EARLY EXCLUSIVELY NON-INVASIVE INHALED NITRIC OXIDE IN SPONTANEOUSLY BREATHING PRETERM AND TERM NEONATES WITH ARTERIAL PULMONARY HYPERTENSION

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Background and aims

Inhaled nitric oxide (iNO) is an approved therapy for neonates with mechanical ventilation for hypoxic respiratory failure (HRF). Little is known about the early non-invasive iNO treatment of persistent pulmonary hypertension (PPH) via nasal cannula or mask. We studied this practice in spontaneously breathing term and preterm infants, hypothesizing that it would be associated with reduced oxygen requirements.

Methods

In our electronic medical records (2011 to 2017) we identified 123 inborn neonates receiving iNO. Whereof 46 singletons with PPH were exclusively spontaneously breathing on respiratory support via nasal continuous positive airway pressure (CPAP) receiving non-invasive iNO treatment starting within their first 12 hours of life. In all infants HRF (persistent supplemental oxygen >30%) was accompanied by echocardiographically proven PPH.

Results

46 neonates receiving non-invasive iNO were studied with a median birth weight of 2629g (740g – 4680g) and a median gestational age of 35 weeks (24+6 weeks – 41+6 weeks) including 10 preterm infants ≤ 30 weeks. Median duration of non-invasive iNO application was 24 hours (1,5 hours – 168 hours) with a mean starting dose of 20 ppm (10ppm – 35ppm). Fractional oxygen requirements dropped with initiation of non-invasive iNO from median 60% [55% – 100%] to 25% [21% – 40%], (p<0.01) and remained stable after discontinuation.

None of the patients developed any-stage of necrotizing enterocolitis, focal intestinal perforation, retinopathy of prematurity requiring treatment, chronic lung disease, intraventricular hemorrhage (≥ grade II), and periventricular leukomalacia. Indications for using non-invasive iNO included idiopathic pulmonary hypertension (83%), meconium aspiration syndrome (10%), Mb. Down (4%), and congenital heart disease (2%). All infants survived without major complications.

Table 1: Study population demographics

Patient	Gender	GA (wk)	BW (kg)	UA-pH	APGAR (10')	NO (ppm)	O2 max	O2 at end of NO	NO (hours)	Surfactant	Catecholamines	Oxygen (up to dol)	Special findings / etiologies
B.P.	f	24+6	0,74	7,32	08	15	60	27	29	Yes	No	50	Congenital infection
B.C.	f	26+1	0,82	7,22	08	20	38	21	12	Yes	No	21	
D.F.*	m	27+2	0,894	7,27	08	10	45	33	6	Yes	No	35	
D.M.	m	28+1	1,14	7,4	08	20	50	21	48	Yes	No	18	
F.L.	f	28+2	1,26	7,29	09	20	35	21	14	Yes	Yes	4	
FW.	f	29+0	1,315	7,31	08	15	36	30	33	Yes	Yes	3	
F.E.	f	29+3	1,49	7,41	08	10	35	30	33	Yes	No	11	
G.J.	m	30+0	1,61	7,33	09	20	34	25	30	Yes	No	3	
H.G.	m	30+5	1,664	7,2	09	20	65	21	29	Yes	No	5	
H.L.	f	30+5	1,7	7,15	07	20	50	24	16	No	No	4	
G.A.S.	f	31+5	1,72	7,43	08	20	60	25	11	Yes	Yes	2	
H.J.	m	31+3	1,74	7,33	08	20	70	21	6	No	No	1	
H.D.	m	31+6	1,85	7,1	07	20	45	21	20	Yes	No	1	
L.K.	f	31+1	1,9	7,13	08	20	100	21	25	No	No	1	
H.K.	f	32+0	1,99	7,41	08	20	60	21	4	Yes	No	1	
J.M.	m	32+2	2,09	7,3	09	20	40	23	31	Yes	Yes	3	
K.C.	m	32+1	2,13	7,44	08	20	80	25	30	No	No	2	
L.H.*	f	33+6	2,13	7,18	09	15	60	25	21	No	No	1	Anemia
L.L.	m	35+5	2,16	7,09	07	20	100	21	64	No	Yes	3	
R.A.	m	35+0	2,31	7,39	08	20	35	21	6	Yes	No	1	
H.J.M.	m	36+2	2,42	7,37	08	20	97	28	11	No	No	2	Anemia Down Syndrome
R.T.	f	36+3	2,47	7,34	09	25	46	30	26	No	No	12	
K.K.E.	f	37+2	2,48	7,32	08	10	30	28	45	No	Yes	2	
L.L.	f	37+6	2,74	7,21	08	20	58	25	22	No	No	1	Transposition of the great arteries
L.J.	m	37+2	2,8	7,26	09	20	40	21	27	No	No	1	
P.A.	f	38+0	2,9	7,16	07	20	100	28	22	Yes	Yes	8	MAS
S.N.	f	38+0	2,93	7,24	09	15	41	21	2	No	No	1	Pulse oximetry screening
T.M.	m	38+5	2,93	7,37	10	20	51	21	41	No	No	1	
W.H.	f	38+2	3,098	7,14	09	20	40	21	19	No	No	1	Pulse oximetry screening
N.M.*	m	39+2	3,16	7,18	08	20	40	34	17	No	No	9	MAS, Infection
W.L.	f	39+2	3,26	7,35	09	30	95	33	24	No	No	1	
Z.M.*	f	39+1	3,29	7,03	08	20	50	25	9	No	No	1	
R.K.K.	m	40+5	3,29	7,2	10	20	66	25	4	No	No	2	Pulse oximetry screening
R.K.*	f	40+0	3,348	7,23	08	35	42	21	19	No	No	1	
S.K.	f	40+0	3,47	7,18	08	20	100	28	5	No	No	2	Congenital infection Pulse oximetry screening, congenital infection
S.P.	m	40+5	3,51	7,1	10	20	100	21	16	No	No	3	
S.E.*	f	40+2	3,58	7,01	08	20	73	24	1	No	No	1	
S.G.*	m	40+0	3,61	7,34	09	20	42	21	41	No	Yes	1	
V.M.	f	40+0	3,66	7,11	10	20	100	21	47	No	Yes	2	Down Syndrome MAS
Z.J.	m	40+2	3,78	7,37	10	20	100	40	14	No	Yes	10	
L.K.	m	41+0	4	7,03	07	20	100	25	30	No	Yes	5	MAS
M.K.	f	41+5	4,02	7,17	09	20	70	21	24	No	Yes	1	Pulse oximetry screening
P.J.	f	41+2	4,16	7,28	10	20	60	30	49	No	No	1	Drug abuse Perinatal acidosis
S.L.	f	41+6	4,24	7,15	09	20	80	25	14	No	Yes	4	
V.O.*	m	41+3	4,47	6,97	08	20	85	30	24	No	Yes	2	MAS
Z.K.	m	41+6	4,68	7,09	08	20	100	21	33	No	Yes	1	

Abbreviations: * = Out-born; GA = Gestational age; BW = Birth weight; UAph = Umbilical artery-pH; NO = Nitric oxide; O2 = Oxygen; dol = Day of life;

Figure 1: CPAP-system prepared for non-invasive iNO.

Figure 2: Non-invasive iNO via pharyngeal tube.

Figure 3: Patient data (GA 28+2 wk) receiving non-invasive iNO.

Conclusions

Non-invasive iNO improved oxygenation in spontaneously breathing newborn infants with persistent pulmonary hypertension receiving respiratory support for hypoxic respiratory failure. Non-invasive iNO therapy was simple, safe, and without detectable adverse effects.