REVIEW

Hemodilution, kidney dysfunction and cardiac surgery

Hemodiluição, disfunção renal e cirurgia cardíaca

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ABSTRACT

Hemodilution has been used in cardiac surgery to reduce blood viscosity and peripheral vascular resistance, decrease the need for blood transfusions, attenuate the risk of transfusions and diminish systemic inflammatory response syndrome and hospital costs. The lowest hematocrit level during cardiopulmonary bypass has been stated as 20%. However, severe hemodilution in cardiopulmonary bypass for patients undergoing cardiac surgery has been recognized as a risk factor for hospital deaths and reduced long-term survival. The introduction of normothermia restarted the debate about the lowest acceptable hematocrit during cardiopulmonary bypass. The objective of this review is to evaluate hemodilution during cardiac surgery as a risk factor for the development of post-operative acute renal failure.

Keywords: Thoracic surgery; Cardiac surgery procedures; Hemodilution; Renal failure; Hematocrit

RESUMO

A hemodiluição em cirurgia cardíaca tem sido utilizada por reduzir a viscosidade sanguínea e resistência vascular periférica, diminuir a utilização de sangue e derivados, atenuar o risco transfusional e resposta inflamatória sistêmica e, ainda, pela redução do custo hospitalar. O nível de menor hematócrito durante a circulação extracorpórea tem sido estabelecido como ideal em 20%. Entretanto, a hemodiluição durante a circulação extracorpórea em pacientes submetidos à cirurgia cardíaca é fator de risco conhecido para o aumento da mortalidade hospitalar e diminuição da sobrevivência tardia. Com a utilização da normotermia, o debate em torno do menor hematócrito aceitável durante a CEC foi revivido. O objetivo desta revisão é avaliar a importância da hemodiluição durante a cirurgia cardíaca como fator de risco para o desenvolvimento de insuficiência renal aguda no pós-operatório.

Descritores: Cirurgia torácia; Hemodiluição; Insuficiência renal; Hematócrito

INTRODUCTION

Hemodilution in cardiac surgery

The use of crystalloid solutions to reduce blood transfusions in cardiac surgery was introduced by Panico and Neptune, in 1959[1]. Cooley et al., in 1962, reported a hundred consecutive cases of cardiac surgery with hemodilution in cardiopulmonary bypass and improvement in pulmonary, renal and neurological functions were noted[2].

Hemodilution is routinely done in cardiac surgery, a situation that uses cardiopulmonary bypass and reduces metabolism induced by hypothermia. Hemodilution decreases blood viscosity and improves regional blood flow[3-7].

The lowest hematocrit considered ideal during cardiopulmonary bypass is 20%[8]. Nevertheless, hemodilution during cardiopulmonary bypass in patients who undergo cardiac surgery is a well known risk factor to increase in-hospital mortality[9-10] and to decrease survival[11]. With the use of normothermia, the debate around the lowest acceptable hematocrit during cardiopulmonary bypass was reassessed[12-13].

OBJECTIVE

The objective of this article is to evaluate the importance of hemodilution during cardiac surgery as a risk factor for the development of postoperative renal dysfunction after cardiac surgery.

METHODS

Literature review was performed by searching articles on hemodilution and renal dysfunction in cardiac surgery.

Study carried out at Hospital do Servidor Público Estadual "Francisco Morato de Oliveira" – HSPE-FMO, São Paulo (SP), Brazil.

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Strategy to identify the studies

The strategy to retrieve the studies was applied to the databases Medline®, through Pubmed, and Lilacs®, and through Virtual Health Library, up to January 2007.

The strategy was designed based on keywords, synonyms and acronyms for thoracic surgery, renal failure and hematocrit, which proved to be a high-sensitivity and low-specificity filter. No limits regarding date or country of origin were established, thus reducing publication bias. The searching strategy presented was applied to the database Medline® and was modified according to the standards required at the Lilacs® database.

Study selection

Cardiopulmonary bypass has evolved immensely since its beginning. Many factors interfere in the development of renal dysfunction during cardiopulmonary bypass. Some factors, such as the use of crystalloids and/or colloids, bypass temperature, type of oxygenator, heparin-coated circuits, the alpha method or pH stat and the use of centrifugal pumps are variables known to interfere in the degree of renal injury during cardiac surgery[14].

Hence, to conduct the analysis of the results, the studies selected were those which used total hemodilution with crystalloids, with membrane oxygenators and which did not use heparin-coated circuits.

Systematic review and meta-analysis

Meta-analysis was not carried out because only two randomized controlled studies assessing hemodilution during cardiac surgery and renal dysfunction were identified.

RESULTS

The articles identified for analysis enabled identification and analysis of renal dysfunction considering the hematocrit levels defined for the groups and not by the groups, what would be a bias.

Eight articles were identified. Six were observational studies and two randomized controlled trials.

The type of study, temperature during cardiopulmonary bypass, arterial blood flow, target mean arterial blood pressure, are depicted on Table 1. The frequency of acute renal failure (ARF), for each study, is shown on Figure 1.

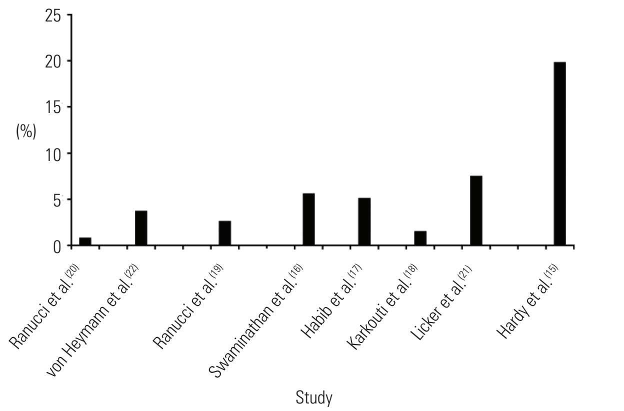


Figure 1. Frequency of acute renal failure in selected studies.

Hardy et al.[15], in an observational study, noticed that post-operative low hemoglobin concentration after cardiac surgery with cardiopulmonary bypass increased kidney and abdominal complications. ARF occurred in 19.8% of patients. When hemoglobin was below 6 g/dl; between 6 and 6.9 g/dl, from 7 to 7.9 g/dl, from 8 to 8.9 g/dl and higher than 8.9 g/dl, ARF occurred in 11.4 %; 6.36 %;

Table 1. Studies found and its characteristics

Author	Year	Type	n	Temperature	Arterial flow	Target MBP
Ranucci et al.[20]	2006	Observational multicenter	n = 1766	Not reported	Not reported	Not reported
von Heymann et al.[22]	2006	Randomized controlled	n = 54	35.5-36 ºC (95.9 -96.8 ºF)	Not reported	55-60 mmHg
Rannucci et al.[19]	2005	Observational	n = 1048	32-34 ºC (89.6-93.2 ºF)	2.0-2.4 L/min/m²	60 mmHg
Habib et al.[17]	2005	Observational	n = 1760	35.5-36 ºC (95.9-96.8 ºF)	2.5-3.0 L/min/m²	Not reported
Karkouti et al.[18]	2005	Observational	n = 9080	34 ºC (93.2 ºF)	2.0-2.4 L/min/m²	50-70 mmHg
Licker et al.[21]	2005	Randomized controlled	n = 80	32-34 ºC (89.6-93.2 ºF)	2.2-2.5 L/min/m²	50-70 mmHg
Swaminathan et al.[16]	2003	Observational	n = 1404	28-34 ºC (82.4-93.2 ºF)	2.0-2.4 L/min/m²	50-70 mmHg
Hardy et al.[15]	1998	Observational	n = 2661	32-34 ºC (89.6-93.2 ºF)	Not reported	Not reported

MBP: mean arterial blood pressure

6.04 %; 3.87 % and 3.54% of patients. There is a bias in the study of Hardy et al., which is the assessment of the lowest hemoglobin concentration during cardiopulmonary bypass and the first postoperative day [15]. Swaminathan et al., in an observational study using multivariate linear regression for the association between lowest hematocrit and serum creatinine variation, in patients who underwent myocardial revascularization with moderate hypothermia and arterial blood flow between 2.0 and 2.4 l/min/m^2, the lowest hematocrit in cardiopulmonary bypass between 22 and 24% was the risk factor for renal dysfunction[16]. Habib et al., in a retrospective study using logistic regression evaluated five thousand patients who were submitted to cardiac surgery under normothermia and arterial blood flow between 2.5 and 3.0 l/min/m^2, and observed that when the lowest hematocrit in cardiopulmonary bypass was lower than 22%, the incidence of ARF was four-fold higher[11]. In a later publication, Habib et al. determined that ARF was more frequent in elderly patients, those with larger body surface area, women, patients with hypertension and/or diabetes, with cardiac failure, those submitted to re-operations, longer cardiopulmonary bypass and anoxia and blood transfusion. They also demonstrated that when the hematocrit was lower than 24% during cardiopulmonary bypass, the risk of developing ARF was higher. When the lowest hematocrit was between 20 and 24%, the risk for ARF was of 1.8 fold higher and when the lowest hematocrit was lower than 20%, the risk for ARF was of 2.45 fold higher[17]. In those studies, the groups were composed of quintiles (one thousand patients in each group). Karkouti et al., in patients who underwent cardiac surgery under mild hypothermia and arterial blood flow between 2.0 and 2.4 l/min/m^2, divided the patients into three groups according to the hematocrit level and each group was assessed by logistic regression. It was noticed that when the lowest hematocrit in cardiopulmonary bypass was between 21 and 25%, the incidence of ARF was lowest, with an odds ratio of 2.34 times in intense hemodilution ($Ht \leq 21\%$) and 1.88 times in mild hemodilution ($Ht > 25\%$)[18]. Ranucci et al. noticed an association between oxygen delivery (OD) and lowest hematocrit level in cardiopulmonary bypass and renal failure. In this study, the lowest hematocrit and renal dysfunction were also assessed. A receiver operating curve (ROC) was prepared and identified that 26% was critical for the development of ARF[19].

In a multicenter retrospective study, Ranucci et al. described that when the lowest hematocrit during cardiopulmonary bypass was lower than 23%, 4.3% of patients needed dialysis. When hematocrit was higher than 23%, 2.1% of patients required dialysis (RR = 1.93, 95% CI = 1.231-3.926, p = 0.011)[20].

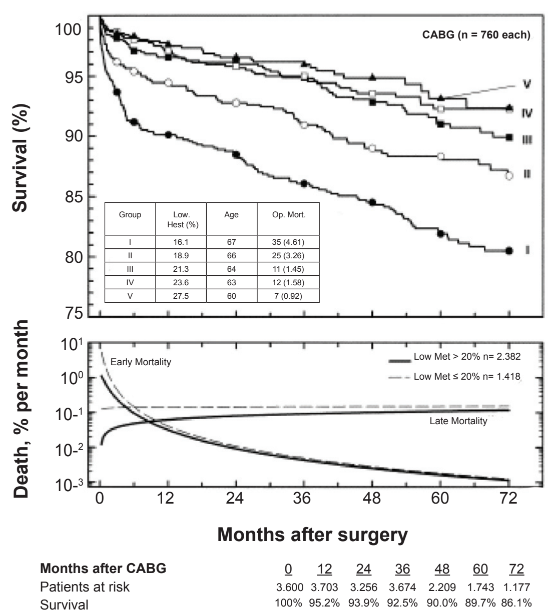
The next two studies were prospective, controlled and randomized. In both investigations the patients were allocated into groups with hematocrit of 20 and 25%.

Licker et al.[21] published a study with 80 patients who were divided into one group of 41 patients with hematocrit of 20% and another group with 39 patients and hematocrit of 25%. Patients with creatinine clearance lower than 20 ml/min were not included in the study. Six (7.5%) patients suffered acute renal failure, three in each group (p = 0.7). Von Heymann et al.[22] also published a study with 54 patients divided into one group with 28 patients with predicted hematocrit of 20% and 26 patients in the group with hematocrit of 25%. Patients with serum creatinine higher than 1.5 mg/dl, renal failure or anuria were not included in the study. Acute renal failure was seen in two patients (3.7%), one from each group (p = 0.99).

DISCUSSION

There is a renewed interest in assessing the importance of hemodilution level during cardiopulmonary bypass as a factor triggering complications and mortality[9-11] in cardiac surgery. Figure 2 depicts the importance of the lowest hematocrit for survival in cardiovascular surgery. Postoperative renal dysfunction after cardiac surgery increases morbidity and mortality[23-25].

A low hematocrit during cardiopulmonary bypass is used as a marker for blood transfusion. Nevertheless, blood is a complex biologic product that triggers systemic inflammatory response and non-specific immune suppression[26-27]. Low hemoglobin



Source: Habib et al.[11]

Figure 2. Months after surgery

concentration reduces oxygen delivery to the tissues and can lead to ischemia and tissue injury. Perioperative anemia in the presence of cardiac disease is a well-known risk factor for mortality[28].

The observational studies presented a significant number of patients who progressed to renal dysfunction due to higher hemodilution level. Nevertheless, Karkouti[18] reports that moderated hemodilution (Ht = 21 to 25 %) is favorable when compared to mild hemodilution (Ht > 25%) or intense hemodilution (Ht < 21%). Prospective randomized controlled studies presented important limitations, such as the small number of patients and the fact that those patients are at low risk for postoperative events[21-22]. The definition of ARF in each study was different, since Licker et al.[21] defined it as an 120% increase in baseline serum creatinine and von Heymann et al.[22] defined ARF as the need for dialysis or a 2.0 mg/dl increase in creatinine.

Pathophysiological mechanisms

The mechanism by which renal dysfunction occurs is not clearly understood. The low oxygen concentration in the hypoxemic environment of the renal medulla[29-30] may worsen due to low hematocrit during cardiopulmonary bypass. The renal blood flow during cardiopulmonary bypass increases with hemodilution, increasing energy consumption used in tubular transportation[31-32]. The reduction of plasma oncotic pressure results in fluid retention in the interstitium, with capillary decrease and lower oxygen delivery to tissues[33]. Kidney susceptibility to hypoperfusion increases vulnerability of the renal medulla to hypoxia with cell injury and renal failure.

Reperfusion injury that happens after renal ischemia causes blood congestion in external renal medulla, hyperemia which is visible micro and macroscopically. Mason et al., in an experimental study in rats, noticed that erythrocyte aggregation occurs without the demonstration of hemostatic mechanisms. The set of aggregated erythrocytes decreases renal perfusion, causing functional and structural defects, with a decrease in renal function[34].

Hellberg et al.[35] demonstrated that erythrocytes aggregation in the renal medulla is associated with decreased renal blood flow. The duration of ischemia increases the intensity of erythrocyte aggregation. When hemodilution is used, a longer period of ischemia is necessary to produce the same extension of renal lesion in relation to normal hematocrit. When the hematocrit is higher, the ischemia time to produce the same extension of medullary congestion is smaller[35-36].

Moderated hemodilution may be a protective factor against renal ischemia during cardiopulmonary bypass in cardiac surgery through the mechanisms herein described.

CONCLUSIONS

The correlation between hemodilution during cardiopulmonary bypass and the development of pos-operative renal failure is well established. Nevertheless, the level of safe hemodilution during cardiopulmonary bypass is a current issue of debate to determine procedure safety during cardiopulmonary bypass.

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