JOURNAL OF SURGICAL RESEARCH 186 (2014) 452–457

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.JournalofSurgicalResearch.com

The effect of arginine vasopressin on organ donor procurement and lung function

Devon S. Callahan, MD, Angela Neville, MD, Scott Bricker, MD, Dennis Kim, MD, Brant Putnam, MD, Frederic Bongard, MD, JD, and David S. Plurad, MD*

Department of Surgery, Division of Trauma/Acute Care Surgery and Surgical Critical Care, Harbor-UCLA Medical Center, Torrance, California

ARTICLE INFO

Article history:
Received 26 June 2013
Received in revised form
2 September 2013
Accepted 12 September 2013
Available online 7 October 2013

Keywords:
Transplantation
Hormone replacement therapy
Arginine vasopressin
Thyroxine
Outcomes

ABSTRACT

Background: Hormone replacement therapy (HRT) is becoming more common when managing brain-dead donors. Arginine vasopressin (AVP) is associated with benefits but is not consistently used. We hypothesize that AVP is associated with the maintenance of lung function and successful recovery in donors and enhanced lung graft performance in recipients.

Methods: The Organ Procurement and Transplantation Network database was used. Study donors were those treated with HRT and procured from January 1, 2009 to June 30, 2011. AVP (+) and AVP (−) donors were compared. Donor lung function, the rate of successful lung procurement, and the incidence of graft failure in recipients were studied.

Results: There were 12,322 donors included, of which 7686 received AVP (62.4%). Cerebrovascular accident (4722 [38.3%]) was the most common cause of donor death. There was a significant increase in high yield (≥4 organs) (51.0% *versus* 39.3%, <0.001), mean number of organs (3.75 *versus* 3.33, <0.001), and rate of successful lung recovery (26.3% *versus* 20.5%, <0.001) with AVP. Lung function was preserved to a greater degree in donors receiving AVP. Adjusting the significant factors, AVP was independently associated with lung procurement (1.220 [1.114–1.336], <0.001). The incidence of early graft failure was not changed.

Conclusions: AVP with HRT is associated with the maintenance of lung function and a significant increase in successful organ recovery in donors without untoward effects in the recipient. AVP should be universally adopted as a component of HRT in the management of donors with neurologic death.

1. Introduction

Transplantation is the preferred treatment for end-stage organ failure. Donation after neurologic death provides a considerable number of high-quality grafts. Despite an increasing inclusion of living related donors, donation after cardiac death [1], and expanded criteria donors (ECDs) [2], graft availability does not approach demand [3]. Improvements in preprocurement medical management offer a means to close this gap with improved graft function before procurement [4].

Catastrophic brain injury is associated with severe vasoregulatory dysfunction, hemodynamic instability, and the subsequent cardiovascular collapse [5]. Therefore, hormone replacement therapy (HRT) has been advocated, as it is associated with a higher rate of procurement [4], particularly for heart and lung grafts [6,7]. The current regimens for HRT

* *Corresponding author*. Department of Surgery, Harbor-UCLA Medical Center, 1000 West Carson Street, Torrance, CA 90509. Tel.: +1 347 432 2389; fax: +1 310 533 1841.
E-mail address: devon.callahan.md@gmail.com (D.S. Callahan).
0022-4804/$ – see front matter © 2014 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jss.2013.09.028

involve infusions of dextrose, insulin, methylprednisolone, and thyroxin in brain-dead donors with hemodynamic instability. Arginine vasopressin (AVP) is a peptide hormone that has potent vasoconstrictor effects, enhances renal fluid resorption, and regulates corticotrophin levels [8]. AVP infusion in the brain-dead organ donor is associated with the restoration of vascular tone in vasodilatory shock that is unresponsive to catecholamine administration, with a subsequent preservation of organ perfusion and a decreased or eliminated need for exogenous vasopressors [9–11]. However, AVP has yet to be adopted universally in patients receiving HRT [12–14]. Although there are series examining the independent effect of AVP on organ procurement in small groups for specific organs [10,11], recent series demonstrated an association with increased procurement in a generalized donor population [15]. However, despite a theoretical benefit of AVP on graft procurement, there are few studies on the effects of AVP on maintenance of preprocurement graft function, with only an animal model study [16]. We hypothesized that the AVP-related increase in organ recovery is associated with an improved maintenance of preprocurement lung graft function, enhanced rate of lung procurement in donors, and improved lung graft survival in recipients.

2. Methods

The Organ Procurement and Transplantation Network (OPTN) deceased donor and thoracic recipient databases were used. The donor group was defined as those diagnosed with brain death who received HRT having any organ successfully procured from January 1, 2009 to June 30, 2011. ECDs (age $\geq$ 60 y without comorbidities or 50–59 y with comorbidities) and Centers for Disease Control (CDC) high-risk (history of IV drug use, hemophilia, high-risk sexual activity, exposure to human immunodeficiency virus, and jail sentencing) donors were included in this study. HRT was defined as an infusion of dextrose, insulin, methylprednisolone, and thyroid hormone during resuscitation. Procurement outcomes from donors who received AVP (AVP+) were compared with those that did not receive AVP (AVP−). A successful recovery is defined as a procurement of a graft that is subsequently transplanted to a recipient. High-yield procurement was defined as the recovery of $\geq$4 organs. Any lung donor having at least one graft successfully transplanted was counted as a single donor with regard to calculating the incidence of successful lung recovery. However, each lung was counted as a single organ with regard to calculating the number of organs per donor successfully transplanted. Lung donors were matched to their recipients and outcomes were compared between transplanted patients who received a lung graft from either an AVP (+) or an AVP (−) donor. All recipients having at least 1-mo follow-up data were included in this study. Donor study variables included gender, age, ethnicity, cause of death, donor cardiac arrest before procurement, donor obesity (BMI >30), ECD status, CDC high-risk donor status, human leukocyte antigen (HLA) match level ($\geq$2 markers) with the recipients and the presence of infection. Recipient variables included age, gender, diagnoses leading to lung failure, any episodes of acute rejection before discharge, requirement for life support before transplant (mechanical ventilation, intra-aortic balloon pump, ventricular assist devices, inotropic infusions), panel reactive antibody results, and warm ischemia time. Study endpoints were the incidence of organ procurement (lung and overall), preprocurement pulmonary function in donors, and the incidence of graft failure in lung recipients. The OPTN deceased donor and thoracic recipient databases represent information gathered on all transplants performed in the United States in an internet-based secure application. There is an internal data validation process on submission. In addition to this built-in validation process, data collection is uniformly submitted to minimize the rate of missing data points.

Groups were statistically compared with bivariate analysis and any variable with a P value <0.2 was subsequently entered into the logistic regression to determine an independent association with lung procurement. Results are expressed as means ± standard deviations, percentages, odds ratios with 95% confidence intervals (CIs), and P values, or raw data where applicable. Analysis was performed using χ^2, Cramer ϕ for categorical variables, or analysis of variance for continuous variables where appropriate. A P value <0.05 was considered statistically significant and all P values were two-sided. Logistic regression was performed to determine factors independently associated with study endpoints. SPSS for Mac version 21.0 (IBM Corporation, Armonk, NY) was used for statistical analysis.

3. Results

There were 12,322 brain-dead donors meeting inclusion criteria. Most were male (7282 [59.1%]), with cerebrovascular accident (4722 [38.3%]) and traumatic brain injury (4469 [36.3%]) being the leading causes of death. Mean age was 39.6 ± 18.4 y. There were 2974 lung grafts recovered (24.1%) (Table 1). AVP was infused in 7686 donors (62.4%). A comparison with AVP (−) donors is depicted in Table 2. AVP infusion was associated with improved donor lung function, a significantly higher number of lung grafts recovered, and a higher mean number of organs recovered overall. AVP (+) donors were more likely male, younger, and had a BMI <30. They were less likely to receive phenylephrine infusions, but more likely to receive norepinephrine and epinephrine. In donors that received AVP, mean PO_2 on 100% was higher (239.9 ± 154.2 *versus* 228.8 ± 149.3, <0.001), with a greater number having a $P/F > 200$ (45.3% *versus* 42.0%, 1.141 [1.060–1.228], <0.001). There was no significant difference in the rate of bacteremia, CDC defined high-risk donors, or dopamine infusion between the AVP (+) and AVP (−) donors. There was a slight tendency for Hispanic donors to receive AVP. On logistic regression, adjusting the significant differences between the AVP (+) and AVP (−) groups, AVP infusion was independently associated with successful lung procurement (Table 3).

The association of AVP and an increase in organ procurement was observed even in donors who traditionally have a lower organ yield (not shown in tables). In donors with a BMI >30, AVP infusion was associated with a greater number of high-yield donors (39.4% *versus* 26.5%, 1.807 [1.556–2.099], <0.001) and a greater mean number of organs recovered (3.37 ± 1.20 *versus* 2.99 ± 1.22, <0.001). In donors with