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Editorial

Physiology Principles Underlying Goal Directed Therapies in Children

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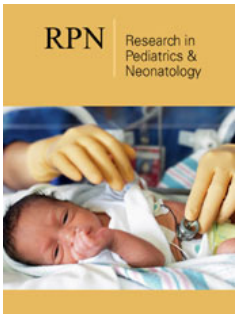

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Abstract

Background: Goal directed therapies (GDT) include goal directed fluid and hemodynamic therapy (GDFHT), transfusion goal directed protocols (TGDP) and enhanced recovery after surgery (ERAS). These GDT share common aims which are to optimize tissular oxygen delivery (DO_2), oxygen consumption (VO_2) and extraction ratio (O_2ER).

Objectives: This editorial on the Thesis Project entitled ´Do goal directed therapies improve postoperative outcome in children' highlights the physiology and rationale of GDT.

Methods: Editorial on the rationale of the Thesis Project in GDT in children.

Result: GDFHT, TGDP and ERAS have the same aim which is the optimization of tissular DO_2, VO_2 and O_2ER to avoid and prevent organ dysfunction.

Conclusion: Understanding the physiology of GDT is important for optimal patients management.

Keywords: Goal directed fluid and hemodynamic therapy; Transfusion goal directed protocols; Enhanced recovery after surgery; Postoperative outcomes, Children; Oxygen delivery; Oxygen consumption; Oxygen extraction ratio; Tissular perfusion pressure

Introduction

A Thesis Project has been undertaken which has the objectives to determine the impact of Goal directed therapies on postoperative outcome in children [1]. The background of this Thesis Project were the results of five retrospective observational studies realized in the pediatric surgical settings [2-6]. These studies had the objectives of determining predictors of adverse postoperative outcomes in the surgical pediatric population. The aim of this Thesis Project is to bring improvement measures in domains where predictors of postoperative adverse outcomes were identified. In order to implement these measures prospective and randomized controlled trials need to be developed. The hypothesis of the Thesis is by implementing goal directed therapies in fields were predictors of pejorative postoperative outcome have been identified, outcome in terms of postoperative morbidity and length of hospital stay will be improved.

Rationale of Goal Directed Therapies

Goal directed therapies (GDT) include goal directed fluid and hemodynamic therapy (GDFHT), transfusion goal directed protocols (TGDP) and enhanced recovery after surgery (ERAS) [7-33]. GDFHT, TGDP and ERAS share common goals. These aims are to optimize oxygen delivery (DO_2), oxygen consumption (VO_2) and oxygen extraction in different tissues of the organism. Considering the following equations, one will understand the physiology and the basis of GDT [14,22,23,34,36].

$$DO_2 = COxCaO_2 = COx(Hbx1.31xSaO_2+0.0031xPaO_2)$$

$$VO_2 = CO(CaO_2-CvO_2)$$

$$CaO_2 = Hbx1.31xSaO_2+0.0031xPaO_2$$

$$CvO_2 = Hbx1.31xSvO_2+0.0031xPvO_2$$

$$O_2ER = CaO_2-CvO_2/CaO_2 = SaO_2-SvO_2/SaO_2 = VO_2/DO_2$$

CO= SV x HR= VTIxD^{2}x Π /4xHR

SV= Aortic Velocity Time Integral x area of the aortic valve=VTIxD^{2}x Π /4

PP= SVR x CO

Where CO= Cardiac output, SV= Stroke volume, HR= Heart rate, PP= Tissular perfusion pressure, SVR= Systemic vascular resistance, VTI= Aortic velocity time integral, D= Diameter of the aortic valve, CaO_2= Arterial oxygen content, CvO_2= Venous oxygen content, Hb= Hemoglobin levels, PaO_2= Arterial oxygen partial pressure, PvO_2= Venous oxygen partial pressure, SaO_2= Arterial oxygen saturation, SvO_2= Venous oxygen saturation, O_2ER= Oxygen extraction ratio.

The determinants of DO_2 are CO, Hb, SaO_2, PaO_2.

The determinants of VO_2 are CO, Hb, SaO_2, PaO_2, SvO_2, PvO_2.

The determinants of CO are SV and heart rate.

The determinants of SV are afterload [ventricular relaxation and compliance (diastolic function); systemic arterial blood pressure, systemic vascular resistance; pulmonary arterial pressure, pulmonary vascular resistance], preload (volemia) and heart contractility (systolic function). The determinants of tissular perfusion pressure are SVR and CO.

Optimizing DO_2, VO_2 and O_2ER means that the demand (VO_2) has to be fulfilled by the offer (DO_2) [23]. If VO_2 exceeds DO_2, the tissues have to increase oxygen extraction in order to fulfill the demand [23]. If VO_2 exceeds DO_2 and oxygen extraction does not increase, a deficit in oxygen will occur which will lead to anaerobic metabolism which will increase lactate production and decrease tissular perfusion which will lead to organ dysfunction [22,23,34-36]. In normal states, VO_2 is independent of DO_2. If DO_2 decreases to a critical state, VO_2 becomes dependent on oxygen delivery. In this situation O_2ER increases to fulfill VO_2. However O_2ER cannot increase continuously when DO_2 decreases under the critical point. In this state of DO_2 dependency, hypoxia occurs and leads to organ dysfunction and lactate levels increase due to anaerobic metabolism [22,23,34-36].

Considering the goal directed fluid and hemodynamic therapy (GDFHT) point of view [9-20]. The objectives of the GDFHT are to optimize DO_2 to the tissues and tissular VO_2. DO_2 can be optimized in GDFHT by increasing CO. CO can be increased by optimizing SV. SV can be assessed echocardiographically with aortic peak velocity variation (ΔVpeak), aortic velocity time integral (VTI) and distance minute (DM) at the aortic valve [9-20]. Assessing aortic velocity time integral (VTI) and aortic peak velocity variation (ΔVpeak) will determine fluid responsiveness if fluid therapy with crystalloids and or colloids is necessary or vasopressor-inotropic therapy to increase SV and thus cardiac output [14]. As precised here above the determinants of tissular perfusion are systemic vascular resistance and cardiac output. Tissular perfusion pressure can decrease if SVR is low and or if CO is low. Optimizing SV with fluid and or inotropic therapy and SVR with vasopressor therapy will increase tissular perfusion pressure. In GDFHT, DO_2 can be optimized by increasing CO as explained here above. GDFHT aims to avoid DO_2 dependency states and prevent organ dysfunction [22,23,34-36].

Considering the transfusion goal directed protocols (TGDP) point of view [23-28,33,36]. Optimizing DO_2 and VO_2 will be achieved by optimizing hemoglobin levels. The ideal hemoglobin level is one that avoids situations where VO_2 is dependent on DO_2 and depends on the clinical context [22]. Since transfusion of all sorts of blood products has been related to postoperative morbidity in terms of organ dysfunction among others, it is important to transfuse the right product at the right time [2-5]. Using point of care viscoelastic methods can be helpful to guide and transfuse correctly [24-28]. These point of care devices have been shown to reduce length of hospital stay in hemorrhagic surgeries in children [28]. Maintaining the optimal hemoglobin levels to avoid situations where VO_2 exceeds DO_2 is mandatary since anemia has been related to increased mortality in children [26].

The important issue is to avoid unnecessary blood product administration which increases morbidity [2-5] and also avoid unnecessary anemia which can increase mortality [26]. In hemorrhagic settings like surgery, point of care devices can be useful to detect coagulation disorders which can be promptly treated with the appropriate blood products. Correcting coagulation disorders will further reduce bleeding which will avoid hemoglobin level decrease and thus avoid red blood cell transfusion. The use of TGDP is beneficial in bleeding situations to guide the correct use of blood products. Transfusion of red blood blood cells has been shown to reduce oxygen extraction ratio in cardiac surgical children with high extraction ratio [33]. The ideal hemoglobin level is the one that avoids to reach the oxygen delivery dependency state and depends on patients clinical context. The objectives of TGDP are to avoid and prevent situations where VO_2 becomes dependent on DO_2. DO_2 dependency state can lead to organ dysfunction (Table 1).

Table 1: Factors influencing determinants of DO_2 and VO_2.

Determinants of DO_2	Determinants of VO_2	Influencing Factors
CO	CO	Goal directed Fluid and hemodynamic therapy: Fluid therapy and or vasopressor-inotropic therapy
Hb	Hb	Transfusion Goal Directed Protocols
SaO_2	SaO_2	ERAS: Protective ventilation, optimal oxygen therapy, physiotherapy, optimal pain therapy
PaO_2	PaO_2	ERAS: Protective ventilation, optimal oxygen therapy, physiotherapy, optimal pain therapy
	SvO_2	ERAS: Protective ventilation, optimal oxygen oxygen therapy, physiotherapy, optimal pain therapy, temperature, sepsis, stress
	PvO_2	ERAS: Protective ventilation, optimal oxygen therapy, physiotherapy, optimal pain therapy

Considering enhanced recovery after surgery (ERAS) point of view [23,29-36] The objectives of ERAS is to reduce the perioperative stress which can have adverse consequences on postoperative recovery [23,29,30]. ERAS englobes measures which aim to reduce perioperative stress. These measures include optimal pain therapy, minimal invasive techniques whenever possible, optimal prevention and treatment of postoperative nausea and vomiting, prevention of postoperative organ dysfunction including infections, reducing fastening periods, favoring oral intake whenever possible, favoring early mobilization, respiratory physiotherapy to prevent pulmonary dysfunction which can lead to hypoxemia and hypoxia. Increasing oxygen saturation with oxygen therapy can increase DO_2, CaO_2 and decreases oxygen extraction ratio [33,35,36]. Oxygen consumption can be increased with the above mentioned stress situations. Reducing these situations and favoring states where DO_2 is optimal is mandatory to avoid the DO_2 dependency state which can have adverse effects on postoperative recovery [23].

Conclusion

GDFHT, TGDP and ERAS share the same goals. These are optimization of DO_2, VO_2 and O_2ER to prevent morbidity due to organ dysfunction. These goal directed therapies are related via the VO_2-DO_2 interaction. To reach ERAS, GDFHT and TGDP are necessary. The aimed outcome of GDFHT, TGDP and ERAS is the prevention of postoperative organ dysfunction and the reduction of postoperative length of hospital stay and thus the improvement of outcome. Determinants of DO_2, VO_2, oxygen extraction and perfusion pressure underly the physiology of goal directed therapies in children. Understanding these determinants are important for optimal patient management.

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