Adrenocortical Function before and after Cardiac Operations of Infants under Hypothermia

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Adrenocortical functions were studied in 15 infants under 1 year of age, operated on under hypothermia for congenital cardiac diseases consisting mainly of ventricular septal defect. Adrenocortical functions were examined pre- and postoperatively, by eosinophil cell count in the peripheral blood and determination of urinary output of 17-OHCS and 17-KS. Thorn's test was also done before operation. As controls, the same examinations were performed in general surgical cases of infants, on cases of open heart surgery in young children operated on under hypothermia and in general surgical cases of adults.

Insufficiency of the adrenocortical function was found preoperatively in children and adults with acquired or congenital heart diseases of long duration, while in infants a latent hypofunctional state was observed only in cyanotic or very severe cases. The other cases, in general, had well maintained adrenocortical function as was revealed in large urinary 17-OHCS output.

Infants with congenital heart diseases seemed to have adrenocortical functions enough to tolerate open heart operation under hypothermia. Even in such cases, however, hormonal balances were liable to be disturbed as indicated by retarded recovery with conspicuous fluctuations of the eosinophil count and of excretion of 17-OHCS and 17-KS.

In recent years, pathophysiological investigations before and after operation have acquired an increasing importance in pediatric surgery. In regard to the pituitary-adrenocortical response of infants to surgical operations, a number of problems still remain to be clarified. Since 1961, we have mainly performed radical operations for ventricular septal defect under hypothermia, and satisfactory results have been obtained. In the present study, responses of the patients under the above operative procedure were studied in association with the adrenocortical function.

MATERIALS AND METHODS

Fifteen cases with congenital heart diseases, comprising five males and ten females, were investigated. All the patients were under a year of age. Their age
distribution was: 2 in the 5th month, 1 in the 6th, 2 in the 7th, 6 in the 8th, 2 in the 9th and 2 in the 12th. They included 12 cases with ventricular septal defect, 1 with single ventricle, 1 with total anomalous pulmonary venous return and 1 with atrial septal defect associated with pulmonary stenosis. All infants were deeply anesthetized with ether, and hypothermia was induced by means of the surface cooling method. Radical operation under direct vision was performed in all instances but one with single ventricle in which the superior vena cava was anastomosed with the right pulmonary artery. The lowest temperature achieved varied from 22 to 29°C. In the majority of instances the body temperature was kept at between 24 and 25°C. The shortest time for circulatory occlusion was 6 minutes and 40 seconds, while the longest was 38 minutes. In this series, death occurred in a case with total anomalous pulmonary venous return and in 3 cases with ventricular septal defect.

Twenty general surgical cases of infants served as controls. They comprised 5 cases with congenital biliary atresia, 4 with inguinal hernia, 2 with intussusception, 2 with pyloric stenosis, 1 with duodenal stenosis, 1 with colon polyp, 1 with congenital megacolon, 1 with choledochus cyst, 1 with cleft lip, 1 with foreign body in the stomach, and 1 with congenital diaphragmatic hernia. In addition, 12 open heart-hypothermic cases of children and adults, and 11 adult cases of major operations in general surgery were also studied.

Eosinophil cell count in the peripheral blood was estimated using Hinkelman’s solution and Fuchs-Rosenthal’s disc. Glenn and Nelson’s method modified by Kanbegawa was adopted for determination of 17-OHCS of 24 hour urine.

Total 17-KS urinary output was also determined by Kanbegawa’s method using 24 hour urine specimens.

Thorn’s test was done by intramuscular injection of ACTH-Z in an amount of 40 units. To cases under 14 years of age, 20 units were given. The count of eosinophils in the peripheral blood was performed before and immediately after operation, on the 1st, 2nd, 3rd, 5th, 7th and 14th postoperative days, while urinary 17-KS and 17-OHCS levels were determined by the above mentioned method at regular intervals up to the 7th postoperative day.

RESULTS

According to Kanbegawa, the normal value of 17-OHCS is 0.7 to 3 mg per day in men and 0.5 to 2.5 mg per day in women. The normal value of total 17-KS urinary output is 3 to 6 mg per day (Kanbegawa, personal communication). In the present investigation, comparative analysis of postoperative 17-OHCS and 17-KS excretion in patients with congenital heart diseases indicated that the output of both 17-OHCS and 17-KS in 24 hour urine was lower in infants than in children or adults in general. With regard to the values of 17-OHCS per
kg of body weight, a mean of 39γ/kg/day was excreted in those above 10 years of age, a mean of 47γ/kg/day in children between 1 and 9 years and a mean of 57γ/kg/day in infants below one year of age, respectively, indicating higher values in the younger age group. On the contrary, 17-KS showed lower values in the younger age group (Fig. 1). This is presumably due to the immaturity of the gonads and of the reticular zone of the adrenal cortex.

Both in cases of children and adults with ventricular septal defect or mitral stenosis low excretion levels of both 17-OHCS and 17-KS were observed. Cases with a larger shunt volume presented moderately low levels. Fatal cases due to operative intervention showed lower values than the survivors. In infantile cases, those with cyanosis and pulmonary hypertension did not always present low values, but the majority of severe cases which could not withstand operative procedures, had already shown low levels of both 17-OHCS and 17-KS prior to the operation.

Ten infantile cases were subjected to Thorn’s test, but the evidence of functional insufficiency of the adrenal cortex could not be obtained in all except one case with congenital biliary atresia. Its functional insufficiency was verified in 5 of 21 cases of children and adults with heart diseases. They were 2 cases with mitral insufficiency, 1 with constrictive pericarditis falling into cardiac failure, 1 with ventricular septal defect seen in the relatively high age group (16 years of age) and 1 with tetralogy of Fallot (22 years of age).

Postoperative alterations of adrenocortical function were evaluated by the
eosinophil count of the peripheral blood, which was considered to reflect the function of the adrenal cortex fairly well. As was shown in Fig. 2, eosinophils decreased immediately after operation in both infantile cases (A) and adult cases (D) and almost completely disappeared, but started to increase after 2 days postoperatively and returned to the preoperative level around the 5th days after operation. In the hypothermic group (infantile cases (B) and child and adult cases (C), somewhat slower recovery was seen than in normothermic group. Of the infantile cases operated on under hypothermia in particular, the majority could not restore preoperative levels until 2 weeks after operation, indicating a greater sensitivity of the adrenal cortex to operative stress. In addition, markedly slow recovery was documented in cases with postoperative complications such as pericarditis or bronchopneumonia.

In general, urinary output of 17-OHCS increased markedly postoperatively. Except for the child and adult hypothermic group (C) it reached to the peak on the operative or the 1st postoperative day and gradually decreased thereafter. By the 7th postoperative day, however, it did not return to the preoperative level (Fig. 3). In the infantile hypothermic cases (B), urinary output of 17-OHCS per kg of body weight on the 1st postoperative day was twice larger than that in
children and adults (C). Postoperative response was low in a cyanotic case (single ventricle) of an infant and 2 cyanotic cases of a child and adult. It might probably due to reduced hormonal reserve which was frequently observed. Poor response was also observed postoperatively in a case who developed pericarditis. Three infants operated on under hypothermia had poor cardiac resuscitation. Nearly all of them showed larger output postoperatively than before the operation. The output of 17-OHCS was found to have no relation with clinical course, operative technique, etc.

Fluctuations of urinary 17-KS output are shown in Fig. 4, which are similar to those of 17-OHCS. However, they had not always a parallel relationship to each other. The period during which the peak of 17-KS excretion was attained tended to become somewhat prolonged in comparison with that of 17-OHCS. In most of the cases, the peak appeared on the 2nd postoperative day or thereafter. Daily changes of 17-KS excretion were insignificant. Particularly in the infantile hypothermic group (B), no marked response was demonstrated such as seen in 17-OHCS.
Fig. 4. Mean urinary output of 17-KS per kg of body weight.
A: General surgical cases of infants.
B: Infants operated on under hypothermia.
C: Children and adults operated on under hypothermia.
D: Control group of adult cases.

DISCUSSION

It has been generally accepted that even cases with chronic diseases such as pulmonary tuberculosis or malignant tumor do not develop functional insufficiency of the adrenal cortex except in extremely advanced stages. There are a number of reports indicating that patients with cardiac diseases in general have hypofunction of the adrenal cortex. There are, however, the observations that the adrenocortical function is within the normal range in cardiac patients in the compensatory period. The author's study revealed poor responses to a stress in relatively severe cases with acquired heart diseases such as rheumatic heart disease, especially in the older age group. Lasche and his associates recognized a parallel relationship between the adrenocortical hypofunction and the duration of illness. In addition to this, the fact that infantile cases with pulmonary hypertension or cyanosis did not always show adrenocortical hypofunction seems to indicate that adrenocortical activity falls gradually in a state of exhaustion after long duration of disease as a result of excessive response to continuous stress in the infantile period. In severe cases which could not tolerate operative stress, 17-OHCS level had been low prior to operation. Poor postoperative responses were found among blue babies. From these facts, cardiac diseases...
per se act undoubtedly as a great stress.

It is 3 years of life when the three perpetual layers of the adrenal cortex are formed. The infantile cases dealt with in the present study were all within a range of 5 to 12 months of life, the period which corresponded to the time when the fetal cortex disappeared and the adult type zona glomerulosa was first formed. Anatomically, however, this zona glomerulosa is apparently immature. The zona fasciculata develops in a relatively early period. In fact, it has been recognized that a good adrenocortical response to surgical operation occurred after one week of life. One of the present authors (Kimura) recognized a good response of the pituitary-adrenocortical system in general surgical cases of infants except for newborns and older children. The author's study further indicated that 17-OHCS level per kg of body weight was higher in infants than in adults. The elevated level persisted over one week after operation. This was attributed either to high activity of the adrenal cortex of infants or to high sensitivity to operative intervention. Even in 3 cases with relatively low postoperative 17-OHCS output, complications suggesting functional insufficiency of the adrenal cortex did not take place. Those who succumbed to postoperative complications had shown marked increase of 17-OHCS output until a day prior to death. It could not be assumed consequently that the production of adrenocortical hormones could not meet the bodily demand.

In the cases of unsuccessful cardiac resuscitation or retarded resumption of cardiac action, postoperative adrenocortical response was good. No sequela in the form of adrenocortical hypofunction seems to persist in infants subjected to circulatory interruption within 30 minutes under hypothermia of 24° to 25°C, the condition under which we operated on.

The infants with congenital heart diseases seem to have the adrenocortical function sufficient to tolerate open heart operation under hypothermic anesthesia, except for extremely severe cases in which latent hormonal insufficiency was suspected on account of the long duration of disease.

References


