Journal of Pediatric Surgery Case Reports 32 (2018) 75–78

Contents lists available at ScienceDirect

Journal of Pediatric Surgery Case Reports

journal homepage: www.elsevier.com/locate/epsc

Continuous double volume exchange transfusion is a safe treatment for ECMO-induced hemolysis

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ARTICLE INFO

Keywords:
Veno-arterial extracorporeal membrane oxygenation
Hemolysis
Exchange transfusion

ABSTRACT

Extracorporeal membrane oxygenation (ECMO)-related hemolysis is a recognized complication and remains a source of significant morbidity and mortality in the neonatal population. This is the first description of continuous double-volume exchange transfusion (ET) performed for profound hemolysis that developed in a neonate with congenital heart disease on VA ECMO for sepsis. The aim of this report is to demonstrate the safety and efficacy of performing ET on a physiologically frail patient on ECMO support.

1. Introduction

Extracorporeal membrane oxygenation (ECMO)-related hemolysis has been a recognized complication for over 25 years and remains a source of significant morbidity and mortality in the neonatal population [1]. Hemolysis, defined as a rise in plasma-free hemoglobin (PFH) and total bilirubin, has an incidence of 7.8–13% in pediatric patients on ECMO [2–4]. It results in increased blood product transfusion requirements, pigment induced renal injury and need for renal replacement therapy (RRT), longer ICU and hospital stays, and higher mortality [5–7]. Despite recognition of risk factors leading to hemolysis and subsequent refinements in the circuitry, hemolysis remains a significant and increasing complication of ECMO [4,8].

Exchange transfusion (ET) is an established treatment for neonatal hyperbilirubinemia, immune and non-immune red cell hemolysis, and severe sepsis [9]. It is important to rapidly and effectively lower serum bilirubin levels in neonates to minimize secondary injury in the form of kernicterus and neurodevelopmental abnormalities such as hearing loss, movement disorders, and, intellectual deficits [10,11] as well as renal injury resulting from impaired glomerular filtration and tubular function [12]. Efficacy and complications of exchange transfusion vary based on the size of aliquots (single vs double volume exchange) [9], route (peripheral vs. umbilical) [13], and method of exchange (continuous vs. push-pull) [14]. Mortality directly attributable to ET is estimated to be approximately 1% and is most often due to cardiac arrest, cardiac arrhythmia, or air embolism [15]. There is a paucity of literature on the applicability of ET to ECMO-induced hemolysis in the neonatal, pediatric, or adult populations.

From our review of the current literature and to the best of our knowledge, this is the first description of continuous double-volume exchange transfusion on a neonatal patient on veno-arterial (VA) ECMO with profound hemolysis. Our aim is to demonstrate the safety and efficacy of performing ET on a physiologically frail patient on VA ECMO.

1.1. Case report

The patient is a 54 day-old male with Noonan's Syndrome, parachute mitral valve, hypoplastic transverse arch, atrial septal defect (ASD) and ventricular septal defect (VSD), placed on veno-venous (VV) ECMO (13 Fr Origen in right internal jugular vein) for respiratory failure initially, and subsequently converted to VA ECMO with addition of arterial cannula (8 Fr Biomedicus arterial cannula in left common carotid artery) for increased cardiovascular support. The ECMO circuit consisted of 1/4 by 1/16 SMART coated PVC tubing pack with a CARDIOHELP System (Maquet Medical Systems USA, Wayne, NJ) and a Quadrox-ID Adult PMP Oxygenator (Maquet Medical Systems USA, Wayne, NJ). The infant received heparin anticoagulation per an

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https://doi.org/10.1016/j.epsc.2018.02.012
Received 18 December 2017; Received in revised form 10 February 2018; Accepted 15 February 2018
Available online 17 February 2018

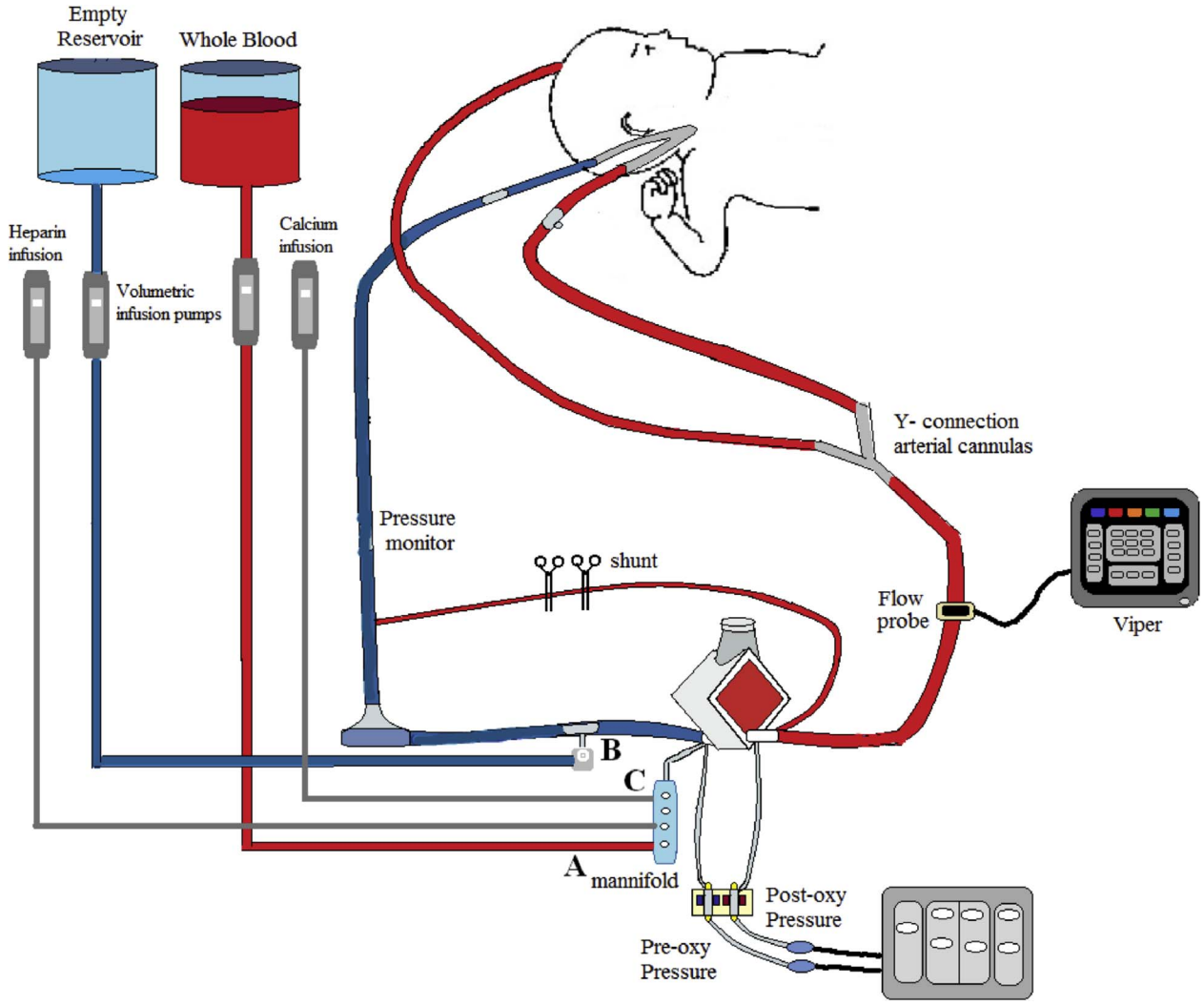

Fig. 1. Exchange transfusion configuration. A post-pump, pre-oxygenator "infusion return" (A) was configured to infuse blood at 7 cc/hr. The "reservoir pull" (B) configured pre-pump, pre-oxygenator pulled blood at 7 cc/hr. Continuous calcium and heparin infusions (C) were attached to the post-pump, pre-oxygenator manifold.

institutional protocol to target therapeutic levels of 0.3–0.7 IU/mL based on a heparin assay. Notable events on ECMO included a circuit exchange on ECMO day 2 for extensive thrombi and fibrin stranding, and the placement of a hemoconcentrator (Minntech, Minneapolis, MN) on ECMO day 12. Following addition of the hemoconcentrator, the patient experienced significant hemolysis, diagnosed by clinical jaundice, rise in plasma free hemoglobin (peak 195 mg/dL) and high serum levels of total bilirubin (peak 66.6 mg/dL). Given worsening renal failure, presumed to be acute tubular necrosis from byproducts of hemolysis, and severely elevated bilirubin, a double volume exchange transfusion was performed on ECMO day 16 using the configuration noted in Fig. 1.

1.2. Exchange transfusion

The transfusion volume was determined based on patient's weight (80 mL/kg) and the circulating volume of ECMO circuit (350 mL). A double volume exchange was calculated to be 1270 mL and was carried over 3 h at a rate of 7 mL/min. Per institutional policy, we used irradiated reconstituted, CMV-free, and sickle cell negative, whole blood less than 10 days old, with a final hematocrit of 50%.

We configured a "reservoir pull", a volumetric infusion pump which instead of infusing, pulls fluid at a predetermined rate. This was attached to a three-way stopcock on the ECMO circuit located on the pre-pump and pre-oxygenator tubing (Fig. 1: A). The "infusion return" was an infusion pump that infused whole blood at the same rate as the reservoir pump pulled (Fig. 1: B). This was attached to a manifold located on the post-pump and pre-oxygenator tubing. A continuous calcium and heparin infusion was also attached to the post-pump and pre-oxygenator manifold. The calcium drip was titrated based on ionized calcium (iCa) levels measured on serial patient arterial blood gases (ABGs) using epoc Reader (Epocal, Inc. Ottawa, ON Canada), which were collected at 15-min intervals.

The total blood volume to be exchanged, 1270 mL, was sent in sequence in 3 units of whole blood. ABGs were obtained on each of the 3 units to ascertain starting pH, potassium, ionized calcium, and lactate prior to starting procedure.

Bag 1: pH < 6.8, pCO2 65, pO2 45, HCO3 22.6, BE -27.5, lactate 3, K 3.8, iCa and glucose unmeasurable.

Bag 2: pH < 6.8, pCO2 > 90, pO2 48, HCO3 12.4, BE -28.5, lactate 17, K unmeasurable, iCa < 0.25, and glucose > 599.

Bag 3: pH < 6.8, pCO2 > 90, pO2 45, HCO3 12.3, BE -28.9, lactate 16.1, K > 11.2, iCa < 0.25, and glucose > 599.

The whole blood infusion was started at 7 mL/min and the calcium gluconate infusion at 10 mg/kg/h. After 5 min, withdrawal was initiated from the reservoir pump at a rate of 7 mL/min. The serial ABGs were collected at 15-min intervals and are graphed in Fig. 2. Through the length of the procedure, the calcium drip was titrated from 10 mg/kg/hr to 55.9 mg/kg/h based on the iCa on ABGs to a goal iCa level of 1.2–1.7.