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Research Article

A RETROSPECTIVE ANALYSIS OF PROFILE AND MANAGEMENT OF BRAIN-DEAD ORGAN DONORS IN A TERTIARY CARE SETUP IN NEW DELHI

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Abstract

Overview: Organ harvesting from brain dead donors has significantly developed over the years due to a constant increase in the demand of transplantation. This has led to various recommendations and strategies to improve donor management after brain death. Brain dead trauma patients are ideal organ donors due to relative young age and absence of life-threatening comorbidities. **Methods:** The aim of our retrospective study was to gather and analyze the case profiles of all brain-dead patients at our hospital between January to December 2022. Their demographics, mode of injury, time from injury to diagnosis of brain death and time from brain death to organ harvesting were noted. **Results:** Our findings revealed that only 7.9% of the brain dead patients eventually became organ donors. The rest were lost due to lack of consent, hemodynamic instability or other procedural problems. **Discussion:** Various strategies have been adopted to increase the organ donor pool. Amongst them, education of population and awareness about the value of donation is foremost. Hemodynamic and endocrine management of the brain dead organ donors is also crucial for better graft survival.

Keywords: Brain death, Organ donor, Organ harvesting, Transplant, Trauma.

INTRODUCTION

Organ harvesting from brain dead individuals and their subsequent transplantation into patients with terminal illnesses has evolved manifold over the years. However, due to the constant shortage of available donors, solid-organ transplantation remains limited. Three main reasons are identified for the loss of potential donors: (a) family refusal for organ donation, (b) loss of donors due to hemodynamic collapse and subsequent cardiac arrest, and (c) unfit donors according to acceptance criteria. [1] Improvements in donor management with early recognition of donors, hemodynamic support, improvements in surgical techniques and more effective immunosuppressive therapy may go a long way in increasing the success rate of transplantations. [2] However, one of the most important steps that can significantly increase the number of donors is population awareness about organ donation and counseling of families of brain-dead patients. Management of potential donors after the confirmation of brain death is crucial. There is a shift in emphasis from cerebral protection to optimization of organ function for subsequent transplantation. Brain death induces various cardiovascular, respiratory, hormonal and metabolic changes. These changes, if untreated, may lead to cardiac death and somatic changes rendering the organs unfit for transplantation. Hence, management of a potential brain-dead organ donor presents a unique challenge to the anesthesiologist and intensivist. The purpose of this article is to review the case records of brain-dead organ donors in a tertiary level trauma center between January to December 2023. Based on this, the physiological alterations and consequences of brain death will be elaborated and current management strategies of brain-dead potential organ donors will be addressed.

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METHODOLOGY

The objective of this retrospective study was to analyze the case profiles of brain dead organ donors in a tertiary level trauma center over a period of one year. Institutional Ethical Committee clearance was obtained before starting the study. The case records of all brain-dead trauma patients within the period January to December 2023at the author's institute were reviewed. Inclusion of subjects was based on fulfillment of brain death criteria (Form-8) as per Transplantation of Human Organs and Tissue (Amendment) Act, 2011. Consent from near relatives (Form-6) and no-objection from investigating police officer from concerned jurisdiction were also obtained. The exclusion criteria included all patients deemed medically unfit for donation or those without consent for donation. Patient demographics (age and sex), mode of injury, duration between time of injury and diagnosis of brain death, duration between diagnosis of brain death and organ retrieval, consequences and complications of brain death were observed in all brain dead organ donors. All parametric data was recorded as arithmetic mean ± standard deviation (SD). Statistical analysis was performed using Student's *t* test for parametric data and Chi square test for categorical data. Tabulation and graphical analysis were done with the help of Microsoft Office and latest version of SPSS.

RESULTS

A total of 63 patients were declared brain dead as per the provisions in Chapter-II (Clause-6) of Transplantation of human organs and tissues Amendment Act 2011. Out of these 63 patients, only seven were identified as potential donors. Two patients amongst these were lost to cardiac arrest due to hemodynamic instability before the process of organ retrieval could be started. **Table 1** elaborates the clinical profile all identified donors.

Table 1. Demographic profile of organ donors (n=5) in our institute

Demographic variable	(n=5)
Mean Age	31.2 ± 3.77 years
Males	4 (80%)
Females	1 (20%)
Cause of Death	
- Road Traffic Accidents	3 (60%)
- Fall From Height	2(40%)
Surgery before brain death	4 (80%)
Haemodynamics requiring vasopressor/inotropic support	5 (100%)
Average time between injury and brain death declaration	89.8 ± 11.7 hours
Average time between brain death declaration and organ retrieval	26.6 ± 3.65 hours

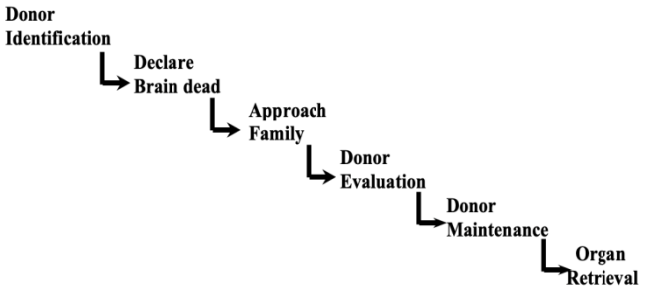

Fig. 1. The Organ-Donation Process. Each step is vital, and donation may fail because of a roadblock at any stage

All the donors were adults, the mean age being 31.2 ± 3.77 years. Out of the five donors, four were males and one was a female. All the donors were declared brain-dead with the antecedent cause of traumatic brain injury (100%). The mode of injury included road traffic accidents (60%) and fall from height (40%). Four out of the five patients were operated upon for head injury prior to declaration of brain death. The average time recorded between the injury and the diagnosis of brain death was 89.8 ± 11.7 hours. All patients (100%) showed signs of hemodynamic instability and required varied degree of inotropic/vasopressor support. Average time gap between diagnosis of brain death and organ retrieval was 26.6 ± 3.65 hours. The organs harvested included heart, kidneys, heart valves, liver, cornea and vessel grafts.

DISCUSSION

Very few data regarding brain dead organ donors is available in India. This study was carried out to shed light on the organ donation scenario in one of the major trauma centers of a metropolitan city. On review of the above data, we found that only 7.9% of brain-dead patients eventually become organ donors at our institution in the year 2023. The main reasons behind the loss of other potential organ donors were lack of consent, unstable hemodynamics, various comorbidities, higher age group and procedural problems. Figure 1 illustrates the organ donation process. Obstacle at any one step may result in failure of the whole transplant process. Improvements in donor management protocols will bring about an increase in the number of organ donations. Amongst these protocols, the most important is increasing awareness amongst the general population regarding the value of donation. Family bereavement counseling and education goes a long way in giving consent for organ donation. [3] Other interventions that can increase the chances of organ donation are related to the consequences and complications of brain death on various organ systems of the body, which are discussed below.

Cardiovascular response to brain death

The cardiovascular changes after brain death result from brain stem ischemia secondary to the rise in intracranial pressure (ICP) and cerebral herniation. The mean arterial pressure rises to maintain cerebral perfusion. As midbrain ischemia progresses, parasympathetic activation occurs causing sinus bradycardia. Subsequent pontine ischemia causes sympathetic stimulation resulting in hypertension (Cushing's reflex). This is followed by an unopposed "sympathetic storm" as the ischemia progresses towards the medulla oblongata, resulting in ischemia of vagal motor nucleus. This period is characterized by extreme hypertension and tachycardia, which may even cause myocardial ischemia. Complete ischemia of the spinal cord then follows, causing loss of all sympathetic vascular tone, leading to progressive hypotension and cardiovascular collapse. This stage is of particular concern since it causes reduced tissue perfusion and end organ damage. [4] Cardiac function is also compromised after brain death due to "catecholamine cardiotoxicity" brought about by the sympathetic storm. [1]

Pulmonary changes after brain death

Pulmonary changes in brain dead patients occur both as result of unrelated causes as well as directly as a result of brain death. Unrelated causes include aspiration, pneumonia, contusion and ventilator induced injury. Brain death induced lung injury is mainly related to neurogenic pulmonary edema (NPE) and inflammatory acute lung injury. [5] NPE is a result of the sympathetic storm, which causes systemic vasoconstriction, increasing cardiac afterload and hence, elevated left ventricular and left atrial pressures. The resultant pulmonary edema is a combined result of elevated hydrostatic pressure and structural damage to the capillary endothelium.

Endocrine changes after brain death

Apart from changes in plasma catecholamine levels, brain death may also cause endocrine dysfunction reflecting anterior and posterior pituitary failure. Although cortisol and insulin levels remain normal, subnormal T3 levels have been recorded in 60-80% of brain dead patients. Although some authors have recommended routine use of T3 supplementation for hemodynamic support in the past, [6] many recent studies have shown no improvement in cardiac function after T3 therapy in brain deadpatients.[7-9] Plasma cortisol levels remain normal, but the capacity for cortisol to increase after adrenocorticotropic hormone (ACTH) is attenuated. [10] In contrast, posterior pituitary function is lost in as many as 80% of brain-dead patients. [1] Diabetes insipidus with resulting hypovolemia, circulatory instability and electrolyte abnormalities is a major problem in these patients. This occurs due to diuresis caused by loss of arginine vasopressin secretion, which also amplifies the circulatory collapse by causing systemic vasodilatation.

Inflammatory and immunological aspects

Severe cerebral injury and brain death is associated with release of various inflammatory mediators and cytokines such as tumor necrosis factor TNF-α, interleukin IL-6, IL-8, IL-1βand IL-2R. [11] This can cause apoptosis, hemodynamic instability, increased organ dysfunction and organ rejection. [12]

Donor management

Most brain dead potential donors suffer from intracranial hemorrhage or traumatic brain injury, and the treatment will be aimed at saving their cerebral homeostasis. This therapy might include administration of hydroxyethyl starch (HES), which was proposed to cause renal tubular injury and impair early renal graft function. [13] However, some studies have shown little effect of starch solution on kidney function. [14,15] Such treatment may cause hypernatremia, which is associated with an increased risk of graft dysfunction after liver transplantation. [16]After confirmation of brain death, the emphasis shifts from cerebral resuscitation & intravascular volume contraction to maintenance of cellular perfusion & oxygenation. The goal of hemodynamic management of brain dead organ donors is to maintain circulatory stability and proper perfusion pressure to ensure optimal oxygenation of tissues. This can be achieved with the help of fluid resuscitation, inotropic support, vasopressors and hormonal substitution. Initial hypotension may occur in as many as 80% of donors and sustained hypotension is associated with impaired graft function. Hypovolemia is common and fluid resuscitation is considered as the primary step in management of a brain dead donor. The goal should be normovolemia if thoracic organs are to be harvested, but kidney function benefits with more aggressive fluid regimen. [1] Administration of packed red blood cells to maintain the hemoglobin level above 100g/L (or hematocrit ≥ 30%) is recommended. Gelb et al proposed a "Rule of 100" which included maintenance of systolic blood pressure above 100 mmHg, urine output more than 100 ml/hour, PaO_2 greater than 100 mm Hg and a hemoglobin concentration of more than 100 g/L. [17]

The hemodynamic goals are seldom achieved by fluid resuscitation alone and frequently, inotropic/vasopressor support is required. Traditionally, dopamine has been the inotrope of choice and still defends its position in most recommendations. This is because catecholamines have immunomodulatory effects and may attenuate the immunogenicity of organs, leading to improved organ survival after brain death. [18,19] Similarly, norepinephrine has also been used with good results. Some studies have shown a superior hemodynamic control in brain dead patients with vasopressin as compared to catecholamines. [20] Vasopressin has been recommended as the agent of choice in refractory shock as well as for treatment of diabetes insipidus. [21,22] It has been used in the dose range of 0.5-1.5 U/hour, and doses above 0.04 U/minute cause dysfunction in major organs by causing severe vasoconstriction. The analogue desmopressin has also been used for its antidiuretic action in a dose of 2-6 μg every 6-8 hours. If the hemodynamic goals are still not reached, hormone replacement therapy may be used as the last effort. Traditionally a combination of triiodothyronine, steroids, vasopressin and insulin has been used. [23] Insulin is started in the intensive care to achieve a tight sugar control. Although the use of thyroid hormone remains controversial, but good outcomes have been reported in circulatory unstable donors on high dose vasoactive therapy. [24,25] Administration of methylprednisolone to brain dead donors is associated with improved outcome for most transplanted organs. [23,26,27] It may be given as a single bolus dose of 15 mg/kg body weight, or 250 mg bolus followed by an infusion of 100 mg/hour. Other issues that need to be addressed in brain dead organ donors are avoidance of hypothermia, treatment of coagulopathy and use of lung protective ventilation. The ventilator strategy should aim to avoid barotrauma while using moderate positive end-expiratory pressures and recruitment maneuvers to reverse the micro-atelectasis. [28] Intra-operatively, the main goal is maintenance of hemodynamic stability throughout the duration of organ procurement. This is achieved with the help of proper invasive monitoring, such as arterial line, central venous catheter and pulmonary artery catheter wherever feasible, along with the use of vasoactive drugs. Spinally mediated reflexes might be intact in these donors mandating the use of analgesics and muscle relaxation. [29] Volatile anesthetic agents may also be used to control the hemodynamic surges in response to intense stimuli. All anesthetic agents are discontinued after the cross clamping of aorta. To summarize, proper donor management in the intensive care unit as well as intra-operatively is necessary to increase the organ procurement and graft survival. Maintenance of circulatory stability with adequate fluids, vasoactive drugs and invasive monitoring along with hormonal substitution and immunosuppressive therapy is required.

Conflicts of Interest: None

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