
2. Patients and Methods

2.1. Study Population

Adult traumatic brain-injured patients who had been admitted to the intensive care unit (ICU) with post-resuscitation Glasgow Coma Scale (GCS) scores 4-8 were considered for inclusion. This study is a prospective, was carried out in (ICU) department in each of Hawler Teaching Hospital, Rizgary Teaching Hospital and Hawler Private Hospital performed on patients with severe traumatic brain injury admitted to (ICU) from January 1, 2008 to July 1, 2009 after obtaining scientific Committee approval from college of medicine. A total of (57) TBI patients (patient with their GCS 4-8 and with closed type of head injury, who belonged to ASA class I-II category, having no indication for neurosurgery were included in this study.

Severe head trauma was defined as GCS 4-8. All patients included in the study had their trachea intubated and lungs ventilated mechanically with the intention to prevent hypoxemia as well as hypocapnia and hypercapnea with a history of not more than 24hrs from the time of injury. Such patients admitted to respiratory care units after recommendations from neurosurgeons when the patient's Glasgow Coma Scale 4-8 for which computerized tomography done prior to admission.

2.2. Study Design

A standardized data collection sheet was utilized that included demographic data, mechanism of injury, GCS on admission to ICU, pupil reaction to light, brain CT findings, six hourly electrolyte arterial blood gas (ABG) analyses, drugs received (anesthetic, inotropic, antihypertensive, antiarrhythmic, Insuline injections) , 4th ; 6th day GCS, follow up CT finding any events during ICU management and lastly daily Chest X-Ray .

2.2. Patients.

Total number of patients were fifty seven (57), sixteen (16) patients were excluded from the study (**five** patients developed unilateral pupil unreactivity after been included because of bilateral reactivity, **three** patients get bilateral pupil dilation after 6-12 hours after admission , **three** patient had multiple trauma requiring surgical intervention rather than neurosurgery , **three** patients had shooting in blood pressure uncontrolled by recommended therapies purposed in the study and last **two** patients excluded as they developed hypoxia because of multiple bilateral lung contusion diagnosed by CT on forth day). Forty one (41) patients enrolled in the study were subdivided into five groups according to pathological type of brain injury documented by CT findings, these subgroups are:

Group 1: are patients with brain concussion.

Group 2: are patients with brain contusion.

Group 3: are patients with Intracerebral Hemorrhage (ICH).

Group 4: are patients with Diffuse Axonal Injury (DAI)

Group 5: are patients with multiple brain pathology.

Their ages were ranged from 3-63 years.

2.3. Materials:

2.3.1. Drugs and dose used in ICU for management of TBI with some example in figure (2.1).

1. Thiopental (Tiopental 1g B.P.[®])

(SANDOZ). Sandoz. GmbH, Kundl Austria. (Powder for reconstitution for injection 2.5%)

was given in a dose of 3-4mg/Kg as an induction agent.

It's Pharmacologic class: Barbiturate, Therapeutic class: Anesthetic

2. Atracurium (ATACURE[®])

(HIKMA Pharmaceuticals). Amman Jordan. (10 mg/mL in 5mL ampoule)

was given in a dose 0.4mg/Kg/hr as infusion in 0.9% isotonic sodium chloride solution.

3. Fentanyl injection. (Fentanyl-Janssen[®])

Janssen-Cilag. Belgium. (0.05 mg (50mcg)/1mL, 2mL ampule)

Was given in a dose 2 mcg/kg bolus on induction followed by 0.5-1mcg/kg/hr.

4. Midazolam injection. (Dormicum[®])

Roche (F. Hoffmann-La Roche Ltd, Basel). Switzerland. (5mg/1ml, 1ml ampoule).

Was given in a dose 0.1-0.3 mg/kg/hr as infusion in 0.9% isotonic sodium chloride solution.

5. Lidocaine injection. (LIDOCAINE[®])

Rotexmedica. Germany. (Lidocaine injection BP 2%, 20 ml vial).

Was given in a dose 1-1.5 mg/kg as bolus doses as required.

6. Esmolol injection. (Brevibloc[®])

Baxter healthcare Lt.Baxter .(Esmolol HCl 250mg/mL, 10mL vial)

Was given as infusion titrated to effect

7. Metoprolol injection. (Beloc[®])

Rotexmeica.Germany. (Mrtoprolol injection 5mg/5mL ampoule)

Was given as slow infusion titrated to effect

8. Dobutamine injection (Dobutamine HCL injection[®])

MEDICOLAB S.P.R.L.Rue Joeseph Bensstraat 83A.(40mg/mL, 5mL ampoule).

Was given as infusion as inotropic agent.



Figure-2.1. Drugs used in ICU for anesthetic management for TBI patients.

2.3.2. Osmetech OPTI™ Blood Gas Analyzer

Osmetech Inc. Critical Care Division 235 Hembree Park Drive .Roswell, GA 30076 USA. www.osmetech.com

This machine was used for analyzing arterial blood samples regarding blood gas content and electrolyte level as shown in figure (2.2)



Figure-2.2. Osmetech OPTI™ Blood Gas Analyzer and Cassette

2.4. Exclusion Criteria:

- Patient in ASA IV, V, & VI (Explained in 2.7)
- Patient with brain death from the start but admitted to ICU medico-legally for controlled ventilation.
- Patient with GCS 3 from the start.
- Patients with brain stem injury.
- Patients with unilateral dilatation, of a pupil or other signs of impending brain herniation.
- Patients with multiple injury especially lung injury.

2.5. Methods:

After admission of such patients these patients are hemodynamically stabilized by putting three venous access, central venous line under aseptic technique, an arterial sample taken for ABG analysis.

Anesthesia was induced by Thiopental (given in dose 3-5 mg/kg) with Lidocaine (Lidocaine, given in a dose 1.5 mg/kg (given 2 minutes prior to intubation)), then Suxamethonium was given in a dose 1-1.5 mg/kg (Suxamethonium given approximately 30-60 second before ETT) i.e., rapid sequence induction supposing all patients with full stomach, then Atracurium was given in a dose 0.4 mg/kg, and induction was confirmed by loss of eyelash reflexes mean while doing cricoid pressure, then the patients are intubated endotracheally with suitable internal diameter cuffed endotracheal tube and ventilated mechanically by Intermittent Positive Pressure Ventilation (IPPV) mode with Zero PEEP (positive end expiratory pressure) Ventilatory machine used were [Dräger Evita 2 and Taema HORUS], as shown in figure (2.3), starting by an FiO₂ (fractional Oxygen concentration) of 100% with Tidal Volume (VT) of 10ml/Kg and a respiratory rate of not less than 12 respiration /minute according to the age with an I:E ratio of 1:2 (1 Inspiration :2

Expiration) aiming at maintaining ‘optimal oxygenation’ i.e., arterial PO₂ > 83 mmHg (11kPa) and an ‘adequate ventilation’ i.e. arterial PCO₂ between 34.2 -38 mmHg (4.5-5kPa) (Oertel *et al*, 2002), blood sugar monitoring every four hours maintaining blood sugar between 4-7 mmol/L with non-invasive continuous blood pressure monitoring, Electrocardiography, pulse oxymetry , temperature measuring and Central venous pressure monitoring especially in those patients who have fluctuation in their blood pressure .

Maintenance of anesthesia achieved by each of Medazolam infusion in 0.9% NaCl isotonic saline (0.1-0.3mg/kg/hr), Atracurium infusion in 0.9% NaCl isotonic saline (0.4mg/kg/hr), and Fentanyl (1-2mcg/kg/hr)



Figure-2.3. Mechanical ventilator showing zero PEEP.

2.5.1. Hemodynamic stabilization maintained by:

1. Giving $\frac{2}{3}$ rd normal daily requirement in the form of 0.9% NaCl isotonic saline calculated for maintenance and replacement of concomitant losses.
2. Colloid as blood or Albumine when Mean Arterial Blood Pressure less than 60mmHg. $MAP = DBP + \frac{1}{3}(SBP - DBP)$ (systolic blood pressure (SBP), diastolic blood pressure (DBP)).
3. Giving i.v. infusion of beta blocker drugs as propranolol or Metoprolol for controlling rise in mean arterial blood

2.5.2 Anesthetic agents

used was Thiopental and Suxamethonium as induction agents, atracurium as maintenance muscle relaxant, Medazolam as maintenance sedative agents and lastly Fentanyl as an analgesia the whole anesthesia was for about 72hrs.

Lidocaine used as an antiarrhythmic and for abolishing upper airway reflex during intubation. Other types of antiarrhythmic was available incase of any type of arrhythmia such as Amiodaron or Verapamil.

Certain Guidelines and approach for the Management of Severe Traumatic Brain Injury was developed as shown in figure (2.4) and table (2.1) (2.2)

2.6. Statistical Analyses.

Paired t-test was used to compare between means of certain parameters in two occasions. Chi square of association was used when applicable. When the expected count of $> 20\%$ of the $r \times c$ table were < 5 , Chi square test was not used.

2.7. ASA Classification.

Physical Status Classification System according to American Society Of Anesthiologists (ASA)}

ASA I: A normal healthy patient.

ASA II: A patient with mild systemic disease and no functional limitations.

ASA III: A patient with moderate to severe systemic disease that result in some function limitation.

ASA IV: A patient with severe systemic disease that is a constant threat to life and functionally incapacitating.

ASA V: A moribund patient who is not expected to survive 24 hours with or without the operation

ASA VI: A declared brain-dead patient whose organs are being removed for donor purposes.

2.8. Some Protocols and Guidelines for Management of TBI patients in ICU as shown in table (2.1) (2.2) and figure (2.4)B.

Table-2.1. Recommendations from Guidelines for the Management of Severe Traumatic Brain Injury (Bullock RM et al, 2000).

Standards based on class I evidence:

1. If intracranial pressure (ICP) is normal, avoid chronic prolonged hyperventilation therapy ($Paco_2 < 25$ mm Hg).
2. Administration of steroids does not improve outcome or reduce ICP.
3. Prophylactic use of anticonvulsants does not prevent late posttraumatic seizures.

Guidelines based on class II evidence:

1. All regions should have an organized trauma care system.
2. Avoid or correct immediately hypotension (systolic blood pressure < 90 mm Hg) and hypoxia ($SpO_2 < 99\%$ or $Pao_2 < 60$ mm Hg).
3. Indications for ICP monitoring include Glasgow Coma Score 3-8 with abnormal CT scan or 2 or more of the following adverse features: age > 40 years, motor posturing, systolic blood pressure < 90 mm Hg.
4. Initiate treatment for ICP at an upper threshold of 20-25 mm Hg.
5. Avoid the use of prophylactic hyperventilation ($C < 35$ mm Hg) therapy during the first 24 hours after severe traumatic brain injury.
6. Mannitol is effective for control of raised ICP after severe TBI, in doses ranging from 0.25 g/kg body weight to 1 g/kg body weight.
7. High-dose barbiturate therapy may be considered in hemodynamically stable salvageable severe TBI patients with intracranial hypertension refractory to maximal medical and surgical ICP lowering therapy.

Provide nutritional support (140% of resting energy expenditure in nonparalyzed patients and 100% of resting energy expenditure in paralyzed patients) using enteral or parenteral formulas containing at least 15% of calories as protein by day 7 after injury.

ICP, intracranial pressure; TBI, Traumatic Brain Injury; Pao_2 , Partial arterial pressure of Oxygen; $Paco_2$, Partial arterial pressure of Carbon Dioxide

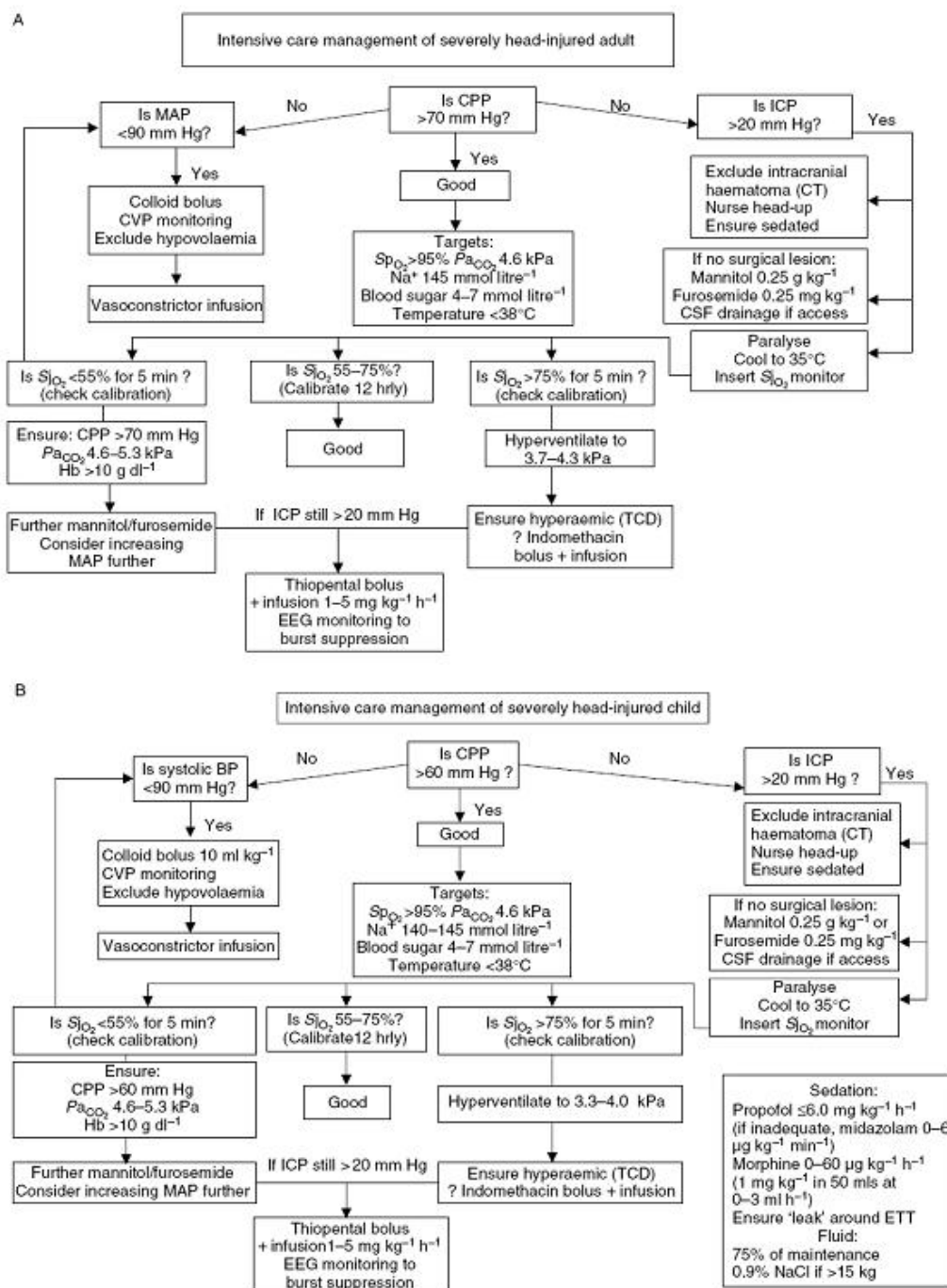


Figure-2.4. The Frenchay ICU head injury management protocols for (A) adults and (B) children. (Clayton et al, 2004)

MAP, mean arterial pressure; CPP, cerebral perfusion pressure; ICP, intracranial pressure; CVP, central venous pressure; CT, computed tomography; SpO₂, pulse oximetry; SjO₂, jugular venous oxygen saturation; TCD, transcranial Doppler; EEG, electroencephalogram.

Table-2.2. Comparison of Therapeutic Approaches to Management of Traumatic Brain Injury (Richard S and James M, 2008).

<i>Therapeutic Approaches to Management of Traumatic Brain Injury</i>				
	<i>Traditional</i>	<i>CPP Management</i>	<i>Lund Therapy</i>	<i>Individualized Therapy</i>
Intracranial homeostasis				
Mean arterial blood pressure	Not considered,	>70-80 mm Hg	>50-60 mm Hg	Ischemia/Hypoperfusion-increase CPP to improve CBF
Arterial hypertension	Treat SBP >160 mm Hg	no	metoprolol + clonidine	Ischemia/hypoperfusion pattern -don't treat Adequate perfusion-treat
Barbiturate coma	yes	no	no	Hypoperfusion/edema pattern-no Hyperemia/vascular engorgement pattern-yes
CSF drainage	yes	yes	no	Yes
Extracranial homeostasis				
Goal for CPP	ICP <20 mm Hg Normal BP	(above lower limit of autoregulation)	(whatever provides adequate perfusion)	Adequate perfusion-normal CPP
Head position	15-30° elevation	flat	flat	position with best CPP and ICP
Hyperventilation	yes	no	no	Ischemia/hypoperfusion pattern-no Adequate perfusion-yes
Neuromuscular blockade	yes	yes	no	yes
Nutritional support	yes, avoid hyperglycemia	no	yes, avoid hyperglycemia	yes, avoid hyperglycemia
Osmotherapy	yes	yes	no	Hypoperfusion/edema pattern-yes Hyperemia/vascular engorgement pattern-no
Sedation	morphine + lorazepam	none	low dose thiopental	morphine + lorazepam

BP, blood pressure; CBF, cerebral blood flow; CCP, cerebral perfusion pressure; CSF, cerebral spinal fluid; ICP, intracranial pressure; SBP, systolic blood pressure