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Sterility Duration of Preprimed Extracorporeal Membrane Oxygenation Circuits

Vi Ean Tan, MD; Alan T. Evangelista, PhD, D(ABMM); Dominick M. Carella, BSN, MBA; Daniel Marino, BSN, CCRN; Wayne S. Moore, PharmD; Nadji Gilliam, BSN; Arun Chopra, MD; and Jeffrey J. Cies, PharmD, MPH

OBJECTIVES There is a lack of standardization and supporting data regarding the duration preassembled and preprimed extracorporeal membrane oxygenation (ECMO) circuits are expected to be sterile. Therefore, the purpose of this study was to prospectively evaluate whether preassembled and preprimed ECMO circuits could maintain sterility for a period up to 65 days.

DESIGN Four ECMO circuits (2 neonatal/pediatric ¼" and 2 adolescent/adult ⅜") were assembled and primed under sterile conditions and maintained at room temperature. Culture samples were obtained from each circuit and plated within 1 hour. Culture samples were obtained on day 0 when assembled and primed then every 5 days up to day 65. Samples were plated on several different media including the following: blood agar plate: trypticase soy agar with 5% sheep blood, MacConkey agar, and thioglycollate broth then incubated at 35°C for 3 days.

RESULTS All cultures obtained from the priming solution from of the ¼" and ⅜" ECMO circuits produced no microbial or fungal growth for the 65-day study period.

CONCLUSION These pilot data suggest preprimed ECMO circuits may maintain sterility for a period up to 65 days. Additional studies evaluating a larger number of ECMO circuits are needed to confirm these findings.

ABBREVIATIONS BAP, blood agar plate; ECMO, extracorporeal membrane oxygenation; ELSO, Extracorporeal Life Support Organization; MAC, MacConkey agar; THIO, thioglycollate broth

KEYWORDS ECMO; extracorporeal membrane oxygenation circuits; pediatric; sterility

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Introduction

Extracorporeal membrane oxygenation (ECMO) circuits are forms of mechanical circulatory support that are progressively evolving in the critical care setting.[1] ECMO is used to provide support to neonates, children, and adults with severe but potentially reversible pulmonary and/or cardiac failure. ECMO is used in the neonatal and pediatric intensive care units when the risk of dying from cardiopulmonary failure is very high despite optimal conventional treatment. Artificial oxygenation and perfusion was described as early as 1954 when Gibbon[2] successfully applied a mechanical heart and lung apparatus during cardiac surgery. Many clinicians have since simulated the concept. Baffes et al[3] described the first use of venoarterial ECMO in 1970 in infants undergoing palliative cardiac surgery. Bartlett et al[4] successfully treated patients including postoperative cardiac failure, infant respiratory distress syndrome, meconium aspiration, and persistent fetal circulation by using ECMO in 1975. The indications for ECMO have since expanded beyond providing support for patients with acute severe heart or lung failure with high mortality risk. In recent years, ECMO has also been used during extracorporeal cardiopulmonary resuscitation to improve outcomes in selected patients as well as a bridge to cardiac assist device or transplantation.[5] The international summary published in January 2016 from the Extracorporeal Life Support Organization (ELSO) reported 251 centers currently providing ECMO support. It also reported an overall ECMO decannulation survival rate totaling neonatal, pediatric, and adult patients of 69% with the survival to discharge or transfer rate being 55%.[6]

ECMO support involves a closed system draining venous blood from a large vein through a tube or cannula, mixing the blood with the priming solution and passing it, with the help of a mechanical pump, into a membrane oxygenator outside of the body, in which oxygen and carbon dioxide are exchanged. The blood is then returned to the body, either through a vein (venovenous) or through an artery (venoarterial) cannula. The ECMO circuit consists of a blood pump with raceway tubing, a venous reservoir, a membrane oxygenator, and a countercurrent heat exchanger. ECMO staff must assemble, prime, and de-air an ECMO circuit using aseptic techniques and conditions prior to connecting the patient to the ECMO circuit for initiation. The entire process is estimated to take 30 to 60 minutes, depending on skill,

experience, and any potential delays in acquiring the necessary components for assembly. The availability of preassembled and preprimed ECMO circuits can significantly reduce the time from the decision to initiate until successful ECMO cannulation. Currently, the ELSO Infectious Disease Task Force recommends preprimed circuits can be maintained for up to 30 days.[7] Therefore, the purpose of this pilot study was to prospectively evaluate whether preassembled and preprimed ECMO circuits can remain sterile for a period up to 65 days.

Materials and Methods

Four ECMO circuits (2 neonatal/pediatric and 2 adolescent/adult with Quadrox-i pediatric and adult oxygenators [Maquet Cardiopulmonary GmbH, Rastatt, Germany], S3 and S5 pump systems [Sorin, Munich, Germany], ¼" and ⅜" tubing [Medtronic, Minneapolis, MN], and heaters [Cincinnati Sub Zero, Cincinnati, OH]), were assembled using aseptic technique in the ECMO supply room at St. Christopher's Hospital for Children by the ECMO coordinator and staff members. The Quadrox-i pediatric ¼" circuit was primed with 750 mL of Isolyte S (Multi-Electrolyte Injection, B. Braun Medical, Inc., Bethlehem, PA), and the Quadrox-i adult ⅜" circuit was primed with 1000 mL of Isolyte S. Each 100 mL of Isolyte S contains sodium chloride USP 0.53 g, sodium gluconate USP 0.5 g, sodium acetate trihydrate USP 0.37 g, potassium chloride USP 0.037 g, magnesium chloride hexahydrate USP 0.03 g, and water for injection USP added in quantity sufficient to final volume. The pH was adjusted to 6.7 (6.3–7.3) by adding tromethamine (Spectrum Chemical Manufacturing Corporation, New Brunswick, NJ) and sodium bicarbonate (Pfizer, New York, NY). The calculated osmolarity was 295 mOsmol/L. The estimated concentration of electrolytes (mEq/L) includes sodium 140; potassium 5; magnesium 3; chloride 98; acetate 27; and gluconate 23. Isolyte S is a sterile and nonpyrogenic solution that does not contain bacteriostatic or antimicrobial agents. The preassembled and preprimed ECMO circuits were covered and stored in the ECMO supply room for the duration of the study period. Authorized research personnel and ECMO staff members were able to enter and exit the supply room without additional infection prevention procedures such as donning personal protective equipment. The supply room was maintained at a controlled room temperature of approximately 22°C (72°F) for the duration of the study.

Culture samples were obtained from each circuit via the prepump access port of the ECMO circuit. Each 2-mL sample was collected using a SmartSite Needle-Free Valve (Carefusion, San Diego, CA) attached to the access port; this apparatus was changed after each sampling procedure and accessed via the access port for culture sampling. Chlorascrub (chlorhexidine gluconate 3.15% and isopropyl alcohol 70%) antiseptic swab (Merit Pharmaceutical, Los Angeles, CA) was used to clean the tip of the SmartSite valve prior to obtaining each sample. Chlorascrub was also used to clean the exterior of the plastic test tube vials used for sample procurement prior to obtaining the sample to prevent any potential contamination of sample from vial. A 5-mL sterile syringe (BD Becton Dickinson, Franklin Lakes, NJ) was used to withdraw each sample from the ECMO circuit and transfer it to the test tube vial. Samples were then labeled and hand delivered to the microbiology lab for further processing of each sample within 1 hour of collection.

Culture samples were obtained on the day of circuit priming and assembly (day 0) and subsequently every 5 days until day 65, accounting for 14 samples per circuit for the study duration. By using a pipette with a sterile tip, 100 mcL of culture sample was removed from the sample tube to inoculate agar plates including a blood agar plate (BAP), which consisted of trypticase soy agar plate with 5% sheep blood, and a MacConkey agar (MAC) plate. The sample fluid was spread over the entire surface of the plates using sterile loops. Three hundred microliters of sample fluid was also used to inoculate a tube of sterile thioglycollate broth (THIO) by using a pipette with a sterile tip. The BAP, MAC plates, and THIO broth were incubated at 35°C for 3 days. The BAP plates, MAC plates, and THIO broth were observed for growth daily for a total duration of 3 days. If turbidity or growth was observed in the THIO broth, then 100 mcL of culture fluid would be inoculated onto BAP and MAC plates and incubated at 35°C for an additional 3 days.

Results

The study results are presented in the Table. All sample cultures obtained from both of the ¼" and both of the ⅜" ECMO circuits remained negative for microbial and fungal growth for the 65-day study period.

Discussion

Many institutions have developed local policies and procedures for maintaining preassembled and preprimed ECMO circuits to minimize the time to successful ECMO initiation. In 1990, Chorak et al[8] reported a nonprimed dry assembled circuit could maintain sterility for a period of 48 to 60 hours. Young et al[9] conducted a study in 1997 to evaluate 12 ECMO circuits (6 dry circuits and 6 wet circuits), for a period of 7 days for potential microbial contamination. They concluded there was no microbiological contamination during the study period, hence the assembled circuits could maintain sterility for a period of 7 days. In 1998, Lonsky et al[10] demonstrated ECMO circuits (N = 100) preassembled and preprimed for approximately 2.5 to 3 days prior to cardiac surgery demonstrated no risk of microbial contamination when standard aseptic technique was used. The following year, Searles et al[11] conducted a 3-phase study with 43

Table. Extracorporeal Membrane Oxygenation Circuit Characteristics and Microbiological Outcomes of 4 Ex Vivo Experiments

Circuit Tubing Size, in	Oxygenator	Approximate Total Circuit Volume, mL	Study Duration, days	BAP Culture	MAC Culture	THIO Culture
1/4	Quadrox-i pediatric	750	65	No growth	No growth	No growth
1/4	Quadrox-i pediatric	750	65	No growth	No growth	No growth
3/8	Quadrox-i adult	1000	65	No growth	No growth	No growth
3/8	Quadrox-i adult	1000	65	No growth	No growth	No growth

BAP, blood agar plate; MAC, MacConkey agar; THIO, thioglycollate broth

circulating preprimed ECMO circuits with no samples being contaminated for up to 72 hours. In 2005, Walczak et al[12] evaluated 10 wet-primed devices for a period of 30 days before adding fresh bovine whole blood to prove efficient oxygen transfer for 6 hours within the preprimed circuits. All cultures obtained during the study period remained sterile after 30 days of stagnant prime. Karimova et al[13] reported wet-preprimed ECMO circuits with a hollow-fiber membrane oxygenator (N = 14) could be stored up to 2 weeks without microbial contamination if standard aseptic precautions were maintained. In 2012, Naso et al[14] conducted studies on 6 ECMO circuits with 2 supplementary circuits deliberately inoculated with a known bacterial strain as a positive control. The group reported ECMO circuit sterility was maintained for up to 35 days. The most recent study from 2015 by Weinberg et al[15] evaluated 5 preprimed ECMO circuits and demonstrating no bacterial growth for up to 4 weeks. The ELSO Infectious Disease Task Force was established in 2008 to address numerous issues including the lack of data on the safety of preassembled and preprimed ECMO circuits from an infection prevention perspective. The task force had 3 members participate in evaluating different ECMO circuits with various culture media for up to 30 days on preprimed circuits.[6] All cultures remained negative for the study duration and based on these results, the task force concluded it is safe to maintain preprimed circuits for up to 30 days, and possibly beyond 30 days.

Many hospitals have relied on infection prevention and infectious disease practitioners for guidance regarding the safe storage duration for preassembled and preprimed ECMO circuits. However, the majority of previous recommendations were based on guidelines developed for peripheral and central intravenous lines.[16] Despite all of these studies being conducted, there is still a lack of standardization and data regarding the duration of time that a preassembled and preprimed ECMO circuit is expected to be sterile. Our data indicate preassembled and preprimed ECMO circuits can maintain sterility for at least 65 days. This may allow for preprimed ECMO circuits to be stored for a longer duration, which could potentially reduce costs associated with circuit equipment waste while maintaining the ability for rapid ECMO initiation.

There are several limitations to this study. First, the study was conducted at a single center and the priming and assembling technique may not be consistent among ECMO centers. Second, the number of circuits evaluated was small (N = 4). Third, priming volumes and equipment may also vary among ECMO centers but theoretically should have minimal impact on affecting the outcome. Fourth, we did not assess for additional organisms such as *Mycobacterium*, *Legionella, Aspergillus,* and molds. While there are investigations and reports demonstrating contamination with *Mycobacterium chimaera,* these occurred as the equipment was contaminated by the manufacturer and delivered contaminated to the end users and not contaminated by the personnel assembling or using the equipment. As such it was not our intent to determine if any of the ECMO equipment was precontaminated with *M chimaera.*[17] Additionally, contamination of an ECMO circuit by personnel assembling the circuit with *M chimaera* would not be expected but could be considered with additional studies evaluating a longer period of potential sterility. However, these preliminary data support the need for additional studies to be conducted involving a larger sample size, additional centers, and additional organisms.

Conclusion

These pilot data suggest preprimed ECMO circuits may maintain sterility for a period up to 65 days. Additional studies evaluating a larger number of ECMO circuits are needed to confirm these findings.

ARTICLE INFORMATION

Affiliations St. Christopher's Hospital for Children (VET, ATE, DMC, NG, JJC), Philadelphia, Pennsylvania; Drexel University College of Medicine (ATE, DMC, JJC), Philadelphia, Pennsylvania; The Center for Pediatric Pharmacotherapy LLC (WSM, AC, JJC), Pottstown, Pennsylvania; NYU Langone Medical Center (AC), New York, New York; NYU School of Medicine (AC), New York, New York

Correspondence Jeffrey J. Cies, PharmD, MPH; jeffrey.cies@gmail.com

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