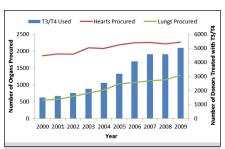
Increased Procurement of Thoracic Donor Organs After Thyroid Hormone Therapy

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Hormonal therapy to the brain-dead organ donor can include thyroid hormone (triiodothyronine [T₃] or levothyroxine [T₄]), antidiuretic hormone, corticosteroids, or insulin. There has been a controversy on whether thyroid hormone enables more organs to be procured. Data on 63,593 donors of hearts and lungs (2000-2009) were retrospectively reviewed. Documentation on T₃/T₄ was available in all donors (study 1), and in 40,124 details of all 4 hormones were recorded (study 2). In this cohort, group A (23,022) received T_3/T_4 and group B (17,102) no T_3/T_4 . Univariate analyses and multiple regressions were performed. Posttransplant graft and recipient survival at 1 and 12 months were compared. In study 1, 30,962 donors received T₃/T₄, with 36.59% providing a heart and 20.05% providing 1 or both lungs. Of the 32,631 donors who did not receive T₃/T₄, only 29.62% provided a heart and 14.61% provided lungs, an increase of 6.97% hearts and 5.44% lungs from T_3/T_4 -treated donors (both P < 0.0001). In study 2, 34.99% of group A provided a heart and 20.99% provided lungs. In group B only 25.76% provided a heart and 15.09% provided lungs, an increase of 9.23% (hearts) and 5.90% (lungs), respectively, in group A (both P < 0.0001). The results of multiple regression analyses indicated a beneficial effect of T₃/T₄ on heart (P < 0.0001) and lung (P < 0.0001) procurement independent of other factors. T₃/T₄ therapy to the donor was associated with either improved posttransplant graft and recipient survival or no difference in survival. T₃/T₄ therapy results in more transplantable hearts and lungs, with no detriment to posttransplant graft or recipient survival.

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Donor treatment with T3/T4 and hearts and lungs procured.

Central Message

In a study of 63,593 brain-dead donors of hearts and lungs, thyroid hormone therapy resulted in procurement of more hearts and lungs.

Perspective

To resolve the question of whether T_3/T_4 is beneficial in procuring more hearts and/or lungs, UNOS data on hormonal therapy in 63,593 brain-dead organ donors were reviewed. The data indicate that T_3/T_4 therapy should be administered to all donors, particularly if combined with ADH and corticosteroids. The number of organs procured is significantly increased, without detriment to transplant outcome.

See Editorial Commentary pages 133-134.

INTRODUCTION

The detrimental consequences of brain death on the heart of the potential donor were first reported in 1984. Following the

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initial experimental and clinical reports from the University of Cape Town of the beneficial effect of thyroid hormone therapy (triiodothyronine $[T_3]$ or levothyroxine $[T_4]$) to brain-dead potential organ donors, ¹⁻³ multiple small studies of hormonal therapy were reported with varying outcomes, ^{2,3} possibly because (1) the methodology to measure plasma-free T_3 was in development, (2) total T_3 may have been measured (whereas only approximately 5% of T_3 is available to the cells as free T_3), or (3) in clinical practice the rates of depletion of T_3/T_4 and other hormones vary greatly, depending on the variability of hypothalamic-pituitary function. ⁴ For several years, relatively few transplant groups administered T_3/T_4 (reviewed fully in Cooper et al² and Novitzky and Cooper ³).

THYROID THERAPY AND THORACIC ORGAN PROCUREMENT

In 2001 the United Network for Organ Sharing (UNOS) performed a retrospective analysis of all brain-dead potential donors from January 2000 to September 2001, inclusive. ^{5,6} When T₃/T₄ had been administered to the donor, multiple studies revealed significant increases in the number of transplantable organs ⁷⁻⁹ and an improvement in the 1-year survival of hearts and kidneys after transplantation. ^{9,10} Guidelines were developed for maximizing the number of organs recovered and transplanted from deceased donors. ^{5,6}

Although hormonal resuscitation therapy gradually became more widely accepted, there remained considerable variability in its use. Indeed, 2 relatively recent meta-analyses 11,12 concluded that there were insufficient data to "support a role for routine administration of thyroid hormone in the braindead potential organ donor"11 or that the study suggested "limited efficacy of interventions focusing on the management of brain-dead donors." 12 There has, however, been a steady increase in the number of potential donors receiving T₃/T₄ therapy. During the course of the present study (2000-2009), there was an increase in the use of T₃/T₄ from approximately 30% to > 60% of all donors. Callahan et al¹³ suggest that this has been associated with increased organ procurement.

Currently, hormonal therapy can include the administration of 4 hormones—thyroid (T₃ or T₄), antidiuretic hormone (ADH, eg, desmopressin—1-deamino-8-D-arginine vasopressin), a corticosteroid, and insulin.

Although it is difficult to determine exact numbers, a significant number of brain-dead potential donors are lost from the donor pool owing to progressive acidosis and hemodynamic instability, which becomes refractory to high-dose inotropic support. There is a constant organ shortage for purposes of transplantation, and any intervention that increases the donor organ pool should surely be welcome.

 T_3/T_4 therapy was originally introduced to improve the hemodynamic status of potential heart donors, and, although there is increasing evidence of its association with increased procurement of several other organs, ¹⁵ arguably it has its greatest effect on procurement of the heart.

In an effort to resolve the question of whether T_3/T_4 is beneficial in procuring more thoracic organs (hearts, lungs), we have now reviewed data provided by UNOS on hormonal resuscitation therapy in the management of 63,593 brain-dead potential organ donors in the 10-year period, 2000-2009. To our knowledge, this retrospective analysis is the largest to date.

METHODS

Data Retrieval

Data were provided from January 1, 2000, to December 31, 2009. All parameters of interest were retrospectively retrieved from the UNOS worksheet "Deceased Donor Registration Worksheet," in which all donor demographics, causes of death, and procured or transplanted organs are included. Other parameters, for example, inotropic support and hemodynamic stability, were not consistently well documented, and therefore they were not analyzed.

A total of 71,571 donors were registered with UNOS, of which 4942 were excluded on the basis of being non-heart-beating donors or donors without heart-beat information (Supplementary Fig. 1). Of 66,629 heart-beating donors, 3036 were without T₃/ T₄ treatment information. Therefore, the initial study analysis (study 1: T₃/T₄ vs no T₃/T₄) was performed on 63,593 donors (mechanisms, circumstances, and causes of death are listed in Supplementary Table 1). Of these, all had documentation on whether T₃/T₄ was administered. However, only 40,124 had documentation of all hormonal managements (ie, of T₃/T₄, ADH, corticosteroids, and insulin), with 23,469 having incomplete documentation, except for T₃/T₄, and these formed the basis of study 2 (in which data on all 4 hormones were analyzed).

Hormonal Treatment Modalities

In both study 1 and study 2, the analysis was focused on the number of (1) hearts and (2) lungs procured and transplanted (for the sake of simplicity, when it is stated that an organ was "procured," this indicates that it was also "transplanted"). In study 1, the effects of T_3/T_4 on the percentages of hearts and lungs procured and transplanted were determined and compared with the percentages procured or transplanted from donors who did not receive T_3/T_4 (irrespective of any other therapy).

In study 2, group A (n=23,022) consisted of donors who received T_3/T_4 either alone or in combination with one or more other hormones (ADH, corticosteroid, and insulin) (Table 1). Group B (n=17,102) did not receive T_3/T_4 but may have received one or more of the other hormones. Comparison of groups was therefore based on the 8 comparable pairs (subgroups) of hormonal treatment modalities with or without T_3/T_4 (Table 1). The percentages of donors from whom hearts or lungs were procured and transplanted were determined.

In both study 1 and study 2, the outcomes of the transplants were determined by documenting both graft and patient survival at 1 and 12 months after the transplantation.

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