Guidelines for
MANAGEMENT OF THE BRAIN DEAD ORGAN DONOR IN INTENSIVE CARE UNIT (ICU)

1. Introduction: Following the diagnosis of brain death, a race against time starts. The process of counseling the relatives and obtaining consent for organ donation progress while the intensivist tries to keep the donor's organ systems viable for donation. This process can be extremely challenging, since a number of physiological changes which occur in the brain dead patient lead inexorably to hypoperfusion of the various organs which are intended for harvesting. It is the duty of the intensive care team to counteract these changes, and optimize the perfusion of these organs for as long as it takes for consent to be obtained for organ donation. The guidelines which follow attempt to provide a road map to allow for the largest possible yield of organs. It will be seen that these guidelines are frequently based on low grade evidence, opinion and anecdote. There is therefore substantial room for variations in practice, and an explicit attempt has been made to avoid a prescriptive approach in areas where the evidence is weak. It should be recognised, that even when everything is done perfectly, conversion from recognition of brain death to actual organ donation is distressingly low in this country.

2. Changes which occur following brain death. Depending on the study quoted, the following changes occur in brain dead, ventilated patients in the incidence mentioned [1].

Derangement	Cause	Approximate Incidence
Hypothermia	Hypothalamic damage; reduced metabolic rate; vasodilation and heat loss Invariable if not prevented	Invariable if not prevented
Hypotension	Vasoplegia; hypovolaemia; reduced coronary blood flow; myocardial dysfunction	81-97%
Diabetes Insipidus	Posterior pituitary damage	46-78%
DIC	Tissue factor release; coagulopathy	29-55%
Arrhythmias	'Catecholamine storm'; myocardial damage; reduced coronary blood flow	25-32%
Pulmonary oedema	Acute blood volume diversion; capillary damage	13-18%

3. Pathophysiology

a. Cardiovascular issues: Raised intracranial pressure causing brain death leads to Cushings Reflex which stimulates a release of epinephrine upto a thousand times normal. This can lead to subendocardial ischemia, arrhythmias, pulmonary edema and a consequent decrease in cardiac output along with hypertension. As the reflex subsides, the epinephrine levels reduce to subnormal levels and the underlying decrease in ejection fraction becomes unmasked causing severe hypotension. Soon, the posterior pituitary stops secreting vasopressin, and the urine output increases, which if not matched by intravenous fluids and corrected with externally administered vasopressin or its analogues can lead to hypovolemiaaggracating the hypotension and systematic hypoperfusion. If hypotension is not corrected, it can lead to as many as 25% of available organs being rendered unusable. [3]

b. Endocrine Changes: Human studies have concluded that the anterior pituitary is more resistant than previously assumed, and the main emphasis is on replacing vasopressin secreted by the posterior pituitary. Methylprednisolone in supraphysiological doses has been associated with decreased extravascular lung water, decreased levels of inflammatory markers, and increase organ retrieval [4], and hydrocortisone in low doses has been shown to reduce vasopressor requiremen[5]. There is some evidence that routine intravenous triiodothyronine (T3) leads to improvement in catecholamine responsiveness and consequently, better organ perfusion, although this effect appears less important than appropriate fluid and vasopressor management[6],[7]. Additionally, a low dose insulin infusion aids in the avoidance of hyperglycemia.

SPECIFIC MANAGEMENT OF THE BRAIN DEAD DONOR

4. Communication Issues: It is important to state to the relatives without ambiguity and equivocation the fact of the patient's brain death. Following this, time should be given for the families to adjust to the fact of the patient's brain death and only then should the process of counseling the patient regarding organ donation. Hirearchy of the family of the donor should be ascertained so that the person responsible for giving consent for organ donation is established. It is preferable that the ICU team which has conveyed the news of brain death, should not be involved in counseling the relatives.

5. General Nursing Care: The general nursing care of the brain dead organ donor (Prevention of decubitus ulcers, skin care, dressing changes, urinary and intravascular catheters and catheter site care) should occur with the same regularity as with a living patient. This will aid in preventing the brain dead patient from developing systematic sepsis. In addition, continuing regular care is very valuable in ensuring that important aspects of management are not lost because of interruption of the normal cycle of care. If not already place, a nasogastric tube should be placed for decompressing the stomach. It is critical to actively warm the patient using either blankets (passive warming), or devices like forced air warmers (active rewarming) and to monitor the core body temperature, as the hypothermia which invariably develops in brain dead organ donors can lead to coagulopathies and worsening of hemodynamics.

6. Monitoring. The brain dead organ donor requires extremely close monitoring to detect decompensation and treat it urgently. The following monitors are desirable.

    a. Core temperature (Either Nasopharyngeal, esophageal, rectal or indwelling bladder catheter)
    b. ECG
    c. Invasive Blood Pressure (Arterial Catheter)
    d. CVP (Subclavian or IJV)
    e. SpO2
    f. End-tidal CO2
    g. Hourly urine output

These should be initiated as soon as possible after brain death is established.

7. Routine Investigations: The following investigations should be performed.

    a. CBC
    b. Blood grouping and cross matching
    c. Coagulation profile- PT/PTTK
    d. RFT-BUN, Creatinine
    e. Complete LFT
    f. S Electrolytes- Ca, Mg, Na, K, Phosphate
    g. Blood Sugar
    h. Urine analysis
    i. ABG with lactate
    j. Cardiac evaluation
        h. ECG
        ii. Echocardiography

    K. Imaging

        i. CXR

        ii. USG for abdominal organs-liver, kidney, pancreas

    l. Microbiology

        i. Surveillance cultures of ET Asp, Blood, urine, any other fluid eg ascetic fluid

        ii. Viral markers
            1. HBsAg
            2. Anti HCV
            3. HIV 1&2

8. Specific Infection Prevention: Aseptic precautions to be continued and antibiotics if required for organ donation to be decided on centre/organ specific basis.

9. Fluid management of the brain dead organ donor:
   a. Maintenance Fluid: Fluid therapy is aimed to preserve organ function whereby they can be transplanted in the recipient. If the serum sodium rises above 150 mEq (as frequently happens when diabetes insipidus supervenes), the fluid can be shifted to 5% Dextrose. In either instance, it is critical not to fall behind the urine output, and it is extremely important to monitor urine output on an hourly basis, an increase the maintenance fluids whenever required.
   b. Replacement of absolute volume deficit: Brain dead patients are frequently hypovolemic (for reasons mentioned in the pathophysiolgy section) and may require large volume boluses of fluid to prevent hypotension. This is best carried out with balanced salt solutions (Ringer's Lacate, or one of its variants). With regards to colloids, as there is a large body of literature showing no evidence of improvement in outcome, and there exists some evidence of increased renal failure, colloids are best avoided [8].
   c. Fluid Targets: No specific end point has been demonstrated conclusively to improve outcome in living patients, or organ retrieval in brain dead patients, whether it be static indicators of preload such as central venous pressure or pulmonary capillary wedge pressure, or dynamic indicators such as systolic pressure variation, cardiac output monitoring or Inferior Vena Cava assessments. It seems prudent to recommend using multiple inputs to assess fluid repletion (including, importantly, a subjective clinical sense of whether the patient seems adequately volume resuscitated or not) rather than depending on any one indicator.

10. Vasopressor choice: It is important to ensure that the patient is adequately volume resuscitated before starting any pressors. Once this is achieved, vasopressors need to be started if the patient continues to be hypotensive. There is little evidence to show the superiority of one pressor over the other in this particular setting. There is some weak, outdated evidence that dopamine may lead to improved kidney retrieval, and some evidence that norepinephrine is associated with less arrhythmias. One of the ways in which brain dead organ donors are different is the routine requirement of physiologic doses of vasopressin (0.5-2.4 units per hour) in order to maintain the blood pressure and responsiveness to the pressor effect of catecholmaines. Norepinephrine and Vasopressin are the first line vasopressors whereas dopamine, dobutamine and epinephrine are used selectively in some patients. By reducing the catecholamine requirements, ATP levels in the hart are maintained, and the salvage rates of the heart are improved [9]. A combined approach of cardiovascular optimization and hormone therapy has been shown to reverse the myocardial stunning which takes place after brain death [10]. A recent trial has shown no difference in cardiac function between organ donors who were supported by either dopamine or nopeinephrine [11].
11. Ventilatory management: Standard lung protective ventilation strategies are suggested, in conjunction with closed suctioning, and targeting of PEEP to allow the FiO2 to be kept as

low as possible to allow an SpO2 of >94% , especially where lung transplantation is being considered. It is important to prevent atelectasis and consequent shunt induced hypoxia by ventilator augmentation and sterile suctioning of mucus plugs.[12] As far as possible, high levels of PEEP and peak inspiratory pressures should be avoided as this could lead to hepatic congestion.

12. Targets for resuscitation: As a general guide, till the results of the Monitor trial are published, the following guidelines for resuscitation may be considered reasonable.

Parameter	Target
Heart Rate	60-120 beats/mt
Arterial Pressure	Systolic pressure>100 mm Hg
Central Venous Pressure	6-10 mm Hg
Urine Output	0.5-3 ml/kg/hr
Electrolytes	Serum Sodium 130-150 mmol/litre Normal Potassium, Calcium, Magnesium, Glucose and Phosphate
Blood Gases	Ph-7.35-7.45 PaCO2-30-45 mmHg PaO2> 80 mmHg SpO2>95%
Temperature	>35°C
Blood sugar	120-180mg%

13. Management of Endocrine Dysfunction And Hormone Replacement
    a. Diabetes Insipidus. The posterior pituitary is particularly prone to stop functioning in brain dead patients. This leads to an absolute deficiency of vasopressin and consequent diabetes insipidus. Diabetes Insipidus is characterized by a urine output of > 4ml/kg/hr, serum sodium of >145 mEq, a serum osmolarity of >300 mosm and a urinary osmolarity of <300 mosm and a urinary specific gravity of less than 1.005. However, as a practical point, valuable time may be lost if treatment is started only after the lab reports are received. Perhaps a better option is to administer nasal puffs or intravenous desmopressin presumptively if two hours of urine output >4 ml/kg/hr have passed. In this context, it should be remembered that there is no role for mannitol or furosemide in the brain dead organ donor. In a hypotensive patient with diabetes insipidus, a vasopressin infusion is a more rational choice, as it achieves correction of both hypotension

and diabetes insipidus.In addition, vasopressin has been demonstrated in a randomized trial to improve organ retrieval rates [9].

b. Methylprednisone: As previously mentioned, methylprednisone may have advantages above and beyond its role in physiological replacement of corticosteroids. Most centres internationally have a protocol of giving methylprednisolone 15 mg/kg every 24 hours [2]. Another suggested option is to give a bolus methylprednisone 250mg followed by 100mg/hr till the time of organ retrieval.

c. Triodothyronine/ Thyroxine: There are some reports of triodothyronine in the dose of 4 microgram bolus followed by infusion at 3 micrograms/hour in the brain dead patient improving vasopressor responsiveness and organ salvage rates, possibly by reducing the incidence of stunned myocardium [13],[14]However, intravenous tridothyronine is generally not available in this country, and its advantages are marginal when the patient is already receiving methylprednisone and vasopressin [7]. Oral thyroxine in the dose of 300-400mcg/8hourly is an alternative to triodothyronine.

d. Hyperglycemia: It is important to avoid extreme hyperglycemia, especially when pancreatic harvesting is considered. A blood sugar of 120-180 mg% should be aimed for with the judicious use of a low dose insulin infusion.

14. Coagulopathies and blood transfusion: A large number of brain dead organ donors have suffered severe head injuries. This results in the release of brain thromboplastin, which induces severe coagulopathies, which in turn can lead to severe bleeding from puncture sites and wounds. It is therefore important to carry out frequent monitoring of the prothrombin time, activate partial thromboplastin time and platelet count, and correct abnormalities in coagulation aggressively with fresh frozen plasma, cryoprecipitate and platelet concentrates. With regards to blood transfusion, while there is a general trend in critical care following the TRICC study, to adopt a conservative blood transfusion protocol, and transfuse only when the hemoglobin drops below 7 gm%, there is no evidence of the optimal transfusion trigger for brain dead organ donors and a transfusion target for 10 gm% is still frequently aimed for [4].

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