Predonation of autologous blood reduces perioperative allogeneic transfusion requirement in grown-up patients with congenital heart disease

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Abstract

Background: Adults with congenital heart diseases have a substantial risk for bleeding upon re-operations. Due to the detrimental effects of allogeneic blood transfusion, reduction of transfusion requirement is a major concern. To investigate the efficacy of autologous blood predonation (ABP), we focussed on a homogeneous subgroup of patients, with right ventricular outflow tract reconstruction. Methods: Prospectively collected data included 76 patients older than 16 years with repeated right ventricular outflow tract reconstruction from May 1995 to November 2006. In 27 patients, ABP was performed without any complication. Results: Primary diagnoses included Tetralogy of Fallot in 50 patients and others in 26 patients. All patients had at least one previous operation, 62% had more than one. All patients received a homograft conduit between the right ventricle and the pulmonary artery. Preoperative haemoglobin was 123 ± 15 g l⁻¹ in patients with ABP and 134 ± 22 g l⁻¹ in the remainder (p = 0.037), but was not significantly different after cardiopulmonary bypass until discharge from the intensive care unit. Significantly more patients without ABP required transfusion of allogeneic packed red cells (PRCs) (26 of 49 patients (53%) vs 4 of 27 patients (15%), p = 0.001) and allogeneic fresh frozen plasma (FFP) (30 of 49 patients (61%) vs 6 of 27 patients (22%), p = 0.002) than patients with ABP. Of 27 patients, 23 (85%) and 25 (93%) with ABP received their predonated PRC and FFP, respectively. Logistic regression analysis identified no ABP (p = 0.005, odds ratio (OR) 5.4, 95% confidence interval (CI) 1.7–17.7) and time on extracorporeal circulation >83 min (p = 0.009, OR 5.0, 95% CI 1.5–16.8) to be predictive for allogeneic blood transfusion. Conclusion: ABP can be safely performed in grown-up patients with congenital heart disease without complications. Patients without predonation of autologous blood exhibit a fivefold increased risk for requiring allogeneic blood transfusion.

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Keywords: Right ventricular outflow tract; Homograft; Blood donation

1. Introduction

Grown-up patients with congenital heart disease may exhibit an increased risk for bleeding complications upon re-operations [1]. Since most of the initial operations are performed in infancy, the majority of the patients who require surgery in adulthood had already undergone prior operations [2]. Marked adhesions and the presence of collateral arteries are frequent. In addition, haemostatic disorders are common, especially in patients with cyanotic heart defects [3]. Since the detrimental effects of allogeneic blood transfusion are well known, transfusion requirement is a major concern in this potentially increasing patient population [4–6]. Another point of concern in allogeneic blood transfusion is the risk of transfusion-transmitted viral infections [7]. Screening programmes have substantially reduced the risk for clinically well-known infections such as hepatitis C virus (HCV) and human immunodeficiency virus (HIV), but new viruses with parenteral modes of transmission may create new problems in the future. A benefit of autologous blood predonation (ABP) has been shown for elective coronary artery bypass surgery and cardiac valve operations [8–11]. Accordingly, we hypothesised that ABP reduces allogeneic transfusion requirement in adults upon re-operation for congenital heart defects. As far as we know, this has not been shown yet. To investigate the efficacy of ABP, we focussed on a subgroup of patients, who underwent re-operations for right ventricular outflow tract reconstruction.
2. Patients and methods

2.1. Inclusion and exclusion criteria

All patients who were re-operated for reconstruction of the right ventricular to pulmonary artery connection with a homograft between 1995 and 2006 were included into this prospective follow-up study. Children below 16 years at the time of the operation were excluded. Furthermore, patients who underwent concomitant procedures other than pulmonary artery plasty, tricuspid valve plasty and residual ventricular septal defect closure were excluded. The study was approved by the ethics committee of the Technical University Munich.

2.2. Blood predonation

ABP is performed routinely at the department of anaesthesiology for adult patients presenting with congenital and acquired heart disease. Patients presenting with severely impaired functional status (New York Heart functional class III and IV) and patients with low body weight (below 50 kg), were considered unsuitable. Depending on haemoglobin concentration and the time frame until surgery, between one and three donations per patient were obtained. The first predonation sampling was usually performed at 5 weeks, the last predonation not later than 1 week prior to the day of admission for surgery. Target volume of each donation was 480 ml whole blood (maximum 10 ml kg\(^{-1}\) body weight). The removed volume was replaced either by crystalloids or by colloids. The whole blood was processed to 1 unit of packed red cells (PRCs) and 1 unit of fresh frozen plasma (FFP). The products were stored under temperature control in a separate storage unit for autologous blood products (maximum storage time for PRC is 42 days and for FFP 1 year). An oral substitution of 200—300 mg ferric sulphate was requested from registration for ABP until admission for surgery. Identical protocols were applied for postoperative transfusion of autologous or allogeneic blood. The cutoff haemoglobin level for transfusion of autologous or allogeneic blood was 90 g l\(^{-1}\).

2.3. Operative data

All patients were operated through a median sternotomy with cardiopulmonary bypass and moderate hypothermia (32 °C). The pulmonary artery of the homograft was cut just above the valve level and sutured to the main pulmonary artery. The ventricular end of the homograft was sutured to the ventriculotomy. A Dacron patch was used when appropriate. In all patients high-dose aprotinin was administered according to the Hammersmith protocol. Intra-operative cell saving and postoperatively shed mediastinal blood retransfusion was performed.

2.4. Clinical follow-up

The patients were followed up until hospital discharge. Haemoglobin concentration was evaluated at the time of hospital admission, at arrival at the operating room, at 5 min after initiating the extracorporeal circulation, at termination of the extracorporeal circulation, at transfer from the operating room to the intensive care unit, at admission on the intensive care unit, on the first postoperative day and at discharge from the intensive care unit. The cumulative blood loss was recorded at 6, 12 and 24 h, postoperatively. The transfusion requirement stratified by allogeneic PRC, allogeneic FFP, autologous PRC, autologous FFP and concentrated platelets was recorded in units.

2.5. Statistical analysis

Frequencies are given as absolute numbers and percentages. Continuous data are expressed as means and SD or as medians with ranges. Fisher’s exact test was performed to detect significant differences between groups. For comparison of continuous variables between two groups, the t-test was used. Two-tailed tests were used for all analyses. The endpoint allogeneic transfusion requirement was analysed by means of a logistic regression model. Variables with p values <0.1 in univariate analysis for the endpoint allogeneic transfusion requirement, and variables with p values <0.1 for the comparison between the groups with and without ABP were entered into the multivariate model. Statistical analysis was performed using SPSS 16.0.

3. Results

3.1. Study population characteristics

The cohort comprised 76 patients, of whom 27 patients (35%) could be included into the ABP programme. Tetralogy of Fallot was the most common diagnosis in both groups. There were no significant differences in the number of diagnoses between both groups (Table 1). Platelet concentration at the time of hospital admission was lower, and haemoglobin concentration at arrival at the operating room was higher preoperatively in patients without ABP compared with patients with ABP (Table 1). There were no statistically significant differences with regard to sex, New York Heart functional class and body weight between both groups. In patients without ABP, exchange of a previously implanted homograft was more frequent, and significantly more patients required more than 83 min on extracorporeal circulation (median) compared with patients with ABP (Table 1). There were no differences in the number of concomitant procedures between patients with and without ABP. Patients, who did not join the ABP programme, refused to postpone the operation and underwent surgery shortly after diagnostic evaluation.

3.2. Haemoglobin concentration

Haemoglobin concentration was not significantly different from immediately after initiation of cardiopulmonary bypass until discharge from the intensive care unit between the groups with or without ABP (Fig. 1).

3.3. Blood loss

The median blood loss at 6, 12 and 24 h was 245, 310 and 400 ml in patients without ABP, and 170, 270 and 360 ml in patients with ABP, respectively (Fig. 2).
3.4. Transfusion requirement

Significantly more patients without ABP required transfusion of allogeneic PRC (26 of 49 patients (53%) vs 4 of 27 patients (15%), \( p = 0.001 \)) and allogeneic FFP (30 of 49 patients (61%) vs 6 of 27 patients (22%), \( p = 0.002 \)), compared with patients with ABP. There was no statistical difference between both groups with regard to transfusion of concentrated platelets. Of 27 patients, 23 (85%) and 25 (93%) with ABP received their predonated PRC and FFP, respectively.

3.5. Risk factors for allogeneic blood transfusion

The following variables were either significantly different between the groups with and without ABP, and/or significantly associated with allogeneic transfusion requirement (Table 2), and therefore entered into the multivariate model: number of prior operations, preoperative platelet and haemoglobin concentration, homograft exchange, extracorporeal circulation time and no ABP. Logistic regression analysis identified no ABP (\( p = 0.005, \text{ OR } 5.4, 95\% \text{ CI } 1.7—17.7 \)) and time on extracorporeal circulation >83 min (\( p = 0.009, \text{ OR } 5.0, 95\% \text{ CI } 1.5—16.8 \)) to be predictive for allogeneic blood transfusion.

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**Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No autologous blood predonation (( n = 49 ))</th>
<th>Autologous blood predonation (( n = 27 ))</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean patient age (years)</td>
<td>25.7 ± 8.4</td>
<td>25.7 ± 4.5</td>
<td>n.s.</td>
</tr>
<tr>
<td>Gender male (patients)</td>
<td>31 (63%)</td>
<td>16 (59%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean body weight (kg)</td>
<td>66.1 ± 16.6</td>
<td>66.5 ± 14.7</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean haemoglobin concentration at hospital admission (g l(^{-1}))</td>
<td>143 ± 21</td>
<td>137 ± 14</td>
<td>n.s.</td>
</tr>
<tr>
<td>Haemoglobin concentration at arrival in operating room (g l(^{-1}))</td>
<td>134 ± 22</td>
<td>123 ± 15</td>
<td>0.037</td>
</tr>
<tr>
<td>Mean platelet concentration at hospital admission (10(^9) l(^{-1}))</td>
<td>200 ± 66</td>
<td>239 ± 61</td>
<td>0.012</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetralogy of Fallot (patients)</td>
<td>26 (53%)</td>
<td>16 (59%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Pulmonary artery with ventricular septal defect (patients)</td>
<td>6 (12%)</td>
<td>2 (7%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Pulmonary stenosis (patients)</td>
<td>4 (8%)</td>
<td>4 (15%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Common arterial trunk (patients)</td>
<td>4 (8%)</td>
<td>1 (4%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Other (patients)</td>
<td>9 (18%)</td>
<td>4 (15%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>More than one prior operation</td>
<td>36 (73%)</td>
<td>11 (41%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Homograft exchange (patients)</td>
<td>27 (55%)</td>
<td>7 (26%)</td>
<td>0.017</td>
</tr>
<tr>
<td>Pulmonary artery plasty (patients)</td>
<td>6 (12%)</td>
<td>3 (11%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Tricuspid valve plasty (patients)</td>
<td>5 (10%)</td>
<td>4 (15%)</td>
<td>n.s.</td>
</tr>
<tr>
<td>More than 83 min on extracorporeal circulation</td>
<td>29 (59%)</td>
<td>9 (33%)</td>
<td>0.054</td>
</tr>
</tbody>
</table>

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**Fig. 1.** Level of haemoglobin concentration in patients with and without autologous blood predonation at the time of hospital admission (admission), at arrival at the operating room (arrival OR), at 5 min after initiating the extracorporeal circulation (5 min ECC), at termination of the extracorporeal circulation (after ECC), at transfer from the operating room to the intensive care unit (transfer OR), at admission on the intensive care unit (admission ICU), on the first postoperative day (1st day), and at discharge from the intensive care unit (discharge ICU). The median is depicted by the horizontal line in the box, the interquartile range is represented by the box, and the range is indicated by the vertical line.

**Fig. 2.** Blood loss within the first 24 h postoperatively in patients with and without autologous blood predonation. The median is depicted by the horizontal line in the box, the interquartile range is represented by the box, and the range is indicated by the vertical line.
CI, confidence interval; OR, odds ratio.

Table 2
Risk factors for allogeneic blood transfusion.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No allogenic</td>
<td>Allogenic</td>
</tr>
<tr>
<td></td>
<td>transfusion</td>
<td>transfusion</td>
</tr>
<tr>
<td>More than one prior operation</td>
<td>12 (41%)</td>
<td>35 (74%)</td>
</tr>
<tr>
<td>Platelet concentration at hospital admission</td>
<td>230 ± 43</td>
<td>204 ± 77</td>
</tr>
<tr>
<td>Haemoglobin concentration at arrival in operating room</td>
<td>128 ± 18</td>
<td>131 ± 22</td>
</tr>
<tr>
<td>Homograft exchange</td>
<td>8 (28%)</td>
<td>26 (55%)</td>
</tr>
<tr>
<td>More than 83 min on extracorporeal circulation</td>
<td>7 (24%)</td>
<td>31 (65%)</td>
</tr>
<tr>
<td>No autologous blood predonation</td>
<td>10 (34%)</td>
<td>39 (83%)</td>
</tr>
</tbody>
</table>

3.6. Clinical outcome

The median stay on the intensive care unit and in the hospital was 4 days and 17 days, respectively; without a significant difference between the groups with and without ABP. Significantly more patients without APB (22 of 32 patients, 69%) required more than 7 h of mechanical ventilatory support (median) compared with patients without APB (7 of 26 patients, 27%, p = 0.003). Two patients died during hospital admittance. Both patients did not perform APB. There was no statistical difference with regard to hospital mortality between both groups.

4. Discussion

The reduction of allogeneic blood consumption in patients who require repeat cardiac operations for congenital heart defects may be beneficial for several reasons. Transfusion-transmitted diseases, namely viral infections such as HIV or hepatitis virus or emerging virus, and the resulting social and economic costs can be prevented [5]. Furthermore, the incidence of postoperative complications, such as infections and pulmonary dysfunction may be reduced [4,6]. Since the demographic trends suggest that future blood demand is increasing, reduction of allogeneic blood consumption may help to prevent blood shortages [12]. Finally, the immune function of the transfusion recipient is altered by transfusion of allogeneic blood [13] leading to the production of antibodies. Hence, especially in patients who require frequent re-operations and blood transfusions, the supply of compatible allogeneic blood is an increasing problem.

In this comparative study of adult patients who underwent re-operations of the right ventricle to pulmonary artery connection, we could demonstrate that patients who performed ABP exhibited a fivefold lower risk for requiring allogeneic blood transfusion. Blood predonation could be performed without complications, and the wastage rate of autologous blood was as low as 15% for PRC and 7% for FFP.

The key finding of the present analysis, the fivefold lower risk for requiring allogeneic blood transfusion in patients who performed ABP, must be discussed with regard to the significant differences between both groups. As one might expect, patients who performed ABP presented with a lower preoperative haemoglobin concentration compared with the remaining patients. Interestingly, the preoperative platelet concentration was higher in patients with ABP compared with the remaining patients. We speculate that repeated blood withdrawal might trigger an increase of platelet proliferation. The increase of platelet proliferation has been attributed to the effects of endogenous erythropoietin by Stohlwet et al. [14]. Patients, who did not perform ABP, had undergone more prior operations. They underwent more frequently a homograft exchange, and the time on the extracorporeal circulation was longer than for the remaining patients. Consequently, longer time on the extracorporeal circulation emerged as the second independent risk factor for allogeneic transfusion requirement in multivariate analysis.

Besides these differences in the potentially influencing factors for allogeneic transfusion requirement between both groups, it is of note that the underlying diagnoses and the number of concomitant procedures did not differ significantly. In addition, there were no statistical differences between both groups with regard to the exclusion criteria for the ABP programme, low body weight and impaired functional status. All patients, who did not undergo the ABP programme, would have been eligible for ABP. However, they refused to postpone the operation for 2 months and underwent surgery shortly after diagnostic evaluation.

The safety of ABP has been shown predominantly in the context of orthopaedic surgery [15,16]. Young adults without any concomitant diseases are regarded as the ideal candidates for ABP. However, there is concern whether patients who exhibit congenital heart disease are just as well suitable as patients scheduled for orthopaedic surgery. By respecting two simple exclusion criteria — severely impaired functional status and low body weight — we did not observe any adverse events in the patients who were included in the ABP programme.

The efficacy of ABP was high in the present study population. Re-transfusion of autologous PRC and of FFP was performed in 85% and in 93% of the patients, respectively. These results compare favourably with the ABP programmes used in orthopaedic surgery. The low wastage rate of autologous blood in the present study was not attributed to excessive transfusion of autologous blood since the haemoglobin concentration at six different times was not significantly higher in patients with ABP compared with the remainder. Hence, an efficient programme of ABP is a cost-effective alternative to reduce allogeneic blood consumption [8].

In conclusion, ABP can be performed in grown-up patients with congenital heart disease without complications. Allogeneic transfusion requirement is determined by a longer time on extracorporeal circulation. However, a fivefold reduction of allogeneic transfusion requirement can be
References


Appendix A. Conference discussion

Dr J. Aramendi (Barakaldo, Spain): Those who are involved with grown-up patients more frequently see many tetralogy patients requiring operation on the outflow tract, and this operation can be achieved nowadays with low mortality and excellent results. And the main complication is bleeding and the need for transfusion.

Therefore, we all should be open-minded regarding new strategies to help reduce the need for transfusions. And you have achieved excellent results, a fivefold reduction in the need for donor blood.

This is a difficult study design to pursue such a long recruitment time, 11 years.

I have three questions. First, the control group is twice as large as the actual treatment group. And being those groups are equivalent in weight and size, which is the reason we would have expected a more even distribution in both groups of patients.

Second, the control group also shows a much larger pump time; therefore, I assume that those were more complex cases. So this may be a confounding factor, for those patients with a longer pump time often bleed more regardless of using autotransfusion or not.

And finally, what is your present policy for autotransfusion? Are you opening the indication to any grown-up patient?

Dr Horer: All patients, including those who did not perform autologous predonation, were suitable for this program. They refused to join the autologous predonation program because they didn’t want to delay surgery. The need for autologous predonation is performed six weeks prior to surgery, and those patients chose to stay at the hospital and to undergo surgery a few days after admittance.

The second question, yes, there were statistical significant differences between the groups. Patients who did not perform autologous predonation more frequently underwent an autograft exchange, and therefore the bypass time was longer.

To correct the analysis to those statistically significant differences between the groups, we included these parameters in the multivariate analysis. Allograft exchange was no risk factor for requiring allogenetic transfusions; however, the complexity of the operation was a risk factor because longer bypass time was a risk factor for requiring allogenetic transfusions.

And your last question, we apply this protocol to all our GUCH patients. All patients who require surgery are asked to present at our outpatient clinic of the Institute for anaesthesiology to perform autologous blood predonation.

We have two simple exclusion criteria. One of them is New York Heart Functional Class above III, and the other is low body weight.