

# Pediatric Donor Management: A Case Study



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# Case presentation

A 4 year old presents to an outside hospital with a chief complaint of headache and lethargy. Parents state that he hit his head playing football with his brother the day prior and complained of a headache at that time. No LOC is reported. On the day of admission he remained lethargic, had a low grade fever and emesis in the early morning. Examination revealed blood pressure of 100/66, heart rate of 96, respiratory rate of 16, temperature 99.6°. This child is lethargic, complains of headache. Pupils are equal and reactive to light. He will talk in sentences. Lungs are clear to auscultation. He is warm and well perfused. A CAT scan of the head is performed and interpreted as normal. He is given a single dose of Ceftriaxone and a lumbar puncture is performed. CSF is cloudy with 120,000 WBC's and gram positive cocci noted on the gram stain. Differential is 90% PMN cells. CSF chemistries reveal a protein of 1500, glucose < 10. Arrangements are made for hospital admission.

# Case presentation (cont)

Two hours following his lumbar puncture the child has an episode of emesis, becomes bradycardic, and develops apnea followed by asystole. Closed chest compressions are initiated, he is intubated with possible aspiration of gastric contents reported. He receives 2 doses of epinephrine and one dose of atropine with ROSC after 6 minutes. His blood pressure is 60/40. He receives a fluid bolus of normal saline and a dopamine infusion is started. Provisions are made for transport to the tertiary care children's hospital.

En route to the children's hospital this child has another cardiac arrest. His dopamine had been escalated to 20 mcg/kg/min and he received an additional dose of epinephrine with ROSC. Upon arrival to the PICU, this child is comatose. Vital signs: blood pressure is 80/36, heart rate is 110, no spontaneous respiratory effort is noted. Temperature is 93.6°. Neurologic exam reveals fixed and dilated pupils. No cough, corneal or gag reflexes are noted. He has minimal movement of his left shoulder with noxious central stimulation. He continues on a dopamine infusion at 20 ug/kg/min an epinephrine infusion at 0.3 ug/kg/min. He has brisk clear urine output.

Supportive care was continued. Central venous access and arterial cannulation have occurred. Inotropic support was continued along with volume resuscitation. Mechanical ventilation continued with increased PEEP due to a PaO<sub>2</sub> of 140 on an FiO<sub>2</sub> of 1.0. Urine output was excessive. Urine output was replaced cc/cc with 1/2 NS. Antibiotic therapy was continued. It was unclear if this child received vancomycin at the referring facility. A vancomycin level on admission was 1.6.

Discussions with the parents occurred throughout the day. The parents understood that their child's condition was critical and that he may not survive this event.

Over the next several hours hemodynamics remained unstable. Inotropic support was titrated to maintain systolic blood pressures > 90 torr. Oxygenation and ventilation were easily controlled. PaO<sub>2</sub> increased to 410 torr on an FiO<sub>2</sub> of 1.0. Lactate was 1.9. Serum Na<sup>+</sup> had increased from 139 to 156 mg/dl. Urine output replacement continued and a vasopressin infusion was started to help control urine output.

# Hormonal replacement therapy

- Consider using HRT early in the course of donor management
- There is no contraindication to using HRT in a patient prior to neurologic death
  - Steroids for sepsis
  - Thyroid hormone in post-operative cardiac patients and patients with hypothyroidism
  - Vasopressin and desmopressin are routinely used for the treatment of DI
- Hormonal replacement therapy decreases the need for inotropic support in children

*Zuppa AF, Nadkarni V, Davis L, et al. The effect of a thyroid hormone infusion on vasopressor support in critically ill children with cessation of neurologic function. Crit Care Med 2004;32:2318-2322.*

- As neurologic death occurs, alteration in the hypothalamic-pituitary-adrenal axis (HPA axis) occurs

# Hormone Replacement Therapy

- Thyroid hormone replacement
  - Levothyroxine (T4)
  - Triiodothyronine (T3)
- Steroid replacement
  - Hydrocortisone or methylprednisolone
- Control of DI
  - Vasopressin (Pitressin)
  - Desmopressin (DDAVP)
- Control of hyperglycemia
  - Insulin

# Thyroid hormone

- Effects of thyroid hormone
  - Increases cardiac output
  - Increases heart rate
  - Increases ventilation rate
  - Increases basal metabolic rate
    - Affects cellular metabolism
- Administration of thyroid hormone
  - Triiodothyronine (T3)
    - Active form of thyroid hormone
    - T3 is converted from T4 (thyroxine) in the peripheral circulation by deiodinase
    - T3 is 4 times more active than T4
    - Dose: 0.05-0.15 mcg/kg/hour titrated to effect
  - Thyroxine (T4)

# Thyroid hormone (cont)

- Levothyroxine (Synthroid, T4)
  - Route of administration: IV continuous infusion
  - Dose: 1 mcg/kg/hour titrated to effect

<b>Age</b>	<b>Bolus (mcg/kg)</b>	<b>Infusion (mcg/kg/hour)</b>
<b>0-6 months</b>	<b>5</b>	<b>1.4</b>
<b>6-12 months</b>	<b>4</b>	<b>1.3</b>
<b>1-5 years</b>	<b>3</b>	<b>1.2</b>
<b>6-12 years</b>	<b>2.5</b>	<b>1</b>
<b>12-16 years</b>	<b>1.5</b>	<b>0.8</b>
<b>&gt; 16 years</b>	<b>0.8</b>	<b>0.8</b>

# Additional considerations

- Dopamine for hemodynamic support
  - Dopamine inhibits TSH production
  - Decreased TSH production results in decreased release of thyroid hormone from therapy to maintain hemodynamic stability
  - Decrease of TSH from CNS insult and alteration of the HPA axis
  - Potential donor is in a relative hypothyroid state

# Steroids

- Steroid production will be inhibited or lost due to CNS insult and loss of the HPA axis
- The use of steroids should be considered early in the course of the child with hemodynamic instability that is minimally responsive to aggressive inotropic support
  - Steroids up-regulate adrenergic receptors making them more sensitive to the effects of catecholamines
  - Enhance response to inotropes
- May provide an important role in stabilization of pulmonary function for the potential donor

# Pharmacologic Management of Diabetes Insipidus

- Vasopressin (Pitressin)
  - Correction of hypernatremia with hemodynamic instability
  - Dose
    - Continuous IV infusion: 0.5 milliunits/kg/hour titrated to effect
- Desmopressin (DDAVP)
  - Correction of hypernatremia without hemodynamic instability secondary to greater ADH effect
  - Correction of hypernatremia with associated bleeding problems ( coagulopathy)
  - Dose
    - Continuous infusion rate: 0.5 µg/hour titrated to effect
- These agents are ineffective when administered by the intranasal or subcutaneous route in this patient population

HRT using levothyroxine and solucortef was initiated. Vasopressin was continued with improved control of urine output. Over the next 12 hours inotropic support had been reduced to 4 ug/kg/min of dopamine. Serum Na<sup>+</sup> had decreased to 140 mg/dl. This child's neurologic exam continued to deteriorate and he eventually lost all movement to noxious central stimulation. An apnea test was performed. There was no spontaneous respiratory effort with a PaCO<sub>2</sub> of 87 torr after 10 minutes.

Supportive care was continued. The parents were present during the examination and understood the clinical implications of the neurologic examination and apnea test. A second brain death examination occurred 24 hours later.

The following morning this child's clinical examination remained unchanged. A second brain death exam including an apnea test was performed. The brain death examination remained consistent with neurologic death. The child was pronounced at 0745 hours.

The parents consented to organ donation. 26 hours after declaration of death, this child went to the operating suite for recovery of kidneys and liver.

# Why start HRT?

- HRT is inexpensive
- Adverse effects to the potential donor are minimal
- It may increase graft function post-operatively
- Continued therapy for the dying child reinforces to the parents that everything humanly possible is being done for their child

- **Early HRT is only part of good donor management**
  - Donor management must be guided with input from the pediatric intensivist and critical care team
  - Collaboration with the transplant coordinator, OPO, chaplain, social and other support services is vital for successful donation to occur
  - Communication with the family is imperative for donation to be successful
  - Hormonal replacement therapy can be initiated prior to declaration of death
  - Hormonal replacement therapy appears to decrease the need for inotropic support
    - Zuppa AF, Nadkarni V, Davis L, et al. The effect of a thyroid hormone infusion on vasopressor support in critically ill children with cessation of neurologic function. Crit Care Med 2004;32:2318-2322.*
  - Does early HRT improve organs available for transplantation?

# The Effect of Hormonal Resuscitation (HR) on Organ Utilization in Pediatric Donors

Cherikh WS, Edwards LB, Sweet SC, Kauffman HM, Rosendale JD

- In 1,903 pediatric donors 3-HR (three-drug combination consisting of corticosteroids, vasopressin, and T3/T4) was used in 1,169 (61%) of the pediatric donors.
- **Summary:** When compared with 0-HR, the use of 3-HR was associated with significantly increased odds of pediatric donors having their livers and at least one of their kidneys and lungs transplanted. The use of 3-HR was not associated with an increased likelihood of pediatric donor hearts being transplanted.

*Abstract 2007*

# Beneficial effects of HRT?

- Use of thyroid hormone (T4) in patients with severe hemodynamic instability resulted in significantly more transplanted organs than in patients who did not receive T4.

*Salim A, Martin M, Brown D, et al. Using thyroid hormone in brain dead donors to maximize the number of organs available for transplantation. Clin Transplant 2007;21:405-409.*

- HRT may result in more transplanted hearts with improved early function
  - Retrospective study 4,543 heart recipients suggests improved 1 month survival rates and less early graft dysfunction.

*Rosendale JD, Kauffman HM, McBride MA, et al. Hormonal resuscitation yields more transplanted hearts, with improved early function. Transplantation. 2003;75:1336-1341.*

# Hormonal replacement therapy

- There is no contraindication to using HRT in a patient prior to neurologic death
  - Steroids for sepsis
  - Thyroid hormone in post-operative cardiac patients and patients with hypothyroidism
  - Vasopressin and desmopressin are routinely used for the treatment of DI
- Studies are indicating more organs recovered and improved graft function from donors receiving HRT

# Conclusions

- Good donor management equals good patient care
- Collaboration between the OPO and the Pediatric Intensivist and critical care team is essential for good outcomes
- Early hormonal replacement therapy can increase the number and quality of organs available for transplantation
- Timely declaration of neurologic death and meticulous care directed towards the preservation of organs for transplantation is essential for positive outcomes