Neonatal Respiratory Extracorporeal Membrane Oxygenation (ECMO) Referrals

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Abstract
Extracorporeal membrane oxygenation (ECMO) is a complex technique for providing life support in neonatal respiratory failure. The UK Collaborative ECMO trial demonstrated cost-effectiveness and substantial improvements in neurological morbidity and mortality. Currently, infants requiring ECMO in Ireland are referred to one of various centres in the UK and Scandinavia. We aimed to review the number of infants referred from Ireland for respiratory ECMO. All infants with a non-cardiac condition referred from Ireland for ECMO were reviewed for diagnosis and outcomes. Eleven infants required ECMO between June 2006 and January 2009 and were referred to the Scandinavian team for ECMO transport although one infant improved and did not require ECMO following the arrival of the team. Four infants died: one infant died prior to arrival of the ECMO team, 3 infants had fatal diagnoses and one infant with congenital diaphragmatic hernia received pre-op ECMO. The median (inter-quartile range) gestational age was 39.7 (38.3 - 40.7) weeks and birth weight of 3.7 (3.2 - 4.0) kg. The median age at the decision to transfer for ECMO was 13h (4-123) and the team arrived at 23 h (12-132). All infants had a normal cranial ultrasound and echo prior to ECMO and 2 infants had an abnormal MRI post-ECMO. The time on ECMO was 9 days (3-17) and total length of hospital stay was 32 d (23-36). There were no pre-ECMO clinical or biochemical predictors of mortality but survival was influenced by the underlying diagnosis leading to respiratory failure. Neonatal respiratory ECMO is unavailable in Ireland and recently infants have been transferred on ECMO support by the transport ECMO team from the Karolinska Institute in Sweden. Continuing audit of infants requiring ECMO is essential to ensure optimal outcomes.

Introduction
Extracorporeal membrane oxygenation (ECMO) provides life support in respiratory failure by oxygenating blood outside the body, thereby facilitating lung recovery, and providing cardiovascular support if necessary used in severe cases of meconium aspiration syndrome (MAS), persistent pulmonary hypertension of the newborn (PPHN), congenital diaphragmatic hernias (CDH), sepsis and idiopathic respiratory distress syndrome (RDS). The UK Collaborative ECMO trial demonstrated cost-effectiveness and substantial improvements in neurological morbidity and mortality. In the UK, 4 supra-regional ECMO centres cater for a population of over 60 million and include ECMO-transport. Currently, infants requiring ECMO in Ireland are referred to centres in the UK and Scandinavia depending on bed-availability. This involves a potential delay in providing ECMO and the transport of a sick neonate by air which is associated with increased morbidity. In addition, the cost incurred on the referring hospital is substantial. We aim to review the number of infants referred for ECMO to determine the costs and cost effectiveness of this treatment for infants in Ireland.

Methods
We included all neonates referred for respiratory ECMO from Ireland between June 2006 and January 2009. Infants with congenital heart disease were excluded as ECMO is available if required in these cases in Dublin. Data collection included: gestational age, birth weight, Apgar scores, gender, mode of delivery, and medical diagnosis. Pre ECMO characteristics including initial arterial blood gases and routine blood tests, delivery room resuscitation, and oxygenation index were also collected. The time from the decision for ECMO to the initiation of therapy was retrospectively obtained from the chart. Outcome measures including time on conventional ventilation, hospital stay, and death was obtained. The cost of transfer to the ECMO referral centre is €25,000. The cost of ECMO provision in the referral centre is €9,000 per day (Astrid Lindgren Children's Hospital, Karolinska University, Stockholm, Sweden). The mean cost of ECMO for each infant and the total cost of the studied time period were calculated. A Mann-Whitney U test was used for continuous variables and a Fischer Exact test was applied for categorical data. The values were represented as medians [range] and absolute number (%) unless stated otherwise. A p value of < 0.05 was considered significant.

CS: Caesarean section; MAS: Meconium Aspiration Syndrome. CDH: Congenital diaphragmatic hernia; PPHN: persistent pulmonary hypertension of the new born.
Results
Eleven infants were referred for ECMO during the study period. Their median birth weight was 3.7 Kg [inter-quartile range (IQR) 3.3 – 4.0] and gestation 39.7 weeks [IQR 38.3 – 40.8]. Four infants (36%) had meconium aspiration syndrome (MAS), three (27%) had a congenital diaphragmatic hernia (CHD), two (18%) had persistent pulmonary hypertension (PPHN), and two infants (18%) had congenital surfactant protein deficiency. Six infants (55%) survived to discharge. Four infants died following institution of ECMO therapy including 2 infants with surfactant deficiency, one infant with CDH who received pre-CDH repair ECMO, and 1 infant with PPHN. There was no difference in the gestational age of the surviving compared with the non-surviving infants (Table 1).

pCO2: partial pressure of carbon dioxide; pO2: partial pressure of oxygen; HCO3: Hydrogen bicarbonate; BE: base excess; MAP: mean arterial pressure; OI: Oxygenation index.

The first arterial pH and pCO2 were similar in the two groups (Table 2). The pre-ECMO Oxygenation Index (OI) of the survivors was higher than the non-survivors (60 vs. 36). There were no differences in the full blood count, urea/electrolytes, and liver function tests. More infants in the survivor groups required saline boluses and delivery room intubations (Table 3). The timing of the decision to initiate ECMO varied amongst the population. The infants with surfactant deficiency were not referred to ECMO until the second week of life. The average time of arrival of the team after the ECMO call was 8 hours with a range of 7 to 11 hours. ECMO was initiated within 2 hours of the arrival of the team. The survivors needed less time on ECMO compared to the non survivors (4 vs. 23 days, p<0.02). 5 of the survivors had an MRI study before discharge with 1 infant having an abnormal finding. The same infant developed seizures. With the exception of time on ECMO, none of the other results reached statistical significance. The total cost of ECMO provision to the 11 infants reported was €1,197,000. The median cost of ECMO provision excluding the cost of transfer was €108,000 [27,000 – 207,000] per infant. The median cost of ECMO including the cost of transfer was €133,000 [52,000 – 232,000] per infant.

Discussion
This is the first review of neonatal ECMO referrals from the Republic of Ireland. The overall survival of the studied cohort was 84%. The Extracorporeal Life Support Organization (ELSO) maintains a registry of all known cases in which ECMO was performed. Over 170 centres from around the world have contributed data to the Registry. Currently, there are over 35,000 cases in the Registry including over 24,000 newborns, 7,000 children, and 2,000 adults with respiratory and cardiac failure. The ELSO registry reports overall survival rates of 75% 4. However, two infants who did not survive had lethal conditions, only diagnosed after ECMO was instituted. The survival rate from Ireland during the study time period after excluding these two cases was 77%. The other 2 non survivors had CDH and PPHN of unknown aetiology. The outcome from Ireland is therefore favourable. This may reflect the early recognition for the need for ECMO and the early referral.

The use of ECMO has seen a decline following the introduction of ECMO-sparing therapies such as nitric oxide and high frequency oscillation 6,7. There is some concern that the use of these ECMO-sparing agents may delay the initiation of ECMO. However, data from the UK and the US have shown that the use of advanced respiratory therapies...
Over a 2 and a half year period, ECMO provision for the neonatal population in the Republic of Ireland has cost the Health Service Executive €1,197,000. The cost of using this overseas service is quite high, and in addition, subjecting these critically ill infants to long transports may increase morbidity. The development of an ECMO service in Ireland therefore warrants debate. Cost-effectiveness of ECMO has been demonstrated in the UK. The United Kingdom Collaborative trial showed that over 7 years, neonatal ECMO was effective at reducing known death or severe disability. Mean health service costs during the first 7 years of life were £30,270 (34,304) in the ECMO group and £10,029 (11,592) in the conventional management group generating a mean cost difference of £20,041 (22,712) that was statistically significant. The incremental cost per life year gained was estimated at £13,385 (15,170). The incremental cost per disability-free life year gained was estimated at £23,566 (26,709). The authors of the paper projected this cost-effectiveness over a 7-year period of the child's life. They argue that extending the projection further into adulthood may in fact increase the cost effectiveness of ECMO by offsetting the cost needed to address long-term disability issues.

Infants treated with ECMO compared to conventional therapies also had lower respiratory morbidities requiring hospitalisations and less behavioural problems requiring community health interventions.

References

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