Hypoxic Respiratory Failure in Term and Near Term Newborns: …Perspective from the London Neonatal Transfer Service

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◆ Background

Hypoxic Respiratory Failure (HRF) is a significant cause of morbidity in neonates. The condition constitutes a major proportion of ECMO referrals. Transfer of these infants for escalation of medical management is common and can be challenging. The data available regarding the transfer of these newborns is limited [1].

Newborns with an oxygenation index (OI) greater than 25 warrant consideration for Extracorporeal Membrane Oxygenation (ECMO) [2] in the event of further clinical deterioration, thus affecting the choice of transfer destination.

◆ Objectives

To identify factors apparent at referral or early in the transfer process that may be predictive of outcome and need for ECMO and would indicate the best destination for transfer.

To explore if any of the interventions by NTS had a significant effect on the oxygenation index (OI).

◆ Methods

Retrospective data was collected on all babies with HRF who were ≥34/40 gestation at referral, and ≤ 72 hours of age, using the NTS database and case notes. Infants with congenital abnormalities other than congenital diaphragmatic hernia and those without an arterial blood gas at the time of referral (to allow calculation of OI) were excluded. Patient demographics as well as ventilatory and physiological data were collected at initial **referral**, on the transfer teams **arrival** and at **departure** from the referring hospital and then again on arrival at the **destination**.

◆ Statistical Analysis

Data was assessed for normal distribution and summarised using median and ranges. Continuous non-parametric data was analysed using Wilcoxon signed ranks test for related paired measures and Friedman's ANOVA by ranks for related multiple measures. Logistic regression was used to predict factors at referral that were associated with a persistently raised OI. Positive and negative predictive values were calculated in relation to OI.

◆ Results

83 newborns met the criteria for this study (Figure 1 and Table 1)

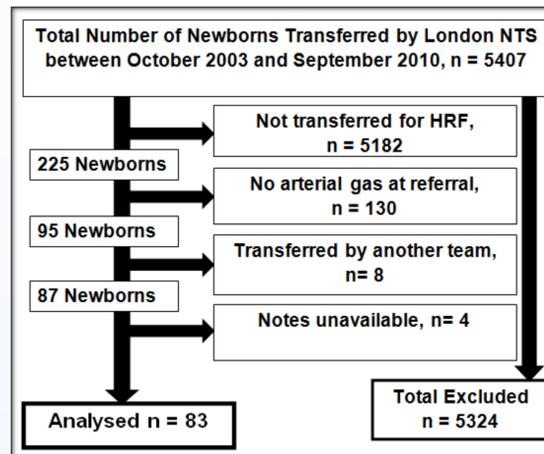Figure 1 – Flow diagram showing details of patient selection

Table 1 – Patient demographics. Figures are shown as Median and Interquartile range in brackets.

	(N=83)
Age at referral (hours)	8 (1-72)
Gestational Age (weeks)	40.2 (34.3 – 42.1)
Birth weight (kg)	3.35 (2.3 – 4.8)
Response Time* (minutes)	73 (20 – 396)
Stabilisation time** (minutes)	148 (65 – 490)

* Time from referral to arrival
** Time from arrival to departure

There was no difference between the median FiO_2 and Mean Airway Pressure (MAP) at the different time points during the transfer (Table 2). However, there was a significant rise in median PaO_2 from referral through arrival, departure and destination (Friedman's ANOVA: $\chi^2 = 17.9$, $p<0.001$) and a significant fall in OI from arrival to departure of NTS (p=0.008).

Table 2 Ventilation parameters of newborns during 4 stages of transfer. Values are given as median (ranges).

Ventilation parameters	At referral to NTS (n = 82)	At NTS Arrival (n=83)	At NTS Departure (n=82)	At destination (n=63)
MAP (cm of H_2O)	13.3 (7.0 - 26.0)	14.2 (6.5 - 26.0)	14.2 (7.3 - 22.3)	14.0 (7.9 - 22.3)
Peak Inspiratory Pressure (cm of H_2O)	28 (16 - 36)	28 (18 - 36)	29 (18 - 36)	28 (18 - 37)
PaO_2 (kPa)	6.4 (2.5 - 18.0)	6.8 (2.7 - 51.0)	8.3 (2.0 - 36.4)	8.7 (3.0 - 43.2)
$PaCO_2$ (kPa)	5.8 (2.3 - 10.3)	5.3 (3.1 - 12.8)	5.2 (3.0 - 9.8)	5.5 (3.4 - 22.1)
pH	7.29 (7.00 - 7.56)	7.32 (6.98 - 7.53)	7.34 (7.07 - 7.53)	7.31 (6.80 - 7.50)
Oxygenation Index	26.0 (5.2 - 89.8)	26.4 (2.2 - 98.0)	20.5 (1.9 - 100.7)	17.5 (2.8 - 74.7)

Interventions by NTS
The additional interventions by NTS are shown in table 3. 57 newborns (69%) were commenced on inhaled nitric oxide (iNO) by NTS. There was a significant improvement in median OI between arrival and departure in this group (p=0.008) (Figure 2).

Table 3 Showing the NTS interventions.

Intervention	iNO	Surfactant	Morphine Infusion	Muscle Relaxation	Changes to Inotropes
Number (%)	57 (69%)	17 (20%)	5 (6%)	23 (28%)	43 (52%)

Figure 2: Box and whisker plot of OI at arrival and departure

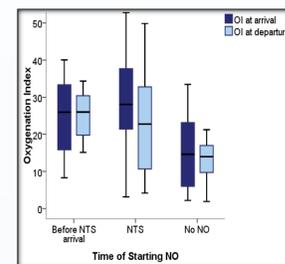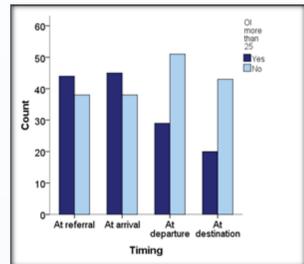Figure 3: Newborns with OI>25 and OI<25 during transfer

The proportion of newborns with OI>25 decreased significantly from arrival to destination (Figure 3). Logistic regression with OI>25 at departure as dependent and OI, PIP, MAP, PEEP, PaO_2 and pH on the teams arrival as predictors showed that OI at arrival was the only significant predictor.

ROC curves (Figure 4) were used to determine optimal cut-off value of referral OI and OI at NTS arrival to predict newborns requiring ECMO. Using an OI at referral of 22 produced a positive predictive value of 16% with a negative predictive value of 100% for babies requiring ECMO (table 4). This would involve discussing six newborns for every one who would deteriorate to require ECMO.

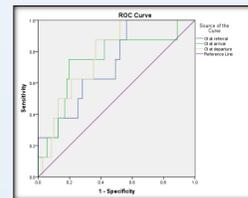Figure 4 ROC curve to determine OI cut off value

Table 4 Positive and Negative Predictive Values for the OI time points

OI at discussion point for ECMO	Positive Predictive Value (%)	Negative Predictive Value (%)
OI = 22 at Referral to NTS	16	100
OI = 25 at Referral to NTS	14	95
OI = 26 at Arrival of NTS	18	98
OI = 17 at Departure of NTS	17	100
OI = 23 at Departure of NTS	21	98

◆ Conclusions

- **There was a significant improvement in OI during stabilisation and the transfer. The significant improvement in arterial PaO_2 appears to be associated with commencing iNO and is unrelated to MAP and FiO2.**
- **The OI on team arrival predicted the likelihood of the OI being greater than 25 at departure but no other parameters were found to be predictors, consistent with previous studies [1].**
- **An OI threshold of 22 selected all newborns that went on to require ECMO. Using this threshold would have involved discussing six newborns for every one that eventually required ECMO.**

◆ References

1. Mills L *et al.* Predictors of Clinical Outcome for infants transferred for ECMO. Arch Dis Child Fetal Neonatal Ed 2007;92:F233-F234.

2. Chapman RL *et al.* Patient selection for Neonatal ECMO: beyond severity of illness. J Perinatol 2009;29 :606-611.