Brief Communication

Brain death in ICU patients: Clinical significance of endocrine changes

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ABSTRACT

Numerous studies have been carried out among patients admitted in intensive care unit (ICU) having primary endocrine pathology, endocrine manifestations of systemic diseases or post-endocrine tissue surgery. However, minimal literary evidence is available highlighting the endocrine changes occurring during brain death in critically ill patients. A precise and timely diagnosis of brain death is required to convey the relatives about the prognosis and also to possibly plan for organ retrieval for transplantation purposes. The diagnosis of this condition as of today remains largely a clinical one. Brain death is associated with a multitude of endocrinological alterations which are yet to be completely unraveled and understood. Evaluating these endocrinological modifications lends us an added vista to add to the existing clinical parameters which might help us to confirm the diagnosis of brain death with a higher degree of precision. Moreover, since the efficacy of hormone replacement therapy to benefit in organ retrieval remains yet unproven, newer diagnostic modalities and research studies are definitely called for to strategize the optimal dosage and duration of such therapies.

Key words: Brain death, blood glucose, catecholamines, thyroid hormones

Introduction

Brain death is a common unfortunate clinical entity encountered in day to day practice of intensive care. It is defined as "irreversible loss of all functions of brain including brainstem" and is established with the presence of three essential findings of coma, absence of brainstem reflexes and apnoea. This scenario is linked with various clinical and ethical dilemmas which can have significant social impact.[1]

The admission pattern of critical care units is highly variable and many a times number of patients with primary endocrine pathology, endocrine manifestations of systemic diseases, endocrine emergencies or post surgical resection of endocrine tissues get admitted to ICU.[2-6] Moreover, patients with severe systemic diseases, poisoning and terminal pathology with or without endocrine involvement may get admitted to ICU.[7,8] The prognosis in such patients is guarded and they invariably have a higher morbidity and mortality. Literary evidence is studded with patho-physiological and endocrine changes in these patients; however, the least studied is the significance of endocrine changes in patients with brain death. Besides these facts, care of such patients throws numerous socio-clinical, legal and administrative challenges to the attending intensivist.

Euthanasia is not legalized in our country and as such intensivists are bound to act within these ethical norms in spite of clinically declaring a critically ill patient as brain dead. The decision is invariably imposed by the relatives, majority of whom do not want to take patients from the ICU or consent to withdraw life support. In a resource-starved nation like ours and with the growing public awareness regarding organ transplantation, necessity of diagnosing brain-dead patients promptly and accurately is the need of the hour.

The diagnosis of brain death is primarily done on clinical grounds which involve conclusively performed clinical

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examination, two assessments of brainstem reflexes and a single apnea test.[1] However, in the absence of clinical findings or confirmatory tests consistent with brain death, the diagnosis or brain death becomes a predicament. Under such conditions, additional parameters, if available would be invaluable to proceed toward the diagnosis with a degree of certainty. From an endocrine perspective, pathophysiological processes associated with brain death and the hormonal milieu is highly significant. Various endocrinological alterations occur, whose analysis might help us to formulate our diagnosis or in making the existing diagnosis concrete. The present article is an attempt to highlight the various endocrinological changes occurring in brain-dead patients and also to explore the possibility of adding this as an added dimension for consideration in such patients.

Disruption of blood supply of hypothalamus and pituitary gland along with the stress response of critical illness cause steady alterations in hormonal production and regulation. Among catecholamines, dopamine, noradrenaline, and adrenaline levels shoot up initially for 15 minutes after brain death.[9] After the initial "catecholamine storm" subsides, circulating levels of catecholamines (noradrenaline and adrenaline) levels start declining but dopamine levels remain elevated for up to 90 minutes. Once vasoparesis sets in, addition of dopamine, noradrenaline and adrenaline infusions can be considered to maintain perfusion pressure and cardiac output which might be beneficial in liver and renal transplant patients.[10]

Diabetes is a frequent accompaniment of multisystem disorders in patients admitted to ICU either due to some medical disease or post-operatively.[11] However, 80% of brain-dead patients experience another diabetes entity, diabetes insipidus, following these pathophysiological changes due to exhaustion of antidiuretic hormone (ADH) which is associated with hypovolemia, hyperosmolarity, and hypernatremia.[12] As such vasopressin infusion is often initiated in such situations to maintain vasopressor support, to reduce the diuresis and also to withdraw potentially detrimental catecholamine support.[13]

The effect of brain death on the hypothalamic pituitary adrenal (HPA) axis is not uniformly elucidated with conflicting outcomes in different researches. Levels of cortisol have been reported to be normal, low or high.[14,15] This leaves the method of cortisol level measurement prone to inaccuracies and hence other tests like serum cortisol, free cortisol index and free cortisol performed by equilibrium dialysis, stimulation tests utilizing ACTH are employed to measure the functioning of HPA axis even though they have their own advantages and disadvantages.[16,17]

The levels of circulating thyroid hormones demonstrate a variable response before and after brain death. Free T3 (fT3) levels fall, fT4 levels and TSH remain normal while reverse T3 levels are erratic.[18] T3 levels decline to 50% of their values 24 hours after death and stabilize at 40% of the original over next 7 days.[19] T4 levels, however, remain normal.

Thirty-nine percent of the brain-dead patients experienced a blood glucose level of more than 250 mg/dl.[18] Thus, a sizeable proportion of this population is prone to hyperglycemia. Hence, aggressive management of hyperglycemia (120-180 mg/dl) is kept as one of the primary targets of United Network for Organ Sharing (UNOS).[20]

Thus, it can be seen that a number of well documented endocrinological changes are associated with brain death. However, whether hormonal replacement to increase the quality of donated organ is beneficial in this subset of patients or not remains a matter of debate as available evidence in this regard remains limited. Nonetheless, this dimension of endocrinological evaluation of suspected brain-death patients to confirm the diagnosis for withdrawal of life support or preparation for organ donation still remains an unexplored frontier. As the precision of our investigative modalities increase and knowledge and understanding of the hormonal alterations become advanced, the option of using endocrinological changes as a marker of predicting brain death opens up. The field of hormone replacement therapy in brain-dead patients to improve the quality of donated organ also deserves analysis as the precise variety and amount of supplementation required still remains to be elucidated. Among the existing hormones, thyroid hormones' have a clear-cut salutary effect on cardiovascular system, corticosteroids have attenuating effect on pulmonary injury and tight glucose control is desirable but in spite of their postulated benefits, further evaluation to ascertain their dosage and treatment strategies is needed.

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