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The effect of skin-to-skin care on cerebral oxygenation during nasogastric feeding of preterm infants

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Short title: Feeding during skin-to-skin care

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ABSTRACT

Aim: To describe cerebral oxygenation during gavage feeding of preterm infants during incubator and skin-to-skin care.

Methods: Further analysis of data from two crossover studies comparing cerebral oxygenation, heart rate and oxygen saturation during skin-to-skin care with incubator care. Data were analysed in three epochs; 10 mins pre-feed, during-feed, and 10 mins post-feed. Measurements from infants fed during incubator care were compared with those obtained during skin-to-skin care.

Results: In 39 infants (median (IQR) 27.8 (26.1-30.0) weeks' gestation) there was no difference in cerebral oxygenation between pre-, during- and post-feed. Heart rate increased by 3 beats per minute post-feed compared with during-feed. Twenty infants received two gavage feeds, one feed in the incubator and another during skin-to-skin care. There was no difference in cerebral oxygenation and heart rate whilst peripheral oxygen saturation decreased by 3% during feeding whilst skin-to-skin care compared with feeding in the incubator.

Conclusion: Cerebral oxygenation remained stable before, during and after gavage feeding in an incubator and during skin-to-skin care. The small decrease in oxygen saturation whilst receiving gavage feeding during skin-to-skin care is unlikely to be clinically important, providing reassurance that preterm infants maintain physiological stability during skin-to-skin care.

Key Words: cerebral oxygenation, gavage feeding, near-infrared spectroscopy, preterm, skin-to-skin care

Key Notes:

- Preterm infants often receive gavage feeds during skin-to-skin care but there are concerns about physiological stability during gavage feeding, especially whilst infants are receiving skin-to-skin care.
- Regional cerebral oxygenation ($rStO_2$) measured with near infrared spectroscopy remains stable during gavage feeding including whilst infants are receiving skin-to-skin care.

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- Timing of gavage feeds does not need to be factored in determining the duration of skin to skin care

Abbreviations:

bpm	beats per minute
cFTOE	cerebral fractional tissue oxygen extraction
CI	confidence interval
HR	heart rate
IQR	interquartile range
NICU	neonatal intensive care unit
NIRS	near-infrared spectroscopy
$rStO_2$	regional cerebral oxygenation
SD	standard deviation
SpO_2	peripheral oxygen saturation
SSC	skin-to-skin care

BACKGROUND

Gavage feeding in preterm infants is associated with peripheral oxygen desaturations (1, 2). These recurring episodes of hypoxaemia may impair cerebral oxygenation (3) and have been implicated in long term neonatal brain injury (4, 5).

Regional cerebral oxygenation ($rStO_2$) is a measure of cerebral oxygen delivery and consumption and can be measured continuously with near-infrared spectroscopy (NIRS). NIRS relies on the differential absorption of near-infra-red light by oxygenated and deoxygenated haemoglobin (6). In neonates, this technology is most commonly used for cerebral tissue oxygenation (7). It is reassuring that $rStO_2$ seems to remain unchanged during and after gavage feeding (8-10). There however, remains a paucity of information about the effect of bolus gavage feeding on $rStO_2$ and other physiological parameters during skin-to-skin care (SSC).

SSC is becoming more common in the neonatal intensive care unit (NICU) setting. SSC is defined as placing an infant prone, in direct skin contact with their mother or father's chest (11). SSC has many proven benefits for preterm infants, including increased maternal bonding and breastfeeding

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performance (12, 13). In the NICU environment, intermittent SSC is practiced for extended periods of time (14), meaning the infant is often fed while in the SSC position. There are concerns about infant's physiological stability during gavage feeding (15) and whilst receiving SSC (16).

Our aims were to firstly determine how bolus gavage feeding in the incubator affects preterm infant physiology and secondly, to compare this to feeding during SSC. We hypothesised that $rStO_2$, peripheral oxygen saturations (SpO_2) and heart rate (HR) would remain stable during both incubator and SSC feeding.

METHODS

Study design and population

Two prospective, non-inferiority, crossover trials were performed at the Royal Women's Hospital in Melbourne, Australia (17, 18). Written informed prospective parental consent was obtained and both studies were approved by the hospital human research and ethics committee. Primary outcome results have been presented elsewhere (17, 18). Data collected during these studies were used to compare $rStO_2$ and other physiological parameters in preterm infants (<33 weeks' gestation) before, during and after SSC (Figure 1).

Continuous recordings of $rStO_2$, HR, and SpO_2 for 10 minutes before the start of the feed (pre-feed), for the duration of the feed (during-feed) and for 10 minutes after the end of the feed (post-feed) were analysed. Gavage feeds were given via an indwelling nasogastric tube and the duration of feeding determined by gravity and recorded.

Infants were included in this study if the pre-/during- and post-feed period was during either incubator period (control or post-intervention, Figure 1). When available, paired comparisons of physiological recordings during feeding in the incubator were made with those made during SSC.

Equipment and definitions

NIRS (Fore-sight, CAS Med. Medical Systems Inc., Branford, CT, USA) was used to continuously measure $rStO_2$. The NIRS sensor was placed on the right tempoparietal area of the infant's forehead and fixed with a firm fitting

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hat. SpO_2 and HR were measured by pulse oximetry (Radical7 V5; Masimo, Irvine, California, USA). Bradycardic events were defined as HR < 100 beats per minute (bpm) for > 5 seconds and hypoxic events were defined as SpO_2 < 80% for > 5 seconds. 'Cerebral hypoxia' was defined as $rStO_2$ < 55% and 'cerebral hyperoxia' as $rStO_2$ > 85% (17-19). Cerebral fractional tissue oxygen extraction (cFTOE) is a measure of cerebral oxygen delivery and consumption. For each data point, cFTOE was calculated by: (SpO_2 - $rStO_2$)/SpO_2 (20). Standard deviation (SD) around each infant's mean $rStO_2$ was used as an estimate of the variability of the parameter.

All signals ($rStO_2$, SpO_2, HR) were digitised and recorded at 200Hz using the NewLifeBox Neo-RSD physiological monitor (Advanced Life Diagnostics UG, Weener, Germany), the sampling rate of $rStO_2$, SpO_2, HR was 1 data point every 2 seconds.

Statistical analysis

Continuous data of $rStO_2$, HR, SpO_2, and cFTOE were summarised as mean (SD) if normally distributed and median (IQR) if skewed, for each patient and for each defined feeding period (pre-, during- and post-feed). For comparison of the intra-individual average value between pre-/during- and post-feed periods and between during-feed periods in the incubator and during SSC, a paired t-test and 95% confidence interval (CI) were used, as the differences were normally distributed.

A p value < 0.05 was considered significant, no adjustments for multiple testing were performed. All analyses were performed using STATA software (Intercooled 13, V.13, Stata Corp, Texas, USA).

RESULTS

80 infants were recruited between September 2015 and September 2016 for the two primary studies (17, 18). Of the 80 infants, 39 had their pre-/during- and post-feed period in one of the two incubator periods and 20 infants were fed both during incubator and SSC. Demographic characteristics of both groups are summarised in Table 1. The centiles of $rStO_2$ in the incubator of this study population (n=39) are shown in Table 2. Physiological outcomes

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during the pre-/during- and post-feed period in the incubator and during SSC are shown in Table 3.

Feeding in the incubator

There was no difference in $rStO_2$ [mean difference (95% CI) -0.06 (-0.6 to 0.5) %, p=0.8], SpO_2 [-0.4 (-1.2 to 0.4), p=0.3] %, HR [-0.3 (-1.8 to 1.3) bpm, p=0.7] and SD of $rStO_2$ [0.07 (-0.3 to 0.5), p=0.7] between the during-feed period and pre-feed period in the incubator. There was a small decrease in cFTOE in the during-feed period compared with the pre-feed period [mean difference (95% CI) -0.005 (-0.009 to -0.001), p=0.02].

There was no difference in $rStO_2$ [mean difference (95% CI) 0.01 (-0.5 to 0.5) %, p=1.0], SpO_2 [0.04 (-0.5 to 0.6) %, p=0.9], cFTOE [0.001 (-0.005 to 0.006), p=0.9] and SD of $rStO_2$ [0.2 (-0.1 to 0.6), p=0.2] between the during-feed period and the post-feed period. There was an increase in HR in the post-feed period compared with during-feed [mean difference (95% CI) 3 (1 to 5) bpm, p<0.01].

Feeding during SSC

There was no difference in $rStO_2$ [mean difference (95% CI) -0.4 (-1.2 to 0.4) %, p=0.3], HR [-0.9 (-3.3 to 1.4) bpm, p=0.4], cFTOE [-0.003 [-0.011 to 0.005, p=0.4) or SD of $rStO_2$ [0.08 (-0.4 to 0.5), p=0.7] between during-feed values with pre-feed values. There was a small decrease in SpO_2 in the during-feed period compared with the pre-feed period [-0.8 (-1.3 to -0.2) %, p=0.01].

When comparing during-feed with post-feed periods, there was no difference in $rStO_2$ [mean difference (95% CI) 0.5 (-0.8 to 1.8) %, p=0.4] SpO_2 [-1.4 (-5.4 to 2.7) %, p=0.5], cFTOE [-0.004 (-0.282 to 0.021), p=0.7) and SD of $rStO_2$ [0.1 (-0.6 to 0.9), p=0.7]. There was an increase in HR in the post-feed period compared with during-feed [mean difference (95% CI) 4 (2 to 7) bpm, p<0.01].

Comparison of feeding in the incubator and SSC

There was no difference in $rStO_2$, HR, SD of $rStO_2$, number of hypoxic and bradycardic events between feeding periods in the incubator and during

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SSC. There was a decrease in SpO_2 and cFTOE during SSC feeding compared with incubator feeding. The proportion of time spent in cerebral hypoxia and hyperoxia were very low during both conditions (Table 4). Mean $rStO_2$ over all feed periods in the incubator and during SSC are shown in Figure 2.

DISCUSSION

To the best of our knowledge, this is the first study analysing the effect of gavage feeding during SSC on $rStO_2$ and other physiological parameters.

Similar to previous studies, $rStO_2$ remained unchanged before, during and after feeding in the incubator (8, 10). The current study however highlights that $rStO_2$ and the variability in $rStO_2$ remained unchanged when feeding during SSC. Moreover, the proportion of time spent in cerebral hypoxia and hyperoxia were very low pre-/during- and post-feed during incubator and SSC according to these relatively wide normative values. Other data shows that even in the most immature preterm infants, $rStO_2$ remains stable during feeding and gestational age does not seem to have an influence on this parameter (21).

Similarly, HR remained unchanged between pre-feed and during-feed but increased in the post-feed period by 3-4 bpm both in the incubator and during SSC. These findings are unexpected, since feeding increases parasympathetic activity and therefore, may be expected to lead to lower HR. An impaired parasympathetic response to feeding in immature preterm infants, however, has been described previously (22). The observed increase in HR after feeding might be related to compensatory systemic haemodynamic changes in response to feeding caused by an increase in mesenteric blood flow with consequent increase in splanchnic oxygenation (8, 10, 23).

SpO_2 remained unchanged between pre-, during- and post-feed periods in the incubator. Conversely, during SSC SpO_2 dropped during-feed compared with pre-feed (by less than 1%). Furthermore, SpO_2 was lower during-feed in SSC (1.5%) compared with in the incubator. This might be explained by the

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lower SpO_2 values observed during SSC in the original studies (-0.5% and -1.1%) (17, 18) which are unlikely to be clinically important.

The strengths of this study were that continuous recording pre- / during and post-feeding intervals were compared with equal time periods for pre- and post-feed. The duration of the during-feed period (determined by gravity) was accurately documented instead of analysing a fixed time period. Moreover, we did not include any feeds that occurred within 30 minutes of handling (i.e. during washout periods).

This report takes the opportunity of combining data from two randomized trials. However, it was not pre-planned and the number of infants studied is limited to a subset of those recruited to the original trials and therefore it is a small retrospective secondary analysis.

CONCLUSION

Preterm infants are able to maintain stable cerebral oxygenation before, during and after gavage feeding in the incubator and during SSC. SSC is becoming more popular in the NICU and we now know that gavage feeding during SSC has no effect on cerebral oxygenation. Our study provides reassurance regarding gavage feeding during SSC in preterm infants.

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COMPETING INTERESTS

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FIGURES:

Figure 1: Study design showing the different study periods of the original two prospective, non-inferiority, crossover trials

Figure 2: Mean regional cerebral oxygenation ($rStO_2$) by feed period in the incubator and during SSC. The long dash lines represent the reference ranges for $rStO_2$. The line in the boxplot is the median, the end of the boxes are the 25^{th} and 75^{th} percentiles (Q1 and Q3) and ends of the whiskers (the upper and lower adjacent values, which are the most extreme values within Q3+1.5(Q3-Q1) and Q1-1.5*(Q3-Q1), respectively. The dotted lines within the boxplots represent the mean.

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Table 1: Patient Demographics

	Infants with feeds in the incubator only (n=39)	Infants with feeds in the incubator and during SSC (n=20)
Gestational age (weeks)[1]	27.9 (26.1 – 30.1)	27.6 (26.0 – 29.7)
Birth weight (g)[1]	988 (838 – 1450)	960 (817 – 1134)
Postmenstrual age (weeks)[1]	30.7 (28.6 – 33.7)	29.2 (28.2 – 32.6)
Postnatal age (days)[1]	10 (7 – 38)	11 (8 – 21)
Multiple birth, n(%)	9 (24)	7 (35)
Male, n(%)	17 (45)	9 (45)
Caffeine treatment, n(%)	29 (76)	17 (85)
Number of infants requiring any respiratory support at time of study, n(%) Mechanical ventilation CPAP HFNC	20 (53) 6 (15) 8 (21) 6 (15)	13 (65) 3 (15) 6 (30) 4 (20)
Feed amount (mL)[1]	16 (6 – 33)	12 (4 – 21)
Feed duration (mins)[1]	7.4 (4.2 – 12.3)	5.7 (3.0 – 9.3)

[1] median (IQR)

CPAP = continuous positive airway pressure

HFNC = high flow nasal cannula

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Table 2: Centiles of rStO2 in the incubator

	n	5th	10th	25th	50th	75th	90th	95th
$rStO_2$	39	63	66	70	75	78	81	82

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Table 3: Physiological parameters during feeding

	Incubator care n=39			Skin-to-skin care n=20		
Physiological Parameter	**pre-feed**	**during-feed**	**post-feed**	**pre-feed**	**during-feed**	**post-feed**
$rStO_2$ [%] [1]	74.1 (5.0)	74.0 (5.4)	74.0 (5.3)	73.5 (6.2)	73.1 (6.1)	72.6 (5.9)
SpO_2 [%] [2]	97 (94-98)	96 (94-98)	97 (94-98)	95 (92-98)	93 (92-98)	94 (92-97)
HR [bpm] [1]	159 (11)	159 (12)	162 (10)	161 (12)	160 (12)	164 (12)
cFTOE [1]	0.2 (0.05)	0.2 (0.05)	0.2 (0.06)	0.2 (0.06)	0.2 (0.06)	0.2 (0.08)
$rStO_2$ SD [1]	1.6 (1.0)	1.7 (1.0)	1.9 (1.0)	1.9 (0.8)	2.0 (1.1)	2.1 (1.5)
Number of hypoxic events	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-1.5)	0 (0-1.5)
Number of bradycardic events	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Proportion of time spent in cerebral hypoxia ($rStO_2$< 55%) [%]	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Proportion of time spent in cerebral hypoxia ($rStO_2$< 60%) [%]	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
Proportion of time spent in cerebral hyperoxia ($rStO_2$ > 85%) [%]	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)

$rStO_2$ = regional cerebral oxygenation

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SpO_2 = oxygen saturation

HR = heart rate

cFTOE = cerebral fractional tissue oxygen extraction

SD $rStO_2$ = standard deviation around each infant's mean $rStO_2$

[1] mean (SD)

[2] median (IQR)

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Table 4: Physiological parameters during incubator vs. SSC feeds

Physiological Parameter	Incubator feed	SSC feed	Mean difference (95% CI)	p-value
$rStO_2$ [%] [1]	73.3 (6.0)	73.1 (6.1)	-0.2 (-1.6 to 1.2)	0.7
SpO_2 [%] [2]	96 (94-98)	93 (92-98)	-1.5 (-2.9 to -0.2)*	0.03
HR [bpm] [1]	160 (9)	160 (12)	0.04 (-4.9 to 5.0)	0.9
cFTOE [1]	0.214 (0.058)	0.228 (0.062)	-0.014 (-0.025 to -0.004)	0.01
$rStO_2$ SD [1]	1.7 (1.0)	2.0 (1.1)	0.3 (-0.2 to 0.8)	0.2
Number of hypoxic events	0 (0-0)	0 (0-1.5)	0.7 (-0.3 to 1.6)	0.2
Number of bradycardic events	0 (0-0)	0 (0-0)	0 (-0.2 to 0.2)	1.0
Proportion of time spent in cerebral hypoxia ($rStO_2$< 55%) [%]	0 (0-0)	0 (0-0)	**	
Proportion of time spent in cerebral hypoxia ($rStO_2$<60%) [%]	0 (0-0)	0 (0-0)	**	
Proportion of time spent in cerebral hyperoxia ($rStO_2$>85%) [%]	0 (0-0)	0 (0-0)	**	

$rStO_2$ = regional cerebral oxygenation

SpO_2 = oxygen saturation

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HR = heart rate

cFTOE = cerebral fractional tissue oxygen extraction

SD $rStO_2$ = standard deviation around each infant's mean $rStO_2$

[1]Mean (SD)

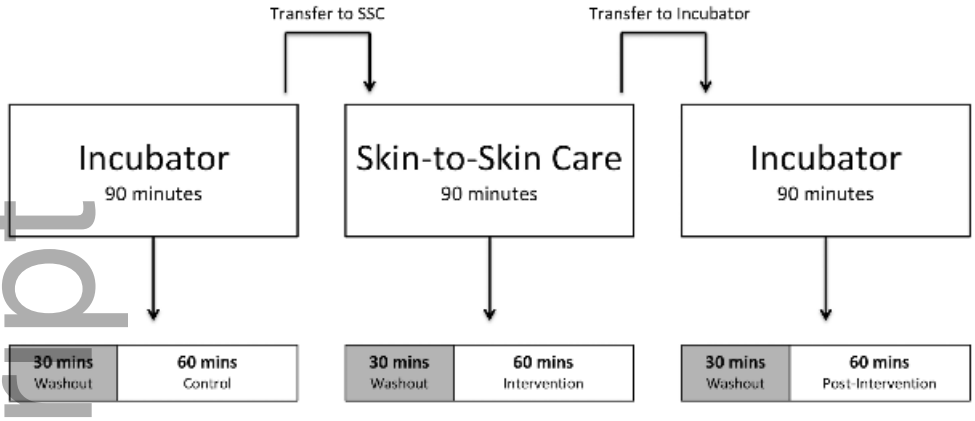
[2] Median (IQR)

[*] a paired t-test for the difference in means was used even though SpO_2 was skewed because the difference was normally distributed

** difference could not be tested with a statistical test since the data were skewed due to a high proportion of zero

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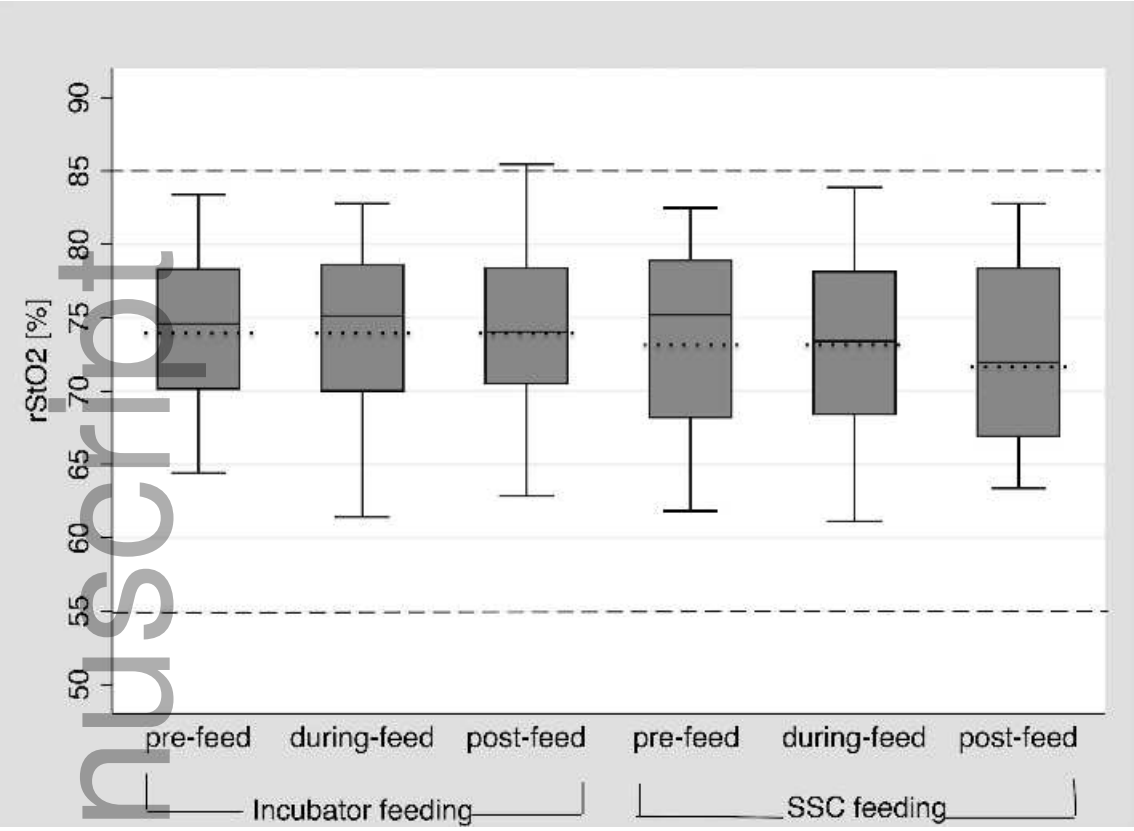
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