mL, total $V = 0.2$ mL) made into a double lumen intraventricular balloon catheter. Once a stable average has developed, the device produces a minute by minute measure of intracranial compliance.[4] The monitoring was done continuously until the ICP, cerebral perfusion pressure (CPP) and cerebral compliance (CI) were normalised and the patients were reversed from sedative effects unless the patients died. Systemic arterial pressure was concomitantly monitored. CPP was calculated as the difference between mean arterial pressure (MAP) and ICP. Interventions were adjusted to achieve the target of an ICP of less than 25 mmHg, a CPP of more than 60 mmHg and a CI of more than 0.5 mL/mmHg.[5–8] Initial stage management included nursing the patient with their head elevated at 30 degrees, mechanical ventilation, adequate sedation, analgesics with or without paralysing agent. In resistant cases, an option of drainage of cerebrospinal fluid, administering mannitol, loop diuretics, intermittent hyperventilation, inotropes, hypertonic saline or hypothermia were used singly or in combination.[6] Barbiturate coma and decompressive craniectomy were kept as the last options to control cerebral oedema. All patients received a repeat of non enhanced CT within 72 hours of surgery for radiological assessment of cerebral oedema. The degree of cerebral oedema was classified according to the Marshall classification with emphasised on the effacement of the basal cistern and the degree of midline shift. The Glasgow outcome scales[9] of the patients which were either unfavourable (death and persistent vegetative state) or favourable (severe disability, moderate disability and good recovery) was assessed at 1 month post trauma.

Statistical analysis

Data analysis was completed using commercially available software (SPSS Version 12.0.1; SPSS, Inc., Chicago, IL). A non parametric test (Mann-Whitney) was applied to analyse the relationship between ICP, CPP, cerebral compliance and the degree of post operative cerebral oedema represented by midline shift, state of the basal cistern, and the Marshall classification. The level of significance was set at 0.05.

Results

Thirty severely head injured patients with a Glasgow coma score (GCS) of 8 or below were admitted into Neurosciences Intensive Care Unit (NICU) after surgery to remove a mass lesion. The youngest was 13 years old while the oldest was aged 65 years with mean age of

32 years old. Twenty four (80.0%) of them were male and six (20.0%) were female.

The initial GCS scorings after adequate resuscitation showed one (3.3%) patient had GCS 3, eight (26.7%) patients had GCS 4, five (16.7%) had GCS 5, 6 or 7, and six (20%) had GCS 8. Nine of them (30%) suffered critical head injury and 21 (70%) had severe head injury. Among them, seven (23.3%) patients actually initially had moderate head injury which further deteriorated, and was hence reclassified into severe head injury upon reassessment in emergency room at Hospital Universiti Sains Malaysia (HUSM).

In the patients where the post operative CT scans showed an opened basal cistern, the minimum and maximum age was 13 and 65 years respectively with a median interquartile range (IQR) of 22.5 (31.0), 16 (53.3%) and four (13.3%) were male and female respectively, two (6.7%) were critical and 18 (60.0%) had severe head injuries, nine (30.0%) and 11 (36.7%) documented equal and unequal pupils respectively, 13 (43.3%) had a craniotomy and seven (23.3%) had a craniectomy done, nine (30.0%) had favourable and 11 (36.7%) had unfavourable GOS at first month. In this group, preoperative CT scans showed seven (23.3%) had extra parenchymal haematoma, six (20.0%) intra parenchymal haematoma and seven (23.3%) multiple lesions. In the group with an effaced basal cistern, the minimum and maximum age was 15 and 62 respectively with median (IQR) of 25 (43), eight (26.7%) and two (6.7%) were male and female respectively, seven (23.3%) were critical and three (10.0%) had severe head injuries, one (3.3%) and nine (30.0%) noted equal and unequal pupil respectively, two (6.7%) had a craniotomy and eight (26.7%) had a craniectomy done, all 10 (33.3%) had a unfavourable outcome in the first month. A preoperative CT scan showed six (20.0%) had extra parenchymal haematoma, one (3.3%) intra parenchymal haematoma and three (10.0%) multiple lesions.

In the patient where the post operative CT scan demonstrated midline shift (MLS) of less than 0.5 cm, the minimum and maximum age was 13 and 65 years respectively with median (IQR) of 20 (20.0), 16 (53.3%) and two (6.7%) were male and female respectively, four (13.3%) were critical and 14 (46.7%) had severe head injuries, seven (23.3%) and 11 (36.7%) documented equal and unequal pupils respectively, 11 (36.7%) had craniotomy and seven (23.3%) had a craniectomy done, seven (23.3%) had favourable and 11 (36.7%) had unfavourable GOS at first month, and eight (26.7%) had favourable outcomes and 10 (33.3%) had unfavourable outcomes when reassessed at sixth month. Preoperative CT scan showed six (20.0%) had extra parenchymal haematoma, five (16.7%) intra parenchymal haematoma and five (23.3%) multiple lesion.

In the group with MLS of more than 0.5 cm, the minimum and maximum age was 17 and 65 respectively with median (IQR) of 33 (40.0), eight (26.7%) and four (13.3%) were male and female respectively, five (16.7%) were critical and seven (23.3%) were severe head injuries, three (10.0%) and nine (30.0%) noted equal and unequal pupils respectively, four (13.3%) had craniotomy and eight (26.7%) had craniectomy done, two (6.6%) had favourable and 10 (33.3%) had unfavourable outcomes at first month while reassessment at sixth month revealed three (10.0%) favourable and nine (30.0%) unfavourable outcomes. A preoperative CT scan showed seven (23.3%) had extra parenchymal haematoma, two (6.7%) intra parenchymal haematoma and three (10.0%) multiple lesions.

In the patients where the post operative CT scan displayed Marshall I and II, the minimum and maximum age was 13 and 65 respectively with median (IQR) of 20 (30.0), 15 (50.0%) and three (10.0%) were male and female respectively, one (3.3%) was critical and 17 (56.7%) were severe head injuries, eight (26.7%) and 10 (33.3%) possessed equal and unequal pupils respectively, 12 (40.0%) had a craniotomy and six (20.0%) had a craniectomy done, nine (30.0%) had a favourable and unfavourable GOS each in the first month. A preoperative CT scan showed six (20.0%) had extra parenchymal haematoma, five (16.7%) intra parenchymal haematoma and seven (23.3%) multiple lesions (Table 1).

In the group with Marshall III and IV which indicated more severe brain injury, the minimum and maximum age was 15 and 62 respectively with median (IQR) of 25 (43.0), nine (30.0%) and three (10.0%) were male and female respectively, eight (26.7%) were critical and four (13.3%) had severe head injuries, two (6.7%) and 10 (33.3%) possessed equal and unequal pupils respectively, three (10.0%) had craniotomy and nine (30.0%) had a craniectomy done, all 12 (40.0%) had unfavourable outcomes in the first month. A preoperative CT scan showed seven (23.3%) had extra parenchymal haematoma, two (6.7%) intra parenchymal haematoma and three (10.0%) multiple lesions.

The median (IQR) ICP in the group with an opened and effaced basal cistern was 17.27 (7.42) mmHg and 37.1 (40.76) mmHg respectively while the median (IQR) CPP

Table 1. Distribution characteristics of study population

Variables	State of basal cistern		Midline shift		Postoperative CT scan	
	Opened	Effaced	≤ 5 mm	> 5 mm	Marshall I–II	Marshall III–IV
Age[a]	22.5 (31)	25 (43)	20 (20)	33 (40)	20 (30)	25 (43)
GCS[b] score						
3–5 (Critical)	2 (6.7)	7 (23.3)	4 (13.3)	5 (16.7)	1 (3.3)	8 (26.7)
6–8 (Severe)	18 (60.0)	3 (10.0)	14 (46.7)	7 (3.3)	17 (56.7)	4 (13.3)
Sex[b]						
Male	16 (53.3)	8 (26.7)	16 (53.3)	8 (26.7)	15 (50.0)	9 (30.0)
Female	4 (13.3)	2 (6.7)	2 (6.7)	4 (13.3)	3 (10.0)	3 (10.0)
Pupil[b]						
Equal	9 (30.0)	1 (3.3)	7 (23.3)	3 (10.0)	8 (26.7)	2 (6.7)
Unequal	11 (36.7)	9 (30.0)	11 (36.7)	9 (30.0)	10 (33.3)	10 (33.3)
Preoperative CT scan[b]						
Extraparenchyma	7 (23.3)	6 (20.0)	6 (20.0)	7 (23.3)	6 (20.0)	7 (23.3)
Intraparenchyma	6 (20.0)	1 (3.3)	5 (16.7)	2 (6.7)	5 (16.7)	2 (6.7)
Multiple	7 (23.3)	3 (10.0)	7 (23.3)	3 (10.0)	7 (23.3)	3 (10.0)
Operation[b]						
Craniotomy	13 (43.3)	2 (6.7)	11 (36.7)	4 (13.3)	12 (40.0)	3 (10.0)
Craniectomy	7 (23.3)	8 (26.7)	7 (23.3)	8 (26.7)	6 (20.0)	9 (30.0)
GOS at 1 month[b]						
Favourable	9 (30.0)	0	7 (23.3)	2 (6.6)	9 (30.0)	0
Unfavourable	11 (36.7)	10 (33.3)	11 (36.7)	10 (33.3)	9 (30.0)	12 (40.0)

[a]Median (IQR); [b]*n* (%).

with an opened and effaced basal cistern was 73.6 (9.88) mmHg and 59.23 (31.02) mmHg respectively. The median (IQR) cerebral compliance in the group with an opened basal cistern was 0.72 (0.19) mL/mmHg while in the effaced basal cistern, 0.7 (0.37) mL/mmHg. Both ICP and CPP were statistically correlated with the state of the post operative basal cistern, p value = 0.001 and p value = 0.022 respectively. There was a lower cerebral compliance in the group of patients with an effaced basal cistern as compared to the group with an opened basal cistern but it was not statistically significant.

The median (IQR) ICP in the group with MLS less than 0.5 cm and MLS more than 0.5 cm was 19.96 (9.24) mmHg and 18.33 (22.21) mmHg respectively while the median (IQR) CPP with MLS less than 0.5 cm and more than 0.5 cm was 71.98 (10.59) mmHg and 71.1 (17.68) mmHg respectively. Median (IQR) cerebral compliance in the group with MLS less than 0.5 cm was 0.72 (0.19) mL/mmHg and MLS more than 0.5 cm was 0.7 (0.41) mL/mmHg. None of the analyses of the relation between MLS with ICP, CPP or cerebral compliance were significant.

The median (IQR) ICP in the group with Marshall I and II and Marshall III and IV were 16.6 (7.79) mmHg and 33.43 (35.11) mmHg respectively while the median (IQR) CPP with Marshall I and II and Marshall III and IV were 73.63 (8.22) mmHg and 63.89 (29.36) mmHg respectively. The median (IQR) of cerebral compliance in the group with Marshall I and II was 0.72 (0.19) mL/mmHg while Marshall III and IV was 0.7 (0.42) mL/mmHg. There was a statistically significant correlation between Marshall Classification and ICP value; the p value = 0.001. Cerebral perfusion pressure and compliance were better in a less severely oedematous brain (Marshall I and II) as compared to a more oedematous brain (Marshall III and IV) but not statistically significant (Table 2).

Discussion

The process that occurs at cellular level following brain injury includes release of amino acids, glutamate and aspartate, free radicals, lactate and hydrogen ions above toxic levels. These processes eventually result in an influx of

Table 2. Relationship between ICP, CPP and cerebral compliance with state of basal cistern, midline shift and Marshall classification, *n* = 30

States of basal cistern	Opened (*n* = 20) Median (IQR)	Effaced (*n* = 10) Median (IQR)	Mann-Whitney U	*p* value*
ICP (mmHg)	17.27 (7.42)	37.1 (40.76)	27.0	0.001
CPP (mmHg)	73.6 (9.88)	59.23 (31.02)	48.0	0.022
Compliance (mL/mmHg)	0.72 (0.19)	0.7 (0.37)	88.0	0.598
Midline shift	≤ 5 mm (*n* = 18) Median (IQR)	> 5 mm (*n* = 12) Median (IQR)		
ICP (mmHg)	19.96 (9.24)	18.33 (22.21)	98.0	0.672
CPP (mmHg)	71.98 (10.59)	71.1 (17.68)	94.0	0.553
Compliance (mL/mmHg)	0.72 (0.19)	0.7 (0.41)	99.0	0.703
Marshall classification	I–II (*n* = 18) Median (IQR)	III–IV (*n* = 12) Median (IQR)		
ICP (mmHg)	16.6 (7.79)	33.43 (35.11)	30.0	0.001
CPP (mmHg)	73.63 (8.22)	63.89 (29.36)	62.0	0.051
Compliance (mL/mmHg)	0.72 (0.19)	0.7 (0.42)	103.0	0.832

*The level of significant was set at a probability value of 0.05.

calcium ions into cells and subsequent cell swelling. The presence of intracranial haematoma and cerebral oedema distort the anatomy of brain and blood vessels which worsen the cerebral hypoxia, responsible for inflammation and micro vascular dysfunction. The extra vascular blood also predisposes to large vessel spasms and a further reduction in cerebral blood flow, hypo perfusion and ischemia, and eventually cerebral oedema and brain swelling.[10,11]

Evacuation of blood clots or contusions remove a significant amount of the mass lesion and restores the brain anatomy. The evacuation of mass lesions therefore may result in reduced chances of developing cerebral oedema and minimise micro vascular dysfunction and large vessel spasms. The degree of oedema shortly after evacuation of the haematoma can be easily assessed on a CT scan brain based on the effacement of the basal cistern and shift of the midline structure. Effacement of the basal cistern and the degree of midline shift also signify the severity of brain injury.[12] Marshall and colleagues classified the degree of oedema in diffused injury (DI) into DI I having a normal CT scan and no visible pathology; DI II has a cistern open with less than a 5 mm midline shift and a lesion present under 25 mL; DI III has a cistern compressed or absent, a midline shift less than 5 mm and a lesion present that was less than 25 mL; and DI IV has a midline shift of more than 5 mm and a lesion less than 25 mL.[13]

In our study, a univariate analysis showed a statistically significant relationship between mean ICP as well as CPP with both states of basal cistern, degree of diffuse injury and oedema based on Marshall Classification System. The ICP was higher while CPP and compliance were lower whenever the basal cisterns were effaced in cases of cerebral oedema with Marshall III and IV. In comparison, the study revealed lower ICP, higher mean CPP and better mean cerebral compliance if the basal cisterns were opened or a post operative CT scan brain showed Marshall I and II. These findings suggested the surgical evacuation of a clot to reduce the mass volume and the restoration of brain anatomy may reduce vascular engorgement and cerebral oedema therefore preventing intracranial hypertension, improved cerebral perfusion pressure and cerebral compliance. Nevertheless the study did not find any significant relationship between midline shifts and mean ICP, CPP or cerebral compliance even though lower ICP, higher CPP and compliance were frequently observed when the MLS was less than 0.5 cm. As the majority of our patients had multiple and diffuse brain injuries, the absence of the MLS did not necessarily mean lower ICP as the pathology were bilateral. An abnormal CT scan brain that showed cerebral hemispheric swelling, compression of the basal cistern and diffuse injury with Marshall III–IV were associated with raised ICP higher than 20 mmHg and a CPP of less than 70 mmHg.[14–16] In another study by Hiler M et al found that the degree of oedema on the CT scan associated with ICP only in the first 24 hours but not with the mean ICP over the total time of treatment in the intensive care unit.[17]

Post operative CT features in our study also demonstrated significant association between the state of the basal cistern and Marshall classification with the patient outcome the first month after the injury. The effaced basal cistern as well as the group of patients with Marshall III and IV after surgical evacuation of mass lesions had unfavourable outcomes as compared to those with opened cisterns and Marshall I and II. Collectively post operative CT scans which showed mild cerebral oedema (opened basal cistern, MLS of less than 0.5mm and Marshall I/II) or severe cerebral oedema (closed basal cistern, MLS of more than 0.5 mm and Marshall III/IV) also showed significant association with Glasgow Outcome Score at first month. Collectively post operative CT scans which showed mild cerebral oedema (opened basal cistern, MLS of less than 0.5 mm and Marshall I/II) or severe cerebral oedema (closed basal cistern, MLS of more than 0.5 mm and Marshall III/IV) also showed significant association with the Glasgow outcome score in the first month. However when variables were subjected to logistic regression, none appeared as an independent survival outcome predictor.

We assumed the CT brain scan obtained after evacuation of the mass lesion to assess the state of the basal cistern and classify the diffuse oedema may prognosticate the intracranial pressure and cerebral perfusion pressure thus assisting in the acute postoperative management of a severely head injured patient. Hence a CT brain scan may be done to verify the ICP and CPP reading postoperatively. Subsequently, withdrawal of sedation for neurological assessment after surgery could be done if the CT brain showed an opened basal cistern and Marshall I and II coupled with ICP of less than 20 mmHg.

References

1. Klauber MR, Toutant SM, Marshall LF. A model for predicting delayed intracranial hypertension following severe head injury. *J Neurosurg* 1984;61:695–9.
2. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974;2:81–4.
3. Jennett B, Teasdale G, Braakman R, et al. Predicting outcome in individual patients after severe head injury. *Lancet* 1976;1:1031–4.
4. Piper I, Spiegelberg A, Whittle I, et al. A comparative study of the Spiegelberg compliance device with a manual volume-injection method: a clinical evaluation in patients with hydrocephalus. *Br J Neurosurg* 1999;13:581–6.
5. Chesnut RM, Marshall LF. Management of head injury. Treatment of abnormal intracranial pressure. *Neurosurg Clin N Am* 1991;2:267–84.
6. Dearden NM. Management of raised intracranial pressure after severe head injury. *Br J Hosp Med* 1986;36:94–103.
7. Miller JD, Piper IR, Dearden NM. Management of intracranial hypertension in head injury: matching treatment with cause. *Acta Neurochir Suppl (Wien)* 1993;57:152–9.
8. Ratanalert S, Phuenpathom N, Saeheng S, et al. ICP threshold in CPP management of severe head injury patients. *Surg Neurol* 2004;61:429–35; discussion 434–5.
9. Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet* 1975;1:480–4.
10. Obrist WD, Langfitt TW, Jaggi JL, et al. Cerebral blood flow and metabolism in comatose patients with acute head injury. Relationship to intracranial hypertension. *J Neurosurg* 1984;61:241–53.
11. Chambers IR, Treadwell L, Mendelow AD. The cause and incidence of secondary insults in severely head-injured adults and children. *Br J Neurosurg* 2000;14:424–31.
12. Toutant SM, Klauber MR, Marshall LF, et al. Absent or compressed basal cisterns on first CT scan: ominous predictors of outcome in severe head injury. *J Neurosurg* 1984;61:691–4.
13. Marshall LF, Marshall SB, Klauber MR, et al. The diagnosis of head injury requires a classification based on computed axial tomography. *J Neurotrauma* 1992;9(Suppl 1):S287–92.
14. Lubillo S, Bolanos J, Carreira L, et al. Prognostic value of early computerized tomography scanning following craniotomy for traumatic hematoma. *J Neurosurg* 1999;91:581–7.
15. Lobato RD, Sarabia R, Cordobes F, et al. Posttraumatic cerebral hemispheric swelling. Analysis of 55 cases studied with computerized tomography. *J Neurosurg* 1988;68:417–23.
16. Hiler M, Czosnyka M, Hutchinson P, et al. Predictive value of initial computerized tomography scan, intracranial pressure, and state of autoregulation in patients with traumatic brain injury. *J Neurosurg* 2006;104:731–7.
17. Miller MT, Pasquale M, Kurek S, et al. Initial head computed tomographic scan characteristics have a linear relationship with initial intracranial pressure after trauma. *J Trauma* 2004;56:967–72; discussion 972–3.