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A series of 23 consecutive neonates undergoing the arterial switch operation with and without blood transfusions: A pilot study on the impact of transfusions on clinical outcome

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Результаты 23 операций у новорожденных по артериальному переключению с применением переливания крови и без него: пилотное исследование о влиянии транфузий на клинический исход болезни

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The detrimental impact of blood transfusions on the outcome of patients is increasingly being appreciated. Miniaturized cardiopulmonary bypass systems facilitate transfusion free cardiac surgery even in neonates. We assessed the possible impact of transfusions on the duration of ventilation and of stay on the intensive care unit in a series of neonates undergoing the arterial switch operation at our institution. Charts of 23 consecutive patients diagnosed for transposition of the great arteries without concomitant cardiac malformations who underwent the arterial switch operation at our institution in an 18 month period after the implementation of a new miniaturized cardiopulmonary bypass circuit were studied. Patients were divided into three groups: group I consisted of patients without any transfusions, group 2 patients who underwent the intra-operative period without transfusions but received transfusions postoperatively and group III patients with intra-operative transfusions. There were 4 patients in group I, 7 patients in group II and 12 patients in group III. .All patients had an uneventful clinical course. Patients of group I had significantly shorter duration of mechanical ventilation and stay on the intensive care unit than those in the other groups. There was no significant difference between group II and group III in this regard. Avoidance of any transfusions in neonates undergoing complex cardiac surgery with cardiopulmonary bypass appears to reduce duration of ventilation and length of stay on the intensive care unit, while the timing of the transfusion has no impact on these outcomes.
Key words: transfusion, cardiopulmonary bypass, congenital heart disease

В настоящее время большое внимания уделяется проблеме неблагоприятного влияния переливания крови на исход болезни у пациентов. Применение миниатюрных систем искусственного кровообращения обеспечивает проведение кардиохирургических операций без использования переливания крови даже у новорожденных пациентов. Мы проанализировали фактор влияния переливания крови на продолжительность вентиляции и длительность нахождения пациента в отделении интенсивной терапии на примере целого ряда новорожденных пациентов, которым была сделана операция артериального переключения в нашем лечебном учреждении. Нами были исследованы данные 23 пациентов с диагнозом «транспозиция магистральных артерий без сопутствующего порока сердца», которые были прооперированы в нашем кардиоцентре. Исследование проводилось на протяжении 18 месяцев с момента установки новой миниатюрной системы искусственного кровообращения. Пациенты были выделены в 3 группы. В первую группу вошли пациенты, которым не проводилось переливание крови. Вторую группу составили пациенты, которым переливание крови было проведено после операции. В третьей группе были пациенты, которым проводилось переливание крови во время операции. В первой группе наблюдалось 4 пациента, во второй – 7, а в третьей -12 пациентов. У всех пациентов курс лечения протекал без каких-либо осложнений. У пациентов первой группы показатель продолжительности механической вентиляции и длительности пребывания в отделении интенсивной терапии был значительно ниже, чем у пациентов в двух других группах. Существенных различий по показателю такого плана между пациентами второй и третьей группы не зафиксировано. Отказ от переливания крови у новорожденных, которым проводилась комплексная кардиохирургическая операция с применением системы искусственного кровообращения, как установлено, снижает показатель продолжительности вентиляции и длительности пребывания в отделении интенсивной терапии. Проведение переливания крови не приводит к получению таких показателей.
Ключевые слова: трансфузия, кардиопульмональное шунтирование, врожденный порок сердца

In recent years, increasing evidence has been accumulated that suggests a detrimental effect of the transfusion of autologous blood products on the outcome of patients undergoing cardiac surgery [1;2]. Additionally, strong data suggest that not only the fact that autologous blood products are transfused but also that the age of stored

autologous red blood cell concentrates impacts the outcome of patients who underwent cardiac surgery dramatically [3]. In consequence the development of strategies to reduce the consumption of donor blood products as well as re-evaluation of lower "critical" hemoglobin values as a trigger for transfusions are of increasing importance [4]. However, particularly in small infants and neonates, the goal of transfusion free cardiovascular surgery is usually limited by the extreme hemodilution caused by the relatively large priming volume of the CPB system. During recent years, we have demonstrated that implementation of small components in the CPB circuit resulting in reduction of the CPB priming volume facilitates transfusion-free cardiovascular surgery in selected cases in neonates and small infants [5].

Purpose. In the current study of 23 consecutive neonates undergoing the arterial switch operation at our institution, we assessed the effect of transfusions and the timing of the transfusion on selected clinical outcome data.

Materials and methods

After approval by the local ethics committee and having obtained informed consent from the patients' parents, we analyzed the data of 23 consecutive neonates diagnosed for with transposition of the great arteries without concomitant malformations (ventricular septal defect etc) who underwent the arterial switch operation at our institution employing a miniaturized CPB set-up [5]. Patients were divided into three groups. Group I were patients without any transfusions, group 2 patients who had no transfusions in the intra-operatively but received transfusions postoperatively and group III patients with intra-operative transfusions.

Surgery was performed by a single surgeon, anesthesia by three different anesthetists and CPB by three different perfusionists. In accordance with departmental standards, surgery was done in moderate hypothermia of 24°-28° C. Cardioplegia was performed with 10 ml/kg body weight (BW) of crystalloid cardioplegic Kirsch solution (Mg-Aspartat Procain, Köhler-Chemie, Alsbach, Germany) and 10 ml/kg BW cardioplegic perfusion solution (Fresenius AG, Bad Homburg, Germany).

The set-up of the miniaturized CPB circuit was designed as described before, resulting in the requirement of a priming volume of between 90 and 120 ml depending on the weight of the patients [5]. In all procedures, a pump flow of 2.5-3 l/m^2 was maintained with the aid of vacuum-assisted drainage. In accordance with departmental standards, during CPB the "critical" hemoglobin (Hb) value was 7-8 g/dl, and after CPB, under the condition of normothermia (36-37 °C) and normovolemia (central venous pressure of 6-10 mmHg), dependent on the overall clinical situation of the patient: 8-10 g/dl in patients needing only minimal inotropic support (adrenalin 0.01-0.1 μg/kg/min) and 10-12 g/dl in patients needing moderate inotropic support (adrenalin 0.1–0.2 μg/kg/min) and >12 g/dl in patients needing high (adrenalin >0.2 μg/kg/min) inotropic support. During the operation regional oxygenation was monitored via near-infrared spectroscopy (NIRS) optodes placed on the forehead and leg.

During CPB heparin management and after the procedure protamine calculation was performed according to the results of the Hepcon HMS™ (Medtronic, Minneapolis, Min, USA). After CPB, the circuit was flushed with saline and the volume processed with a small volume cell bowl (55 ml, Dideco, Mirandola, Italy). No modified ultrafiltation was performed after the procedure.

If autologous blood was given, packed red cell concentrates were washed in the cell saver before transfusion. If red blood cell concentrates were transfused, comparable volumes of virus inactivated fresh frozen plasma were given.

Statistical analysis was performed using the Mann-Whitney-Wilcoxon test. A p value of <0.05 was defined as significant.

Results and discussion

In all patients the chest could be closed primarily and all patients arrived on the intensive care unit (ICU) with minimal inotropic support with adrenalin (0.02-0.06 μg/kg/min) and milrinone (0.75 μg/kg/min). The overall clinical course of all patients was uncomplicated and all patients were discharged from hospital on schedule.

Demographic data and baseline clinical data are presented in table 1. There was no significant difference among these data except for that in the pre-operative hemoglobin value which was significantly increased in patients of group 2 compared to group 3. Intra-operative data are given in table II. There was no significant difference in the priming volume of the CPB circuit, duration of ischemia, surgery etc. However, there were significant differences in the hemoglobin value 30 min after initiation of CPB and after chest closure. After chest closure patients in group III had higher hemoglobin values while there were no differences with regard to the central venous oxygen saturation and serum lactate concentrations between the groups.

Regarding the clinical outcome data (fig. 1), patients of group I had significantly shorter duration of mechanical ventilation and stay on the intensive care unit compared to the other groups, while there was no difference between groups II and III.

Conclusions

The current investigation shows a significant reduction in the duration of mechanical ventilation and length of stay on the ICU in the group of patients who received no blood transfusions during the entire clinical course.

While a large number of publications on adults undergoing cardiac surgery have provided convincing evidence that transfusion of donor blood products are associated with adverse outcomes such as increased morbidity and mortality, scant data are available from the

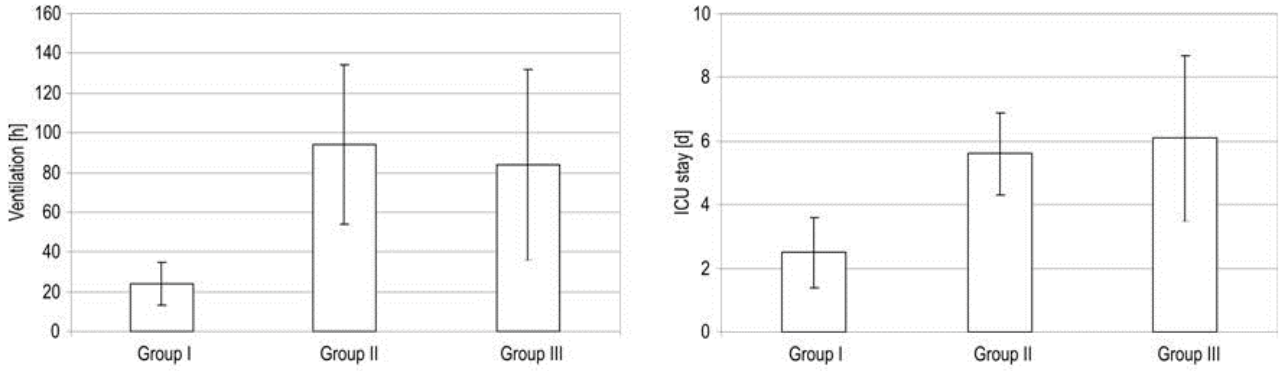

Fig. 1. Duration of mechanical ventilation (h) and stay on the intensive care unit (d).

	P (I vs. II)	P (I vs. III)	P (II vs. III)
Ventilation [h]	0.016	0.004	ns
ICU stay [d]	0.041	0.024	ns

Table 1

Demographic and clinical baseline data

	Group I	**Group II**	**Group III**	**P (I vs. II)**	**P (I vs. III)**	**P (II vs. III)**
N patients	4	7	12	ns	ns	ns
Gender	f=1; m=3	f=1; m=6	f=3; m=9	ns	ns	ns
Age [d]	10.0 ± 1.9	10.1 ± 4.5	8.3 ± 4.0	ns	ns	ns
Weight [kg]	3.95 ± 0.7	3.10 ± 0.7	3.27 ± 0.6	ns	ns	ns
Baseline Hb [g/dl]	16.3 ± 2.1	15.5 ± 0.7	13.8 ± 1.4	ns	ns	0,021

Legend: CPB=cardiopulmonary bypass, hb=hemoglobin level, sat. 02 cv=central venous oxygen saturation, re-op=re-operation, ICU=intensive care unit. Ns=not significant (p value of <0.05 was determined for significance).

Table 2

Perioperative data

	Group I	**Group II**	**Group III**	**P (I vs. II)**	**P (I vs. III)**	**P (II vs. III)**
Priming volume CPB [ml]	110±12	108±7	114±10	ns	ns	ns
Duration ischemia [min]	80±8	79±9	88±9	ns	ns	ns
Duration CPB [min]	115±5	113±12	132±24	ns	ns	ns
Hb [g/dl] before CPB	14,4±1,4	12,8±1,4	12,4±0,2	ns	ns	ns
Hb [g/dl] 30 min after start CPB	10,2±1,03	8,7±1,0	7,5±0,9	ns	ns	
Hb [g/dl] 30 min after end CPB	11±1,7	8,8±1,1	13±1,1 2	ns	0,005	0,013
Hb [g/dl] After chest closure	10,9±1,3	9,8±1,0	13,1±0,5	ns	0,0023	0,001
Sat 02 cv [%]	60±5,8	62±6,3	68±6,6	ns	ns	ns
Lactate [mmol/l]	1,9±0,8	2,6±1,2	3,1±0,8	ns	ns	ns

Legend: CPB=cardiopulmonary bypass, hb=hemoglobin level, sat. 02 cv=central venous oxygen saturation, re-op=re-operation, ICU=intensive care unit. Ns=not significant (p value of <0.05 was determined for significance).

pediatric world and particularly with regard to neonates. One recent investigation in pediatric patients after open heart surgery demonstrated a correlation between transfusions and infections but not with mortality [6]. In a larger series of 150 children undergoing cardiac surgery with miniaturized CPB, Durandy et al showed a reduction in the duration of ventilation time when patients were not transfused [7]. A recent observational study in 295

critically ill children (non-cardiac diseases) demonstrated an independent association of transfusions with prolonged need for mechanical ventilation, inotropic support, duration of ICU stay and mortality [8].

In our investigation a remarkable percentage (40%) of patients left the operation room without transfusions; most of them, however, required transfusions in the further clinical course.

The development and implementation of specially designed miniaturized CPB systems form the technical basis for transfusion free cardiac surgery in neonates and small children. In addition to this technical aspect, one central question remains the definition of the "critical" hemoglobin value and therefore the "transfusion trigger" under this special condition. In the investigation by Kneyber et al. a large number of patients received transfusions at a hemoglobin value higher than 9.6 g/dl, whereas in 2007 Lacroix et al. showed that in a mixed population of children requiring ICU treatment that with a hemoglobin value of >7.0 g/dl as a restrictive transfusion regimen clinical outcomes were comparable to a a more liberal transfusion regimen with a hemoblobin value of >9.5 as transfusion trigger [4]. These results also applied for the small subgroup of ICU patients following cardiac surgery (patients older than 28 days and with a non-cyanotic cardiac malformation) [9]. Szekely defined the critical hemoglobin value as 35% for neonates, 30% for infants and 25% for children [6]. In neonates undergoing complex cardiac surgery with deep hypothermic cardiac arrest (DHCA) Jonas et al. reported adverse neurological outcomes in patients with a hematocrit of 20% while a hematocrit of 25% appeared to be safe [10-12]. In our study, although no DHCA was performed, the critical hematocrit was defined as 21-24%, correlating to hemoglobin values of 7-8 g/dl. However, as these critical levels apply for the period during the controlled conditions of CPB the critical values for the period after surgery, particularly for neonates, remain undefined. Broader use of recently introduced methods of monitoring tissue oxygenation such as NIRS may help to better define critical values in this regard.

Although we condensed patient selection to a rather homogenous clinical syndrome and well standardized surgical and CPB procedure, our investigation is clearly limited by the relatively particularly for neonates small number of patients and lack of long term data for evaluation of neurological outcomes. Nevertheless, we believe that our data further confirm the possible adverse effect of transfusions on clinical outcomes even in neonates and small children. Based on this set of data we believe that further strict care must be taken to implement all possible blood saving strategies and reduce transfusions in this patient population. Further studies are needed to confirm these data and to better define the critical hemoglobin level in the complex and versatile population of children with congenital heart disease.

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