NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of extracorporeal membrane oxygenation for postneonatal children

Introduction

This overview has been prepared to assist members of IPAC advise on the safety and efficacy of an interventional procedure previously reviewed by SERNIP. It is based on a rapid survey of published literature, review of the procedure by specialist advisors and review of the content of the SERNIP file. It should not be regarded as a definitive assessment of the procedure.

Procedure name

Extracorporeal membrane oxygenation (ECMO)

Synonyms: extracorporeal lung assist, extracorporeal CO_2 removal, extracorporeal life support

Specialty society

Royal College of Paediatrics and Child Health

Indications

Extracorporeal membrane oxygenation (ECMO) is indicated for respiratory or cardiac failure unresponsive to all other measures, but considered to have a reversible cause. Most children treated with ECMO are very ill and are considered likely to die.

ECMO may also be used following heart surgery to ease the transition from cardiopulmonary bypass.

It is rare for a child to require ECMO. The causes of respiratory and cardiac failure that lead to a need for ECMO in children include: pneumonia; septic shock; congenital heart disease; cardiomyopathy; severe burns; pulmonary haemorrhage.

Summary of procedure

ECMO is a temporary life support technique. It involves connecting the child's internal circulation to an external blood pump and artificial lung. A catheter placed in the right side of the heart carries blood to a pump, then to a membrane 'lung', known as the oxygenator, where gas exchange of oxygen and carbon dioxide takes place. The blood then passes through tubing back into either the venous or arterial circulation. Patients are given a continous infusion of an anticoagulant, normally heparin, to prevent blood clotting in the external system. Bleeding is therefore a common adverse effect. Others include blood infection and haemolysis (breaking up of blood cells).

Conventional treatment is maximal intensive care support without ECMO. Ventricular assist devices, which pump the blood externally but do not allow gas transfer, may be

used in addition to standard ventilation, where circulatory rather than respiratory failure is prominent.

In randomised controlled trials, ECMO has been shown to improve survival compared with conventional management in babies under the age of 28 days with severe respiratory failure. It is argued that it would also improve survival in older children.

Literature review

Appraisal criteria

We searched for studies examining clinical effects on extracorporeal membrane oxygenation in children.

We excluded studies that only examined babies younger than 28 days. We excluded studies that examined neonates as well as older children, unless outcomes in the neonatal and postneonatal age groups were analysed separately, or the majority of the study population was postneonatal.

We excluded studies that only examined babies with bronchopulmonary dysplasia.

List of studies found

We found one systematic review, published by the Alberta Heritage Foundation for Medical Research in 1997.[1] We were unable to obtain the full text of this report. It concluded that 'the quality of the available evidence of benefit [in postneonatal children] remains limited'.

We found no controlled trials.

We found one retrospective comparison of case series that met our inclusion criteria.[2]

We found 13 case series that met our inclusion criteria and included more than 50 patients. We have extracted data from the six largest case series that we found.[3-7] References to smaller studies are listed in the annex.

Summary of key efficacy and safety findings (1)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Duncan BW[2] Retrospective comparison of case series Boston, USA Date 1987 to 1996 n=95 people with heart disease: mainly congenital heart disease or cardiomyopathy • ECMO (n=67), median age 3 months • ventricular assist device (VAD), (n=29), median age 20 months Some people in both groups were over 16 years (complete data not provided)	Survival to hospital discharge: • ECMO: 40% • VAD: 41%	Complications: Haemorrhage • ECMO: 40% • VAD: 44% Any severe infection: • ECMO: 27% • VAD: 31% Renal failure: • ECMO: 21% • VAD: 9%	• Non-random allocation • Neonates included • Outcome data not presented separately for neonatal children, postneonatal children and adults • More neonates in ECMO group than VAD group
Zahraa JN[3] Case series International database Date 1986 to 1997 n=763 postneonatal children with respiratory failure, age range not provided	Survival (time period not provided): 57%	Complications: • stroke: 6% • fits: 10% • renal failure or dialysis: 45% • cannula-related 114 (15%)	• Large uncontrolled case series • Includes entirely postneonatal children • No long term follow up data provided
Meyer DM[4] Case series International database Date 1987 to 1993 n=655 patients with respiratory failure (age range 14 days to 17 years)	Survival (time period not provided): 50% Survival reduced as age increased: • <24 months: 55% • 24 to 72 months 47% • 72 to 156 months: 38% • >156 months: 28% ($p<0.05$)	Complications: No data provided for whole group	• Large uncontrolled case series • Some neonates included • Limited information on complications • Patient population may overlap with that included in reference 3 • No long term follow up data provided

Summary of key efficacy and safety findings (2)

Authors, location, date, patients	Key efficacy findings	Key safety findings	Key reliability and validity issues
Green TP[5] Case series International database Date 1982 to 1992 n=382 children with respiratory failure, age 1 week to 18 years, number of neonates not provided	Survival at hospital discharge: 48%	Complications: No data provided for whole group	• Large uncontrolled series • Neonates included • No long term follow up reported • Limited data on complications • Patient population may overlap with that included in reference 3
Bartlett RH[6] Case series Michigan, USA Date 1980 to 1998 n=237 postneonatal children with cardiac or respiratory failure, age 1 month to 18 years	1 year survival: • respiratory patients: 70% • cardiac patients: 48% 5 year lung function: 'normal'	Complications: • Neurological deficit at discharge: 2% • Stroke: 5% • Non-stroke bleeding: 58% • Haemolysis: 10% • Dialysis or renal failure: 45% • Pump malfunction: 2% • Blood leaks: 7%	• Uncontrolled case series • Includes entirely postneonatal children • Limited baseline data reported • No long term follow up data provided
Swanniker F[7] Case series Michigan, USA Date 1985 to 1998 n=128 children with respiratory failure, age 2 weeks to 17 years	Survival to hospital discharge: 71%	Complications: • Renal failure: 14% • Liver failure: 3%	• Includes some neonates • Uncontrolled case series • Limited data on complications
Meyer TA[8] Case series International database Date 1988 to 1994 n=127 children with viral pneumonia confirmed by culture or serology, n=105 postneonatal	Survival (time period not provided): 57%	Complications: • Stroke: 15% • Other bleeding: 41% • Fits: 17% • Pneumothorax: 9% • Renal failure requiring dialysis: 34%	• Includes some neonates • Ucontrolled case series • Patient population may overlap with that included in reference 3

Validity and generalisability of the studies
All the studies were carried out in settings appropriate to the UK.

In our opinion, the effectiveness of ECMO compared with maximal intensive care management or ventricular assist device (in predominantly cardiac disease) in postneonatal children remains uncertain. There is detailed information on incidence of complications from the database held by the Extracorporeal Life Support Organisation. Information on long term outcomes is very limited.

The retrospective comparison of case series of children with cardiac disease who had ECMO or ventricular assist devices provides limited evidence of effectiveness, because the decision on type of treatment was not made by random allocation, so confounding may have occurred, particularly by age, diagnosis or severity of disease.[2]

Some of the case series are likely to include duplicate patient data. Four of the case series report outcomes in children registered on the Extracorporeal Life Support Organisation database, which collects data from recognised centres around the world.[3,4,5,8] The other two case series[6,7] report on children who are also likely to be registered on the database.

Only three of the studies we found provide evidence that is directly generalisable to postneonatal children.[3,4,6] The other three studies included some neonates as well as postneonatal children, and did not provide outcome data by age.[2,5,7]

Only one of the studies[6] provided data on long term outcomes.

Bazian comments
Two of the case series looked at outcomes in people with heart disease,[2,6] and five in people with respiratory failure,[3-7] including one examining children with viral pneumonia only.[7] Effectiveness of ECMO may vary by indication.

One of the case series found that survival after ECMO fell as age increased.[4] This highlights the issue ECMO in postneonates may not be as effectives as in neonates.

A UK randomised controlled trial of ECMO in adults is in progress, funded by the NHS Health Technology Assessment programme.

Specialist advisor's opinion / advisors' opinions
Specialist advice was sought from the Royal College of Paediatrics and Child Health

There are two main groups of postneonatal patients who may benefit from ECMO: children who need life support for respiratory or cardiac failure; and children who have had cardiac surgery, in whom ECMO may provide a more gentle transition from bypass to ventilation.

About 15 to 20 postneonatal children per year nationally are likely to require ECMO.

Attempts at randomised controlled trials have failed because of low recruitment and heterogeneity of eligible population.

Issues for consideration by IPAC

None other than those discussed above.

References

1. Alberta Heritage Foundation for Medical Research. Extracorporeal life support for children and adults. Technote TN11:15. Canada, 1997

2. Duncan BW, Hraska V, Jonas RA, Wessel DL, Del Nido PJ, Laussen PC et al. Mechanical circulatory support in children with cardiac disease. J Thorac Cardiovasc Surg 1999; 117(3):529-542

3. Zahraa JN, Moler FW, Annich GM, Maxvold NJ, Bartlett RH, Custer JR. Venovenous versus venoarterial extracorporeal life support for pediatric respiratory failure: are there differences in survival and acute complications? Crit Care Med 2000; 28(2):521-525

4. Meyer DM, Jessen ME. Results of extracorporeal membrane oxygenation in children with sepsis. The Extracorporeal Life Support Organization. Ann Thorac Surg 1997; 63(3):756-761

5. Green TP, Moler FW, Goodman DM. Probability of survival after prolonged extracorporeal membrane oxygenation in pediatric patients with acute respiratory. Crit Care Med 1995; 23(6):1132-1139

6. Bartlett RH, Roloff DW, Custer JR, Younger JG, Hirschl RB. Extracorporeal life support: the University of Michigan experience. JAMA 2000; 283(7):904-908

7. Swaniker F, Kolla S, Moler F, Custer J, Grams R, Barlett R et al. Extracorporeal life support outcome for 128 pediatric patients with respiratory failure J Pediatr Surg 2000; 35(2):197-202

8. Meyer TA, Warner BW. Extracorporeal life support for the treatment of viral pneumonia: collective experience from the ELSO registry. Extracorporeal Life Support Organization. J Pediatr Surg 1997; 32(2):232-236

Annex: Case series including 50 to 100 postneonatal children

Reference	Number of study participants
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Kulik TJ, Moler FW, Palmisano JM, Custer JR, Mosca RS, Bove EL et al. Outcome-associated factors in pediatric patients treated with extracorporeal membrane oxygenator after cardiac surgery. Circulation 1996; 94(9 Suppl):II63-II68	64
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Del Nido PJ. Extracorporeal membrane oxygenation for cardiac support in children. Ann Thorac Surg 1996; 61(1):336-339	53
Kirshbom PM, Bridges ND, Myung RJ, Gaynor JW, Clark BJ, Spray TL. Use of extracorporeal membrane oxygenation in pediatric thoracic organ transplantation. J Thorac Cardiovasc Surg 2002; 123(1):130-136	65
Moler FW, Palmisano JM, Greene TP, Custer JR. Predictors of outcome of severe respiratory syncytial virus-associated respiratory failure treated with extracorporeal membrane oxygenation. J Pediatr 1993; 123(1):46-52	53

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