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ORIGINAL ARTICLE

Immediate skin-to-skin contact may have beneficial effects on the cardiorespiratory stabilisation in very preterm infants

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Abstract

Aim: Our aim was to investigate what effect immediate skin-to-skin contact with a parent had on the cardiorespiratory stabilisation of very preterm infants.

Methods: This randomised clinical trial was conducted during 2018–2021 at two university hospitals with three neonatal intensive care units in Norway and Sweden. Infants born from 28+0 to 32+6 weeks of gestation were randomised to immediate skin-to-skin contact with a parent for the first six postnatal hours or standard incubator care. The outcome was a composite cardiorespiratory stability score, based on serial measures of heart and respiratory rate, respiratory support, fraction of inspired oxygen and oxygen saturation.

Results: We recruited 91 newborn infants with a mean gestational age of 31+1 (range 28+4–32+6) weeks and mean birth weight of 1534 (range 555–2440) g: 46 received immediate skin-to-skin contact and 45 received incubator care. The group who received skin-to-skin contact had an adjusted mean score of 0.52 higher (95% confidence interval 0.38–0.67, $p < 0.001$) on a scale from zero to six when compared to the control group.

Conclusion: Immediate skin-to-skin contact for the first six postnatal hours had beneficial effects on the cardiorespiratory stabilisation of very preterm infants.

KEYWORDS
cardiorespiratory stabilisation, kangaroo mother care, neonatal intensive care unit, preterm infant, skin-to-skin contact

Abbreviations: CI, confidence interval; CPAP, continuous positive airway pressure; GA, gestational age; IQR, interquartile range; NICU, newborn intensive care unit; SCRIP, stability of the cardiorespiratory pressure in the preterm; SSC, skin-to-skin contact; VPT, very preterm.

Wibke Jonas and Siren Rettedal shared the last authorship.

1 | INTRODUCTION

In Sweden, 0.9% of all infants were born very preterm (VPT), before 32 weeks of gestation, in 2020.[1] VPT infants have a good prognosis, with improved survival and long-term outcomes.[2] However, they still have higher morbidity than term infants[1] with an increased risk of neurodevelopmental impairment.[3–6]

Transitioning from foetal to newborn life is a period of rapid physiological change, which can continue for hours to days.[7] The first hour of life is referred to as the golden hour, because initial strategies in newborn care may lead to a better start to life.[8] In high-resource settings, VPT infants are typically cared for in incubators in the immediate period following birth and with intermittent SSC for 2–3 h per day during the first postnatal days.[1] This results in mother-infant separation.[9] In a study from two Scandinavian neonatal intensive care units (NICU), infants with a median gestational age (GA) of 32 weeks had a median time to first SSC of 6 h.[10] Reasons for not practicing SSC in the early postpartum period have included logistic challenges.[11]

In healthy preterm infants, SSC helps maintain cardiorespiratory stability.[12] A recent review suggested that mother-infant regulation of physiological systems is desirable immediately after birth,[9] and potentially harmful effects of separation have been described.[13] Such effects of regulation could be captured by the stability of the cardiorespiratory system in the preterm (SCRIP) score, a composite score including the variables heart rate, oxygen saturation and respiratory rate. The original SCRIP score was published by Fischer et al. and used to describe the physiological state in stable preterm infants.[14] Bergman et al. modified the SCRIP score to study physiological transition immediately after birth for low birth weight infants and demonstrated better SCRIP scores when cared for in SSC.[15,16]

Studies on the effects of immediate SSC at birth in VPT infants are scarce.[17] Mehler et al.[18] showed that 60 min of SSC in the birth room compared to 5 min of visual contact improved mother-infant interaction. The aim of this study was to describe the cardiorespiratory effects of immediate SSC in VPT infants in a high-resource setting.

Key notes

- There are few studies investigating the cardiorespiratory effects of skin-to-skin contact immediately after birth in the high-resource setting.
- Skin-to-skin contact between the very preterm infant and a parent may be associated with improved cardiorespiratory stabilisation.
- Improved cardiorespiratory stabilisation during the period of rapid physiological change after birth may have positive implications for neonatal and long-term health.

2 | METHODS

The immediate parent-infant skin-to-skin study was registered on ClinicalTrials.gov (NCT03521310) and the study protocol has been published.[19] This paper presents the results of the primary study outcome: cardiorespiratory stabilisation in accordance with the SCRIP score.

2.1 | Study design

This study was a randomised clinical trial (RCT) that compared the cardiorespiratory effects of care in immediate SSC between the VPT infant and a parent to the same medical and nursing care in an incubator or cot during the first six postnatal hours. The study was conducted at three NICUs at two university hospitals in Norway and Sweden. The Swedish hospital had two sites. Inclusion criteria were inborn at 28+0 to 32+6 gestational weeks regardless of the mode of birth and a parent or surrogate caregiver prepared to start SSC in the first postnatal hour. Exclusion criteria were triplets or higher order births, congenital malformations that required immediate intervention or known severe congenital infection.

To obtain consent for study participation, screening was conducted for women admitted for risk of preterm labour. When the birth was imminent, randomisation was performed. The electronic randomisation tool had variable block sizes, a 1:1 ratio, three strata for the sites and two strata for GA at each site. The GA strata were 28+0 to 30+6 and 31+0 to 32+6 weeks. Twins had the same allocation.

2.2 | Sample size calculation

The sample size was estimated based on a study by Chi Luong et al.[16] In this study, 100 infants were needed to show a 10% difference in SCRIP score between the immediate SSC and control groups at six postnatal hours with a significance level of <0.05 and a power of 90%. The effect size was expected to be less in the current setting because of the higher medical and nursing care level. To compensate for this and attrition, a sample size of 150 was determined to be adequate.

2.3 | Procedures

2.3.1 | All infants

Medical care for newborn infants independent of allocation followed guidelines.[20,21] These guidelines included nasal continuous positive airway pressure (CPAP), nasogastric tube feeding and monitoring with electrocardiography electrodes and pulse oximetry.

2.3.2 | Immediate skin-to-skin contact

The intervention was immediate SSC with a parent after birth and continued throughout the first 6 h. The neonatologist in charge decided whether to initiate SSC immediately or to first assess the newborn infant on a resuscitaire under radiant heat. This decision was based on the infant's GA and expected immediate need of medical interventions. This was justified by prior research by our group showing that temperature control in room air for a VPT infant in immediate SSC may be a challenge.[22] If the mother had a vaginal birth, the infant was placed on the mother's chest, dried and covered with warm textiles. The infant was initially cared for in the birth unit and later transferred to the NICU attached to the mother's or father's chest with a wrap. If the birth mode was a Caesarean section, immediate SSC was with the father from the start and the mother continued SSC as soon as she was transferred to the NICU. The mother received postpartum care by the attending midwife. Twins were either cared for with one parent each or placed together with one of the parents. The nurse was encouraged to place the nasogastric tube and perform peripheral venous blood sampling and insertion of lines with the infant in SSC. SSC was interrupted for umbilical catheterisation, endotracheal tube placement and radiology.

2.3.3 | Control

Infants allocated to control were placed in an Omnibed incubator (GE Healthcare) or cot, in accordance with unit routines. Partners were bedside throughout and mothers when considered stable enough by the obstetric team. Parents were allowed to hand hold their infant in the incubator and encouraged to take an active part in the care.

2.4 | Data collection

Data were collected by the SCRIP method described in the protocol.[19] In summary, bedside observations were performed during 16 five-min periods. The frequency of observations was every quarter of an hour during the first and last of the first six postnatal hours and every half hour between the first and sixth hour. In Norway, one of two research team members or one of six NICU nurses collected data. In Sweden, one of four research team members collected data. Data collection methodology had been harmonised in initial training sessions.

The current place of the infant and any ongoing interventions were documented at each observation time point. The lowest and highest heart rate and oxygen saturation were collected by monitor readings for 4 min. The monitors used were Propaq M (ZOLL; Asahi Kasei) in Norway and Intellivue MX800 (Koninklijke Philips, N.V.) in Sweden. During the fifth minute, respiratory rate was manually counted. Heart rate generated one of three subscores. Oxygen saturation and fraction of inspired oxygen were pooled to another subscore that described the oxygenation. Respiratory rate and support were pooled to a third subscore describing work of breathing. The least favourable of each parameter gave a subscore graded zero to two, adding to a composite score of zero to six points, where six points indicated optimal cardiorespiratory stability.[19]

An attrition factor arose during the initiation period of the study when a single cardiorespiratory parameter rather than a range was recorded at the Norwegian site. The available parameter was used for scoring in these 24 cases. For the remainder, missing data were less than 5%, equally distributed between study groups and imputation of the most frequent response was used for missing SCRIP scores.

2.5 | Data analysis

The data were analysed by intention to treat using Stata/IC 15.0 (StataCorp LLC). Descriptive statistics were used to present baseline variables. The primary outcome was analysed with multilevel mixed-effects linear regression with random effects and an independent structure. The variables considered clinically significant were first tested in univariable models, then stepwise in multivariable models with a judgment of collinearity. Adjustments were ultimately made for country, GA strata, preterm prolonged rupture of membranes, sex and Apgar score at 5 min. A p-value <0.05 was considered statistically significant with a two-sided hypothesis test.

Exploratory subgroup analyses were conducted for GA strata and country. No adjustments for multiple comparisons or clustering were made.

2.6 | Data monitoring

The research staff was trained in Good Clinical Practice. Any unexpected medical event was considered an adverse event and reported. Adverse events were graded and assessed in terms of their relation to the study. Serious adverse events, risking disability or death or leading to prolonged length of stay or readmission to the hospital, were reported to the sponsor within 24 h and other adverse events were reported to the sponsor monthly. The Karolinska Trial Alliance designed and initiated the monitoring process in 2018–2019. The study was conducted according to Consolidated Standards of Reporting Trials guidelines[23] and the study had approval from ethical review boards.

2.7 | Study closure

Recruitment started in April 2018, with imposed pauses due to the COVID-19 pandemic and staffing issues. A preliminary data analysis was conducted in June 2021 and presented to a data safety monitoring board. The rationale for the preliminary data analysis was the publication of a large RCT on SSC from other settings[24] and hence

expected increasing recruitment challenges. On the data safety monitoring board's recommendation, recruitment was stopped in October 2021 at a sample size of 91 infants, because of benefit of the intervention.

3 | RESULTS

A large proportion of women who had consented to study participation gave birth after 32+6 gestational weeks and they were not randomised. A total of 101 infants from 82 mothers were randomised, of which 91 infants from 73 mothers were analysed (Figure 1).

3.1 | Infant characteristics

The mean GA was 31+1 (range 28+4–32+6) weeks, and the mean birth weight was 1534 (range 555–2440) grams. A skewed distribution of sex was seen with more boys in the immediate SSC group, 33/46 (72%) compared to 18/45 (40%) in the control group, $p = 0.002$. Other baseline variables were equally distributed between the groups (Table 1). All infants had respiratory support: 45/46 infants in the immediate SSC group had CPAP and one infant had high-flow nasal cannula. The corresponding proportions in the control group were 44/45 and 1/45. Two infants in the immediate SSC group and two in the control group were intubated for mechanical ventilation during a part of the intervention period.

3.2 | Initiation and duration of skin-to-skin contact

The median SSC initiation time with interquartile range (IQR) was 0.4 (IQR 0.3–1) h. In the younger infants born at GA 28+0–30+6 weeks, the median SSC initiation time was 1.0 (IQR 0.5–1.3) h and in the older infants born at GA 31+0–32+6 weeks, the median SSC initiation time was 0.3 (IQR 0–0.4) h. The median SSC duration during the intervention was 5.0 (IQR 4.5–5.5) h; 4.5 (IQR 4.0–5.0) h in the younger and 5.5 (IQR 4.7–5.7) h in the older GA strata. Maternal and paternal median SSC duration was 0.6 (IQR 0–2.8) and 3.4 (IQR 2.3–4.8) h respectively.

3.3 | Cardiorespiratory stability

Infants allocated to immediate SSC had higher SCRIP scores than infants allocated to control. The adjusted difference in mean SCRIP score with 95% confidence interval was 0.52 (95% CI 0.38–0.67, $p < 0.001$) and the interaction effect of the intervention and time was 0.003 (95% CI 0.003–0.004, $p < 0.001$). The multivariable regression model including the effect of immediate SSC with adjustments and the contribution of each independent variable to the SCRIP score, is presented in Table 2. The cardiorespiratory stabilisation is presented as unadjusted mean SCRIP scores in Figure 2A. The median and mean SCRIP scores for each time point are presented in Table 3. Significant differences were observed from 2.5 to 6 postnatal hours, during which infants of the immediate SSC group had higher stability scores than infants in

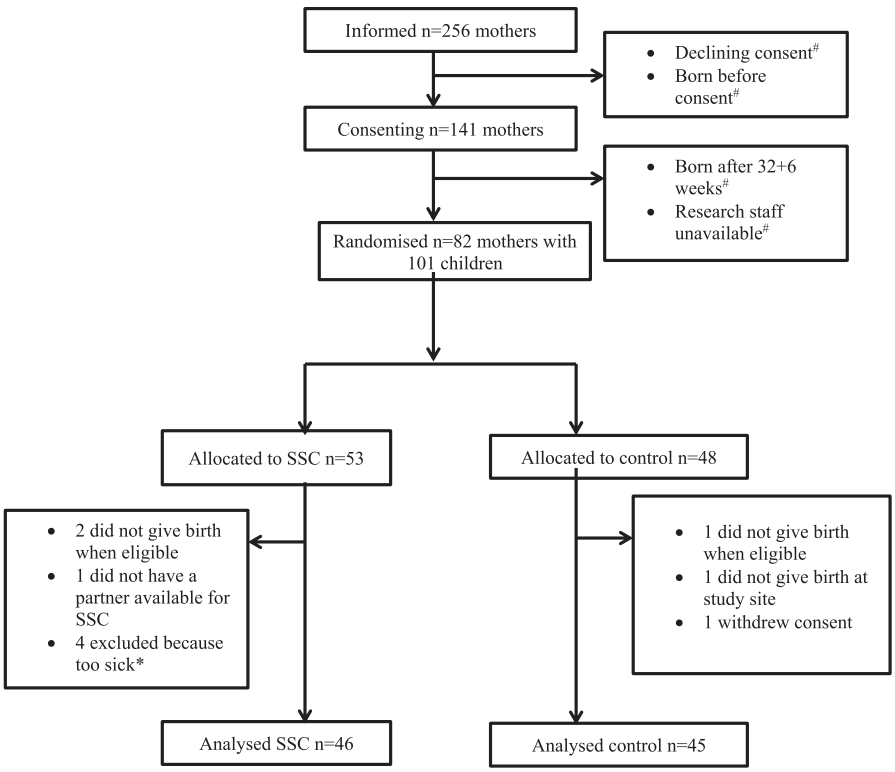

FIGURE 1 Flow chart. Flow chart showing numbers of parental couples informed, consenting and infants randomised, allocated and analysed. #Numbers not available. *The second infant recruited in Sweden was excluded by mistake (data collection was stopped) when the infant needed ventilator care. Three infants in Norway were excluded due to a later diagnosed metabolic disease, interpreted as a exclusion criteria

TABLE 1 Mother and infant characteristics

	SSC (*n* infants = 46, mothers = 38)	Control (*n* infants = 45, mothers = 35)
GA, mean (SD, range), weeks+days	31+2 (1, 28+6–32+5)	31+0 (1, 28+4–32+6)
BW, mean (SD, range), g	1571 (395, 702–2352)	1494 (400, 555–2440)
Apgar score 5 min (median, IQR)	9 (7–9)	9 (8–10)
Vaginal birth, No (%)	14 (37)	8 (23)
Twins, No (%)	16 (35)	20 (44)
Female, No (%)	13 (28)	27 (60)
PE, No (%)	10 (26)	16 (46)
PPROM, No (%)	10 (26)	7 (20)
Antenatal corticosteroids, No (%)	46 (100)	43 (96)
Primiparous, No (%)	27 (71)	16 (46)
Maternal age, mean (SD, range)	31 (5, 21–40)	32 (5, 22–45)

Abbreviations: BW, birth weight; GA, gestational age; IQR, interquartile range; PE, preeclampsia; PPROM, preterm prolonged rupture of membranes; SD, standard deviation; SSC, skin-to-skin contact.

TABLE 2 Multivariable model

Variable	Coefficient (95% CI)	*p*
Constant	2.03 (1.60-2.46)	
Allocation	0.13 (−0.12-0.38)	0.30
Time	0.00 (0.00-0.00)	0.001
Allocation#time	0.00 (0.00-0.00)	<0.001
Country	−0.16 (−0.25-0.07)	<0.001
GA strata	0.22 (0.08-0.36)	0.002
Sex	−0.22 (−0.36-−0.07)	0.003
PPROM	−0.27 (−0.42-−0.13)	<0.001
Apgar 5 min	0.14 (0.10-0.18)	<0.001

Note: The covariables effect on the SCRIP score with 95% confidence intervals (CI): Allocation (immediate skin-to-skin contact), time in minutes, the interaction effect of allocation and time, country (Norway), gestational age (GA) strata (GA 31+0–32+6), sex (male), preterm prolonged rupture of membranes (PPROM) and Apgar at 5 min.

the control group. The differences between groups were of a magnitude of 10% during the above time.

3.4 | Results of exploratory analyses

The effect size was robust across GA strata, but not across countries. While there was a difference in effect at the Swedish sites, no significant difference between allocations was seen at the Norwegian site. Respiratory rates and SCRIP scores by GA strata and country are presented in Figure 2B-E.

3.5 | Safety

An independent researcher revised all adverse event reports. No difference in occurrence or grade of adverse events was observed between randomisation arms. Four infants needed endotracheal intubation, either for apnoea or for surfactant installation. Two of them were in the intervention group and two in the control group. The incidence of hypoglycaemia was similar in the intervention and control groups. There was no significant difference between allocations in proportion of infants with temperature under 36.0°C.

4 | DISCUSSION

To our knowledge, this is the first RCT investigating the effects of immediate SSC in VPT infants in a high-resource setting. Infants of both allocations received the same state-of-the art medical and nursing care, as well as equal opportunities for parental presence and involvement. The study found that cardiorespiratory stabilisation as per the SCRIP score was better in the immediate SSC group compared to in the control group. We have interpreted the effect size of 0.52 on the scale from zero to six as clinically significant. However, the SCRIP is a scale with ordinal data and comparisons of means should be interpreted with caution.

Earlier research has mainly focused on mother-infant SSC, whereas in this study infants spent more time in SSC with their fathers. This was due to that VPT infants were most often transferred to the NICU during the first postnatal hour, before the mothers were well enough to accompany. Previous research has shown beneficial effects of paternal SSC,[25] which this study confirms.

Our results were consistent with previous studies in middle-resource settings.[15,16] Other studies have shown that stable VPT infants have a higher cardiac output during SSC[26] and a more regular respiratory pattern.[27] This suggested that autonomic regulation when in SSC may be due to the activation of the nurturing deep touch sensor system, mediated by unmyelinated C-tactile fibres.[28] Its activation of the parasympathetic nervous system would, in terms of cardiorespiratory parameters, present as a decrease in

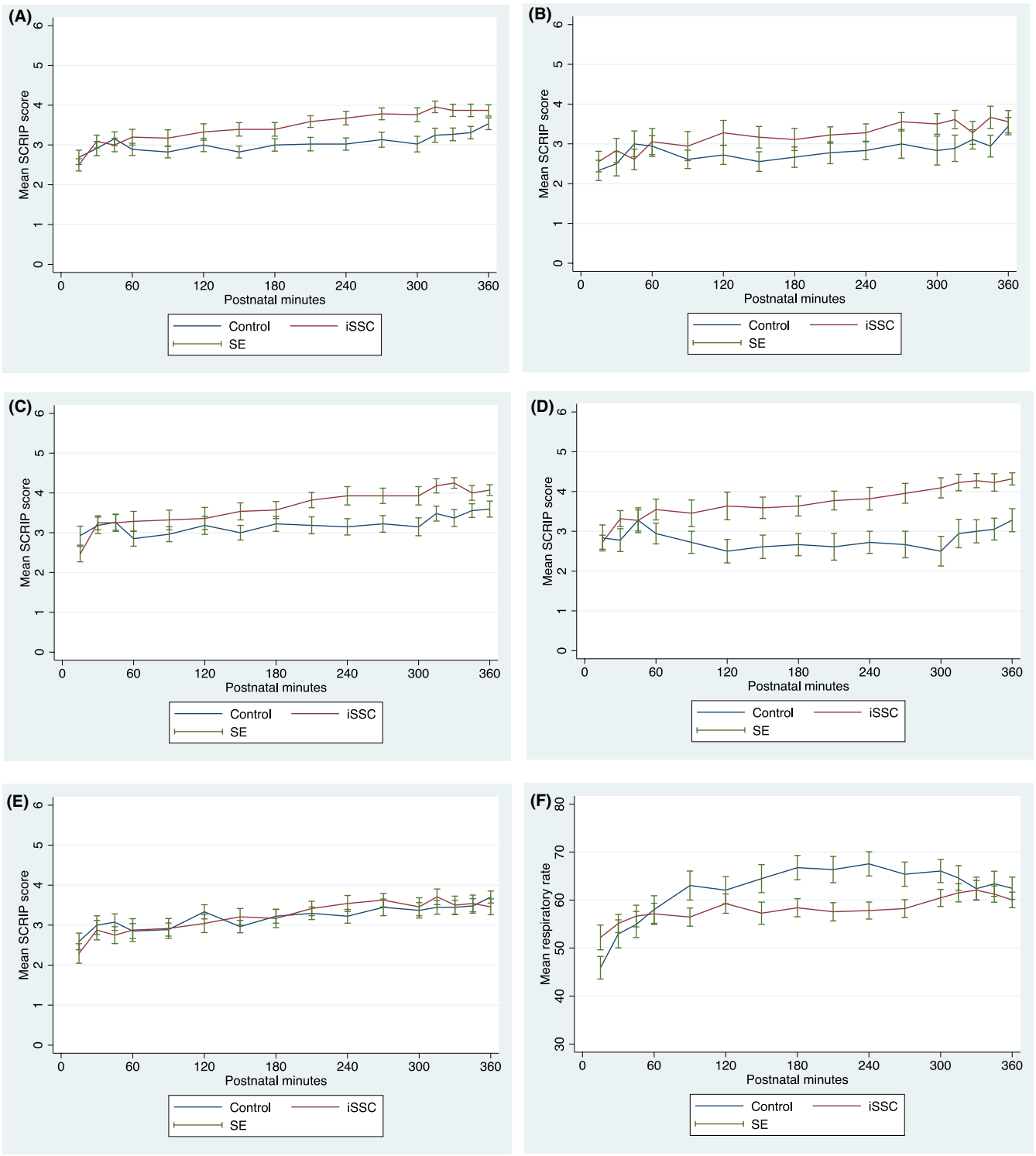

FIGURE 2 Mean SCRIP scores during the first 360 min. (A) All ($n = 91$); (B) GA 28+0–30+6 ($n = 36$); (C) GA 31+0–32+6 ($n = 55$); (D) Sweden ($n = 40$); (E) Norway ($n = 51$); (F) Mean respiratory rates during the first 360 min ($n = 91$). Abbreviations: iSSC, immediate skin-to-skin contact; SCRIP, stability of the cardiorespiratory system in the preterm; SE, standard error

heart rate and an increase in oxygenation. In a longer perspective, it is suggested to have a positive effect on stress handling and parent-infant interaction.[28] Early activation of this system may be important, because the first hours following birth are critical. Disturbances may lead to complications requiring additional potentially stressful, painful and high-risk procedures.[13]

A recent review suggested that mother-infant regulation of physiological systems is essential immediately after birth, and

TABLE 3 Unadjusted median and mean SCRIP scores

Median (IQR) SCRIP score				Mean (95% CI) SCRIP score		
Postnatal minutes	SSC, $n = 46$	Control, $n = 45$	Diff (%)	SSC, $n = 46$	Control, $n = 45$	Diff (%)
15	3 (2–3)	3 (2–4)	0	2.5 (2.2–2.8)	2.7 (2.3–3.1)	−0.2 (−3)
30	3 (3–4)	3 (2–4)	0	3.1 (2.8–3.4)	2.9 (2.5–3.3)	0.2 (3)
45	3 (2–4)	3 (3–4)	0	3.0 (2.7–3.3)	3.2 (2.8–3.5)	−0.2 (−3)
60	3 (2–4)	3 (2–4)	0	3.2 (2.8–3.6)	2.9 (2.6–3.2)	0.3 (5)
90	3 (2–4)	3 (2–4)	0	3.2 (2.8–3.6)	2.8 (2.5–3.1)	0.4 (7)
120	3 (2–5)	3 (3–4)	0	3.3 (2.9–3.7)	3.0 (2.7–3.3)	0.3 (5)
150	3 (3–4)	3 (2–3)	0	3.4 (3.1–3.7)	2.8 (2.5–3.1)	0.6 (10)
180	3.5 (3–4)	3 (2–4)	0.5 (8)	3.4 (3.0–3.7)	3.0 (2.7–3.3)	0.4 (7)
210	4 (3–4)	3 (2–4)	1 (17)	3.6 (3.3–3.9)	3.0 (2.7–3.4)	0.6 (10)
240	4 (3–5)	3 (2–4)	1 (17)	3.7 (3.3–4.0)	3.0 (2.7–3.3)	0.7 (12)
270	4 (3–5)	3 (2–4)	1 (17)	3.8 (3.5–4.1)	3.1 (2.8–3.5)	0.7 (12)
300	4 (3–5)	3 (2–4)	1 (17)	3.8 (3.4–4.1)	3.0 (2.6–3.4)	0.8 (13)
315	4 (4–5)	3 (3–4)	1 (17)	4.0 (3.7–4.2)	3.2 (2.9–3.6)	0.8 (13)
330	4 (4–5)	3 (3–4)	1 (17)	3.9 (3.6–4.2)	3.3 (2.9–3.6)	0.6 (10)
345	4 (3–5)	3 (3–4)	1 (17)	3.9 (3.6–4.2)	3.3 (3.0–3.6)	0.6 (10)
360	4 (3–5)	4 (3–4)	0	3.9 (3.6–4.2)	3.5 (3.2–3.8)	0.4 (7)

Abbreviations: CI, confidence interval; Diff, difference; IQR, interquartile range; SCRIP, stability of the cardiorespiratory system in the preterm; SSC, skin-to-skin contact.

described mechanisms for potentially harmful effects of separation.[9] Stressful exposures can programme the infant through epigenetic mechanisms and have implications later in life.[29] VPT infants may be negatively affected by the stress of parent-infant separation in conventional care. On the other hand, an adequate environment may elicit protective mechanisms with improved parent-infant bonding and long term health.[30] Thus, subtle differences in cardiorespiratory stabilisation may reflect these processes.

4.1 | Strengths and limitations

The major strength of this study was the randomisation and intention to treat design ensuring decreased selection bias and reversed causality. The study was well controlled, the only difference between the groups being the place of care. Bedside observations enabled registration of short deviations in vital parameters.

There were some limitations to the study. The antenatal consent procedure led to the selection of prepared infants and parents to the study. Blinding was not possible. Any expectations regarding the allocation may have affected the parent, consequently affecting the infant, and may also have biased data collection. However, observers were present at the bedside and available to the same extent, and data from intervention and control infants was collected using the same method. Interobserver reliability was validated only during the study initiation phase, which may have contributed to the country differences in outcomes. The study was stopped earlier than planned and the smaller sample size had implications for the power of subgroup analyses.

5 | CONCLUSION

Our study in a high-resource setting indicates that infants born very preterm may have improved cardiorespiratory stabilisation when cared for in SSC with a parent immediately after birth. Thus, immediate SSC is feasible and may be the desirable standard of care for the VPT infant.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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