Original Article

Experimental Evaluation of the Medtronic Maxima Forté Hollow Fiber Membrane Oxygenator

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ABSTRACT

A new hollow fiber membrane oxygenator, the Medtronic Maxima Forté, was tested for gas transfer, blood path resistance and blood handling characteristics in a standardized setting with surviving animals.

Three calves (mean body weight: 71±9.6 kg) were placed on cardiopulmonary bypass at a mean flow rate of 50 ml/kg/min for six hours. The circuit included the Maxima Forté oxygenator. The animals were weaned from cardiopulmonary bypass and then from the ventilator. After seven days, the animals were sacrificed electively.

Physiologic blood gas values could be maintained throughout perfusion in all animals. Mean pressure drop through the oxygenator varied between 49 mmHg and 66 mmHg. The respective baseline values for red blood cell count, white blood cell count and platelets were 8.90±1.26 $10^6/mm^3$, 7.46±3.17 $10^3/mm^3$, and 680±216 $10^3/mm^3$. Red blood cell and platelet counts dropped slightly to 7.26±1.61 $10^6/mm^3$ and 400±126 $10^3/mm^3$ at the end of the bypass, whereas the white blood cell count increased up to 9.13±5.25 $10^3/mm^3$. All three cell lines returned to near their baseline values after seven days. Blood trauma evaluated as a function of plasma hemoglobin (plasma Hb) and lactate dehydrogenase (LDH) showed stable values during all the perfusion time. Both peaked at 24 hours before returning to their baseline values at seven days. LDH showed a statistically significant variation: 3255 ± 693 IU at 24 hours versus 2029 ± 287 IU at baseline ($p = 0.04$). The variation of plasma Hb was not statistically significant (93.5 ± 7.7 µmol/l at 24 hours versus 77.3 ± 52.3 µmol/l at baseline) indicating a weak effect of the perfusion on blood trauma.

The Medtronic Maxima Forté hollow fiber membrane oxygenator offered good gas exchange capabilities, a low pressure drop, and low blood trauma over a prolonged perfusion time of six hours in this evaluation.

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INTRODUCTION

The superiority of membrane oxygenators during cardiac surgery with cardiopulmonary bypass has been firmly established and has led to their widespread use (1,2). Their main advantages lie in their predictability of gas exchange and their improved blood handling. Following the Maxima Plus membrane oxygenator (3), Medtronic Inc.[a] has recently added the Maxima Forté membrane oxygenator to its cardiopulmonary product line. It has a compact design, further improvement of the blood handling, a new polyolefin heat exchanger and advanced plasma resistant fibers. The present study was designed to evaluate this new oxygenator in a standardized setting with surviving animals in order to justify the application of these devices.

MATERIALS AND METHODS

The protocols described herein were reviewed and approved by the Committee on Animal Care, Office Vétérinaire Cantonal, Lausanne. All animals received care in compliance with the "Principles of Laboratory Animal Care" formulated by the National Society for Medical Research and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences and published by the National Institutes of Health (NIH Publication No. 80-23, revised 1985).

ANIMALS

This study was conducted on three calves with a mean body weight of 71±9.6 kg (standard deviation). All the animals were premedicated with xylazine (0.15mg/kg, given intramuscularly). General anesthesia was started with thiopentone sodium (10mg/kg, given intravenously) and maintained thereafter with volatile anesthetic (nitrous oxide and halothane) mixed with oxygen-enriched air. A jugular central venous catheter and a femoral arterial catheter were placed in each animal for hemodynamic monitoring. Analgesia with pentazocin was administered as needed.

OXYGENATOR

The Medtronic Maxima Forté is an integrated hollow fiber membrane oxygenator containing a removable hardshell reservoir, a heat exchanger and an oxygenating compartment. Blood enters the oxygenator at the bottom of the heat exchanger. The heat exchanger is made up of polyolefin fibers, without metal components. Blood flows toward the top of the heat exchanger and then radially into the fiber bundles, which are wound in a spiral fashion, and housed in a cylindrical shaped polycarbonate shell around the heat exchanger. Blood follows a top to bottom flow path through the space outside the hollow fiber bundles through which ventilating gas is circulating. Blood is then collected in the arterial outlet at the bottom of the oxygenator. The microporous hollow fibers are made from polypropylene for separation of the gaseous phase from the blood with a total outer surface area of 2.4 m^2. The reduced pore diameters of 0.3 µ make it less likely for plasma to break through the fiber wall. This should ensure more consistent gas transfer throughout the procedure. The cardiotomy filter is made up of a 20 µ polyester screen. A shunt for recirculation is also provided by the manufacturer. The static priming volume for the integrated device is 295 ml, comparing favorably with the 480 ml of the Maxima Plus. Maximum flow rate is 7 l/min.

EQUIPMENT

A primary calibrated roller pump (model 10.10.00)[b] custom 1/2 in and 3/8 in polyvinylchloride (PVC) tubing packs, an open hardshell reservoir (Maxima Forté hardshell venous reservoir[a]) and a gas blender[c] were used on all cases.

CARDIOPULMONARY BYPASS

Closed chest perfusion was selected for this study. For this purpose, the right atrium was cannulated through a jugular vein for venous drainage, while a carotid artery was used for the arterial return. Before cannulation, heparin (Liquemin[d]), 300 IU/kg body weight, was given systemically and the activated clotting time (ACT[e]) was kept above 400 sec throughout perfusion. The cardiopulmonary bypass circuit was connected after being primed with 1500 ml of crystalloid only (NaCl 104 mmol/l, KCl 5.4 mmol/l, $CaCl_2$ 1.6 mmol/l, Mg Cl_2 1 mmol/l, sodium lactate 27 mmol/l, sodium bicarbonate 50 mmol/l). No additional blood was tranfused. Blood flow rate was maintained by a roller pump at 50 ml/kg/min. An FiO_2 of 80% was selected with the gas blender and adjusted only if the target PaO_2 of 94 mmHg was not reached. Arterial pH was kept between 7.4-7.5 and mean femoral arterial pressure was kept between 60-80 mmHg. Oxygen flow was supplied to the oxygenator with the gas blender at a flow rate equal to the blood flow rate.

After perfusion, the animals were weaned and decannulated. Heparin was reversed with protamine under ACT control. Then the animals were weaned from the ventilator and extubated. After seven days survival, the animals were electively sacrificed with a lethal dose of sodium pentobarbital. A necropsy was performed for macroscopic analyses of the lungs, the heart, the liver, the spleen, and the kidneys, with special attention being paid to the latter to detect any focal necrosis suggestive of emboli (4).

MEASUREMENTS

ECG, central venous pressure, femoral artery pressure, arterial line pressure, pump flow, and inlet and outlet pressures of the oxygenator were recorded continuously. A standard battery of blood samples was taken for arterial and venous blood gas analyses, and hematology (white blood cell count, red blood cell

a Medtronic Inc., Anaheim, CA
b Sorin Biomedical, Irvine, CA
c Sechrist Industries, Inc., Anaheim, CA
d F. Hoffman-la Roche & Co., Basle, Switzerland
e Hemochron, International Technidyne Corp., Edison, NJ

count, platelets), before bypass, after mixing (10 min on bypass), after one hr, two hrs, five hrs, and six hrs of perfusion. Blood gas samples were taken again 30 min after bypass (spontaneous breathing) and 60 min after bypass (after extubation). Furthermore, hematology samples were taken 24 hrs after bypass, 48 hrs after bypass, and seven days after bypass.

DATA ANALYSES

All data are presented as mean ± one standard deviation. Statistical analyses using Student's t test were applied to compare values of the parameters with their baseline values. The results were significant when $p < 0.05$.

RESULTS

The three animals could be perfused for six hours according to the protocol with a mean flow of 50 ml/kg/min. All the animals could be weaned from perfusion and extubated. Survival after perfusion of six hours was seven days for all calves, when they were sacrificed electively for post mortem studies.

BLOOD GAS ANALYSES

Physiologic pH could be maintained throughout the runs, as shown in Figure 1. The mean pH values varied between 7.39 and 7.49 for the arterial side versus 7.34 and 7.42 on the venous side. Adequate results were achieved for pCO_2 (Figure 2) with 30 mmHg to 42 mmHg on the arterial side versus 39 mmHg to 50 mmHg on the venous side. Mean pO_2 values throughout perfusion are depicted in Figure 3. Minimum arterial pO_2 was 200 mmHg and maximum was 257 mmHg compared with 36 mmHg and 38 mmHg on the venous side. Arterial and venous oxygen saturation is shown in Figure 4. Mean oxygen saturation (SaO_2) varied between 99.6% and 99.8% for the arterial side of the oxygenator as compared with 65.2% to 68.2% (SvO_2) on the venous side. The values 30 minutes after bypass represent spontaneous breathing of the animals after weaning from perfusion, whereas the values 60 minutes after bypass were taken after extubation of the animals. No blood gas parameter was found to be statistically different from baseline value at any time interval.

Figure 1: Blood gas analysis, pH. For each time point, one sample from each animal (n = 3) was drawn.

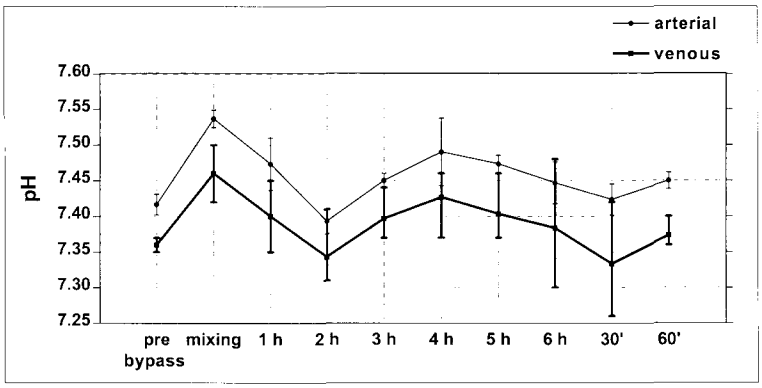


Figure 2: Blood gas analysis, pCO_2. For each time point, one sample from each animal (n = 3) was drawn.

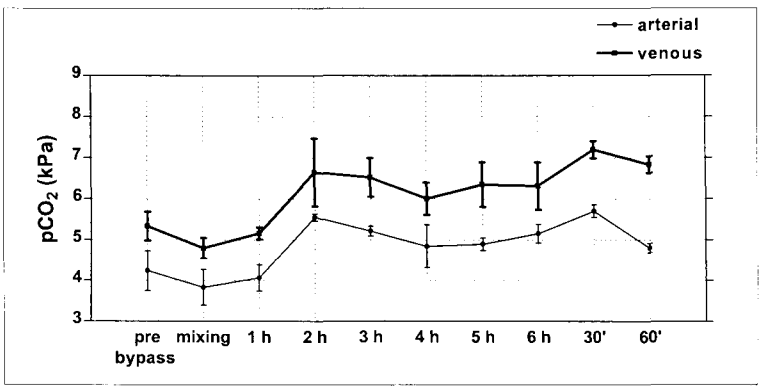
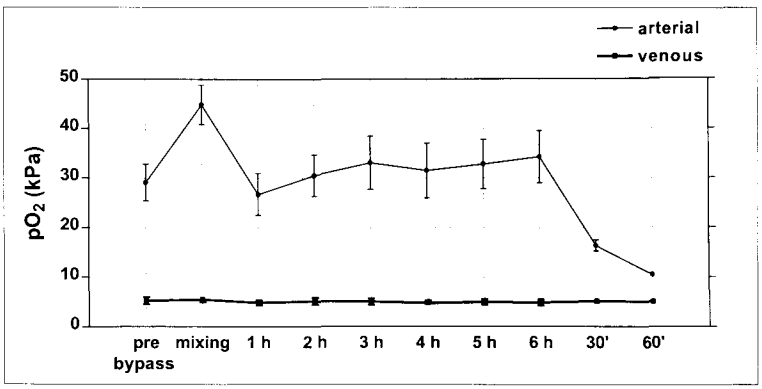


Figure 3: Blood gas analysis, pO_2. For each time point, one sample from each animal (n = 3) was drawn.



HEMATOLOGY

Mean values for red blood cell count, white blood cell count, and platelets are given in Table 1. All three cell lines returned to near their baseline values after seven days. No hematological parameter was found to be statistically different from baseline value at any time interval.

Figure 4: Blood gas analysis, oxygen saturation. For each time point, one sample from each animal (n = 3) was drawn.

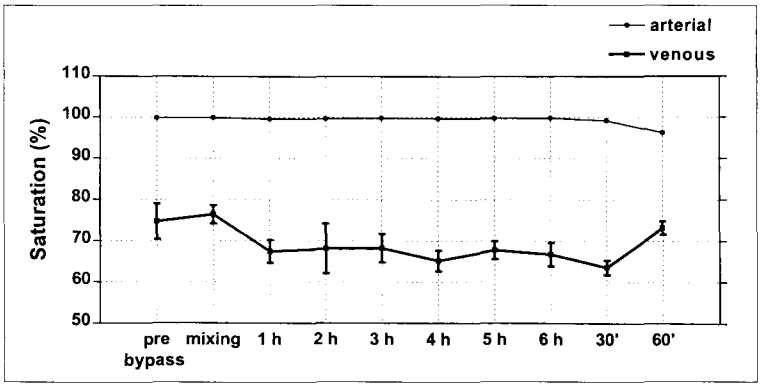


Table 1: Hematology

	Red blood cell count $10^6/mm^3$	White blood cell count $10^3/mm^3$	Platelets $10^3/mm^3$
Prebypass	8.90±1.26	7.46±3.17	680±216
Mixing	7.53±1.14	4.63±4.47	493±244
1 hr	8.03±0.98	5.90±3.80	435±157
2 hr	8.01±1.05	7.69±3.89	493±199
5 hr	7.90±1.05	9.13±5.25	400±126
6 hr	7.26±1.61	9.00±4.54	415±119
24 hr post	9.83±1.58	9.25±5.72	670±311
48 hr post	8.48±0.73	7.45±3.60	512±17
7 days post	9.00±0.70	8.90±4.81	722±272

Table 2: Hemolysis

	LDH IU	Plasma hemoglobin mmol/l	Hct %
Prebypass	1029±287	77.3±52.3	24±5
Mixing	1650±226	53.0±19.9	22±7
1 hr	1725±331	55.3±8.1	20±1
2 hr	1692±403	79.6±25.4	22±3
5 hr	1967±374	6.66±24.8	23±6
6 hr	1928±368	64.3±3.2	23±6
24 hr post	3255±693	93.5±7.7	25±1
48 hr post	2359±507	62.5±3.5	24±1
7 days post	1621±195	42.0±11.3	24±1

HEMOLYSIS

The indices of mechanical erythrocyte destruction are given in Table 2. Plasma hemoglobin and lactate dehydrogenase (LDH) levels were stable throughout the perfusion period. Both had a peak at 24 hours, but dropped back to near their prebypass values in the following days. The peak LDH was statistically different from baseline values ($p = 0.04$). This was not the case for plasma Hb because of an important scatter of the baseline values. For reference, the values of hematocrit and its standard deviations are given in Table 2. The maximal hemodilution was 83%, and no hematological peak value was found to be statistically different from baseline values after correction for hemodilution.

INLET AND OUTLET OXYGENATOR PRESSURES

Mean inlet and outlet pressures before and after the oxygenator as well as mean pressure drop throughout perfusion are shown in Table 3. Minimum mean inlet pressure was 193 mmHg and maximum was 224 mmHg compared to 145 mmHg and 175 mmHg for the outlet pressure. The minimum mean pressure drop was 39 mmHg and the maximum was 49 mmHg, while the maximal single value was 66 mmHg.

NECROPSIES

Post-mortem studies of the five major organs (lung, heart, liver, spleen, and kidney) analyzed in the calves did not demonstrate any macroscopic lesions.

ANALYSES OF THE DEVICES

No macroscopic defects, such as rupture of hollow fibers, cracking of external housing, or deposit of clots, was observed after gentle rinsing of the devices with clear water.

DISCUSSION

In the 1980s, progressive development of membrane oxygenators with higher gas transfer efficiency and integration of heat exchanger and reservoir reversed the dominance of the bubble oxygenator. They have now become the preferred type for cardiopulmonary bypass procedures. Among the different sorts, the hollow fiber oxygenators with extraluminal flow configuration provide compact units with low priming volumes and low surface areas and are therefore the main object of research (1, 5).

The Maxima Forté hollow fiber membrane oxygenator is an integrated device with good gas exchange capabilities by the microporous hollow fibers. Chronic tests of toxicity and blood trauma did not show any deleterious effects. All animals survived seven days after six hours of perfusion. Adequate blood gas values could be maintained throughout perfusion. Mean arterial oxygen saturation for the arterial side of the oxygenator was always above 99%. In accordance with the selected protocol, a high level of PaO_2 was kept throughout the procedures. Of course, in the clinical setting, this would be reduced. Postbypass blood gas analyses showed physiological values for

pH, pCO_2, pO_2, and oxygen saturation. There was no evidence for major lung trauma or pulmonary edema after perfusion of six hours.

The purpose of this study focused mainly on blood trauma rather than gas exchange performance. Therefore, the oxygenators were not challenged, and the animals were allowed to survive for control blood samples. There were no major changes in the hematological cell lines during the experiment. Red blood cell and platelet counts dropped slightly during the perfusion, while white blood cell count slightly increased. All three lines returned to near their baseline values as soon as 48 hrs after the perfusion period. Plasma hemoglobin and LDH were stable during the entire perfusion time. Both peaked at 24 hrs before returning to their baseline values by day seven. However, the variation of plasma Hb was not statistically significant, indicating a weak effect of the perfusion on blood trauma.

This increase in performance was not made at the expense of alteration in priming volume. On the contrary, the low prime design of the oxygenator with blood flow outside the hollow fibers and gas flow inside the hollow fibers allows standard flow rates with low pressure drop. Under the standardized conditions of perfusion with a mean blood flow rate between 3 and 4 l/min, the highest mean pressure drop was 49 mmHg with a maximal single value of 66 mmHg.

An interesting finding has been reported for the use of the Maxima Forté oxygenator in conjunction with the polyvinyl chloride pump tubing, where buildup of static electricity occurred. Eventually, blood to water leakage occurred in the heat exchanger due to the discharge of this capacitor to the water path of the heater-cooler circuit. This problem could be circumvented by grounding the temperature probe. In contrast, traditional metallic heat exchangers provide a direct electrical path to the heater-cooler water path.

In conclusion, the grounded Medtronic Maxima Forté hollow fiber membrane oxygenator offers good gas exchange capabilities, a low pressure drop, and low blood trauma over a prolonged perfusion time of six hours, for the given setup.

Table 3: Inlet and outlet pressure, and pressure drop through the oxygenator (mmHg).

	Inlet	Outlet	D pressure
Mixing	185±24	141±24	44±7
1 hr	193±26	145±21	49±15
2 hr	203±35	159±28	44±7
3 hr	202±22	153±15	49±8
4 hr	204±25	162±25	43±7
5 hr	224±36	175±33	49±15
6 hr	211±24	172±26	39±9

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