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LETTER TO THE EDITOR

Assessment of brain death of organ donors in Iran

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The greatest challenge facing transplant surgery today is how to increase the number of organ donations. On average, 3.6 organs can be recovered from each deceased donor [1]. However, it requires a multifaceted structural organization to put into practice effective donor management protocols. Obviously, brain death is not considered a static condition [2].

In Iran, a Middle East country, the law for allowing transplants using organs from deceased donors was passed in 2000. This new procedure started to compete with a well-established living donor renal transplant program.

A network was developed and the program was gradually settled throughout the country, consisting of 13 organ procurement units (OPUs). There are also five brain death identification units in cities without transplantation centers that refer cases to the OPUs, which have their own brain death identification teams. The organ donation rate in Iran in 2006 was 1.8 per million of the population (PMP), and 23 PMP for brain-dead donors and living donors (LD), respectively. When the brain death identification units are informed about potential brain dead donors, they go to the hospital, approach the potential donor's family, and if the family agrees, the team then takes the responsibility of saving potential suitable organs from the deceased patient. In Tehran, after primary tests, verbal consultation with specialists and especially a satisfactory electroencephalogram (EEG), the identified brain dead donor is transferred to an ICU referred by the OPU. After admission, electrocardiogram monitoring, blood pressure, and urine output is continued as well as measurements of plasma biochemical parameters, such as glucose, electrolytes, phosphorus, and arterial blood gases. To confirm the previous diagnosis of legal brain death, five physicians (internist, neurologist, neurosurgeon, anesthetist, and a specialist in forensic medicine) appointed by the Minister of Health at the OPU in the university hospitals [3,4] carry out neurologic tests and a second EEG to confirm the declaration of brain death. Meanwhile, the family gives their written approval at the OPU. Afterwards, organ procurement takes place. The standard therapeutic interventions for hemodynamic support are mainly intensive administration of intravascular solutions, inotropes and vasopressin in polyuric patients.

The purpose of our study was to define donation patterns and laboratory and electrolyte disturbances during organ procurement from brain-dead patients recorded in the Iranian Tissue Bank since the legislation Act of Deceased donation was passed (December 1999 to December of 2008).

These 132 brain-dead patients had a mean age of 26.3 ± 12.2 years and the gender distribution was 85 (64.4%) men and 47 (35.6%) women. The time between a patient's admission to the ICU of the OPU and organ procurement was 20.1 ± 5.5 h. The leading cause of brain damage was head trauma caused by car accidents (53%), intracranial hemorrhage (14%). Utilization rates were: kidneys 83%, liver 60%, and heart 53%.The recovery rate of organs was 3.4.

Our patients did not experience significant hypotensive periods (the therapeutic goal was systolic blood pressure≥100 mmHg), oliguria (urine output <20 ml/h), or hypothermia. Treatment with vasopressin was required for 79.5%. The mean dose of vasopressin and inotropes (dopamine) 24 h before organ recovery were 7 ± 1 and 4.7 ± 3.1 μg/kg/min, respectively. The frequency of polyuria (urine output of 125 ml/h) was high (70%). There was no correlation between the cause of brain death and organ retrieval. However, the urine volume 12 h before organ recovery correlated with organ appropriateness for recovery (P-value < 0.01).

Hyperglycemia (FBS ≥ 110 mg/dl) was detected in 87% of the donors. Frequency of main electrolyte abnormalities were: hypernatremia Na ≥ 147 mEq/l (58%), hypokalemia K ≤ 3.5 mEq/l (25%), hypocalcemia Ca ≤ 8.5 mg/dl (60%), and hypophosphatemia P ≤ 2.5 mg/dl (60%). Increased serum ALT, AST, direct Bilirubin was found in 87%, 80% and 12%, respectively. The relationships between the number of recovered organs and serum sodium, potassium and direct bilirubin concentration were significant (P-value: 0.006, 0.012, and 0.025, respectively). Observed characteristics of the brain-dead donors are shown in Table 1.

In developed countries with advanced programs of brain-dead organ donor management, a trend toward increasing age of donors and cerebrovascular diseases as the primary cause of brain death is noticeable [5]. In Basque, the mean donor age increased from 32 years in

Table 1. Characteristics of the deceased donors at ICU entrance and before organ recovery.

Laboratory tests	At the ICU entrance	Before organ recovery
Age (year)	26.2 ± 12.2 (7–60)	
Sodium (mEq/l)	149.8 ± 13.6 (115–198)	151.3 ± 11.7 (125–183)
Potassium (mEq/l)	3.7 ± 1.0 (1.6–7.4)	3.9 ± 1.0 (1.5–7.7)
Calcium (mg/dl)	8.6 ± 1.0 (7.0–11.6)	8.3 ± 1.5 (5.9–13.7)
Phosphorus (mg/dl)	3.5 ± 1.4 (1.9–7.1)	2.6 ± 1.1 (1.0–4.8)
Blood sugar (mg/dl)	250.5 ± 134.6 (95–698)	221.3 ± 123.5 (31–689)
Creatinine (mg/dl)	1.2 ± 0.5 (0.5–3.2)	1.1 ± 0.6 (0.4–4.8)
Alkaline phosphatase (units/l)	200.6 ± 140.7 (21–673)	183.4 ± 97.7 (30–572)
Alanine transaminase (units/l)	108.7 ± 167.7 (8–880)	109.3 ± 139.8 (5–722)
Aspartate transaminase (units/l)	109.2 ± 141.5 (10–627)	128.3 ± 164.3 (10–785)
Total bilirubin (mg/dl)	1.0 ± 1.4 (0.2–9.6)	0.8 ± 0.7 (0.1–3.8)
Direct bilirubin (mg/dl)	0.2 ± 0.3 (0.1–1.5)	0.3 ± 0.2 (0.1–1.4)
Albumin (mg/dl)	3.1 ± 0.7 (1.9–4.3)	3.0 ± 0.7 (1.2–4.1)
Hemoglobin (g/dl)	12.0 ± 2.7 (5.3–19.3)	12.0 ± 2.6 (2.2–19.0)
Platelet (per mm^3)	141.3 ± 82.9 (11–419)	136.8 ± 85.0 (21–445)
PT (s)	18.6 ± 20.7 (12–219)	15.7 ± 2.5 (11–25)
PTT (s)	43.4 ± 22.9 (2–120)	43.7 ± 23.4 (16–120)
INR	1.6 ± 0.6 (1.0–4.4)	1.5 ± 0.4 (0.8–3.4)
Mean urine output 12 h before organ recovery (ml/h)	217.1 ± 153.9 (11.5–942)	
Mean blood pressure (mmHg)	82.8 ± 19.0	88.0 ± 20.0

INR, International normalized ratio; PTT, partial thromboplastin time.
Values are expressed as mean ± SD (range).

1987–1992 to 53 in 1999–2004. Moreover, head trauma as the main cause of death decreased from 54% to 30% during the mentioned time period [6]. The story is different in developing countries. The mean age of 132 brain-dead patients of our center was 26.3 ± 12.2 years; Kazemeyni *et al.* reported the median of 29 years of age in 59 donors. Najafizadeh *et al.* reported a mean age of 31.7 ± 15.5 years in donors. In the study by Aldawood *et al.* from Saudi Arabia, the median age was 28 ± 17 years [7–9]. Obviously, we handle younger and possibly more stable donors with a higher potential organ pool. Possibly, we miss some valuable organs.

Despite following strict management protocols for brain-dead patients, metabolic abnormalities are common even in our young patients. Hypophosphatemia (60%) was similar to the Dominguez study (72%), but frequency of hypokalemia in our study (25%) was considerably lower than in other studies [10].

The frequency of polyuria and hypernatremia was also high [10,11]. Further to diabetes insipidus, hyperglycemia by inducing osmotic diuresis and polyuria may be another mechanism of intravascular water deficit. In some experimental models, polyuria occurs within 45 min after brain death [10,12]. It seems that to achieve a higher multi-organ donor rate, submission to the strict therapeutic protocol to maintain homeostasis should not be postponed until the confirmation of brain death. It is possible that the reason for our similar metabolic abnormality rates to those in the other more experienced centers who manage older donors, is our OPUs' unawareness of this phase because they are not informed to start their management protocol and the ICU personnel overlook such potential donor pool.

We are strongly in favor of aggressive fluid resuscitation by ICU staff on potential deceased donors and started to run educational courses on this issue. The other recommended approach was active supervision and looking for potential brain-dead donors in the hospitals covered by our OPUs. This strategy increased the number of organ donations and seems to decrease metabolic complications.

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