Abdominal Problems in Children with Congenital Cardiovascular Abnormalities

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Background: Congenital cardiovascular abnormality is an important cause of morbidity and mortality in childhood. Both the type of congenital cardiovascular abnormality and cardiopulmonary bypass are responsible for gastrointestinal system problems.

Aims: Intra-abdominal problems, such as paralytic ileus, necrotizing enterocolitis, and intestinal perforation, are common in patients who have been operated or who are being followed for congenital cardiovascular abnormalities. Besides the primary congenital cardiovascular abnormalities, ischemia secondary to cardiac catheterization or surgery contributes to the incidence of these problems.

Study Design: Cross-sectional study.

Methods: In this study, we aimed to screen the intra-abdominal problems seen in patients with congenital cardiovascular abnormalities who had undergone surgical or angiographical intervention(s). Patients with congenital cardiovascular abnormalities who had been treated medically or surgically between 2000 and 2014 were analyzed retrospectively in terms of intra-abdominal problems. The patients' demographic data, type of congenital cardiovascular abnormalities, the intervention applied (surgical, angiographic), the incidence of intra-abdominal problem(s), the interventions applied for the intra-abdominal problems, and the results were evaluated.

Results: Fourteen (Group I) of the 76 patients with congenital cardiovascular abnormalities diagnosis were operated due to intra-abdominal problems, and 62 (Group II) were followed-up clinically for intra-abdominal problems. In Group I (10 boys and 4 girls), 11 patients were aged between 0 and 12 months, and three patients were older than 12 months. Group II included 52 patients aged between 0 and 12 months and 10 patients older than 12 months. Cardiovascular surgical interventions had been applied to six patients in Group I and 40 patients in Group II. The most frequent intra-abdominal problems were necrotizing enterocolitis and intestinal perforation in Group I, and paralytic ileus in Group II. Seven of the Group I patients and 22 of the Group II patients died. The patients who died in both groups had more than three congenital cardiovascular abnormalities in the same patient, and 80% of these patients had been operated for congenital cardiovascular abnormalities.

Conclusion: The gastrointestinal system is involved in important complications experienced by patients with congenital cardiovascular abnormalities. The mortality rate was higher in operated patients due to gastrointestinal complications. Gastrointestinal complications are more frequent in patients with cyanotic anomalies. The presence of more than one congenital cardiovascular abnormality in a patient increased the mortality rate.

Keywords: Abdominal surgery, cardiopulmonary, congenital, cardiovascular abnormalities, intestinal ischemia

Congenital cardiovascular abnormality is an important cause of morbidity and mortality in childhood (1). Gastrointestinal system problems are not rare in patients with Congenital cardiovascular abnormalities (2,3). Both the type of congenital cardiovascular abnormality and cardiopulmonary bypass are responsible for gastrointestinal system complications. Heart failure, hypotension, and cardiopulmonary bypass-related hypoperfusion may cause a short- or long-term ischemia in the gastrointestinal system. The tissue injury caused by ischemia may lead to complications ranging from a decrease in intestinal motility to necrosis. In this study, gastrointestinal system problems of patients with congenital cardiovascular abnormalities were investigated regarding predetermined parameters.

MATERIALS AND METHODS

In this study, gastrointestinal system problems of children with congenital cardiovascular abnormalities who underwent surgical intervention and/or cardiac catheterization at a tertiary health care institution between 2000 and 2014 were retrospectively reviewed. All procedures were performed by the same team. All patients received a detailed explanation of the procedure before surgery, and the study was approved by the hospital review board.

After our project had been approved by Başkent Universty Ethical committee. Medical records of the children who had been treated by the Department of Pediatric Surgery were studied. The parameters considered were: age, gender, type of congenital cardiovascular abnormality, interventions performed for congenital cardiovascular abnormality, gastrointestinal complications, and follow-up findings. The results obtained were compared with the findings in the literature.

After the patients with congenital cardiovascular abnormalities were diagnosed to have surgical gastrointestinal system problems, a proper informed consent was taken from their parents and they were transferred to the anesthesia room, and continuous arterial pressure and electrocardiographic monitoring were established before induction of anesthesia by the administration of 1–2 µgr/kg of fentanyl citrate (Fentanyl, Meditera Medical Istanbul, Turkey) delivered intravenously and a titrated dose of Thiopental sodium (PENTAL®Sodyum, I.E. Ulagay, İstanbul, Turkey) (5–7 mg/kg). Muscle paralysis was accomplished with vecuronium (Norcurone, N V Organon, the Netherland) (0.1 mg/kg). After the induction of anesthesia, a central venous access was created. All patients received antibiotic prophylaxis consisting of cefuroxime sodium (Zinnat, Glaxo Smith Kline Medical, London, England) (30 mg/kg every 8 hours for 24 hours) together with prophylactic H_2-receptor blockade using ranitidine (Ulcuran, Abfar Medical, İstanbul, Turkey), with a dose of 50 mg that was intravenously administered at the time of anesthesia induction. We administered positive pressure ventilation with air and oxygen (60:40) with a variable inspiratory concentration of sevoflurane (Sevorane®, Queenborough, England) (0.5–1%).

Statistical analysis

Descriptive statistics are showed as mean ± standard deviation or median (75%) for continuous variables. The t test was performed for normally distributed variables, and the Mann–Whitney U test was performed for variables that did not distribute normally. The continuity correction Chi-square test was used for categoric variables, and results are shown as the frequency and percentage (%). A p-value below 0.05 was accepted as significant.

Logistic regression analysis was performed to find risk factors. IBM SPSS Statistics for Windows, Version 20.0 (Armonk, NY, USA) was used for statistical analysis.

RESULTS

A total of 3373 patients with congenital cardiovascular abnormality had undergone surgical intervention and/or cardiac catheterization. Gastrointestinal complications were recorded in 76 (2.3%) of the total number, 14 (18.5%) of whom were operated (Group I), while 62 patients (81.5%) were treated non-surgically (Group II).

The demographic data of the patients are presented in Table 1. In Group I (10 boys and 4 girls), 11 patients were aged between 0 and 12 months, and three patients were older than 12 months. Group II included 52 patients aged between 0 and 12 months, and 10 patients older than 12 months.

TABLE 1. Distribution of patients according to age and gender

	Group I						Group II					
Age	0–12 months		>12 months		TOTAL		0–12 months		>12 months		TOTAL	
Gender	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
	8	3	2	1	10	4	35	17	6	4	41	21
TOTAL	11		3		14		52		10		62	

Group I: operated patients; Group II: medically managed patients

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Congenital cardiovascular abnormalities of the patients include: ventricular septal defect, atrial septal defect, ductus arteriosus defect, pulmonar stenosis, double outlet right ventricle, transposition of the great arteries, aortic coarctation, fallot tetralogy, and tricuspid atresia.

Eleven (78.5%) of the 14 patients in Group I had cyanotic congenital cardiovascular abnormalities, and 3 (21.5%) had acyanotic congenital cardiovascular abnormalities, while 44 (71%) of the 62 patients in Group II had cyanotic and 18 (29%) had acyanotic congenital cardiovascular abnormalities.

The interventions performed for the diagnosis or treatment of congenital cardiovascular abnormalities are listed in Table 2.

The patients who underwent cardiac operations were divided into two groups: cyanotic and acyanotic. Cardiopulmonary bypass and aortic cross-clamp times were significantly longer in patients who underwent surgical correction for cyanotic congenital malformations (p=0.0017 and 0.023, respectively; Table 3).

Although some of the complications that occurred due to the surgeries and surgical interventions in Group I were not directly related to the gastrointestinal system, they were included in the study because laparotomy was performed in order to treat them. For example, retroperitoneal hematoma secondary to femoral catheterization was drained via laparotomy, and liver laceration occurred during pericardiosynthesis that was performed for pericardial tamponade and was repaired via laparotomy. Two patients with free air in the abdominal underwent explorative laparotomy, but no perforation was detected. Peritoneal opening during mediastinal tube insertion during cardiac surgery was thought to be the reason for the free air in the abdomen in these patients.

In Group I, necrotizing enterocolitis, a serious gastrointestinal system complication, developed in 10 patients. All these patients had cyanotic congenital cardiovascular abnormalities

(Table 4). Visualization of free air in abdominal plain radiograph, intestinal content detection in parasynthesis following extensive dense-liquid detection in abdominal ultrasonography, and edema and color change in the abdominal wall were accepted as laparotomy indications. In these patients, localized or wide necrosis and single or multiple foci of perforation were detected. In two cases abdominal exploration revealed no abnormality, whereas primary repair of intestinal perforation was performed in two patients and ileostomy or colostomy was performed in ten patients.

In Group II, gastrointestinal complications were approximately three times more frequent in patients with cyanotic congenital cardiovascular abnormalities than in patients with acyanotic congenital cardiovascular abnormalities (Table 5).

The patients with abdominal distention, bilious vomiting, bilious nasogastric drainage, jejuno-ileal air-fluid levels on erect plain abdominal radiograms, and immotile bowel on sonography were diagnosed as paralytic ileus. In these patients, oral feeding was stopped, nasogastric decompression was performed, triple-antibiotic therapy (ceftriaxone (Rocephin, Roche Medical, Basel, Switzerland) 50 mg/kg/day or ampicillin/sulbactam (Sulcid, İ.E. Ulagay Medical, İstanbul, Turkey) 50 mg/kg/day, amikacin (Amiketem, İ.E. Ulagay Medical, İstanbul, Turkey) 15 mg/kg/day, and ornidazole (Biteral, Roche Medical, Basel, Switzerland) 20 mg/kg/day) was started, and the patient was followed by plain abdominal radiograms taken every 12–24 hours. Follow-up and medication was ended after gaining intestinal motility with spontaneous gas and stool passage.

Stage I and II necrotizing enterocolitis was defined by deterioration of the patient's status, occult or massive blood detection in the stool, abdominal distention, and bilious vomit-

TABLE 2. Distribution of interventions performed according to the groups

Investigation performed	Group I	Group II
Cardiac catheterization	8 (57.1%)	22 (35.5%)
Surgery	6 (42.9%)	40 (64.5%)
TOTAL	14	62

Group I: operated patients; Group II: medically managed patients

TABLE 3. Cardiopulmonary bypass and aortic cross-clamp times in cyanotic and acyanotic patients

	Acyanotic	Cyanotic	p value
Patients	21	55	
Aortic cross-clamp (median value)	46 minutes	99 minutes	0.0017
Cardiopulmonary bypass (median value)	31 minutes	91 minutes	0.023

TABLE 4. Distribution of the indications of abdominal operations in Group I (operated patients), according to the presence of cyanosis

	Acyanotic	Cyanotic	TOTAL
Necrotizing enterocolitis (Stage III)	-	10	10 (71.4%)
Retroperitoneal hematoma	1	-	1 (7.2%)
Intra-abdominal free air	1	1	2 (14.2%)
Liver laceration	1	-	1 (7.2%)
TOTAL	3	11	14

TABLE 5. Complications developed in Group II (Medically managed patients)

	Acyanotic	Cyanotic	TOTAL
Paralytic ileus	12	30	42 (67.7%)
Necrotizing enterocolitis (Stage I–II)	6	13	19 (30.6%)
Ogilvie syndrome	-	1	1 (1.7%)
TOTAL	18	44	62

ing. Oral feeding was stopped and nasogastric decompression was performed, triple-antibiotic therapy (ceftriaxone 50 mg/kg/day or ampicillin/sulbactam 50 mg/kg/day, amikacin 15 mg/kg/day, and omidazole 20 mg/kg/day) was started and the patient was followed-up by plain abdominal radiographs every 8–12 hours. Parenteral nutrition was started if oral feeding could not be provided for at least 3 days. Medication was ended upon improvement in X-ray findings and bowel motility with stool and gas passage.

In the case with Ogilvie Syndrome, severe abdominal distention was seen and colonic expansion was detected on plain abdominal X-ray. Similarly, oral feeding was stopped and nasogastric decompression was performed, triple-antibiotic therapy (ceftriaxone 50 mg/kg/day or ampicillin/sulbactam 50 mg/kg/day, amikacin 15 mg/kg/day, and ornidazole 20 mg/kg/day) was started, the colon was decompressed via a rectal tube, rectal stimulation, or enema. Treatment was ended after distention disappeared with neostigmine (Neostigmine, Adeka Medical, Samsun, Turkey) infusion (2 mg/kg/day).

Seven patients in Group I (50%) and 22 patients (35.5%) in Group II died. The distribution of these patients according to the type of congenital cardiovascular abnormality is given in Table 6.

The mortality rates of the two groups were compared, and no statistically significant difference was found (p=0.458).

All the patients who died in Group I had cyanotic-type congenital cardiovascular abnormalities. Five (23%) of the 22 patients who died in Group II had acyanotic congenital cardiovascular abnormalities and 17 (77%) patients had cyanotic abnormalities. In both groups, the survival rates in cyanotic and acyanotic patients were not significantly different (p=0.361). In the overall evaluation of the study group, 5 (23.8%) of the 21 acyanotic patients and 24 (43.6%) of the 55 cyanotic patients died. No statistically significant difference was found between the cyanotic and acyanotic patients with regard to survival rates (p=0.122).

Sixty-six patients had three or more congenital cardiovascular abnormalities. In both groups, the number of congenital cardiovascular abnormalities in patients who died was at least three.

TABLE 6. Distribution of the patients who died according to the type of congenital cardiovascular abnormality

	Group I		Group II	
	Acyanotic	Cyanotic	Acyanotic	Cyanotic
Survivors	3	4	13	27
Exitus	0	7	5	17
TOTAL	3	11	18	44
	14		62	

Group I: operated patients; Group II: medically managed patients

DISCUSSION

Gastrointestinal ischemia can cause variable degrees of tissue injury. Ischemia disturbs tissue integrity via mediators appearing in the affected organ depending on the length of the period of exposure. The result can be either temporary, like paralytic ileus, or permanent, like necrosis. We observed that the gastrointestinal system complications were not uncommon in children who were operated for congenital cardiovascular abnormalities. Although congenital cardiovascular abnormalities are a well-known factor for necrotizing enterocolitis development, there is no satisfying data in the literature about its incidence, pathophysiology, and effects (1-6). In our study, gastrointestinal system complications were detected in 76 congenital cardiovascular abnormalities patients. In the 14-year period, the number of patients who underwent a surgical intervention because of congenital cardiovascular abnormalities in our hospital was 3373. The rate of gastrointestinal system complications was 2.3%, which is similar to the previously reported rates (1,7).

Necrotizing enterocolitis, a problem with high mortality, is characterized by translocation of pathogenic enteric bacteria out of the intestinal wall (8-12). Necrotizing enterocolitis is generally seen in newborns, and it constitutes the most important reason for emergent surgery at this age. Intestinal ischemia has an important role in its etiology. One of the theories suggested for the physiopathology of ischemia causing necrotizing enterocolitis is the "diving reflex" (12-14). According to this theory, in the case of a general ischemia, in order to maintain oxygenation of more vital organs, more blood flow is temporarily directed from the splanchnic area to the vital organs, and the result is ischemia in the intestinal wall. A similar situation may occur in patients undergoing surgery for congenital cardiovascular abnormalities. Hypotension during cardiopulmonary bypass or a delay in starting the cardiac functions after ending the pump function may cause ischemia in the splanchnic area via trigger of the "diving reflex". This explains the frequency of intestinal complications in patients with congenital cardiovascular abnormalities. Cheng et al. (3) reported that among the symptomatic newborns with congenital cardiovascular abnormalities, diagnosed as necrotizing enterocolitis, the mortality rate in the cyanotic ones (71%) was apparently higher than the acyanotic ones (39%). They also emphasized that those necrotizing enterocolitis cases with congenital cardiovascular abnormalities had higher birth weights and APGAR (activity and muscle tone, pulse, grimace response, appearance, respiration) scores than the necrotizing enterocolitis cases with no congenital cardiovascular abnormalities.

In this study, necrotizing enterocolitis developed in 10 (71.4%) of 14 patients who underwent surgery for gastrointes-

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tinal system complications, and in 19 (30.6%) of 62 patients who received medical therapy. Eleven (78.5%) of the 14 patients in Group I and 44 (71%) of the 62 patients in Group II had cyanotic-type congenital cardiovascular abnormalities. According to our results, the probability of necrotizing enterocolitis is higher in cyanotic patients, which supports the literature data.

In this study, in 42 (67.7%) of the 62 patients in Group II, paralytic ileus was detected. When the total 76 patients are considered, this rate was 55.2%. Simić et al. (15) reported that paralytic ileus constitutes 36% of the gastrointestinal complications, and so our results are compatible with those in the literature. Twelve (28.5%) of the 42 patients with paralytic ileus had acyanotic-type congenital cardiovascular abnormalities, and 30 (71.5%) of them had cyanotic-type abnormalities.

Both necrotizing enterocolitis and slowed or diminished intestinal motility were more frequently seen in cyanotic congenital cardiovascular abnormalities patients than in acyanotic congenital cardiovascular abnormalities patients. According to the literature, there are two main reasons for this: 1) Cyanotic abnormality directly causes hypoperfusion in the gastrointestinal system, and therefore, causes ischemic complications (16-21); 2) Hypotension and ischemia related to cardiopulmonary bypass, in addition to reperfusion injury, which develops after surgical correction, can cause tissue damage in the gastrointestinal system (1,22-24).

Another clinically proven complication of cardiopulmonary bypass is an increase in intestinal wall permeability (25-27), while another reason for tissue damage after cardiopulmonary bypass is systemic inflammatory response syndrome (28-30). An increase in intestinal permeability due to any reason is one of the important factors in necrotizing enterocolitis pathogenesis. We think that all the reasons mentioned above may have taken a role in the etiology of the gastrointestinal system complications encountered in our patients.

Despite identification of the risk factors, the nature of the gastrointestinal complications varies and the precise etiology is unclear. They may arise de novo or due to preexisting gastrointestinal disorders, visceral hypoperfusion, and free radical-mediated reperfusion injury. Another important factor may be the use of cardiopulmonary bypass using non-pulsatile flow, which is associated with the development of a gastric mucosal acidosis and may have implications for the development of postoperative complications.

One parameter in our study was different from the literature data: the number of coexisting congenital cardiovascular abnormalities per patient. According to our results, the patients with gastrointestinal system complications in both groups had at least three abnormalities, and thus the number of coexistent congenital cardiovascular abnormalities of a newborn is di-

rectly proportional to the risk of gastrointestinal system complications. It is also a negative prognostic indicator. Twenty-one patients had non-complex cardiac anomaly (ASD; Atrial septal defect, PDA; Patent ductus arteriosus), and the rest had complex cardiac malformation. The distribution of the patients according to the type of cardiac vascular abnormalities is summarized in Tables 3 and 6.

Gastrointestinal system complications are not uncommon in patients with congenital cardiovascular abnormalities. Although it was not statistically significant in our study, mortality was higher in patients who underwent laparotomy for gastrointestinal system complications than in patients who were medically managed. Gastrointestinal system complication and mortality rates were higher in cyanotic congenital cardiovascular abnormalities patients than in the patients who had acyanotic congenital cardiovascular abnormalities. Furthermore, cardiopulmonary bypass and aortic clamping times were significantly prolonged in patients who developed gastrointestinal complications. A number of predictive factors contribute to the development of gastrointestinal complications after cardiopulmonary bypass surgery. Knowledge of these factors may lead to earlier identification of patients at increased risk, and may allow more efficient and earlier interventions to reduce mortality. In centers where congenital cardiovascular abnormalities surgery is performed, a multidisciplinary approach and cooperation with pediatric surgeons contribute to early and appropriate detection and treatment of gastrointestinal complications.

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