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A pilot study comparing two polymethylpentene extracorporeal membrane oxygenators

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J Rambaud, J Guilbert, I Guellec and S Renolleau

Abstract

Objective: We compared two polymethylpentene oxygenators being used in our unit: the Maquet Quadrox-iD paediatric® and the Medos Hilite 800LT®.

Study design: A mono-centric, prospective pilot study was conducted on ten consecutive newborn patients who had been admitted to our hospital service for extracorporeal circulation (EC) treatment. We examined the rate of oxygen transfer, the CO_2 removal capacity and the average sweep gas flow required to produce this result. We also assessed the disturbances of haemostasis, the need for labile blood products and the membrane oxygenator lifetime and cost of use.

Conclusions: According to our study, it seems to us that Medos Hilite 800LT® membrane oxygenators demonstrate greater oxygen transfer and CO_2 removal capacity than Maquet Quadrox-iD paediatric® membrane oxygenators, at a similar cost. These results lead us to conclude that it is reasonable to continue using Medos Hilite 800LT® membrane oxygenators. A broader comparison study would be necessary in order to support these initial results.

Keywords

extracorporeal circulation; polymethylpentene membrane; efficiency; neonatal; cost study

Introduction

Extracorporeal circulation (EC) techniques are used as a last resort during paediatric resuscitation in the case of persistent refractory hypoxaemia under maximum mechanical ventilation and during the use of all so-called conventional therapies.[1-4] These techniques can lead to complications, such as haemorrhaging, thromboembolism or oxygenator failure.[5-8] The superiority of polymethylpentene (PMP) membrane oxygenators in relation to silicone membrane has been previously demonstrated.[9,10] Recent in vitro studies have attempted to show the differences between several different models of polymethylpentene EC membrane oxygenators.[11] However, no in vivo study aiming to compare different polymethylpentene EC membrane oxygenators has been carried out. The issue today consists in improving our techniques (with regard to the types of membrane oxygenators, pumps and cannulae being used) in order to reduce the number of serious complications and the overall costs.[12]

The objective of our study, therefore, was to compare two PMP oxygenators widely used in our unit in order to determine whether or not one of them was superior for use in long-term EC treatments.

Materials and methods

Study design

From November 2010 to May 2011, we carried out a mono-centric, prospective study on newborn patients hospitalized for EC treatment in the paediatric resuscitation unit at Armand-Trousseau Children's Hospital. The type of EC treatment to be administered (venovenous EC with single or double cannulae, or venoarterial EC) was determined according to each child's pathology. The membrane oxygenators used were the Medos Hilite 800LT® (Medos Medizintechnik AG, Stolberg, Germany) and the Maquet Quadrox-iD paediatric®

Paediatric Intensive Care Unit, Armand-Trousseau Children's Hospital APHP (Paris Hospitals Public Assistance) UPMC (Pierre and Marie Curie University, Paris VI) Paris, France

Corresponding author:
Sylvain Renolleau
Paediatric Intensive Care Unit
Armand-Trousseau Children's Hospital APHP (Paris Hospitals Public Assistance)
Paris, France
Email: sylvain.renolleau@trs.aphp.fr

Table 1. Characteristics of the two oxygenators

	HILITE 800®	QUADROX-iD®
Maximum blood flow	0.8 L/min	2.8 L/min
Maximum gas flow	1.6L/min	5.6L/min
Fill volume	55 ml	81 ml
Oxygenator		
Materials	Polymethylpentene	Polymethylpenene
Surface	0.32 m 2	0.8 m 2
Heat exchanger	Included	Included
Surface	0.074 m2	0.15 m 2
Connectors		
Blood entrance and exit	3/16-1/4	1/4
Gas entrance and exit	1/4	1/4 (entrance) and 3/8 (exit)
Need for de-bubbling	Yes	No

(Maquet Cardiovascular, Hirrlingen, Germany). The main differences between these two types of membrane oxygenators lie in their conformation, their surface and their cost (Table 1). The pumps used in the course of the study were pumps with distensible tubes (Sofracob®) which work with an alternative clamp for EC treatment with a venovenous single cannula (AREC/extracorporeal respiratory support).[13]

Statistics

All of the statistics cited in this study were produced through a Wilcoxon rank-sum (Mann-Whitney) unpaired test. The significance level was set at $p<0.05$. Meanwhile, we also produced a set of statistics using a Wilcoxon signed-rank paired difference test.

Patients

Ten consecutive patients were prospectively included in this study. Over the course of the study, nine Medos Hilite 800LT® membrane oxygenators and ten Maquet Quadrox-iD paediatric® membrane oxygenators were used. Both types of membrane oxygenators were used on six of our patients undergoing EC treatment. At the time of the connection to the circuit, the selection of the type of membrane oxygenator to be used was randomized. After the initial connection, a different type of membrane oxygenator was used for each EC circuit change. We chose to replace the oxygenator of one brand by the other brand to avoid a "patient effect" on the lifetime of the oxygenator and the need for blood products The characteristics of these patients are presented in Table 2.

Methods

The criteria for EC treatment were established according to the value of the oxygenation index, the alveolar-arterial difference for oxygen ($AaD\text{-}O_2$) and the PaO_2/FiO_2 ratio.[14,15] The rates of oxygen transfer (PaO_2 at the membrane inlet; PaO_2 at the membrane outlet) and CO_2 removal capacity ($PaCO_2$ at the membrane outlet; $PaCO_2$ at the membrane inlet) were conducted with an FiO_2 of 100%. The PaO_2 measurements were carried out at the same blood flow rate and the same haemoglobin levels. The established objectives were to obtain normal blood pH with a $PaCO_2$ of 40-50 mmHg at the membrane inlet. Where there was complete respiratory support, the goal for venous saturation was 65-75% for venoarterial EC and 75-85% for venovenous EC with double cannulae. We also assessed the membrane oxygenator resistance through the pressure differential at the membrane oxygenator inlet and the membrane oxygenator outlet. The resistance corresponds to the pressure loss between the membrane oxygenator inlet and the membrane oxygenator outlet. The average sweep gas flow needed to obtain these results was also examined.

In order to assess the haemostasis disturbances, the levels of platelets, fibrinogen, D-dimers, activated clotting time (ACT) and anti-Xa were analysed. Our

Table 2. Characteristics of the population studied

	HILITE 800®	QUADROX-iD®	p
Boys/girls	4/4	4/4	1
Average age (d)	8 ± 9	8 ± 9	1
Average weight (kg)	3.2 ± 0.4	3.4 ± 0.7	1
Average $AaDO_2$	583 ± 40	581 ± 43	1
Average OI	39 ± 17	41 ± 17	1
Average PaO_2/FiO_2	40 ± 10	41 ± 14	1
Average ventilation index	102 ± 41	94 ± 47	0.9
Average $PaCO_2$	72 ± 28	83 ± 34	0.87
Nitric oxide	8/8	8/8	1
Haemodynamic disorders	7/8	8/8	1

$AaDO_2$: Alveolar-arterial oxygen tension difference; FiO_2: Fraction of inspired oxygen; OI: Oxygen Index; $PaCO_2$ Partial pressure of arterial CO_2; PaO_2: Partial pressure of oxygen.

goals with regard to anticoagulation were to obtain ACT levels that would be three times higher than the norm and anti-Xa levels of 0.3-0.5 IU/ml.[16] Coagulation was monitored every four hours by means of the Hemochron test (Terumo, Essen, Germany). The goal was to have coagulation between 180 and 200 for venovenous EC and between 200 and 220 for venoarterial EC. Before connecting the patient to the circuit, the levels of free and functionally active protein S, of functionally active protein C and of antithrombin III were measured in order to eliminate any congenital disorders of haemostasis which could have interfered with the results.

The blood product needs were assessed through the quantification of the packed red blood cells and platelet concentrates being used per day of EC treatment. The transfusion thresholds were established before the beginning of the study. Levels of 10 g/dl of haemoglobin and 60,000 platelets/mm^3 are customary.[17-18] Whenever the haemoglobin levels were lower than 10 g/dl, a volume of 40 ml/kg of packed red blood cells was transfused, taking into account the child's blood volume and that of the EC circuit. Any decisions to discontinue EC treatment were based on the patient's capacity to maintain stable haemodynamics, as well as efficient CO_2 removal ($PaCO_2$ of 40-50 mmHg) and efficient oxygenation with minimum support or whenever haemodynamic or neurological developments in the patient made it impossible to contemplate permanent weaning from the EC treatment.

The patients were monitored right up to their release from the resuscitation unit and information on any complications was collected: cerebral haemorrhaging, cerebrovascular accidents (CVAs) or death.

In order to assess the cost per day of the two membrane being tested, we took into account the cost of labile blood products as established by annual decree (€ 112.70 per packed blood cell and € 76.06 per platelet unit) as well as the cost of the membranes themselves.

Results

Patient randomisation and protocol

Patient characteristics at the time of connection to the EC circuit and the indications for connection to extracorporeal circulation were similar in the two groups (Tables 2 and 3).

Oxygenator efficiency

Oxygenation: The rate of oxygen transfer per m^2 was significantly better in Medos Hilite 800LT® membrane oxygenators (oxygenation capacity/surface ratios [SD] were 1138 [307] and 538 [115] mmHg per m^2 for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p<0.0001).

Table 3. EC connection information for each patient

Patient 1	Malignant pertussis
Patient 2	Meconium inhalation, PAH
Patient 3	Meconium inhalation, PAH
Patient 4	Diaphragmatic hernia, PAH
Patient 5	Meconium inhalation, PAH
Patient 6	Diaphragmatic hernia, PAH
Patient 7	Septic shock
Patient 8	Meconium inhalation, PAH
Patient 9	Septic shock
Patient 10	Meconium inhalation, PAH, HCM

PAH: pulmonary arterial hypertension; HCM: hypertrophic cardiomyopathy

CO_2 Removal: The Medos Hilite 800LT® membrane oxygenators had a greater removal capacity per m^2 (the removal capacity/sweep gas flow/surface ratios [SD] were 0.038 [0.004] and 0.022 [0.001] mmHg/ml/mn/m^2 for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p<0.0001). However, the ratio for CO_2 removal capacity and sweep gas flow was significantly higher for the Maquet Quadrox-iD paediatric® membrane oxygenators (the CO_2 removal capacity/sweep gas flow ratios [SD] were 0.012 [0.001] and 0.02 [0.002] mmHg/ml/mn for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.01).

The CO_2 removal capacity and the oxygen transfer rate at the membrane oxygenator surface were significantly better in the Medos Hilite 800LT® membrane oxygenators (Table 4).

Oxygenator pressure and resistance

There was no significant difference in membrane oxygenator resistance (the average resistance [SD] was 16.7 [20] and 11.4 [7] mmHg for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.06).

Coagulation data and consumption of blood products

The fibrinogen concentration was not significantly different (the fibrinogen concentration [SD] was 2.9 [0.7] and 2.8 [0.9] g/l for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.89). The D-dimer concentration was similar in both membrane oxygenators (D-dimer concentrations [SD] were 17.6 [16] and 17 [7.6] µg/l for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.76). The medium need for heparin was comparable in the two membrane oxygenators (the medium dose of heparin [SD] was 36 [7.3] and 35 [8.7] U/kg/h for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.5). These results suggest that, with regard to haemostasis

Table 4. Membrane efficiency

	HILITE 800LT® (average/ standard deviation)	QUADROX-iD ® (average/ standard deviation)	p
Oxygenation capacity (mmHg)	363 ± 92	436 ± 97	< 0.0001
Oxygenation capacity / surface ratio (mmHg/m²)	1138 ± 307	538 ± 115	< 0.0001
CO_2 removal capacity (mmHg)	14.49 ± 6	14.45 ± 4	0.88
CO_2 removal capacity / sweep gas flow ratio (mmHg/ml/mn)	0.012 ± 0.001	0.02 ± 0.002	0.01
CO_2 removal capacity / sweep gas flow /surface ratio (mmHg/ml/mn/m²)	0.038 ± 0.004	0.022 ± 0.001	< 0.0001
Average sweep gas flow (ml)	1400 ± 592	1003 ± 394	< 0.0001
Membrane resistance (mmHg)	16.7 ± 20	11.4 ± 7	0.06

Table 5. Membranes and haemostasis disorders

	HILITE 800LT ®	QUADROX-iD®	P
Average fibrinogen concentration (g/l)	2.9 ± 0.7	2.8 ± 0.9	0.89
D-dimers concentration (mg/ml)	17.6 ± 16	15 ± 7.6	0.76
Average heparin (U/kg/h)	36 ± 7.3	35 ± 8.7	0.8
Daily aphaeresis consumption	0.67	0.76	0.58
Daily erythrocyte concentrate consumption	0.23 ± 0.12	0.18 ± 0.12	0.38

disturbances linked to extracorporeal circulation, there is no difference in the two membrane oxygenators. In just half the cases, the haemostasis evaluation was conducted prior to connection to the EC circuit in search of haemostasis anomalies. No anomalies were found.

There was no significant difference in the consumption of packed red blood cells and platelet concentrates (the average daily consumption of packed red blood cells [SD] was 0.23 [0.12] and 0.18 [0.12] for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.38 and the average daily consumption of platelet concentrates [SD] was 0.67 [0.29] and 0.76 [0.30] for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.38) (Table 5).

Without considering the type of oxygenator, there was also no significant difference in the consumption of packed red blood cells and platelet concentrate (excepting patient N° 8 who consumed more platelets, but this patient used both devices in equal ways and didn't alter the result) (data not shown).

Consumption and cost of oxygenators

In the course of the study, we used a total of 19 membrane oxygenators: nine Medos Hilite 800LT® devices and ten Maquet Quadrox-iD paediatric® devices (Table 6). We made nine membrane oxygenator replacements, four of which were made for patient N° 8 alone. The average duration of the EC treatment was 15.7 days.

The average membrane oxygenator lifetime was not significantly different between the two devices (the average lifetime [SD] was 8.6 [6] and 11.1 [4.4] for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.40). If we exclude patients N°7 and N°10, for whom the EC treatment was discontinued, either because the patient quickly achieved independence (patient N°7) or because the patient died (N°10), the membrane lifetimes were still not significantly different (the average membrane oxygenator lifetime [SD] was 9.1 days [6.3] and 11.86 days [4.4] for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.44). Given the small number of patients, making a statement of fact of these results is difficult.

The assessment of the daily costs of EC with regard to the type of membrane oxygenator used and the cost of the labile blood products consumed did not reveal any significant difference (the average daily costs [SD] were € 184.53 [51] and € 214.34 [58] for the Medos Hilite 800LT® versus the Maquet Quadrox-iD paediatric®, p=0.38). The test did not reveal a specific duration after which one of the two membrane oxygenators became more attractive in terms of costs (Figure 1).

Survival outcome

There was no significant difference in the survival and complication rates for the two membrane oxygenators.

Discussion

This prospective pilot study enabled us to demonstrate a better oxygen transfer rate and a better CO_2 removal

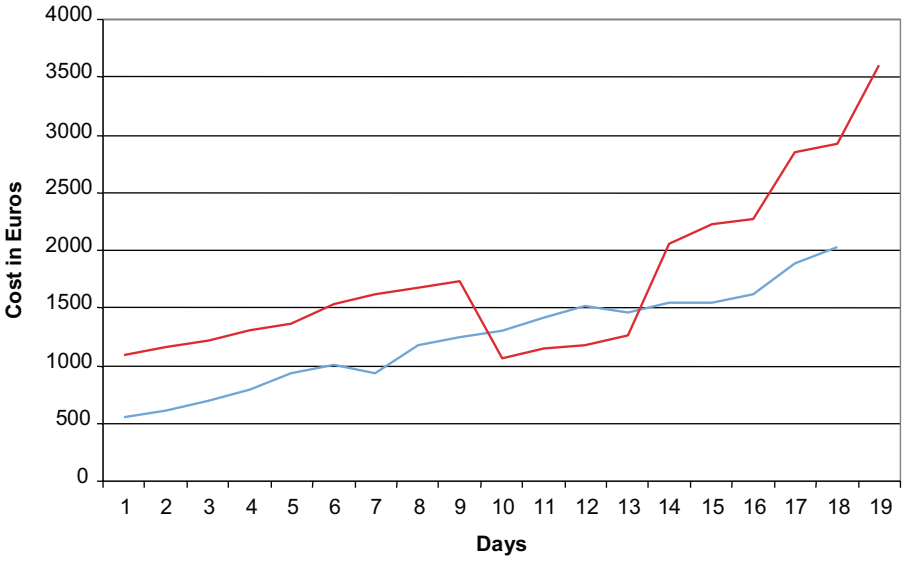

Figure 1. ROC curve comparing the daily costs of each membrane during its usage
Red curve: daily costs for QUADROX-iD® membranes; Blue curve: daily costs for HILITE 800LT ® membranes

capacity in Medos Hilite 800LT® membrane oxygenators when the surface area was taken into consideration.

The oversizing of the Maquet Quadrox-iD paediatric® membrane oxygenator in relation to the corporeal surface of our newborn patients was not negligible and it led to a greater priming volume of 30 ml (10 ml/kg on average) which, consequently, led to an increase in the initial cost of labile blood products. We were particularly interested in studying the lifetime of our membrane oxygenators because we conduct long-term EC treatments with respiratory support. Our study shows that the lifetime of the Maquet Quadrox-iD paediatric® membrane oxygenators seems greater than that of the Medos Hilite 800LT® membrane oxygenators, though not significantly, and at a greater cost. The study did not reveal a delay of use from which a membrane cost less than the other one.

The small number of patients limits the impact of this study. Furthermore, membrane oxygenator lifetime may be affected by certain incidents that are characteristic of studies in vivo. In patient N°8, for instance, the extracorporeal connection time was long because of a technical difficulty in inserting the cannula into the internal jugular vein, which prolonged the use of the membrane oxygenator in closed circuit before connection. Such prolonged use of the membrane oxygenator in closed circuit increases the risk of premature coagulation in the membrane oxygenator, despite the administration of a loading dose of heparin when the circuit is implemented. Indeed, the Maquet Quadrox-iD paediatric® membrane oxygenator coagulated after two days of use. This incident probably skewed the calculation of the membrane oxygenator lifetime and daily cost: the cost of the Maquet Quadrox-iD paediatric® membrane oxygenator is far higher than that of the Medos Hilite 800LT® membrane oxygenator (€ 1000 before taxes versus € 450 before taxes). The amount of time needed for the cannulation procedure is different for each patient and, if it is protracted, may be responsible for premature coagulation in the membrane oxygenator.[19-21]

Moreover, the pre-connection haemostasis evaluation was not conducted on all of the patients. It, therefore, does not allow us to formally rule out the possibility that pre-existing haemostasis disorders might lead to a greater consumption of blood products, greater need for heparin or premature coagulation in the EC membrane oxygenator. In a retrospective study carried out on 20 patients, Vats et al.[22] examined the median hospital stay costs generated in paediatric EC, with the assumption that patients who survived after being released from hospital went on to enjoy a normal lifespan. Their calculations showed a cost of $ 4190 (€ 3331) per year of life saved. It seemed to us that it was relevant to study this cost criterion in the evaluation of the two membranes we were comparing.

Our study did not demonstrate any significant difference in the cost of use between the two membrane oxygenators, even though the Medos Hilite 800LT® membrane oxygenator seems to be less expensive.

Rather than the centrifugal pumps that are more commonly used today, we used EC pumps with distensible tubes.[23,24] Indeed, these are the only types of pumps that can be used for EC treatment with a veno-venous single cannula (AREC/extracorporeal respiratory support). In our experience, there is no difference between centrifugal and extensible concerning the

consumption of platelet units and packed red blood cells. Improvement in centrifugal pumps has enhanced the limitation of haemolysis. [25]

There is currently no single and 100% reliable means of monitoring the quality of anti-coagulation in patients. In order to balance anti-coagulation in our patients undergoing EC treatment, our unit simultaneously monitors several parameters: a twice-daily measurement of ACT and anti-Xa levels, as well as a Hemochron test (rapid measurement of the ACT) every four hours. Our practice is similar to what is recommended in the literature today[26-28]. Thus, we did not modify the membrane oxygenator lifetime by using any protocols or non-recommended methods for monitoring the rate of anticoagulation.

Today, the tendency is to reduce the size of the circuits and of the EC membrane oxygenators[29] and there is some thought being put into the costs generated by such techniques. In light of these preliminary results, it seems reasonable to continue using the Medos Hilite 800LT® membrane oxygenators, which have a lower priming volume, a better oxygenation and CO_2 removal capacity at the membrane surface and a lower purchasing cost.

However, the power of our study is not sufficient to conclude definitively on the superiority of either of the two membranes. Both devices are efficient and any preference should be based on the specifics of the patient. It would be useful to realize a large randomized study to eliminate potential biases associated with the patient.

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Conflict of Interest Statement

The authors have no conflicts of interest to declare

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