INTRODUCTION

Organ transplantation is widely evolving as a mode of treatment for end-stage diseases in modern medical practice. There is a huge imbalance between the demand and supply of organs.[1] To curb this deficit, organ retrieval from brain dead patients is getting increased attention. In our country, despite a significant number of head injuries leading to brain death, the number of organ donations is very less.

The present study was undertaken to address issues related to organ donation and share our experience at a tertiary level trauma care centre with around 6,500 annual trauma admissions and a large number of trauma referrals including significant number of patients with head injury.

METHODS

The objective of our case study was to analyse the profile of brain dead organ donors in tertiary level trauma centre. A retrospective case record analysis of over 5 years from September 2007 to August 2012 was performed. The patients included were those fulfilling brain death criterion (Form-8) as per Transplantation of Human Organs and Tissue (Amendment) Act, 2011 with consent from near relatives (Form-6) and...
no objection from investigating police officer from concerned jurisdiction [Table 1]. Brain dead patients, who were medically unsuitable for donation or did not give consent for organ donation, were excluded from the study. The parameters analysed included patient demographics (age, sex), mode of injury, time from injury to the diagnosis of brain death, time from diagnosis of brain death to organ retrieval, complications secondary to brain death and the organs retrieved.

**Statistical analysis**
In this study, parametric data were recorded as arithmetic mean ± standard deviation (SD). Student’s *t* test was used for parametric data and Chi square analysis was used for categorical data. Graphs were produced using Microsoft Excel for MAC 2011 (version 14.1.2).

### Table 1: Diagnostic criterion for brain death

| Pre-Conditions |  |
|----------------|---|
| **Pre-Conditions** |  |
| 1. Diagnosis: Did the patient suffer from any illness or accident that led to irreversible brain damage? Specify details ............................ |  |
| Date and time of accident/onset of illness .......................................................... Date and onset of no-responsible coma?............................... |  |
| 2. Finding of Board of Medical Experts: |  |
| I. The following reversible causes of coma have been excluded: |  |
| Intoxication (Alcohol) |  |
| Depressant Drugs |  |
| Relaxants (Neuromuscular blocking agents) |  |
| First Medical Examination Second Medical examination |  |
| 1st 2nd 1st 2nd |  |
| Hypothermia |  |
| Hypovolaemic shock |  |
| Metabolic or endocrine disorders |  |
| Primary tests for absent of brain stem functions |  |
| 2. Coma |  |
| 3. Cessation of spontaneous breathing. |  |
| 4. Pupillary size |  |
| 5. Pupillary light reflexes |  |
| 6. Doll’s head eyes movement |  |
| 7. Corneal reflexes (Both sizes) |  |
| 8. Motor response in any cranial nerve distribution, any responses to simulation of face limb of trunk |  |
| 9. Gag reflex, |  |
| 10. Cough (Tracheal) |  |
| 11. Eye movements on caloric testing bilaterally |  |
| 12. Apnoea tests as specified |  |
| 13. Were any respiratory movements seen? |  |
| Date and time of first testing .......................................................... |  |
| Date and time of second testing .......................................................... |  |
| This to certify that the patient has been carefully examined twice after an interval of about six hours and on the basis of findings recorded above, Mr/Mrs. .......................................................... is declared brain-stem dead. |  |
| 1. Medical administrator incharge of the hospital |  |
| 2. Authorised specialist |  |
| 3. Neurologist/ Neuro Surgeon |  |
| 4. Medical officer treating patient. |  |
| **NB.** |  |
| I. The minimum time interval between the first testing and second testing will be six hours. |  |
| II. No. 2 and No. 3 will be co-opted by the administrator in charge of the hospital from the panel of experts approved by the appropriate authority. |  |
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support. Signs of impaired organ perfusion (decreased urine output, fall in blood pressure) was seen in 45% donors and 33.3% had electrolyte imbalance at some point of time. Transfusion of blood products for preoperative optimization was required in 67% cases. The average time recorded from certification of brain death to organ harvesting was 33.47±46.63 hours. The organs harvested were kidney, heart, heart valves, liver, cornea and vessel grafts.

**DISCUSSION**

In our country, the facility of conversion of cadavers to organ donors is available in a limited number of institutes and our centre is one of them. In the present study, total brain dead patients becoming organ donors constituted less than 2%. Though we had ample number of brain dead patients, the actual number of organ donations was very less. The reasons for non-organ donation in the 195 cases were lack of consent, procedural problems, patients not counselled, too unstable for donation, age and co-morbidities, etc. Maximal rate of organ donation is estimated to be 50 donors/million population (dpm), in Western Europe it is 12-20 dpm but no data is available from Indian subcontinent.[2]

**Consent**

As per the transplantation of human organ and tissue Amendment Act 2011, any person may authorise the removal of human organ or tissue of his body for therapeutic purposes before his death. Such authorization should be in writing and in the presence of two or more witnesses (at least one of whom is a near relative of such person). On death, the next of kin of the dead body shall facilitate registered medical practitioner for removal of organs unless he has any reason to believe that the donor had subsequently revoked the authority.

In case of absence of any authority or objection for organ retrieval after death from person during life, the next of kin of the dead body may authorise the removal of any human organ of the deceased person for its use for therapeutic purposes in condition that none of the near relative (spouse, son, daughter, father, mother, brother or sister, grandfather, grandmother, grandson, grand-daughter) has objection to the organs being used for therapeutic purposes.

**Physiological effects and consequences of brain death**

Brain death induces a series of deleterious effects on different organ systems. These are clinically important and need due consideration during the management of potential organ donors and, subsequently, later in organ procurement.

**Cardiovascular changes**

Head injury followed by brain death progressively increases intracranial pressure (ICP). Pontine ischemia results in “cushings reflex with mixed vagal and sympathetic stimulation and hence, bradycardia and hypertension.[2] This is followed by ischaemia of distal medulla resulting in unopposed sympathetic stimulation. “Autonomic storm” is manifested by hypertension, tachycardia and myocardial ischaemia.[3,4] With the completion of herniation, there is a gradual loss of all sympathetic and vascular tone leading to hypotension and cardiovascular collapse.[5] Vasodilation and subsequent afterload reduction cause reduced coronary perfusion and relative hypovolemia followed by deterioration of cardiovascular function.[6] This last phase is of concern because it is characterised by reduced tissue perfusion and end organ damage.

**Pulmonary changes**

Brain death is associated with neurogenic pulmonary edema, systemic inflammatory response simulating...
Acute respiratory distress syndrome (ARDS) and pneumonia. Pulmonary dysfunction may be due to aspiration, pneumonia, contusion or ventilator induced injury. The lung injury is attributed to sympathetic storm induced neurogenic pulmonary oedema following a neurological insult. This is due to stimulation of Alfa receptors causing increased leakage from pulmonary capillaries.

**Endocrine changes**

Anterior pituitary function is well preserved in most donors but posterior pituitary function is lost in 80% of donors. This results in normal values of thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH) and human growth hormone (GH). However, these patients may have diabetes insipidus (DI) with electrolyte disturbances, hypovolemia and circulatory instability. Plasma cortisol levels remain normal but there is decreased capacity to increase cortisol upon ACTH stimulation. Administration of cortisol attenuates immune response and hence in many centres, cortisol is administered to organ donors.

**Immunological consequences**

Release of chemokines and cytokines in response to brain injury results in apoptosis, haemodynamic instability, increased organ dysfunction and likelihood of organ rejection. These are upregulated with time and inflammatory cascade may be initiated after prolonged exposure. Thus, immunologically activated organs may have resultant histological damage, decreased function and reduced graft survival compared to live donors.

**Donor management**

**Haemodynamic monitoring**

It is recommended that every cadaveric donor should have a central venous pressure (CVP) monitoring which can be used in fluid therapy. Guided fluid therapy, is indicated as there is a very high risk of pulmonary oedema due to increased capillary permeability and pulmonary overflow due to reduced pulmonary vascular resistance.

The recommendations by the American society of cardiology is to maintain systolic blood pressure of 90-140 mmHg, CVP of 8-12 mmHg or pulmonary capillary wedge pressure of 12-14 mmHg using pulmonary artery catheter. The rule of 100 which includes systolic blood pressure more than 100 mmHg, heart rate less than 100 beats/min, urine output more than 100 ml/hr and PaO2 more than 100 mmHg, which was followed at our institute also for organ procurement.

Serial echocardiographic examinations may be needed to assess the improvement in myocardial function in patients on cardiovascular support. Coronary angiography is indicated in patients who are above 40 years, require high inotropic support or have risk factors for coronary artery disease. However, serial echocardiography or coronary angiography was not done in any patient in our study.

**Haemodynamic management**

The haemodynamic goals include maintenance of normal intravascular volume, normal cardiac output and perfusion pressures to optimise tissue oxygen delivery. This may require fluid resuscitation, inotropic or vasopressor support and hormonal treatment.

The traditional use of dopamine as the inotrope of choice has been questioned by recent studies as it does not seem to support the renal or hepatosplanchic circulation and suppresses the anterior pituitary hormones. Dopamine has been replaced by vasopressin due to its catecholamine sparing effect. It has been recommended as the initial vasopressor of choice in the vasodilatory shock as well as for the treatment of diabetes insipidus (DI) in donors. Vasopressors are indicated in the setting of low systemic vascular resistance and normal or elevated cardiac output. It has been found that use of vasopressin, glucocorticoids and tridothyronin is successful in converting unsuitable to suitable organ donors.

**Endocrine management**

Pituitary dysfunction is common in brainstem dead patients, which is manifested as a deficiency in anterior pituitary hormones like T3, T4, ACTH, TSH and human GH. Posterior pituitary dysfunction with decreased levels of vasopressin is manifested as DI and usually occurs in 90% of adult and paediatric organ donors. DI in cadaveric donors has been seen associated with cardiovascular collapse and major electrolyte imbalances.

Vasopressin has been used in a dose range from 0.5-1.5 u/hr as it has both vasopressor and antidiuretic action. The use of vasopressin in doses more than 0.04 u/min causes dysfunction in the major organs by causing severe vasoconstriction. The vasopressin analogue 1-desamino 8D-arginine vasopressin, which has got selective antidiuretic action, has also been
used in doses 2-6 μ every 6-8 hrs. A combination of vasopressin and its analogue can also be used.

Hyperglycaemia secondary to insulin resistance is managed with insulin. Tight glycaemic control with insulin regimes is found to increase the survival benefits.[26,27] In our institution, we maintain tight glycaemic control between 80 mg/dL and 110 mg/dL. Severe brain injury is associated with adrenal insufficiency resulting in haemodynamic instability. However, the beneficiary effect of corticosteroids in cadaveric donors is uncertain.

Studies have supported the use of triple therapy with methylprednisolone, T3 and vasopressin in patients who are not improving with a standard management.[28]

Pulmonary care
Prolonged ventilation in the supine position results in hypostatic pneumonia and microatelectasis which is a common finding in the cadaveric donors. It has been found that among the cadaveric donors only about 20% are suitable lung donors.[29] It is recommended that every potential lung donor should undergo aggressive pulmonary toileting, chest physiotherapy, postural changes, bronchoalveolar lavage and culture guided antibiotics against the potential pathogens. Lung recruitment maneuvers using high positive end-expiratory pressure (PEEP) or pressure controlled ventilation for short duration have been proposed as methods of lung protective strategies which were followed at our institution as well. All these factors increase the possibility of the suitable lung donors becoming actual lung donors.[30]

Correction of electrolytic imbalances
It has been found that higher level of serum sodium has been associated with more severe hepatic dysfunction after the transplantation and thus correcting donor serum sodium to levels below 154 mMol/litre has been associated with decreased incidence of liver allograft loss.[31,32]

Transfusion practices
No studies are available regarding the red blood cells (RBC) transfusion in brain dead donors. The recommendations have been to maintain a haemoglobin more than or equal to 10 gm/dL or haematocrit more than 30% in organ donors, which is followed at our institution as well. Similarly, there are no guidelines regarding the threshold for plasma or platelet transfusion.[28,33]

Donor management during organ procurement
Main goal at the time of organ harvesting is to maintain haemodynamic stability using fluid resuscitation and with vasoactive drugs. This is guided by the standard monitoring along with special monitoring like CVP or pulmonary artery catheter and cardiac output monitoring.

In cadaveric donors, it has been found that higher brain and spinal functions are maintained. Thus, there can be wide variations in haemodynamic response if the patients are not anaesthetised during the organ procurement procedure. Sedation, analgesia along with muscle relaxation, is the preferred technique of anaesthesia. The neuromuscular blocking agents are given to prevent reflex muscle contraction. Hypertension associated with the procedure can be treated with volatile agents (isoflurane or sevoflurane) or with agents like sodium nitroprusside.[34]

Organs are surgically retrieved in a stepwise manner so as to maintain proper organ or tissue perfusion. After the cross clamping of aorta, the anaesthetic agents are discontinued.

Why so less organ donation?
All the potential donors do not become actual organ donors because of high familial refusal rate to give consent for organ procurement, haemodynamic compromise subsequently leading to cardiac arrest or associated comorbidities. Different donor management protocols are being development to substantially increase the donor pool.[35,36] As mechanism of injury in these patients is mostly head injury due to motor vehicular accidents or fall from height, they are medico-legal in nature. Thus, a no objection certificate from the competent authority/investigating officer of concerned police jurisdiction is to be taken. All cases included in the present study were medicolegal cases and no objection certificate was taken from investigating police officer before retrieval and retrieval was carried out in presence of consultant of forensic medicine. Regional variation in religious and cultural perspectives about end-of-life care has raised variability in the technique of declaration of brain death.[37]

With the recent amendments in act, physicians have the legal obligation to inform the family members regarding brain death and ask for the option of organ donation. Further, the provision and role of transplant coordinators has also been included in recent amendment. Hence, adequate training of the
Aggressive donor management protocols, multidisciplinary involvement and increasing awareness amongst people about the concept of brain death and organ donation can serve as lifesaving therapy for patients suffering from end-stage organ failure.

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