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Research Article

Blood Product Transfusion and Postoperative Outcome in Pediatric Neurosurgical Patients

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Abstract

Background: Intraoperative and postoperative morbi-mortality factors are multiple in pediatric patients. Studies in pediatric cardiac surgery and intensive care patients have identified transfusion as one factor among others. This study was undertaken to investigate whether transfusion was a risk factor of postoperative outcome in neurosurgical pediatric patients.

Objectives: To identify morbi-mortality risk factors in intraoperatively transfused and not transfused pediatric neurosurgical patients.

Design: Retrospective observational descriptive pediatric cohort study.

Setting: Monocentric pediatric tertiary center, Necker Enfants Malades University Hospital Paris, from 1 January 2014 to 17 Mai 2017.

Patients: 206 patients with a median age of 60 months [13.25 - 135.75] were included.
Inclusion criteria were the presence or the absence of transfusion in the intraoperative period in neurosurgery patients.
Exclusion criterion was transfusion in the postoperative period until discharge from hospital.

Main Outcome Measures: Primary outcome was mortality and secondary outcome was morbidity in transfused and non-transfused patients. Mortality was assessed by deaths occuring intraoperatively or postoperatively during the entire hospitalisation. Morbidity was assessed by intraoperative, postoperative complications, repeat surgery, length of stay in the intensive care unit, in the hospitalisation ward, total length of stay in hospital and length of mechanical ventilation.

Results: ASA score status (odds ratio 2.49; p-value < 0.01) and transfusion (odds ratio 1.33; p-value 0.03) were predictive risk factors for complications. Emergency surgery (odds ratio 6.8; p-value 0.03) was a predictive risk factor for repeat surgery. ASA score, transfusion and emergency surgery were predictive risk factors for length of stay in the intensive care unit, total length of stay in hospital and length of mechanical ventilation (p-value < 0.0001)

Conclusion: Transfusion was identified as a morbidity risk factor among others in this pediatric cohort. Identifying these factors in order to implement improvement measures can upgrade patient postoperative outcome. One of these measures is to implement transfusion protocols in which blood product administration is guided by point of care devices such as viscoelastic methods which can contribute to reduce transfusion intraoperatively and applying blood salvage protocols such as intraoperative tranexamic acid administration and preoperative erythropoietin supplementation in potential hemorrhagic surgical interventions such as craniosynostosis.

Keywords: *Blood Product Transfusion; Postoperative Outcome; Pediatric Neurosurgical Patients*

Introduction

In pediatric patients admitted for surgery under anesthesia, morbi-mortality is related to multiple factors. Several morbi-mortality risk factors have been identified of which transfusion is one of the risk factors in studies concerning pediatric cardiac surgery and critical care patients [1-3]. This study was undertaken to determine whether transfusion was a morbi-mortality risk factor in neurosurgical pediatric patients. The primary endpoint was to identify factors related to mortality and the secondary endpoint was to identify factors related to morbidity in this pediatric population. Mortality (primary outcome) was assessed by deaths occuring intraoperatively or postoperatively until discharge from hospital.

Morbidity (secondary outcome) was assessed by intraoperative and postoperative complications, repeat surgery, length of stay in the intensive care unit (LOSICU), length of stay in hospital (LOSHOSP), total length of stay in hospital (intensive care and standard hospitalisation ward, TLOSHOSP) and length of mechanical ventilation (LMV).

Methods

After approval from the Ethics Committee of Necker Enfants Malades University Hospital, Paris, France, under the registration number 2017-CK-5-R1 on 21 March 2017 (Chairperson Professor Mariane de Montalembert) and after declaration of this study to the National Commission of Liberties and Computer Science, Paris, France (CNIL, Commission Nationale des Libertés et de l'Informatique) under the registration number 2028257 v0 on 21 February 2017 (Chairperson Mrs Isabelle Falque Pierrotin), 206 patients with a median age of 60 months [13.25-135.75] [interquartile range] where included in this study from our Hospital, Necker Enfants Malades, Paris.

Inclusion criteria consisted of patients admitted for neurosurgery and who received blood products [packed red blood cells (PRBC) and/or fresh frozen plasma (FFP) and/or concentrated platelet units (CPU)] in the intraoperative period (transfusion group) and patients admitted for the same surgical speciality and who did not receive any blood transfusion during surgery or in the postoperative period.

We first included the transfused patients and then patients who did not receive blood components, in order to include patients with same surgical operations whenever possible.

The local Transfusion Department (EFS, Etablissement Français de Sang, Hôpital Universitaire Necker Enfants Malades) provided a list of patients who had been transfused in the operation theater from 1 January 2014 until 31 December 2016.

There were 1500 transfused patients identified of which only 103 were finally retained for the study because of complete data and also in order to have the same number of patients with equivalent surgical operations as in the no transfusion group.

We used the operation theater programmation system (IPOP) to identify patients who did not receive blood products intraoperatively and postoperatively. We included 103 patients from 1 January 2014 until 17 Mai 2017 in the no transfusion group. Whenever possible, patients scheduled for similar interventions as in the transfused group where included.

Medical records were analyzed using the computer medical report system (Orbis, Mediweb and Cristalnet).

Data collected consisted of intraoperative and postoperative mortality occuring during hospitalisation regardless of TLOSHOSP (to assess primary outcome), intraoperative and postoperative complications which included organ failure and infections, repeat surgery, number of days spent in the intensive care unit and in the hospitalisation ward, total number of days spent in hospital, number of days spent under mechanical ventilation (to assess secondary outcome).

Factors that could influence primary and secondary outcomes were collected: age, prematurity, type of surgery, comorbidities, ASA score (American Society of Anesthesiologists Score), emergency surgery, number of units of blood products administered [packed red blood cell units (PRBC), fresh frozen plasma units (FFP), concentrated platelet units (CPU)], preoperative and postoperative hemoglobin and platelet levels. The ASA score (I-V) is a scale used in anesthesia to assess patient severity physical status: ASA I: normal healthy patient, ASA II: patient with mild systemic disease, ASA III: patient with severe systemic disease, ASA IV: patient with severe systemic disease which is constantly threatening life, ASA V: moribund patient who is not expected to survive without surgery.

Missing data concerning patient weight, intraoperative blood loss and fluid therapy with crystalloids and colloids, coagulation analysis like international normalized ratio, activated partial thromboplastin time, fibrinogen blood levels which could influence blood transfusion were not taken into account since they were not always available.

XLSTAT 2018.3 software was used for statistics.

Statistical tests included Student's test for parametrical variables, Chi square or Fischer's exact test to compare category variables, propensity score matching analysis to assess for confounding morbi-mortality factors, logistic and log-linear regressions for multivariate analysis. We considered significant a p-value equals to or less than 0.05.

We firstly identified risk factors with univariate analysis. Secondly we proceeded with multivariate measures: logistic and log-linear regressions to assess for predictive risk factors [4].

Variables were expressed in mean values with standard deviation (±SD) or in median values with the interquartile range between the first and the third quartiles q1-q3 and category variables were expressed in proportions.

Four risk factors were identified (ASA score, emergency surgery, transfusion (units of blood products administered PRBC+FFP+CUP) and age) and correlated to the number deaths (mortality) during hospitalisation, number of patients with intraoperative and postoperative complications (complications), repeat surgery, number of days spent in the intensive care unit (LOSICU), in the hospitalisation ward (LOSHOSP), total number of days spent in hospital (ICU plus hospitalisation ward, TLOSHOSP), and the number of days spent under mechanical ventilation (LMV).

Hemoglobin and platelet concentration were not taken into account for analysis since some of the data was not available

Results

We included 206 patients, 103 transfused patients and 103 patients without transfusion. In univariate analysis (Table 1), the number of patients with complications, median LOISCU, median TLOSHOSP, median LMV, the number of ASA IV-V status patients, the number of emergency surgery were significantly higher in the transfusion group.

Patients in the transfusion group were significantly younger. Table 2 shows the type of surgery. Craniosynostosis was the most common surgery in the transfusion group (48 patients of the 103) followed by intracerebral tumor exeresis (16 patients).

In the no transfusion group, intracerebral tumor exeresis was the most common surgery (38 patients of the 103) followed by craniosynostosis (21 patients). In the transfusion group, packed red blood cells were the most transfused blood products (70%), followed by fresh frozen plasma (25%) and platelets were the least administered products (less than 4%) (Table 3).

	Transfusion group (T)	No Transfusion group (NT)	p-value
Number of patients with complications	22	10	0.02
Number of repeat surgery	6	3	0.31
Number of deaths	6	1	0.06
Median length of stay in the intensive care unit in days [interquartile interval]	3 [2 - 4]	2 [1 - 4]	< 0.01
Median length of stay in hospital in days [interquartile interval]	2 [1 - 4]	2 [1 - 3]	0.22
Median total length of stay in hospital in days [interquartile interval]	5 [4 - 9]	5 [4 - 6]	< 0.01
Mechanical ventilation median length in days [interquartile interval]	0 [0 - 1]	0 [0 - 0]	0.01
Number of ASA I patients	34	14	< 0.01
Number of ASA II patients	15	21	< 0.01
Number of ASA III patients	38	60	< 0.01
Number of ASA IV patients	10	7	< 0.01
Number of ASA V patients	6	1	< 0.01
Median number of blood component units per patient [interquartile interval]	1 [1 - 2]	0 [0 - 0]	< 0.0001
Median age in months [interquartile interval]	22 [8 - 61]	122 [60 - 162.5]	< 0.0001
Number of premature patients	0	0	
Number of emergency operations	26	9	< 0.01
Total number of patients	103	103	

Table 1: *General characteristics in transfused and non transfused neurosurgical surgical patients.*

Type of surgery	Number of patients Transfusion Group	Number of patients No Transfusion Group
Peritoneal ventriculostomy/External Ventriculostomy	4	5
Craniosynostosis	48	21
Intracerebral genetical therapy	2	0
Aneurysm/arterio-venous malformation embolisation	2	0
Vertebral arthrodesis, spinal decompression	6	1
Craniotomy	2	5
Central venous catheter placement	1	0
Attached Spinal cord	1	0
Moya-Moya	1	0
Intracerebral tumor exeresis	16	38
Lefort III	1	0
Epileptogen lesion exeresis	2	6
Extradural hematoma	5	0
Subdural hematoma	0	1

Spinal cord Tumor Exeresis	2	1
Brainstem tumor exeresis	2	0
Posterior Fossa Decompression	1	0
Intracerebral lesion biopsy	1	3
Chiari's Malformation	2	10
Orbital tumor exeresis	1	1
Cerebral Cavernoma	1	2
Basal Skull Schwannoma	1	3
Polytrauma (exploration laparotomy)	1	0
Arachnoid cyst	0	1
Cranioplasty	0	2
Intraventricular stenting	0	2
Subdural empyema	0	1
Total	103	103

Table 2: *Type of surgery.*

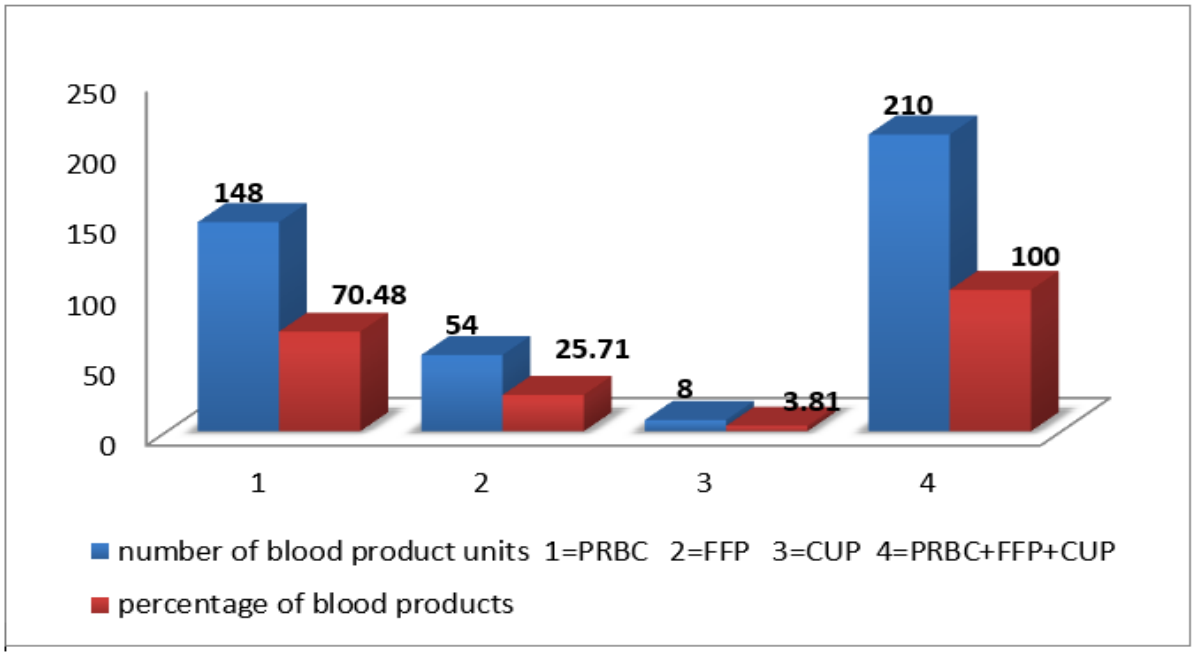

Table 3: *Distribution of blood products administered in neurourgical patients.*

Table 4 shows the average number of blood units per patient. The overall average number of blood units administered per patient was 2.04 ± 1.99. Craniosynostosis patients (48 of 103 patients) were the most commonly transfused with an average of 2.04 ± 1.90 blood units per patient. 5 patients received more than 5 units of blood products.

Surgery	Number of patients	Mean blood products unit per patient ± SD
Ventriculostomy	4	2.5 ± 2.38
Craniosynostosis	48	2.04 ± 1.90
Intracerebral Genetical Therapy	2	1.00 ± 0.00
Angioembolisation	2	1.5 ± 0.71
Vertebral Arthrodesis	6	2.67 ± 1.63
Craniotomy	2	5.00 ± 4.24
Central venous catheter placement	1	1.00 ± 0.00
Attached spinal cord	1	1.00 ± 0.00
Moya Moya	1	2.00 ± 0.00
Intracerebral tumor exeresis	16	1.38 ± 0.89
Lefort III	1	7.00 ± 0.00
Epileptogen lesion exeresis	2	1.00 ± 0.00
Extradural hematoma	5	3.00 ± 2.35
Subdural hematoma	0	0.00 ± 0.00
Spinal cord tumor exeresis	2	1.5 ± 0.71
Brain stem tumor exeresis	2	1.00 ± 0.00
Posterior fossa tumor exeresis	1	2.00 ± 0.00
Intracerebral tumor biospy	1	1.00 ± 0.00
Chiari's Malformation	2	1.5 ± 0.71
Orbital Tumor exeresis	1	2.00 ± 0.00
Cavernoma	1	1.00 ± 0.00
Basal Skull schwannoma	1	6.00 ± 0.00
Arachnoid cyst	1	15.00 ± 0.00
Cranioplasty	0	0.00 ± 0.00
Total	103	2.04 ± 1.99

Table 4: *Type of surgery and the number of blood units per patient.*

Table 5 illustrates the comorbidities, the most common was intracerebral tumor and epilepsia in the two groups.

Table 6 shows the distribution of intraoperative and postoperative complications between the two groups which was similar. This is because some patients had more than one complications. The number of patients with complications was higher in the transfusion group (Table 1).

Comorbidities	Transfusion Group	No Transfusion Group
Intracerebral Tumor	14	36
San Filippo Syndrome	1	0
Cerebral Aneurysm/Arterio-Venous Malformation	3	1
Crouzon Syndrome	3	3
Loeys-Dietz Syndrome	2	0
Trauma	2	2
Sickle Cell Disease	2	0
Obstructive Chronic Apneic Syndrome	1	1
Stroke	2	0
Psychomotor deficiency	0	1
Apert Syndrome	2	1
Hemorrhagic Diathesis	1	0
Bilateral Subdural Hematoma	1	1
Rachitisme	1	1
Epilespisa	6	13
Larsen Syndrome	1	0
Congenital Heart Disease	2	0
Carcinomateous Meningitis	1	0
Asthma	1	1
Neurofibromatosis	2	1
Bourneville's Sclerosis	1	0
Head Trauma	1	1
Endocarditis	1	0
Tracheomalacia	1	0
Brainstem lesion	1	0
Achondroplasia	1	0
Cyphosis/Scoliosis/Vertebrae Hypoplasia	2	0
Klippel-Feil Syndrome	1	0
Metachromic Leucodystrophy	1	0
Spinal Cord Tumor	1	0
Chiari Malformation Type 1	1	12
Intracerebral Hypertension	0	2
Saerthre-Chotzen Syndrome	0	1
Arachnoid Cyst	0	1
Morquio Syndrome	0	1
Ewing Sarcoma C5-S1	0	1
Complexe polymalformation Syndrome with metabolic and heart disease	0	1
Extradural Hematoma	0	1
History of prematurity	2	2
None	41	18
Total	103	103

Table 5: *Comorbidities.*

Intraoperative complications	Transfusion group	No Transfusion group
Hemorrhagic shock	1	1
Cardiac arrest	1	0
Anaphylaxis	0	1
Bronchospasm/Larygnospasm	1	1
Difficult intubation	0	0
Postoperative Organ Failure Complications		
neurological	10	2
cardiocirculatory	0	0
respiratory	2	0
renal	0	0
hepatic	1	0
endocrinologic	0	2
multisystemic	5	1
Hemorrhagic shock	1	0
Anaphylaxis	1	0
Postoperative infectious complications		
Pulmonary sepsis	6	1
Abdominal sepsis	0	0
Uro-genital Sepsis	1	0
Mediastinal Sepsis	0	0
Neuromeningeal sepsis	2	0
Septic Shock	0	0
Local wound site sepsis	0	1
Septicemia	0	1
Deaths	6	1
Repeat surgery	6	3
Total	44	15
p-value	0.28	

Table 6: *Complications.*

After propensity score matching analysis table 7, transfused patients and patients with emergency surgery were 100% matched.

Multivariate analysis with logistic regression (Table 8) demonstrated that, transfusion [odds ratio 1.33; p-value 0.01] and ASA score status [odds ratio 2.49; p-value < 0.01] were predictive risk factors for complications. Emergency surgery [odds ratio 6.8; p-value 0.03] was a predictive risk factor for repeat surgery. There were no significant predictive risk factors for mortality in this cohort.

Variable	Number of matched patients	Percentage of matched patients	Number of unmatched patients	Percentage of unmatched patients	Cost of matching
Transfusion	103	100%	0	0%	78.195
Emergency surgery	35	100%	0	0%	18.511

Table 7: *Propensity score matching for transfusion and emergency surgery.*

Independent variable	Dependent variable	Wald value [95% confidence interval]	Odds ratio [95% confidence interval]	p - value
	Complications			
ASA score		0.91 [0.39 - 1.43]	2.49 [1.49 - 4.16]	<0.01
Emergency		0.61 [-0.46 - 1.68]	1.84 [0.63 - 5.35]	0.26
Transfusion		0.28 [0.03 - 0.54]	1.33 [1.03 - 1.72]	0.03
Age		-0.004 [-0.01 - 0.003]	0.99 [0.99 - 1.003]	0.29
	Repeat surgery			
ASA score		0.28 [- 0.39 - 0.96]	1.33 [0.67 - 2.62]	0.41
Emergency		1.92 [0.20 - 3.63]	6.80 [1.22 - 37.83]	0.03
Transfusion		0.08 [-0.17 - 0.34]	1.09 [0.84 - 1.40]	0.53
Age		-0.007 [-0.02 - 0.006]	0.99 [0.98 - 1.006]	0.31
	Mortality			
ASA score		35.81 [-7853.34 - 7924.97]	NA	0.99
Emergency		0.69 [-11087 - 11088]	NA	1.00
Transfusion		0.10 [-1503 - 15013]	NA	1.00
Age		0.00 [-60.66 - 60.66]	1[0 - $22.2^{E}26$]	1.00

Table 8: *Logistic regression for complications, repeat surgery and mortality.*

Multivariate analysis with log-linear regression showed that ASA score, emergency surgery and transfusion were predictive risk factors for LOSICU, TLOSHOSP and LMV ($p < 0.0001$).

Discussion

Our study has shown that transfusion is a predictive risk factor for complications, LOSICU,TLOSHOSP and LMV. Optimizing transfusion strategies can improve postoperative patient outcome. Studies have reported the physiopathology underlying some transfusion related complications [5,6].

Exposure to blood products can be reduced by applying restrictive transfusion strategies [7], using transfusion protocols based on bedside viscoelastic methods (ROTEM/TEG) to guide blood components administration and also by applying blood salvage protocols such as intraoperative tranexamic acid administration and preoperative erythropoietin supplementation for potential hemorrhagic surgery like craniosynostosis [8-13].

Independent Variable	Dependent Variable	Wald value [95% confidence interval]	p-value
	LOSICU		
ASA score		0.21 [0.15 - 0.27]	< 0.0001
Emergency		0.68 [0.52 - 0.84]	< 0.0001
Transfusion		0.09 [0.08 - 0.12]	< 0.0001
Age		0.00 [-0.001 - 0.001]	0.52
	LOSHOSP		
ASA score		0.12 [0.03 - 0.21]	< 0.01
Emergency		-0.16 [-0.39 - 0.09]	0.21
Transfusion		0.05 [0.007 - 0.09]	0.02
Age		0.001 [0.00 - 0.002]	0.22
	TLOSHOSP		
ASA score		0.18 [0.13 - 0.23]	< 0.0001
Emergency		0.39 [0.26 - 0.52]	< 0.0001
Transfusion		0.09 [0.07 - 0.10]	< 0.0001
Age		0.00 [-0.001 - 0.001]	0.86
	LMV		
ASA score		0.67 [0.54 - 0.80]	< 0.0001
Emergency		1.32 [1.01 - 1.63]	< 0.0001
Transfusion		0.09 [0.07 - 0.12]	< 0.0001
Age		-0.001 [-0.003 - 0.001]	0.55

Table 9: *Log linear regression for LOSICU, LOSHOSP, TLOSHOSP and LMV.*

Emergency surgery was a risk factor for repeat surgery. It has been shown in a previous study that critical events are more frequent during emergency procedures [14]. ASA score status was a risk factor for complications, LOSISCU, TLOSHOSP and LMV. In adults, intra-operative goal directed protocols have shown reduction in complications and length of hospital stay. Studies in this field are lacking in children [15-17]. Randomized controlled trials are necessary in children to demonstrate postoperative outcome improvement when goal directed protocols are applied intraoperatively.

Our survey demonstrated that transfusion, emergency surgery and ASA score status were predictive risk factors for morbidity. There were no significant predictive risk factors for mortality in this cohort.

This study had limits: it was retrospective, not all factors were analysed because of missing data but those which were accessible and analysable can help to identify risks and improvement measures can be applied. More larger prospective trials are needed to complete our findings.

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None.

Conflicts of Interest

None.

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