# Steroids Improve Hemodynamics in Infants With Adrenal Insufficiency After Cardiac Surgery

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***Objective:*** **To investigate whether steroid replacement therapy improved hemodynamics in infants after surgery for congenital heart disease only when they develop adrenal insufficiency. The authors retrospectively investigated adrenal function and evaluated hemodynamic responses to steroid replacement therapy in infants after surgery for congenital heart disease.**

***Design:*** **Retrospective, cohort study.**

***Setting:*** **Intensive care unit in the National Cerebral and Cardiovascular Center Hospital in Japan.**

***Patients:*** **Thirty-two neonates and infants <3 months old who underwent cardiovascular surgery.**

***Interventions:*** **The patients were divided into 2 groups based on corticotropin stimulation test results: group AI with adrenal insufficiency (baseline cortisol <15 μg/dL or incremental increase after testing of <9 μg/dL, with baseline cortisol of 15-34 μg/dL); and group N with normal adrenal function. The corticotropin stimulation test was performed by injecting 3.5 μg/kg of tetracosactide acetate. Hydrocortisone (1 mg/kg) was administered every 6 hours, and hemodynamics were compared before and after steroid administration between the groups.**

***Measurements and Main Results:*** **Seven patients were classified into group AI, and demonstrated a mean blood pressure increase from 53 ± 8 mmHg before treatment to 68 ± 9 mmHg 18 hours after steroid administration ($p < 0.01$). Urine output also increased, from 2.7 ± 1.0 mL/kg/h to 4.8 ± 1.9 mL/kg/h ($p < 0.05$). In group N, neither mean blood pressure nor urine output increased after steroid administration.**

***Conclusions:*** **After surgery for congenital heart disease, one-fifth of infants developed adrenal insufficiency. Steroid replacement therapy improved hemodynamics only in the subgroup with adrenal insufficiency.**



***KEY WORDS: adrenal insufficiency, congenital heart defects, corticosteroids, hemodynamics, infant, postoperative care***

CARDIAC SURGERY INDUCES a systemic inflammatory response.[1] Some reports showed that steroid administration suppressed inflammation and improved hemodynamics in infants undergoing surgery for congenital heart disease (CHD).[2-6] However, steroid therapy includes serious possible side effects, including muscle weakness, impaired wound healing, digestive tract bleeding, and glucose intolerance. In a study of preterm infants, routine steroid use was not recommended because it increased the incidence of intraventricular hemorrhage, neuromotor dysfunction, and delayed growth;[7] and in a study of pediatric patients undergoing cardiac surgery, administration of steroids offered no clinical benefits.[8] Therefore, the indications for steroid replacement therapy in infants after cardiac surgery require clarification.

In adult patients who experience septic shock[9,10] or liver failure,[11] steroid replacement therapy improved mortality and hemodynamics only when patients developed adrenal insufficiency (AI), which was confirmed using the baseline cortisol level and a corticotropin stimulation test. Similarly, in very-low-birth-weight neonates with AI, hemodynamic instability was reversed by steroid administration.[12]

The authors hypothesized that steroid replacement therapy improved hemodynamics in infants after surgery for CHD only when they developed AI. The authors investigated adrenal function and evaluated hemodynamic responses to steroid replacement therapy in infants after surgery for CHD.

## PATIENTS AND METHODS

The authors retrospectively analyzed data collected in an intensive care unit (ICU) of a Japanese national hospital from April 2004 to December 2004. During this period, the authors measured cortisol levels after cardiac surgery in infants, questioning whether steroid replacement therapy would improve hemodynamics. All patients underwent adrenal function testing after surgery for CHD. The retrospective protocol was approved by the Ethical Review Committee of the National Cerebral and Cardiovascular Center. Patient consent was waived for the retrospective analysis.

### Patients

During the study period, the authors enrolled 36 consecutive neonates and infants younger than 3 months old who underwent cardiovascular surgery and blood transfusion. Two patients were excluded because they received extracorporeal membrane oxygenation, which made it difficult to evaluate their hemodynamics. These patients required extracorporeal membrane oxygenation because of airway bleeding and intractable heart failure. One patient who underwent pacemaker implantation for complete atrioventricular block was excluded because he was discharged from the ICU the day after surgery. Another patient was excluded because definitive surgery was scheduled shortly after a modified Blalock-Taussig shunt

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**Table 1. Procedures Performed in Patients With Adrenal Insufficiency (Group AI) and Normal Adrenal Function (Group N)**

| | Group AI (n = 7) | Group N (n = 25) |
|---|---|---|
| Closure of ventricular septal defect | 3 | 8 |
| Repair of atrioventricular septal defect | 1 | |
| Arterial switch surgery | | 4 |
| One-stage repair for IAA/CoA complex | | 3 |
| Norwood procedure | | 1 |
| Modified Blalock-Taussig shunt | 1 | 3 |
| PA banding | 2 | 2 |
| Aortic arch repair + PA banding | | 3 |
| Division of the patent ductus arteriosus | | 1 |

Abbreviations: IAA, interrupted aortic arch; CoA, coarctation of the aorta; PA, pulmonary artery.

procedure. A final total of 32 patients were enrolled, and data from these 32 patients were analyzed retrospectively.

## Clinical Management

The procedures that were performed are listed in Table 1. Cardiopulmonary bypass (CPB) was used in 20 patients who underwent closure of ventricular septal defects, repair of atrioventricular septal defects, arterial switch surgeries, one-stage repair for interrupted aortic arch or coarctation of the aorta with cardiac anomalies, and modified Norwood procedure. Although steroids were not used routinely, methylprednisolone was administered at the initiation of CPB in 4 patients. At weaning from CPB, dilutional and modified ultrafiltration were performed in all patients. Modified Blalock-Taussig shunt procedure, pulmonary artery banding, aortic arch repair with pulmonary artery banding, and division of the patent ductus arteriosus were performed without CPB.

In the ICU, hemodynamic parameters (electrocardiography and arterial and central venous pressures) were monitored continuously. Blood gas, electrolyte, and blood glucose values were analyzed at least every 2 hours, and hematology and blood chemistry were examined every 8 hours. Vasoactive drugs and sedatives were adjusted by the attending physicians who were not authors in this study. Continuous infusion of furosemide was used, if necessary, but the infusion rate remained unchanged throughout the study period.

## Adrenal Function Testing

During the study period, baseline cortisol and corticotropin levels were measured routinely 6 to 12 hours after surgery when circulatory status was stabilized. Based on previous work,[12,13] a corticotropin stimulation test then was performed using a 3.5-μg/kg intravenous bolus of tetracosactide acetate, with cortisol measured 30 and 60 minutes after the tetracosactide stimulation. The incremental response in cortisol after the corticotropin stimulation test was calculated as the difference between baseline and maximal values.

Based on the definition of AI reported by Cooper et al,[14] patients were divided into the following 2 groups: group AI and group N. Group AI included patients with adrenal insufficiency, and group N included patients with normal adrenal function. AI was defined as follows: baseline cortisol $<15$ μg/dL or incremental increase after the corticotropin test of $<9$ μg/dL, with baseline cortisol ranging from 15 to 34 μg/dL. Normal adrenal function was defined as follows: baseline cortisol $>34$ μg/dL or incremental increase after corticotropin testing $\geq 9$ μg/dL, with baseline cortisol ranging from 15 to 34 μg/dL. Patients' demographic data in each group are shown in Table 2. There was no significant difference in demographics between the groups, although the baseline corticotropin level tended to be higher ($p = 0.09$) and the surgery time tended to be longer ($p = 0.07$) in group N than in group AI.

## Steroid Replacement Therapy

Hydrocortisone, 1 mg/kg, was given every 6 hours immediately after completing the stimulation test in all patients. Blood pressure; inotrope score (dopamine [μg/kg/min] × 1 + dobutamine [μg/kg/min] × 1 + epinephrine [μg/kg/min] × 100 + norepinephrine [μg/kg/min] × 100 + milrinone [μg/kg/min] × 15)[6]; hourly urine output; and net fluid balance were compared every hour from 6 hours before hydrocortisone

**Table 2. Demographics of Patients With Adrenal Insufficiency (Group AI) and Normal Adrenal Function (Group N)**

| | Group AI (n = 7) | Group N (n = 25) | p value |
|---|---|---|---|
| Age (day) | 50 (36-65) | 29 (8-64) | NS |
| Male | 43% | 48% | NS |
| Height (cm) | 52.0 (50.9-54.3) | 49.0 (47.0-52.2) | NS |
| Weight (kg) | 3.40 (3.10-3.62) | 2.88 (2.40-3.40) | NS |
| Cardiopulmonary bypass | 57% | 64% | NS |
| Methylprednisolone use | 14% | 12% | NS |
| Baseline corticotropin (pg/mL) | 15.6 (10.5-35.8) | 39.7 (20.4-75.1) | 0.09 |
| Δcortisol by corticotropin test (μg/dL) | 42.8 (34.9-51.2) | 34.2 (17.7-46.9) | NS |
| Surgery time (min) | 170 (140-180) | 190 (170-455) | 0.07 |
| $SaO_2$-$ScvO_2$ on ICU admission (%) | 31.2 (25.6-40.0) | 39.9 (31.6-40.3) | NS |
| Lactate on ICU admission (mmol/L) | 1.8 (1.2-2.3) | 2.4 (1.4-6.2) | NS |
| Total protein on ICU admission (g/dL) | 6.1 (6.0-7.0) | 5.7 (5.6-6.6) | NS |
| Surgical fluid balance (mL) | 85 (29-129) | 95 (25-174) | NS |

NOTE. Values are presented as median (interquartile range) or percent of patients.

Abbreviations: Δcortisol, increments of cortisol; $SaO_2$, arterial oxygen saturation; $ScvO_2$, venous oxygen saturation at superior vena cava; NS, not significant.