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The effects of pulsatile flow characteristics on hemolysis, transfusion requirement, and hemostasis in open heart surgeries

Açık kalp ameliyatlarında pulsatil akım karakteristiklerinin hemoliz, transfüzyon gerekliliği ve hemostaz üzerindeki etkileri

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Background: The aim of this study was to investigate the effects of pulsatile and nonpulsatile perfusion on hemolysis parameters and protection of blood components.

Methods: This randomized, controlled and prospectively designed study included two independent groups, consisting of 27 nonpulsatile (NP) and 24 pulsatile (P) cases who had undergone open heart surgical procedures. Demographic and hemodynamic data were recorded. The effects of perfusion types were evaluated in terms of free hemoglobin (free Hb), haptoglobin (Hp), lactate dehydrogenase (LDH), potassium (K^+), platelet number (plt) and urine Hb. These levels were measured in preoperative period, 30 and 60 minutes after initiation of cardiopulmonary bypass (CPB), two and 24 hours postoperatively. Also, total chest drainage and transfusion requirement were assessed.

Results: Demographic and hemodynamic measurements did not differ between the groups. The mean arterial pressure of the NP group was statistically higher at the 30th minute. Free Hb, Hp, LDH and K^+ levels did not differ in both groups in all time points. The urine Hb levels were significantly higher in the P group in the 30th minute. There was no difference regarding total chest drainage amounts and number of transfused erythrocyte cell packages.

Conclusion: A clinically nonsignificant hemolytic effect of pulsatile perfusion can be outlined, although it is mentioned only in the urine Hb measurements on the laboratory basis.

Key words: Cardiopulmonary bypass; hemolysis; pulsatility.

Amaç: Bu çalışmanın amacı, pulsatil ve pulsatil olmayan perfüzyonun hemoliz parametreleri ve kan komponentlerinin korunması üzerindeki etkilerini araştırmaktır.

Çalışma planı: Randomize kontrollü ve prospektif olarak tasarlanmış bu çalışmaya, açık kalp ameliyatı yapılan 27 pulsatil olmayan (NP) ve 24 pulsatil (P) olgudan oluşan iki bağımsız grup dahil edildi. Demografik ve hemodinamik veriler kaydedildi. Perfüzyon türlerinin etkisi serbest hemoglobin (serbest Hb), haptoglobin (Hp), laktat dehidrogenaz (LDH), potasyum (K^+), trombosit sayısı (plt) ve idrarda Hb açısından değerlendirildi. Bu düzeyler ameliyat öncesinde, kardiyopulmoner baypas (KPB) başlatıldıktan sonra 30. ve 60. dakikalarda ve ameliyat sonrasında iki ve 24. saatte ölçüldü. Ayrıca total göğüs drenajı ve transfüzyon gerekliliği de değerlendirildi.

Bulgular: Demografik ve hemodinamik ölçümler gruplar arasında farklı değildi. NP grubunun ortalama arteriyel basıncı, 30. dakikada istatistiksel olarak yüksekti. Serbest Hb, Hp, LDH ve K^+ düzeyleri tüm zaman noktalarında iki grup arasında da farklı değildi. İdrar Hb düzeyleri, 30. dakikada P grubunda anlamlı düzeyde yüksekti. Total göğüs drenaj miktarları ve transfüze edilen eritrosit hücre paketlerinin sayısı açısından bir farka rastlanmadı.

Sonuç: Laboratuvar esaslı ölçümlerde yalnızca idrarda Hb ölçümü açısından fark olsa da, pulsatil perfüzyonun klinik açıdan anlamlı olmayan hemolitik etkisinden söz edilebilir.

Anahtar sözcükler: Kardiyopulmoner baypas; hemoliz; pulsatilite.

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While performing the cardiopulmonary bypass (CPB) technique in open heart surgery, flow characteristics can be either pulsatile or nonpulsatile. Generally, the nonpulsatile version of flow is used in CPB modes. Alternatively, pulsatile perfusion techniques have been developed as a physiological variation for the human body. Pulsatile flow techniques can enhance the tissue perfusion and oxygen consumption, supplying a more physiological flow character to organ systems. Although many advantageous effects have been reported in various papers, the pulsatile method has not gained satisfactory widespread usage. An important factor may be the presence of studies claiming different disadvantageous effects of pulsatile perfusion. The most widely accepted of these pertains to hemolysis. In this study, we investigated the effects of pulsatile and nonpulsatile perfusion on hemolysis parameters, protection of blood components, transfusion requirement, and hemostasis.

PATIENTS AND METHODS

This was a randomized, controlled, prospective study consisting of two different groups, one with 27 nonpulsatile cases and the other with 24 pulsatile cases, who had undergone open heart surgical procedures in our institution. The effects of perfusion types were evaluated in terms of free hemoglobin (Hb), haptoglobin (Hp), lactate dehydrogenase (LDH), potassium (K^+), platelet number (plt), urine Hb, total chest drainage, and transfusion requirement.

Consent: After informed consent and approval from the local ethics committee, 51 adult patients undergoing elective, first-time coronary artery bypass grafting (CABG) were randomly assigned either to the control or the study group. Exclusion criteria included anemia along with cerebrovascular and chronic renal diseases.

Patient population and operation: The study included 51 patients who underwent open heart procedures between February and May of 2010. Twenty-seven of the patients comprised the control (nonpulsatile; NP) group while the other 24 made up the study (pulsatile; P) group. The two groups were comparable in gender, age, body mass index (BMI), duration of CPB, and aortic cross-clamp (ACC) periods. The patient characteristics and general data are shown in Table 1. Methods of cannulation, surgery, and anesthetic techniques did not differ for the two groups during the study period. Arterial and central venous in addition to rectal and esophageal temperature and urine output were monitored throughout the operation. After a standard midline sternotomy, aortic and bicaval cannulation were done.

Cardiopulmonary bypass: The pump circuit consisted of an oxygenator (Dideco EVO, Mirandola, Italy) with a 40 µm arterial line filter (Dideco D734, Mirandola, Italy) and a roller pump (Stockert S5 D-80939, Munchen, Germany). A Ringer solution constituted the main substance of the prime solution. The prime volume of the CPB circuit was 1200-1350 mL. If the estimated hematocrit level was less than 2%, packed blood cells were added to the circuit. The flow rates were maintained between 1.2 and 2.4 L/m^2/min, depending on the weight. Myocardial preservation was achieved with an

Table 1. Demographic and perioperative parameters

Parameters	NP group			P group			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age			64.04±9.94			60.42±14.28	0.294
Gender							
Male	20	74		10	42		0.242
Female	7	26		14	58		
Body Mass Index			27.88±3.51			29.03±4.11	0.289
Cardiopulmonary bypass time			106.00±36.41			93.13±30.23	0.179
Aortic cross-clamping time			59.44±22.02			57.33±23.51	0.742
Temperature at 30’			31.49±1.43			31.46±1.40	0.94
Temperature at 60’			32.84±2.39			32.82±2.77	0.979
Flow index at 30’			2.31±0.43			2.50±0.25	0.065
Flow index at 60’			2.41±0.30			2.52±0.42	0.111
Mean AP at 30’			64.93±8.94			56.29±5.56	0.000
Mean AP at 60’			63.96±9.60			60.41±8.05	0.162
Δ Systolic-diastolic AP at 30’			6.22±5.7			17.71±9.49	0.000
Δ Systolic-diastolic AP at 60’			6.89±7.5			17.46±11.42	0.000

NP: Nonpulsatile; P: Pulsatile; AP: ’ Minute; Arterial presssure; Numerical data have been described as arythmetical mean ± standard deviation (SD).

intermittent cold sanguineous crystalloid cardioplegic solution during ACC. Circulatory arrest was not used.

Pulsatility: As usual, the CPB was started in the nonpulsatile mode, but in the P group, the flow transformed to the pulsatile type during the ACC period. After termination of the cross-clamp, flow gained its nonpulsatile character again. Body temperature, flow index, mean arterial pressure and systolic-diastolic pressure difference were all recorded.

Parameters: The following variables were noted and compared in both groups: Free Hb, Hp, LDH, K^+, Plt, uHb. These parameters were documented in five different periods: the preoperative period, 30 and 60 minutes after initiating CPB, and at 2 and 24 hours postoperatively. Additionally, total chest drainage and number of transfused erythrocyte cell packages were recorded.

Data analysis

The statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS) for Windows, release 10.1 Student version (SPSS Inc., Chicago, IL, USA). Student's t-test was used for comparing both independent groups. The probability (p) of less than 0.05 was considered significant, and all p values were two-tailed. The results in the text and in the tables were expressed as arithmetical mean + standard deviation.

RESULTS

Patient population and operation: There was no statistically significant difference between the groups in terms of demographic and perioperative data regarding the perfusion parameters. The two groups were comparable in gender, age, BMI, CPB, and ACC periods (Table 1).

Hemodynamic variations: Body temperatures at the 30th and 60th minutes of perfusion did not differ between the groups. Though the difference was insignificant, the flow indexes at 30 and 60 minutes were higher in the P group. The mean arterial pressure of the NP group was statistically higher than the P group at the 30th minute of perfusion (64.9±8.9 versus 56.3±5.6 mmHg). There was no difference at the 60th minute. The pressure differences between systolic and diastolic levels were recorded at the 30 and 60th minutes, and in both groups, the value was significantly higher in the P group (roughly 17 versus 6 mmHg). This is an expected outcome of the pulsatility (Table 1).

Parameters: The biochemical parameters and the platelet numbers were measured during five different periods and demonstrated in Table 2. Regarding the free Hb levels, the results in these time periods were not statistically different. Also, the Hp, LDH, and K^+ levels did not differ in either group in any of these periods. The preoperative mean platelet number value of the P group was lower than in the NP group (189.670 versus 236.960; p=0.038). In the 30 and 60th minutes of the perfusion period, the mean platelet counts were lower in the P group, but the difference did not reach a significant degree, and the other mean values were not different. The urine Hb levels were significantly higher in the P group in the 30th minute of CPB when compared with the NP cases (41.07±86.7 versus 3.86±13.2; p=0.032). Though insignificant, this parameter was also higher in the 60th minute and in the postoperative measurements. There was no difference regarding total chest drainage amounts (974.07±453.8 versus 987.5±573.2 ml) and number of transfused erythrocyte cell packages (3.63±2.45 versus 3.38±2.41) between the groups.

DISCUSSION

The advantages and disadvantages of pulsatility have previously been discussed in various papers. Most results address the favorable effects of the pulsatile version in CPB circuits. Pulsatile circulation has inhibitory effects on cytokine activity, diminishes edema in pulmonary alveoli, and limits endothelial damage. In addition, it has benefial effects on the catecholamine level, renal function, and peripheral circulation.[1] The use of pulsatile perfusion has also been thought to improve microcirculatory flow, myocardial perfusion,[2] oxygenation, and indices of contractility.[3-5] It has also been demonstrated to reduce the commonly seen rise in systemic vascular resistance during CPB by maintaining a normal level of plasma angiotensin, aldosterone,[6] and catecholamines.[7,8] We previously published two papers investigating the effects of pulsatile perfusion on the endocrine system in our institution. In one of them, a more physiological endocrinologic equilibrium was noticed in the pulsatile group.[9] In the second one, more stable glucose levels and a lesser insulin requirement were detected in the diabetic patient group, showing the benefit of pulsatile perfusion.[10] In our current study, though the difference was insignificant, the flow index at 30 and 60 minutes was higher in the P group. The mean arterial pressure of the P group was statistically lower than the NP group at the 30th minute of perfusion. These findings can be related to the lower systemic vascular resistance levels that can be maintained during pulsatile perfusion. The systolic-diastolic pressure differences were significantly higher in the P group (roughly 17 versus 6 mmHg). This is an expected outcome of pulsatile flow; hence, the pulsatility has to

Table 2. Study parameters

Parameters	NP group Mean±SD	P group Mean±SD	*p*
Free hemoglobine			
Preoperative	13.08±1.5	12.52±1.1	NS
30 minute	11.19±3.3	10.58±1.9	NS
60 minute	10.49±1.5	10.27±1.4	NS
2 hours postoperative	10.44±1.2	11.05±1.3	NS
24 hours postoperative	11.15±1.0	11.53±1.1	NS
Haptoglobin			
Preoperative	19.12±32.7	13.3±47.3	NS
30 minute	66.56±72.0	70.04±99.3	NS
60 minute	68.40±73.5	62.70±65.0	NS
2 hours postoperative	60.44±63.5	46.22±56.2	NS
24 hours postoperative	44.00±57.6	32.46±41.8	NS
Lactate dehydrogenase			
Preoperative	159.26±127.8	239.00±216.1	NS
30 minute	222.67±143.2	218.75±85.3	NS
60 minute	321.81±204.1	264.92±133.2	NS
2 hours postoperative	471.12±427.3	434.58±226.9	NS
24 hours postoperative	492.33±368.4	432.79±277.5	NS
Potassium (K^+)			
Preoperative	4.31±0.5	4.35±0.4	NS
30 minute	4.13±0.7	4.51±0.6	NS
60 minute	4.55±0.8	4.52±1.0	NS
2 hours postoperative	4.61±0.8	4.73±0.8	NS
24 hours postoperative	4.47±0.8	4.62±0.7	NS
Platelet Number (x1000)			
Preoperative	236.96±81.8	189.67±75.6	0.038
30 minute	152.44±74.0	135.46±97.6	NS
60 minute	140.52±47.9	116.58±41.9	NS
2 hours postoperative	127.70±38.5	127.54±96.3	NS
24 hours postoperative	143.26±69.1	126.38±45.8	NS
Urine hemoglobine			
Preoperative	5.57±28.8	12.56±51.5	NS
30 minute	3.86±13.2	41.07±86.7	0.032
60 minute	34.23±82.8	58.75±104.7	NS
2 hours postoperative	29.04±70.7	68.99±110.9	NS
24 hours postoperative	35.64±82.8	74.67±110.4	NS
Total chest drainage	974.07±453.8	987.50±573.2	NS
No. of transfused ECP	3.63±2.45	3.38±2.41	NS

NP: Nonpulsatile; P: Pulsatile; SD: Standard deviation; NS: Nonsignificant; ECP: Erythrocyte cell packages; Numerical data have been described as arythmetical mean ± standard deviation.

be demarcated when this pressure difference exceeds 10 mmHg.

On the other hand, this type of pulsatile usage has not gained enough worldwide approval, despite its positive effects. The main reason for such hesitation may be the existence of documents claiming the hemolytic effects of pulsatility. Hemolysis is a fact in all extracorporeal circuits, as shown in various studies by the increasing levels of plasma-free Hb and decreasing levels of Hp both during and after CPB.[11] In our study, the effects of pulsatile and nonpulsatile perfusion were investigated in terms of various hemolysis parameters, amount of chest drainage, and transfusion requirement.

The first of the hemolysis parameters is Hb, which is the major erythrocyte protein. Measurement of free Hb in serum can be used as one of the markers of hemolysis.[12] One study by Zumbro et al.[13] demonstrated that as a marker of blood trauma, the plasma Hb level was significantly higher in the pulsatile group compared with the group receiving

NP perfusion.[14] On the other hand, this investigation detected no significant difference in platelet levels between the P and NP groups. In our study, the two groups were compared in terms of Hb levels in the preoperative stage, 30 and 60 minutes after initiating of CPB, and at 2 and 24 hours postoperatively. There was no statistically significant difference between the groups within these phases.

Because of the oxidative and toxic properties of the iron-containing heme in Hb, free Hb is bound by the plasma glycoprotein Hp, which is released from the erythrocytes. Haptoglobin is involved in promoting the clearance of plasma Hb.[15] It has a strong affinity to bind Hb and, therefore, inhibits its oxidative activity. The Hp-Hb complex is then removed by the reticuloendothelial system (mostly the spleen and hepatic parenchymal cells). When Hb release increases, the rate of Hp clearance also increases, and the plasma Hp concentration falls.[15] Accordingly, decreased plasma Hp concentration is indicative of increased hemolysis. This parameter is widely used to monitor the intravascular hemolytic processes. Haptoglobin was also measured in our study, and its levels were compared in the five periods. Lower levels were detected for the P group at the 60th minute and in the postoperative measurements, but the difference was not significant between the groups.

Lactate dehydrogenase has long been considered a useful clinical marker of intravascular hemolysis. Its serum levels are mildly elevated in extravascular hemolysis, such as immune hemolytic anemia, but are substantially elevated with intravascular hemolysis, for example thrombotic thrombocytopenic purpura and paroxysmal nocturnal hemoglobinuria.[16] Also, the levels of LDH did not differ between the groups during our study.

Raised K^+, similar to hemolysis, refers to a high level of the electrolyte K^+ that points to an underlying cause of excessive breakdown of red blood cells. Although a slight increase has been noticed in the P group, the difference was not statistically significant between the groups.

The platelet count was significantly higher in the NP group, but this measurement was obtained in the preoperative period. Since the patients were randomly assigned to the groups, this result can be stated as accidental. In the 30th and 60th minutes of the perfusion period, the mean platelet counts were lower in the P group, but the difference did not reach significant levels.

Urine Hb was also measured in our study as one of the hemolytic parameters. Hemoglobinuria is associated with indices of intravascular hemolysis. It occurs only after the plasma binding capacity for Hb has been saturated and free Hb is filtered though the glomeruli. It has been suggested that 0.3-0.6 gr/L free Hb is the renal threshold for hemoglobinuria.[17] In the 30th minute of perfusion, urine Hb was significantly higher in the P group, indicating a hemolytic effect. Though the difference was not significant, the urine Hb levels in the P group were higher throughout the study.

The type of perfusion is not always responsible for the hemolysis. For example, a study has shown that excessive usage of a coronary sucker can be blamed for the hemolysis effect. This is dependent on the CPB time and the type of surgical intervention.[18] Our findings showed that total chest drainage amounts and number of transfused erythrocyte cell packages did not differ between the groups.

In conclusion, the only noteworthy finding of hemolytic effect of pulsatile perfusion can be detected in urine Hb measurements. Other findings indicate a clinically insignificant hemolytic effect of pulsatile perfusion which, therefore, supports the recommendation of the pulsatile version of perfusion during CPB.

Declaration of conflicting interests

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