

The Effects of Cardiopulmonary Bypass on Intestinal Absorption

KARDİYOPULMONER BY-PASS'IN İNTESTİNAL ABSORPSİYON ÜZERİNDEKİ ETKİLERİ

Ahmet SARITAŞ*, Ülkü SARITAŞ*, Şeref KÜÇÜKER*, Onurcan TARCAN*, Ahmet AKGÜL*, Oğuz TAŞDEMİR*

*Cardiovascular Surgery Clinic, Türkiye Yüksek İhtisas Hospital, Ankara, TURKEY

Summary

Objective: Following cardiac operations gastrointestinal complications are observed at a rate of %0.4-2.1 and their mortality is reported to be as high as %13-67. In this prospective study, the effect of cardiopulmonary bypass (CPB) procedure on intestinal absorption is investigated on 44 patients.

Method: D-Xylose solution, that is containing 25 gr. D-Xylose in 100 ml of water was given to the patients; and D-Xylose levels were measured in blood sample 2 hours following administration and in urine that was collected for 5 hours. This test was done 2 days before the operation, and on the first hour and third day post-operatively. Patients having second hour blood D-Xylose level below 20 mg/dl and total 5 hours urine D-Xylose level below 5 gr. were regarded as having defective intestinal absorption.

Results: Intestinal absorption was defective in 30 of 44 studied patients (68.18%). Except one all patients blood and urine D-Xylose levels returned to normal levels on third postoperative day. The only patient with defective intestinal absorption on the third postoperative day was lost due to multiorgan failure. Twenty four of the 30 patients with defective intestinal absorption, had abdominal symptoms. There was no statistically significant correlation between absorption defect and age, sex, adjunctive treatment, body weight, cardiac output, hematocrite, intraoperative hypothermia, hypotension, central venous pressure, cardiopulmonary bypass time, cross clamp time and duration of mechanical ventilation. The relation with cardiac index was marginally significant (p=0.0633).

Conclusion: In conclusion, CPB procedure disturbs the intestinal absorption reversibly. This disturbance is more significant among patients low cardiac index and if absorption defect persists, it may cause endotoxemia and multiorgan failure leading to death; as was the case in one of our patients.

Key Words: Gastrointestinal absorption, Cardiopulmonary bypass

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Özet

Amaç: Kalp operasyonları sonrası gastrointestinal komplikasyonların gözlenme oranı %0.4-2.1'dir ve mortaliteleri %13.67 gibi yüksek düzeydedir. Bu prospektif çalışmada kardiyopulmoner bypass'ın (CPB) intestinal absorpsiyon üzerindeki etkisi 44 hastada araştırıldı.

Metod: 100 ml suda 25 gr D-Xyloz içeren, D-Xyloz solüsyonu hastalara verildi; ve 2 saat sonra alınan kan örneklerinde ve 5 saat boyunca toplanan idrarlarında D-Xyloz düzeyleri ölçüldü. Bu test, operasyondan 2 gün önce ve postoperatif birinci ve 3. gün tekrarlandı. 2. saat kan D-Xyloz düzeyi 20 mg/dL'nin altında ve 5 saatlik idrar D-Xyloz değeri 5 gr'ın altında olan hastalarda intestinal absorpsiyon bozukluğu düşünüldü.

Sonuçlar: İntestinal absorpsiyon çalışılan 44 hastanın 30'unda bozuk çıktı (%68.18). Bir hasta dışında tüm hastaların idrar ve kan D-Xyloz düzeyi postoperatif 3.günde normale döndü. İntestinal absorpsiyonu bozuk olan bu hasta postoperatif 3 günde multiorgan yetmezliğine bağlı kaybedildi. Bu 30 hastanın 24'ünde abdominal semptomlar da mevcuttu. Absorpsiyondaki bozukluk ile yaş, cinsiyet, tedavi, vücut ağırlığı, kardiyak debi, hematokrit, intraoperatif hipotermi, hipotansiyon, santral venöz basınç, kardiyopulmoner bypass süresi, kros klemp zamanı ve mekanik ventilasyon süresi ile anlamlı bir istatistikî ilişki mevcut değildi. Kardiyak indeks ile ilişkisi ise anlamlıydı (p=0.0633).

Tartışma: Sonuç olarak, kardiyopulmoner bypass geri dönüşümlü olarak intestinal absorpsiyonu bozmaktadır. Bu durum, düşük kardiyak indeksli hastalarda daha da anlamlıdır ve eğer bir hastamızda olduğu gibi absorpsiyon defekti kalıcı olursa, endoksemi ve multi organ yetmezliğine yol açarak hastanın kaybına neden olur.

Anahtar Kelimeler: Gastrointestinal absorpsiyon, Kardiyopulmoner bypass

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The annual number of open heart surgery cases increases every day and with the advances in cardiac surgical techniques mortality and morbidity of these operations are decreasing. However gastrointestinal complications (GIC) following

cardiopulmonary bypass (CPB) although rare in occurrence are important cause of fatality. Many studies reported the rate of GIC after cardiac operations to be between %0.4 and %2.1 but with high mortality figures ranging between %13-

%67(1-10). Early diagnosis of these complications is not easy leading to delay in treatment and high mortality become inevitable(3,4), so early diagnosis is utmost importance to decrease the mortality.

Lately gastrointestinal tract (GIT) is thought to be the potential source of cardiotoxic molecules and accused to take an important role in multiorgan failure (11). Hypotension during and after CPB may play a role in low cardiac output syndromes seen following open heart surgery (2). Fiddian-Green and Baker showed that %50 of the subjects having cardiac operations had intramucosal acidosis and mucosal transient ischemic attacks (12). A close relation between the duration of intramucosal acidosis and death following open heart surgery was also documented (2). Intraluminal bacteria and endotoxins may easily penetrate the wall when mucosal permeability is disturbed. It was shown that endotoxemia may develop during CPB. The severity of this is related with CPB and cross clamp times (2,11,13,14). In this study the effects of CPB on intestinal absorption and probable risk factors for malabsorption were studied.

Material and Method

Forty-nine patients undergoing open heart surgery at TYIH Cardiovascular Surgery Clinic were included in this study and joint research was conducted with TYIH Gastroenterology clinic. Informed consent was received from all the patients and the study protocol was approved by the Local Ethics Committee of TYIH hospital, where the study was conducted. Patients who had GI symptoms or disorders, hypotension, diabetes and those who were taking corticosteroids were not included. Thirty eight of the patients were male and 11 were female. Mean age was 62 ± 14.5 years ranging between 26 and 76 years. All patients had coronary artery disease (CAD), and none had previous cardiac operation. Five patients were excluded from the study for difficulties in obeying study protocol. Intestinal absorption was measured via D-Xylose test. Before the operation age, sex, body weight, hemotocrit, additional diseases, cardiac pathology, cardiac output, cardiac index, liver and kidney function tests were recorded. Mean arterial pres-

sure (MAP), mean central venous pressure (CVP), level of hypothermia, CPB time, aortic cross clamp time, blood saturations and pH measurements were recorded during intraoperative period. Following the operation, duration of mechanical ventilation, need of inotropic support, intensive care unit (ICU) and hospital stays were recorded.

D-Xylose test was done as following protocol: 100 ml of solution containing 25 grams of D-Xylose was given to the patients with nasogastric tube or orally when possible, 2 hours later blood samples were taken. Total urine output was collected for 5 hours following D-Xylose administration. This test was first done 48 hours before the operation and repeated at first and 72 hours post-operatively.

Patients whose blood D-Xylose levels were below 20 mg/dl or total urine level below 5 gr. at collected urine for 5 hours were regarded as having disturbed intestinal absorption. All patients had sufficient hydration and normal renal functions. Any relation between disturbed intestinal absorption and the recorded variables were investigated.

Statistical Method

The results were analysed by Fisher's exact test and one way analysis of variance. A probability (p value) less than 0.05 was considered statistically significant.

Surgical Technique

Premedication was given as 10 mg diazepam IM. Induction of anaesthesia was achieved with 30 microgram/kg fentanyl, 0.5 mg/kg diazepam and 0.1 mg/kg pancuronium. Maintenance of anaesthesia was provided with fentanyl and pavulon. Patients were operated with median sternotomy and standard aorto-caval cardiopulmonary bypass techniques.

CPB was achieved with hollow fiber membrane oxygenator with nonpulsatile flow, moderate hypothermia (30-32°C) and hemodilution which keeps hematocrite values at 20-25. At 32°C perfusion pressure was 50-70 mmHg, perfusion flow was 2.2lt/min, arterial CO₂ was 40 mm Hg, PaO₂ was 250-300 mmHg. Alpha-stat pH strategy was

utilised. Myocardial protection was achieved with topical hypothermia and intermittent retrograde cold blood cardioplegia at 20 minutes intervals. Terminal warm blood cardioplegia was also given just before removing the aortic cross clamp. Patients are then transferred to intensive care unit following hemostasis and termination of the procedure.

Patients if hemodynamically and neurologically stable, were extubated at 10-12 hours postoperatively. Oral food intake was started 8 to 10 hours following the extubation with liquids and soft foods. Patients usually stayed in the intensive care unit 24-48 hours. Second generation cephalosporines were used as prophylaxis for the ICU stay period.

Results

Of the 44 patients, 30 had disturbed intestinal absorption at first postoperative hour (%68.18) according to urine and blood D-Xylose levels and 29 of them returned to normal levels at 3rd postoperative day. One patient however had sustained absorption disturbance on 3rd postoperative day and this patient was lost due to low cardiac output and multiorgan failure. Of the 30 patients having absorption disturbances at first postoperative hour, 24 have developed abdominal symptoms of varying degree during their intensive care unit follow-up (Table 1).

Preoperative parameters of the patients with and without absorption disturbances are given in Table 2. There was no statistically significant difference between the two groups about the preoperative parameters of age, sex, body weight, cardiac output, and associated diseases. There was marginally significant relation between intestinal absorption and cardiac index.

Intraoperative parameters as arterial pressure, aortic cross clamp time, total perfusion time, degree of hypothermia, central venous pressure and medications used had no effect on intestinal absorption (Table 3).

There was no significant difference between disturbed and normal intestinal absorption groups

Table 1. Postoperative Gastrointestinal Symptoms Observed in Disturbed D-Xylose absorption Group (n=30)

Nausea	17
Vomiting	8
Abdominal pain	21
Diarrhea	1
Constipation	7
Distortion	2

Table 2. Preoperative Parameters

	Normal absorption n=14	Disturbed absorption n=30	P value
Age	62.64±14.35	59.42±14.70	NS
Sex (F/M)	6/8	13/17	NS
Body weight (kg)	58.07±17.38	64.43±12.55	NS
Cardiac output	5.49±0.7	5.44±0.7	NS
Cardiac index	3.6±0.36	3.33±0.44	p=0.06
Hematocrit	44±7.6	43±4.6	NS

Abbreviation: NS=not significant.

regarding mechanical ventilation duration, intensive care unit stay, use of inotropic agents, postoperative hospital stay and other complications (Table 4).

Twenty four of the 30 patients having absorption disturbances at first postoperative hour developed abdominal symptoms, most frequently abdominal pain and nausea (Table 1).

Discussion

Although gastrointestinal complications are rare following cardiac operations under CPB (%0.4-2.1) mortality rates of these complications are high (%13-67) (1,4,7-9,15-17). Most important reason for GI complications following cardiac operations is organ hypoperfusion. Extended CPB time is an important risk factor for postoperative GI complications (1,8,10).

Low cardiac output, hypotension due to bleeding, vasopressor agent infusion, intraaortic balloon

Table 3. Intraoperative Parameters of the Groups

	Normal D-Xylose absorption (n=14)	Disturbed D-Xylose absorption (n=30)	P value
CVP	4.35±3.1	3.01±1.9	p=0.0941
Mean Arterial Pressure	67.14±10.1	68.27±9.45	NS
Cardiopulmoner bypass time	85.93±37.35	74.86±37.24	NS
Aortic cross-clamp time	52.6±30.52	48.2±28.08	NS
Degree of hypothermia (°C)	29.57±1.55	29.8±2.42	NS
Adjuvent therapies			
Hydromorphin	11	26	NS
Dopamin-Dobutrex	7	13	NS
Corticosteroids	2	4	NS
Norepinefrin	1	4	NS
Fentanyl	7	17	NS

Abbreviations: CVP central venous pressure, NS not significant.

Table 4. Postoperative Parameters

	Normal Absorption (n=14)	Disturbed absorption (n=30)	P value
Mechanical ventilation (hrs)	13.35±3.36	13.66±2.69	NS
ICU (days)	2.5±1.39	2.5±2.16	NS
Hospital (days)	8.2±5.08	9.9±11.09	NS
Hemotocrite	30.3±4.3	29.4±3.4	NS
Inotropic support requirement	7	13	
Complications			
Bleeding	1	-	
Tamponade	-	1	

Abbreviations: ICU intensive care unit, NS not significant

pump (IABP) usage, may all reduce blood flow in the splanchnic vascular bed and this ischemia may lead to GI complications following cardiac surgery (1,8,10,17,18).

Developments in the cardiac surgical techniques and CPB gradually reduced operative mortality and morbidity of cardiac surgery. Initial physiologic cardiac output of 3.5-5.0 l/min is reduced to 2.4 l/min with the initiation of normothermic CPB. Systemic response to this situation is as in hypovolemic shock. To hold the blood pressure above 30-50 mmHg flow is shifted to vital organs such as brain (2,19). Renal hypoperfusion developing due to low blood flow during CPB results in activation of renin-angiotensin mecha-

nism. Angiotensin II which is a powerful systemic and mesenteric arterial vasoconstrictor agent is elevated during and after CPB (19-22).

Measurements made with laser doppler flowmeter showed %20 and %46 reduction in hepatic and gastric mucosal flows respectively during hypothermic CPB (19,22). The most affected site of intestines of this hypoperfusion during hypothermia CPB is the apical parts of villi which has the major role in absorption (2,19). Hypothermic CPB may also lead to villus atrophy due to hypoxia. Therefore just after CPB important reduction in intestinal transcellular transport of monosaccharides occurs and intestinal permeability increases. Many studies have demonstrated signifi-

cant dysfunction in transcellular transport and increase in permeability due to splanchnic ischemia (2,19-21). As Anderson, Roche et al demonstrated that the main reason for endotoxemia is bacterial translocation resulting from increased intestinal permeability (10,11,13,14).

Ohri et al defined intestinal hypoperfusion and monosaccharide malabsorption during postoperative period following CABG surgery under CPB and showed that all parameters returned to normal on postoperative 5th day (19). Same group in another study demonstrated that in patients with more than 100 minutes of CPB intestinal permeability was significantly disturbed and this situation was reversible and was due to intestinal mucosal hypoperfusion (2).

In our study, cardiac surgery with cardiopulmonary bypass have resulted with absorption disturbances in 30 patients (68,18%). However in 29 patients, absorption returned to normal in three days. In one case (2,27%) however absorption disturbance persisted, this case was lost due to multiorgan failure and sepsis.

During CPB even when hemodynamic parameters were held on universally accepted limits there occurs an intestinal hypoperfusion which is even more aggravated with intestinal hypothermia (19). In our study group there was statistically significant relation between intestinal absorption disturbances and CI with univariate analyses.

Whatever the risk factors may be, this study nevertheless demonstrates that CPB disturbs intestinal absorption significantly but reversibly. Oral drug therapy or oral nutrition during early postoperative period must therefore be carefully considered. In 1 to 2 % of cases absorption disturbances may be irreversible and the clinical course of these patients is fatal. Therefore all hemodynamic parameters must be carefully followed up during early postoperative period and necessary manipulations must be made to prevent fatal complications.

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Yazışma Adresi: Dr. Ahmet SARITAŞ

Türkiye Yüksek İhtisas Hastanesi
Kardiyovasküler Cerrahi Kliniği
06100, Sıhhiye, ANKARA