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ORIGINAL ARTICLE

Enteral hydration in high-flow therapy for infants with bronchiolitis: Secondary analysis of a randomised trial

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Aim: Nasal high-flow oxygen therapy is increasingly used in infants for supportive respiratory therapy in bronchiolitis. It is unclear whether enteral hydration is safe in children receiving high-flow.

Methods: We performed a planned secondary analysis of a multi-centre, randomised controlled trial of infants aged <12 months with bronchiolitis and an oxygen requirement. Children were assigned to treatment with either high-flow or standard-oxygen therapy with optional rescue high-flow. We assessed adverse events based on how children on high-flow were hydrated: intravenously (IV), via bolus or continuous nasogastric tube (NGT) or orally.

Results: A total of 505 patients on high-flow via primary study assignment (n = 408), primary treatment (n = 10) or as rescue therapy (n = 87) were assessed. While on high flow, 15 of 505 (3.0%) received only IV fluids, 360 (71.3%) received only enteral fluids and 93 (18.4%) received both IV and enteral fluids. The route was unknown in 37 (7.3%). Of the 453 high-flow infants hydrated enterally patients could receive one or more methods of hydration; 80 (15.8%) received NGT bolus, 217 (43.0%) NGT continuous, 118 (23.4%) both bolus and continuous, 32 (6.3%) received only oral hydration and 171 (33.9%) a mix of NGT and oral hydration.

None of the patients receiving oral or NGT hydration on high-flow sustained pulmonary aspiration (0%; 95% confidence interval N/A); one patient had a pneumothorax (0.2%; 95% confidence interval 0.0–0.7%).

Conclusions: The vast majority of children with hypoxic respiratory failure in bronchiolitis can be safely hydrated enterally during the period when they receive high-flow.

Key words: bronchiolitis; enteral hydration; high-flow.

What is already known on this topic

1 In infants admitted with bronchiolitis not on high flow nasogastric hydration has been shown to be effective and safe.
2 It is unclear if children receiving high-flow in bronchiolitis can be safely hydrated enterally as well.

What this paper adds

1 We assessed the form of hydration in 505 infants who received high flow for hypoxic respiratory failure within a randomised trial.
2 Enteral hydration was safe and the majority of infants on high flow were exclusively hydrated via nasogastric tube.

Bronchiolitis, an acute lower airway lung disease is the most common reason for non-elective hospital admission in infants. No interventions have shown efficacy[1,2] and American Academy of Pediatrics and Australasian Bronchiolitis guidelines recommend only supportive therapy including oxygen therapy for hypoxia, respiratory support and the maintenance of hydration.[3,4]

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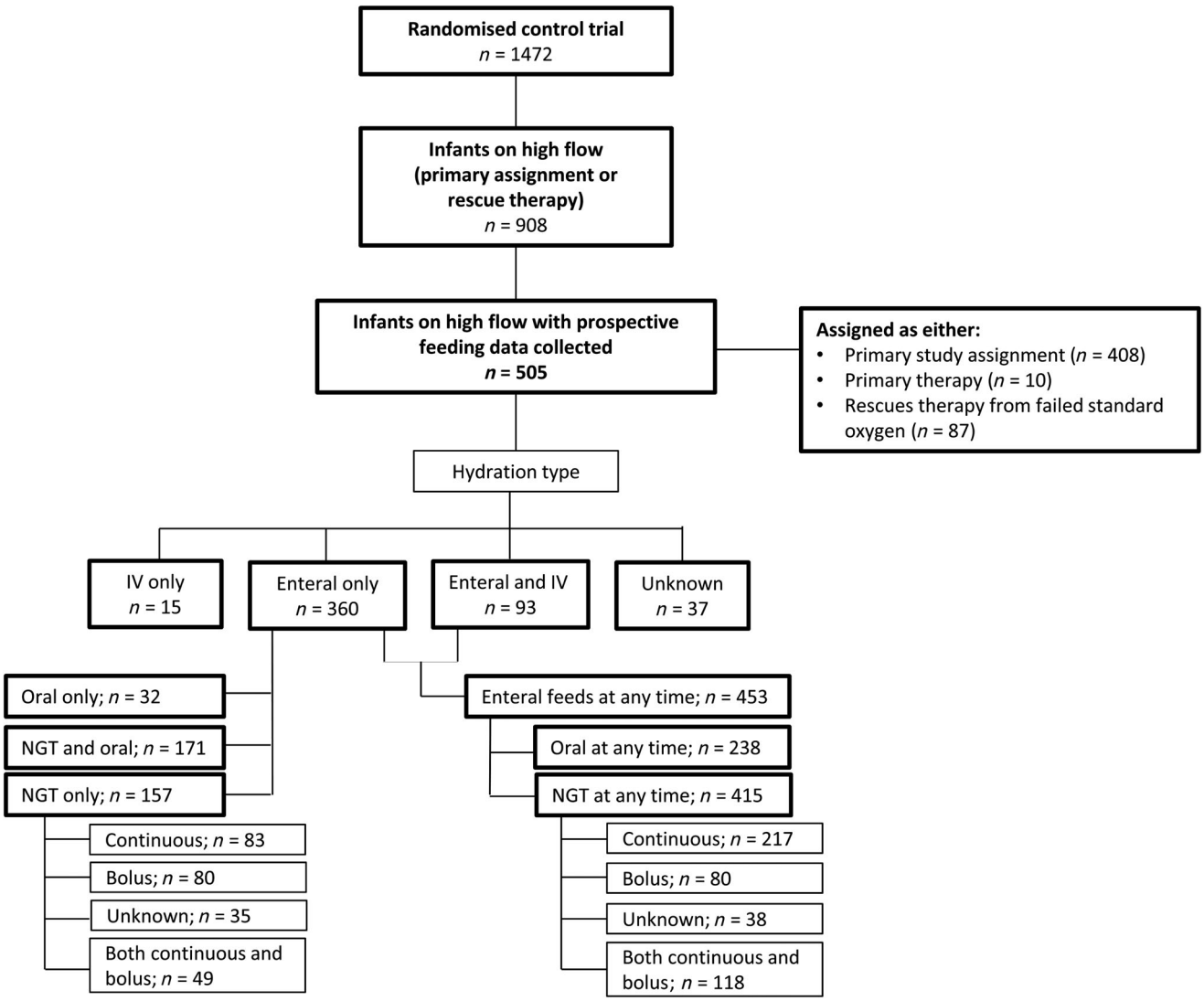

Fig. 1 Numbers of infants who received high flow oxygen via nasal cannula and had hydration status assessed. IV, intravenous; NGT, nasogastric tube.

Three methods of hydration and feeding are available for infants diagnosed with bronchiolitis including intravenous (IV), enteral hydration via nasogastric tube (NGT) or oral hydration. Enteral hydration has several theoretical advantages such as physiological benefits and allowing the additional administration of calories. In infants not requiring respiratory support, IV and NGT hydration have been shown to be equally efficacious and safe in bronchiolitis infants.[5,6] Oral hydration remains controversial, particularly in infants with more severe disease due to either inadequate intake or the perceived risk of aspiration.

Nasal high-flow oxygen therapy has emerged as a means to provide respiratory support in bronchiolitis.[7–12] We have recently conducted a multi-centre randomised controlled trial (RCT) which demonstrated that high-flow oxygen therapy can be provided safely in ward settings with a lower risk of treatment failure than standard oxygen therapy but no difference in hospital length of stay or duration of oxygen therapy.[13] It is unclear, however, if enteral hydration via NGT or orally can be safely administered in infants on high-flow oxygen therapy. In a secondary analysis of the RCT we set out to assess if infants on high-flow oxygen therapy can safely receive enteral hydration.

Methods

Study design

The parent study was an unblinded RCT comparing high-flow oxygen therapy with standard-oxygen therapy in emergency departments and general paediatric inpatient units in 17 tertiary and regional hospitals in Australia and New Zealand between October 2013 and August 2016.[13] The human research ethics committee at each participating site approved the study. The study protocol has been published.[14] The study protocol was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12613000388718).

Patients

Infants less than 12 months of age were eligible for inclusion upon presentation to emergency or paediatric inpatient units with clinical signs of bronchiolitis and an oxygen requirement. Bronchiolitis was defined according to the American Academy of Pediatrics[3] criteria as an infant with symptoms of respiratory distress associated with symptoms of a viral respiratory tract infection.[2] We excluded critically ill infants with immediate need for respiratory support and intensive care admission, infants with cyanotic heart disease, apnoeas, basal skull fracture, upper airway obstruction, craniofacial malformations and infants receiving home oxygen therapy. Written informed consent was obtained from all parents or guardians.

Study intervention

High-flow group infants received heated and humidified high-flow oxygen therapy at a rate of 2 L/kg/min delivered via the Optiflow system (Fisher and Paykel Healthcare, Auckland, New Zealand) using an age-appropriate Optiflow Junior cannula and the Airvo2 high-flow device (Fisher and Paykel Healthcare, Auckland, New Zealand). The standard-oxygen group infants were placed on subnasal oxygen via nasal cannula up to a maximum of 2 L/min. Details of the study protocol are available in a separate publication.[14]

For all infants who received high-flow a NGT placement was recommended for venting of the stomach at least 4 hourly to avoid gastric hyperextension. IV placement was not mandated or encouraged. Depending on the clinician's preference oral intake was allowed if tolerated, particularly during weaning of the treatment. Nursing care management was to continue NGT feeding during high-flow delivery and to stop high-flow and change to low-flow humidified oxygen via the same high-flow Airvo2 device during oral feeding. In this case, the infant would remain undisturbed with the same nasal cannula for this time period and up to a maximum of 20 min before ceasing oral hydration and returning to previous high-flow settings via the Airvo2 device. Type of hydration during high-flow and low-flow humidified oxygen was recorded. Information as to whether or not the flow rate was turned down during enteral hydration was turned down was not collected. Data on the type of hydration during high-flow and low-flow humidified oxygen were obtained where accurately recorded in the medical charts. This was at times difficult to adhere to and collect data on, as parents may have fed their infant when the nurse was not present.

Study outcomes

The primary outcome of the parent study was treatment failure resulting in the escalation of care during the current hospital admission. At the point of care, the treating clinicians determined the presence of treatment failure if at least three of four clinical criteria were met and the escalation of care was required.[13] The clinicians were allowed to escalate therapy if they were concerned for other clinical reasons not captured in the four clinical criteria. For children in the standard-oxygen group who received escalation of care, it was suggested to use rescue high-flow in the inpatient ward environment.

For this study, we assessed all infants who received high-flow oxygen therapy either as their primary commencement therapy regardless of randomised study assignment or as rescue high-flow therapy if they failed standard-oxygen therapy. Detailed hydration data were collected and included in the clinical report form (CRF) from November 2015. Primary analysis of this study was adverse events based on how children on high-flow were hydrated, either via IV route, via bolus or continuous NGT or orally. We collected adverse events by specifically asking for certain adverse events. A serious adverse event was defined as any event that was fatal, life-threatening, permanently disabling, incapacitating or resulted in a prolonged hospital stay.

Table 1 Baseline characteristics of infants with bronchiolitis receiving high flow therapy

	n = 505
Age, months, means ± SD	5.8 ± 3.6
≤3 months, *n* (%)	151 (29.9)
>3–6 months, *n* (%)	120 (23.8)
>6 months, *n* (%)	234 (46.3)
Weight, kg, means ± SD	7.3 ± 2.3
Sex: female, *n* (%)	186 (36.8)
Ethnicity, *n* (%)	
Caucasian	216 (42.8)
Aboriginal/Torres Strait Islander	15 (3.0)
Maori/Pacific Islander	176 (34.9)
Other/Unknown	98 (19.4)
Prematurity < 37 weeks, *n* (%)	92 (18.2)
Need for neonatal respiratory support	69 (13.7)
Oxygen only	15 (3.0)
Non-invasive ventilation	54 (10.7)
Invasive ventilation	15 (3.0)
Previous hospital admissions for respiratory disease post-natal, *n* (%)	122 (24.2)
Intensive care admission for respiratory support	25 (5.0)
Invasive ventilation	1 (0.2)
Non-invasive ventilation	3 (0.6)
High-flow therapy	21 (4.2)
Chronic lung disease	10 (2.0)
Congenital heart disease	7 (1.4)
Patient history of wheeze	110 (21.8)
Family history of asthma	227 (45.0)
Family history of allergy	99 (19.6)
Currently attending child care	64 (12.7)
Viral aetiology,† *n* (%)	
Respiratory syncytial virus	217/393 (55.2)
Other viruses	138/393 (35.1)
Multiple viruses	99/393 (25.2)
No virus detected on nasopharyngeal aspirate	76/393 (19.3)

†Viral testing was not mandated. Multiple options possible. SD, standard deviation.

Table 2 Modalities of hydration in infants with bronchiolitis receiving high flow

	n = 505, *n* (%)	*n* (%)	*n* (%)
IV fluids only	15 (3.0)		
Enteral fluids only	360 (71.3)		
NGT only	157 (31.1)		
Continuous	83 (16.4)		
Bolus	25 (5.0)		
Both continuous and bolus	49 (9.7)		
Unknown	35 (6.9)		
Oral only	32 (6.3)		
NGT and oral	171 (33.9)		
IV and enteral fluids	93 (18.4)		
Fluid administration unknown	37 (7.3)		
Enteral feeds at any time	453 (89.7)		
NGT at any time	415 (82.2)		
Continuous	217 (43.0)		
Bolus	80 (15.8)		
Both continuous and bolus	118 (23.4)		
Unknown	38 (7.5)		
Oral at any time	248 (49.1)		
Age, months	NGT only	IV only	Enteral at any time
≤3	42/151 (27.8)	8/151 (5.3)	136/151 (90.1)
>3–6	34/120 (28.3)	5/120 (4.2)	106/120 (88.3)
>6	81/234 (34.6)	2/234 (0.9)	211/234 (90.2)
Adverse events, *n*	157	15	453
Serious adverse events	0	0	0
Pulmonary aspiration	0	0	0
Pneumothorax	0	0	1 (0.2)
Emergency intubation	0	0	0
Cardiac arrest	0	0	0
Respiratory arrest	0	0	0
Apnoeas	1 (0.6)	1 (6.7)	5 (1.1)

IV, intravenous; NGT, nasogastric tube

Statistical analysis

Descriptive statistics were used to report on the baseline characteristics of the infants who received high-flow and their means of hydration with 95% confidence intervals (CIs) for key proportions.

Results

Patient characteristics

Of 1638 infants, randomised 166 parents/guardians (10%) declined consent to use data, thus 1472 infants were included in the analyses of the parent study. Of these, 739 were primarily randomised to the high-flow group and of whom 728 actually received high-flow, and 733 were primarily randomised to the standard-oxygen group and of whom 18 actually received high-flow in the first instance and 162 received rescue high-flow for a total of 908 receiving high-flow (Fig. 1).

Prospective hydration data were collected for 505 patients who received high-flow and represent the study cohort analysed. Demographic and basic clinical characteristics are shown in Table 1. The average age of the infants was 5.8 months and 217 of 393 tested (55.2%) were respiratory syncytial virus positive. A history of prematurity or previous hospital admission was 92 (18.2%) and 122 (24.2%), respectively. The mean peripheral oxygen saturation level on room air at enrolment was 88%.

Hydration on high flow

While on high-flow 15 of 505 (3.0%) received only IV fluids, 360 (71.3%) received only enteral feeds and 93 (18.4%) received both IV and enteral feeds (Fig. 1). For 37 (7.3%) route of fluid administration was unknown. Of the 453 who had at least at some point been enterally fed while on high-flow 80 (15.8%) received NGT bolus, 217 (43.0%) NGT continuous, 118 (23.4%) both bolus and continuous, 32 (6.3%) received only oral feeds without NGT hydration and 171 (33.9%) received a mix of NGT and oral feeds (Table 2). Infants less than 3 months of age had higher IV rates than older infants.

Adverse events

None of the patients receiving oral or NGT feeding on high flow sustained pulmonary aspiration (0%; 95% CI N/A); one patient had a pneumothorax (0.2%; 95% CI 0.0–0.7%) which was unrelated to NGT insertion and did not require a chest tube. Of note in the parent study, there was one pneumothorax noted in the standard oxygen group. No life-threatening serious adverse events were observed, specifically no emergency intubations or cardiac arrests (Table 2).

Discussion

In this secondary analysis of a multi-centre RCT in infants with bronchiolitis and hypoxaemia, we found that the vast majority of patients – 71.3% – were solely fed and hydrated enterally during high-flow administration and that IV hydration was infrequently used. Most enteral hydration was via an NGT. None of the enterally fed children had a clinical aspiration or other adverse events attributable to enteral hydration.

There are several reasons why NGT feeding was used at a high rate in this study. In the first instance, NGT insertion was recommended by the protocol to allow intermittent venting of the stomach. Furthermore, in Australia and New Zealand NGT hydration is used for a variety of conditions in preference to IV fluids, including in bronchiolitis and gastroenteritis,[5,6,15–17] and it became obvious very quickly in this study that enteral feeding could be safely conducted during high-flow delivery. A further advantage of hydration via NGT is that fewer attempts are needed in infants with bronchiolitis to achieve successful placement compared to IV insertion.[5] A concern in NGT placement in children in contrast to adults[18,19] is that there are no demonstrated means of reducing the pain and distress associated with NGT insertion.[20] Anecdotally, after insertion infants fed via an NGT seem less irritable than IV hydrated infants, without the caloric content provided by formula, though there are no data to support this.

Our study has some limitations. As set out in methods we started collecting feeding data only once a section of the patients had already been enrolled in the trial when the study team realised that these data would be important secondary information. While for the majority of infants only one type of hydration was provided, for some children multiple modalities were used, and sometimes alternating modalities occurred. In addition, we did not record how long different modalities were used in children who had received more than one modality. In this group of infants, it was difficult to determine the predominant feeding modality during high-flow. The protocol recommended to decrease flow rates for feeds; this was proscribed as a safety measure when no data on high flow and feeding were available prior to this study. We did not collect why clinicians chose one modality over another nor if they adhered to the study protocol in terms of reducing high-flow during NGT bolus feeds or oral feeds. We cannot comment specifically on the advantages/disadvantages of bolus versus continuous feeds neither was associated with adverse events. We did not collect details of the type of enterally used fluids.

Conclusions

In conclusion, we aimed to investigate how infants managed on high-flow therapy are hydrated and if enteral feeding, and NGT feeding in particular, is safe during high-flow therapy support. Our data indicate that the vast majority of children with hypoxic respiratory failure in bronchiolitis can be safely fed enterally during the period when they receive high-flow.

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