Original Article

Cardiopulmonary Bypass Factors Affecting the Development Of Choreoathetosis in Pediatric Patients

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ABSTRACT

Choreoathetosis (CHO) in pediatric patients following cardiopulmonary bypass (CPB) has no known etiology, although several causal factors have been suggested. The infrequent occurrence in any one institution and the inability to perform prospective studies have made the etiology of CHO difficult to discover. This paper discusses a retrospective analysis of eleven cases of CHO following CPB. To form a control group for matched comparison, each of the eleven CHO patients was matched with a patient who did not develop CHO. Matching parameters included: age at operation within 10%, diagnosis (cyanotic, not cyanotic), race, gender, operation, and date of operation within 12 months.

Fifteen preoperative and CPB variables were evaluated to determine differences between the CHO patients and the control patients. Statistical analysis included odds ratios for matched pairs and two sample t-tests. A p value of 0.05 was chosen to assess statistical significance. Variables found to be significantly different between the study and control groups were: lowest rectal temperature, cooling and warming rates, and lowest arterial blood temperature. From these results, it is concluded that cooling to rectal temperatures less than 15°C or a cooling rate greater than 0.4°C/min is associated with the development of CHO following CPB in these patients.

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INTRODUCTION

The main cause of non-cardiac complications during cardiopulmonary bypass (CPB) is neurologic injury, having a variety of etiologies. Some types of injury have very apparent causes, while others remain a mystery due to the variety of diagnoses, techniques used during surgery, and individual patient responses to treatment involved in open heart surgery (1).

Choreoathetosis (CHO) is one post-CPB neurological complication with no known etiology (1-5), although several studies suggest some type of damage to the basal ganglia region as a general cause. The onset of CHO is delayed, most commonly occurring between the second and seventh day post-CPB (1). Symptoms include generalized loss of tone, abnormal jerky or writhing movements in the facial area and/or the trunk and extremities, tongue protrusion, and random eye movements, not present during sleep (2). The syndrome has been known to resolve itself, completely in most cases, after a period of time ranging from two weeks to several years (2). All reported cases have occurred in children under the age of six years (2).

Hypoxia during circulatory arrest, uneven cooling, no-flow phenomenon, hyperglycemia, excessive dopaminergic activity (3), and cerebral excitatory amino acid neurotoxicity (4) are the possible mechanisms of CHO. Contributing factors may be age beyond infancy (4), cyanotic heart disease (4), depth and duration of hypothermia, pH management during CPB (6), pharmacologic agents used, and blood flow rates (3).

The purpose of this study is to compare preoperative and intraoperative variables between patients who developed postoperative CHO and a matched control group who did not develop CHO.

MATERIALS AND METHODS

There have been eleven cases of CHO following CPB at the Medical University of South Carolina between 1986 and 1992. Each CHO patient was matched with a patient not developing CHO based on the criteria listed in Table 1. The parameters listed in Table 2 were recorded from hospital and clinic charts and perfusion records. Two-sample t-tests were used to evaluate the continuous data. Odds ratios and chi-square for matched pair analysis were used to analyze discrete data. Linear regression and correlation were used to determine associations between variables. A p value of <0.05 was considered significant.

RESULTS

CHO patient demographics are shown in Table 3. Two of the patients were older than six years; the oldest was 17.5 years old. There were five black, five white, and one Asian-American patient. Eight of the eleven patients were male, and three were female. Three of the patients were cyanotic.

Mean ages of the two groups were 4.0 years for the CHO group and 3.5 years for the control group. The mean age of the CHO group is skewed by one patient, the 17.5 year old, who could not be matched on age at operation. Cyanotic versus noncyanotic diagnoses were matched in all but one pair. Race was matched in all but two pairs. Operation was matched in all

Table I : Criteria used to match each study patient with a control patient.

Age at operation within 10%, not less than 6 months old.
Diagnosis (cyanotic, noncyanotic)
Race
Gender
Operation
Date of operation within 12 months and after 1986

Table 2: Factors that were evaluated between each pair to determine their relationship to the development of CHO. (CPB = cardiopulmonary bypass)

Surgeon, anesthesiologist, perfusionist
Anesthetic agents
Total CPB time
Total cooling time
Minimum temperatures: rectal, arterial blood
Rate of cooling/warming
Circulatory arrest time
Blood flows when cold
Mean arterial pressures while cold/warm
Blood gas values when cold

Table 3: Patient demographics.

Summary of Clinical Data on Patients Developing Choreoathetosis

AGE (yrs)	RACE	GENDER	DIAGNOSIS
0.8	White	Male	Tetrology of Fallot
11.6	White	Male	Wolff-Parkinson-White
0.4	White	Male	ASD,VSD
5.3	White	Female	Single Ventricle
0.7	Black	Male	ASD,VSD,PDA
0.8	Black	Female	VSD,Double-chambered RV
1.1	Asian-Am	Male	TAPVR
1.7	Black	Female	Single atrium
17.5	Black	Male	Single atrium,single ventricle, TAPVR
0.5	White	Male	Anomolous left coronary artery
6.2	Black	Male	Tetrology of Fallot

ASD=atrial septal defect; RV=right ventricle; PDA=patent ductus arteriosus; TAPVR=total anomalous pulmonary venous return; VSD=ventricular septal defect)

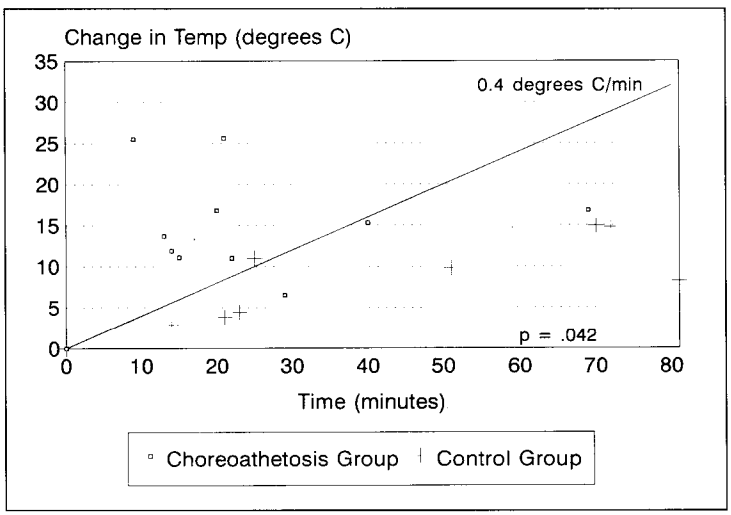
pairs and the date of operation was matched within twelve months, except for one pair that had surgery thirteen months apart.

Four factors were found to be significantly different between the groups (Table 4). Although matched for the same procedure, six of the CHO patients underwent circulatory arrest whereas only two of the control patients underwent circulatory arrest. Minimum rectal temperature was found to be lower in the CHO group ($p<0.05$) (Table 4). The mean minimum rectal temperatures of each group are skewed by one pair (the patients with Wolff-Parkinson-White syndrome), whose surgeries were performed at normothermia. The medians (shown in parentheses) are more indicative of each group's average minimum rectal temperatures. The CHO group was cooled ($p=0.042$) and warmed more rapidly ($p=0.041$) than the control group. The cut-off values of 0.4°C/min and 0.3°C/min respectively were found to be significant by chi-square for matched pair analysis (Figures 1 and 2). The mean lowest arterial blood temperatures were lower in the CHO group ($p=0.038$) (Table 4).

Table 4: Factors found to be significantly different or approaching significance between the two groups. Circulatory arrest numbers are the actual number of patients undergoing/not undergoing circulatory arrest. For the other parameters, the mean ± 1 standard deviation is shown with median in parenthesis where applicable. (min = minute)

Variable	Study group	Control group	p value
Circulatory arrest (yes/no)	6 / 5	2 / 9	0.10
Minimum rectal temperature (°C)	19.2 ± 7.7 (15.5)	24.4 ± 6.3 (25.9)	0.05
Cool rate (°C/min)	0.8 ± 0.9	0.2 ± 0.2	0.042
Warm rate (°C/min)	0.4 ± 0.2	0.2 ± 0.1	0.041
Lowest arterial blood temperature (°C)	11.3 ± 9.1 (7.6)	18.6 ± 9.3 (18.7)	0.038

Figure 1: Cool rates shown as the change in temperature from initiation of cooling to desired hypothermic temperature / amount of time to reach minimum temperature. (min = minute; temp = temperature)



DISCUSSION

The direct cause of neurologic injury leading to CHO has been a mystery for years. There are questions concerning the location of injury, the reason for the delayed onset, the varying degrees of recovery, and the age of the patients. Wong, et al. concluded that age beyond early infancy was associated with more severe persistent CHO (4). They suggest that the most vulnerable time period for CHO was between 6-9 months and 5-6 years. Based on the literature, this conclusion appears accurate; however, we have observed incidences of CHO in patients older than this at our institution. Although the majority of our patients fell within this range, two of the eleven were not within this range. One of our patients was 17.5 years old and is the oldest reported case of CHO following CPB.

If age is not a contributing factor, there may be something else, possibly age related, that causes this syndrome in young people but not in adults. Wong, et al. also found that patients with cyanotic heart disease were more at risk of developing CHO (4). We found that there was no trend toward any one diagnosis, nor a trend toward cyanotic lesions. Use of circulatory arrest was also not a significant variable. This was not statistically significant; however, it is approaching significance ($p=0.10$), so an increase in sample size may find that use of circulatory arrest is a predictor of the development of CHO.

Swain suggested pH management as a possible cause of CHO, noting that some surgeons have observed CHO in association with the use of alpha-stat blood gas management. (J. Swain, M.D.*) Our institution began using alpha stat management prior to any occurrences of CHO; therefore, we were unable to compare type of blood gas management. An analysis of actual blood gas values during cooling showed no significant difference between those developing CHO and the control group.

DeLeon, et al. found that cooling to rectal temperatures less than 25°C and cooling times greater than one hour were associated with CHO (3). This conclusion is not consistent in our patients. Almost all of our patients, control group and study group, were cooled to temperatures less than 25°C. However, we did find a significant difference between the two groups' minimum rectal temperature. The CHO group was cooled to lower temperatures, and statistical analysis showed that cooling to rectal

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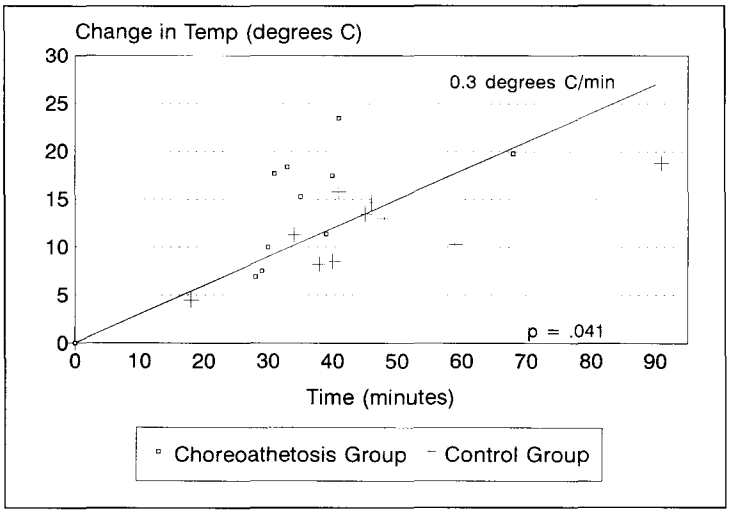
temperatures less than 15°C was associated with CHO. Duration of hypothermia was evaluated and found not to be significantly different between the two groups.

The rate of cooling (°C/min) was found to be significantly different, with more rapid cooling associated with CHO. At the time of these incidences, our institution had no specific protocol regarding cooling rate; patients were maximally cooled (water temp of 3° C) until the desired rectal temperature was obtained. Using this method, cooling to lower rectal temperatures resulted in lower arterial blood temperatures, which resulted in more rapid cooling. Warming also occurred more rapidly in the CHO group due to the lower temperatures, although water temperature was kept within ten degrees of venous blood temperature to prevent air from coming out of solution (7).

In January 1993, a change in our protocol was instituted based on research at another institution (8). The change required that the arterial blood not be cooled to temperatures less than 13°C. The water temperature in the heater cooler is set to 13°C instead of 3°C, which results in a slower cooling rate. It is hoped that since we found that a faster cooling rate was related to the development of CHO that this change may have an effect on the development of CHO. There is not enough information available at this time to assess the effect of the change in protocol.

From the information obtained in this study, we conclude that cooling to rectal temperatures less than 15°C or a cooling rate greater than 0.4°C/min may lead to CHO following CPB. Warming at a rate greater than 0.3°C/min was also associated with CHO following CPB at our institution. These findings appear to be one step towards an answer to eliminating CHO post-bypass. However, this is a very complex problem with many contributing factors, and more research is necessary to discover other possible causes. By learning more about the factors involved in the development of CHO, we can work to prevent its occurrence.

Figure 2: Warm rates shown as the change in temperature from start of rewarm to normothermia / amount of time to reach normothermia. (min = minute; temp = temperature)



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