

Thrombocytopenia related to multiple organ failure (TAMOF) related to extracorporeal circulation in cardiac surgery in paediatrics

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Abstract

Aims and objectives: To determine the frequency of thrombocytopenia associated multi organ failure without infection criteria and its impact on the evolution and survival of patients undergoing cardiac surgery with extracorporeal circulation and prognosis.

Methods: Longitudinal, prospective, observational study to determine the frequency in the presentation of thrombocytopenia associated with multiple organ failure in patients undergoing cardiac surgery under extracorporeal circulation without positive infection rates, admitted to the intensive care unit surgical (ICU). and its impact in the evolution of these patients in the Hospital Federico Gómez.

Results: A total of 47 patients under extracorporeal circulation were analysed. Proportion for low cardiac output syndrome 23% (n = 11) being this complication most frequent presented by our patients, with a direct relationship to the appearance of TAMOF with a p <0.05, there is a direct relationship between the appearance of TAMOF in patients with > 140 minutes of extracorporeal circulation time, the presence of deep hypothermia, lactate more than 5 mmol / L on admission, a PSOF score of more than 8 points, and a higher score on the RASCH risk scale with a p <0.05. There was a significant difference with a p <0.05 in the days of stay in therapy intensive, and mortality among patients who developed TAMOF and those who did not.

Conclusions: The incidence of TAMOF associated with extracorporeal circulation during cardiac surgery in children and its role in impoverishment within the prognosis makes it important to identify this entity to establish action measures with appropriate therapies for these patients. It is necessary to normalize the ADAMTS 13 activity tests in children undergoing extracorporeal circulation.

Introduction

Thrombocytopenia related to multiple organ failure (TAMOF) is a complication associated with sepsis, due to the decrease in the activity of factor ADAMTS 13, which is a metalloprotease that breaks the structure of von Willebrand factor, which leads to thrombotic microangiopathy microvascular ischemia, thrombocytopenia and intravascular haemolysis with subsequent organ dysfunction and impoverishment of the patient's prognosis. This entity has been recognized in recent years, by the exposure of blood flow to artificial membranes, devoid of the biological characteristics of the vascular endothelium, that favour the activation of inflammatory response mechanisms such as neutrophil chemotaxis, and activation of the pathways of coagulation [1-5].

There exist a few studies of TAMOF related to cardiac surgery in paediatrics, one of them is that of Kawai et al, he conducted the study in a single centre with a series of cases of patients with TAMOF treated in combination with ECMO and plasmapheresis; recently there is another retrospective study, that of Mei Chong in Pittsburg with a n = 41 patients, with an average age of 0.6 years (0-17 years), they made the biochemical diagnosis of TAMOF based on the decrease in the activity of ADAMTS13, with the intervention of plasmapheresis and ECMO, reporting a general survival of 53.7%, 73.3% for those with heart failure, 34.8% for those with congenital heart disease, and 100% for other types of heart disease (p = 0.016) Federico Gómez Children's Hospital in Mexico, is a congenital heart disease reference centre; in 2018, 235 cardiovascular interventions were carried out, 155 were performed under extracorporeal circulation, so it is essential to

establish the incidence of thrombocytopenia associated with multiple organ failure. in these patients as well as the impact on the prognosis and their evolution.

Physiology of thrombocytopenia associated with multiple organ failure

Thrombocytopenia associated multiple organ failure (TAMOF) is a clinical phenotype that encompasses a spectrum of syndromes associated with microvascular thrombosis, one of them thrombotic microangiopathies with thrombotic thrombocytopenic purpura / haemolytic uremic syndromes and intravascular coagulation [6-8].

TAMOF is characterized by thrombocytopenia with progression to multiple organ failure in critically ill patients. The decrease in platelet counts by consumption reflects their involvement in the origin of disseminated microvascular thrombosis, which lead to ischemia and organic dysfunction [8-13].

ADAMTS-13 is a metalloprotease with regulatory action of microvascular thrombosis by excision of the von Willebrand

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coagulation factor (VWF) making it smaller and less hemostatically active multimers. Within the pathophysiology of thrombotic thrombocytopenic purpura and thrombotic microangiopathy, it has been attributed to deficiency of ADAMTS-13 levels at <10% of normal activity and an inability to cleave high molecular weight VWF factor, platelets they adhere to ultra-large VWF multimers (ULVWF) that are not cleaved and form microvascular aggregates in endothelial cells, resulting in microvascular occlusions that are rich in platelets and FvW, and lead to generalized thrombosis with subsequent organ dysfunction [13-20].

Methods

Longitudinal, prospective, observational study to determine the frequency in the presentation of thrombocytopenia associated with multiple organ failure in patients undergoing cardiac surgery under extracorporeal circulation without positive infection rates, admitted to the intensive care unit surgical (ICU). and its impact in the evolution of these patients in the Hospital Federico Gómez.

Primary outcome

To determine the frequency of thrombocytopenia associated multi organ failure without infection criteria and its impact on the evolution and survival of patients undergoing cardiac surgery with extracorporeal circulation and prognosis.

Statistical analysis

The collected data were entered into a database using the Microsoft Excel 2013 program and analysed in the STATA program.

Univariate analysis: measures of central tendency and dispersion of quantitative variables were obtained, while relative frequencies were calculated from qualitative variables.

Bivariate analysis: For the correlation between the exposure time to extracorporeal circulation pump, as well as the clamping time, such as the appearance of thrombocytopenia associated with multiple organ failure, the initial sofa and maximum sofa as well as for age and initial diagnosis the association tests between two variables with independent means of chi² and t of student were used.

Results

Cardiac surgery was analysed from January to April 2019 with the following epidemiological results: 66 surgeries were performed, 29 male patients representing 43% and 37 female patients representing 53%, the average age of surgery was 28.8 months.

With regard to pre-surgical diagnoses, the most frequent was interventricular communication with (n = 18) the interventricular defect closure surgeries representing a proportion of 27% of the total surgeries, the surgical risk based on the RACHS scale, the most frequent risk was RACHS 2 with 30 surgeries representing 45.4%, RACHS 1 18.1%, RACHS 3 31.82% and for RACHS 4 4.5% (Table 1).

Table 1. Patient’s diagnosis

Cardiopathy	n=	Cardiopathy	n=
Interventricular communication	18	Total Anomalous pulmonary veins connection	8
Falot tetralogy	2	Great vessel transposition	3
Persistent arteriosus ductus	9	Interauricular communication	3
Tricuspid atresia	7	Atrioventricular canal	1
Pulmonary atresia/stenosis	11	Common arterial trunk	1
Aortic stenosis	1	Myocardiopathy	2

Chi² and t student tests were used to statistically relate the presence of TAMOF with sociodemographic variables, the same analysis was conducted with related to extracorporeal circulation (circulation time, clamping and circulatory arrest) as well as follow-up for the variables within the intensive surgical therapy (Table 2 and Table 3) finding an incidence of TAMOF of 4.2% with an associated mortality of 50%, related to a longer hospital stay and impoverishment of the clinical prognosis.

Discussion

For this study and in our Hospital Federico Gómez, the mortality rate for cardiac surgery corresponds to 6%, which is discreetly higher than the one reported in the world literature from 4.5 to 5.5%, within the cardiological diagnoses our population has the same characteristics as reported worldwide, because the most frequent diagnosis was the interventricular communication in its different forms (n = 21) in a proportion of 34%, with respect to the age of the patient undergoing surgery, surgeries are performed on average at 20 months of age, which in most of them represents a delay in surgical management. Regarding the exposure to extracorporeal circulation, our population has longer time variables than recommendation for these procedure (circulation time, clamping time, time of cardiac arrest) longer for them, which represents a risk factor associated with more morbidity and a higher mortality, with a positive association between the duration of these procedures and the incidence of low cardiac output syndrome, how has been demonstrated in our cohort that syndrome present in a frequency of 11/47, (23%), which is comparable with reported in the literature, and very important it was the most frequently complication associated in our patients with TAMOF (X², p <0.05) [17].

There are a direct association between a total circulation time > 140 minutes with the presentation of TAMOF, other statistically significant associations were the presence of deep hypothermia, lactate of more than 5mmol / L at the admission to ICU. , a PSOFA score of more than 8 points, as well as a higher score on the RACHS risk scale (X², p <0.05) There was a significant difference (p = <0.05) in the days of ICU stay (20.5 vs. 4.2 days).

There is no reported incidence in the literature of thrombocytopenia associated with multiple organ failure in paediatric patients undergoing extracorporeal circulation so our study sets the basis for this measure for this pathology, we found a frequency of 4.2%, with an associated mortality of 50%, which corresponds to what is reported in the literature in the study by Chong et al. There was a statistically significant difference between the mortality of patients who developed TAMOF (1/2) and those who did not develop it (p = <0.05).

Conclusions

The frequency of TAMOF associated with extracorporeal circulation during cardiac surgery and its role in impoverishment within the patient’s prognosis makes it important to identify this phenotypic response of thrombotic microangiopathy to establish action measures with appropriate therapies for this group of patients.

It is necessary to standardize the evidence of the activity levels of the ADAMTS 13 factor in children undergoing extracorporeal circulation and mainly in those patients who encounter the risk factors described in this study. Likewise, in this study it was found that extracorporeal circulation times longer than those recommended for this type of procedures are translated as greater comorbidities such as the presence of low cardiac output syndrome.

Table 2. TAMOF contingency table for demographic and clinical evolution variables

Variable		TAMOF n=2	No TAMOF n= 45	Ch ²	P value	IC
Gender	Male	0	22	1.832	0.175	95%
	Female	2	23			
Age	≤6 months	1	26	0.047	0.828	95%
	≥6 months	1	19			
Extracorporeal Circulation	≤140 min	1	41	3.404	0.065	95%
	≥140 min	1	4			
Aortic clamping	≤40 min	0	20	1.547	0.214	95%
	≥40 min	2	25			
Cardiac Arrest	Yes	1	41	3.40	0.065	95%
	No	1	4			
Deep hypothermia	Yes	2	1	30.634	0.001	95%
	No	0	44			
SBGC *	Yes	2	9	6.836	0.009	95%
	No	0	36			
Haemorrhagic shock	Yes	0	0	0.031	0.859	95%
	No	0	45			
Septic shock	Yes	0	43	0.092	0.761	95%
	No	2	2			
Serum lactate	≤5 mmol/L	0	37	7.72	0.005	95%
	≥5 mmol/L	2	8			
Initial SOFA score	≥8 points	2	1	30.637	0.001	95%
	< 8 points	0	44			
Maximum SOFA score	≥8 points	2	23	1.838	0.175	95%
	< 8 points	0	22			
Risk scale	RACHS 1	0	4	30.637	0.001	95%
	RACHS 2	0	25			
	RACHS 3	0	15			
	RACHS 4	2	1			
ICU Discharge	Yes	1	1	30.637	0.008	95%
	No	1	44			

*Sbg (low output syndrome)

Table 3. Comparison of means for independent variables in patients with TAMOF

Variable	TAMOF n=2	No TAMOF N=45	Dif. Med.	P value	IC
Age	27 months	62.04 months	35.04	0.45	41.61-79.48
Aortic clamping	82 min	53.31 min	-28.68	0.098	47.49-61.56
Temperature	32°C	31.07°C	-0.92	0.716	30.10-32.13
Cardiac Arrest	38 min	5.11 min	-32.89	0.012	1.08-11.93
Extracorporeal circulation	95.5 min	96.91 min	1.41	0.958	85.94-107.75
Initial SOFA score	5.5 puntos	5.8 puntos	0.36	0.666	5.51-6.19
Maximum SOFA	7.5 puntos	9.31 puntos	1.81	0.489	8.18-10.28
Days in ICU	20.5 días	4.2 días	-16.3	0.001	3.38-6.40
Serum Lactate	7.35 mmol/L	3.85 mmol/L	-3.49	0.082	3.18-4.82
Platelets account	73.5 cell/mm ³	218.4 cell/mm ³	144.92	0.013	188.02-236.48

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