



# **INDIRA GANDHI INSTITUTE OF MEDICAL SCIENCES**

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## The Brain Dead Organ Donor In Intensive Care Unit (ICU)

### 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. A recent single center study showed a conversion rate of 10 out of 205 brain dead patients.

### Changes which occur following brain death:

Depending on the study quoted, the following changes occur in brain dead, ventilated patients in the incidence mentioned.

Approximate Incidence	Cause	Derangement
Invariable if not prevented	Hypothalamic damage; reduced metabolic rate; vasodilation and heat loss Invariable if not prevented	<b>Hypothermia</b>
81-97%	Vasoplegia; hypovolaemia; reduced coronary blood flow; myocardial dysfunction	<b>Hypotension</b>
46-78%	Posterior pituitary damage	<b>Diabetes Insipidus</b>
29-55%	Tissue factor release; coagulopathy	<b>DIC</b>
25-32%	“Catecholamine storm”; myocardial damage; reduced coronary blood flow	<b>Arrhythmias</b>

13-18%	Acute blood volume diversion; capillary damage	<b>Pulmonary oedema</b>
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**Patho-physiology:**

**a.**

**Cardiovascular issues:** Raised intracranial pressure causing brain death leads to Cushing's Reflex which stimulates a release of epinephrine up to 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 hypovolemia aggravating the hypotension and systematic hypoperfusion. If hypotension is not corrected, it can lead to as many as 25% of available organs being rendered unusable.

**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 [3]. There is some evidence that routine intravenous triiodothyronine (T3) leads to improvement in catecholamine responsiveness and consequently, better organ perfusion. Additionally, a low dose insulin infusion aids in the avoidance of hyperglycemia.

**SPECIFIC MANAGEMENT OF THE BRAIN DEAD DONOR**

**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. It is preferable that the ICU team which has conveyed the news of brain death not be involved in counselling the relatives.

**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 placed, 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.

### **Monitoring:**

The brain dead organ donor requires extremely close monitoring to detect decompensation and treat it urgently. The following monitors are required at a minimum.

- a. Core temperature (Either Nasopharyngeal, esophageal, rectal or indwelling bladder catheter)
- b. ECG
- c. SBP (Arterial Catheter)
- d. CVP (Subclavian or IJV)
- e. Arterial line
- f. SpO<sub>2</sub>
- g. Hourly urine output
- h. In addition, echocardiography is invaluable to detect impairment in cardiac contractility and to assess the inferior vena cava for fullness. Besides helping in the differential diagnosis of hypotension, it also aids in assessing the suitability of the heart for harvesting.

### **7. Routine Investigations:**

The following investigations should be performed at a minimum.

- 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
- g. Blood Sugar
- h. Urine analysis
- i. ABG with lactate
- j. Cardiac evaluation
  - i. 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

### **Specific Infection Prevention:**

All unnecessary indwelling devices (ventriculostomy drains and intracranial pressure monitors) should be removed. If any invasive device (central line, arterial catheter or urinary catheter) was placed in suboptimal conditions, it is important to change it expeditiously using

complete aseptic precautions. Antibiotics should be given presumptively if there is evidence of infection, while waiting for positive cultures. Prophylactic antibiotics and nephrotoxic antibiotics, should however be avoided.

### **Fluid management of the brain dead organ donor:**

**a. Maintenance Fluid:** A sensible choice for the primary maintenance fluid is half normal saline with 20 mEq/litre of potassium. This, administered as per Holiday and Segars formula should provide both volume and electrolytes to replace urine losses. 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 pathophysiology section) and may require large volume boluses of fluid to prevent hypotension. This is best carried out with balanced salt solutions (Ringer's Lactate, 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.

**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. Greater clarity may be achieved following publication of the MONITOR study, which randomizes brain dead organ donors to either usual management or intensive management with lithium dilution based cardiac output monitoring. While awaiting the findings of this study, 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.

**d. Wet or Dry?-** If the donors lungs are not being harvested, a fairly liberal approach to fluid resuscitation can be adopted. If, on the other hand, the lungs are being harvested, a far more cautious approach to fluid resuscitation is required, since increased lung water can make the lungs unsalvageable. As a purely illustrative example, in a sanitation where the lungs are not being harvested, a CVP of 6-10 cm.

H<sub>2</sub>O is frequently targeted, while when the lungs are being considered for harvesting, a CVP of 2-4 cm H<sub>2</sub>O would be more appropriate.

### **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. Either is an acceptable choice, although the personal preference of the authors is to use norepinephrine. 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 catecholamines. By reducing the catecholamine requirements, ATP levels in the heart are maintained, and the

salvage rates of the heart are improved. A combined approach of cardiovascular optimization and hormone therapy has been shown to reverse the myocardial stunning which takes place after brain death.

### **Ventilatory management:**

Standard lung protective ventilation strategies should be used. It is important to prevent atelectasis and consequent shunt induced hypoxia by ventilator augmentation and sterile suctioning of mucus plugs. As far as possible, high levels of PEEP and peak inspiratory pressures should be avoided as this could lead to hepatic congestion.

### **Targets for resuscitation:**

As a general guide, the following guidelines for resuscitation may be considered reasonable.

<b>Target</b>	<b>Parameter</b>
60-120 beats/mt	Heart Rate
Systolic pressure >100 mm Hg Mean pressure >70 mm Hg	Arterial Pressure
6-10 mm Hg	Central Venous Pressure
0.5-3 ml/kg/hr	Urine Output
Serum Sodium 130-150 mmol/litre Normal Potassium, Calcium, Magnesium and Phosphate	Electrolytes
Ph-7.35-7.45 PaCO <sub>2</sub> -30-45 mmHg PaO <sub>2</sub> > 80 mmHg SpO <sub>2</sub> >95%	Blood Gases

### **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, and furosemide and mannitol have been excluded as causes for the increased urine output. 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.
- 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

- c. **Triiodothyronine:** There are some reports of triiodothyronine 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. However, intravenous triiodothyronine is generally not available in this country, and its advantages are marginal when the patient is already receiving methylprednisone and vasopressin
- 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.

### **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.

### **THE BRAIN DEAD ORGAN DONOR IN AUSTRERE CIRCUMSTANCES**

All that has mentioned above is what should be done in ideal circumstances. It should however be accepted that brain dead patients in this country are often being managed in conditions which are less than ideal, in hospitals which do not have the full panoply of investigations and monitoring, and that the staff caring for the patient is frequently not optimally trained. In such situations, a good deal of ingenuity and diplomacy is called for, in order to ensure that the process of organ donation takes place with the least possible mishaps and miscommunications. Options available could include.

- a. Is transferring the brain dead organ donor to a tertiary care ICU in order to stabilize the condition an option?
- b. Is transferring portable monitoring equipment (portable arterial blood gases and portable echocardiography) from the tertiary care hospital to the bedside of the patient an option? Will clearance be made available to carry the echocardiography machine (which under the PNDT act is to be used only in the hospital in which it is certified)?
- c. Will the staff in the admitting hospital be amenable to allowing the intensive care team from an outside hospital to take over the management of the patient for a few hours in order to optimize parameters?

These and other questions can only be answered as time passes and more experience is accumulated. It should be remembered that while protocols can be drafted in a large number of areas, the process of organ donation is very highly dependent on the cultural, social and economic characteristics of the community in which it takes place, and there will always be room for practice variation. 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. A recent single center study showed a conversion rate of 10 out of 205 brain dead patients, with the major hurdle being cultural values and ignorance of brain death as a concept in the community. Clearly, we have a long way to go.

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