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Immediate parent-infant skin-to-skin study (IPISTOSS): study protocol of a randomised controlled trial on very preterm infants cared for in skin-to-skin contact immediately after birth and potential physiological, epigenetic, psychological and neurodevelopmental consequences

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ABSTRACT

Introduction In Scandinavia, 6% of infants are born preterm, before 37 gestational weeks. Instead of continuing in the in-utero environment, maturation needs to occur in a neonatal unit with support of vital functions, separated from the mother's warmth, nutrition and other benefits. Preterm infants face health and neurodevelopment challenges that may also affect the family and society at large. There is evidence of benefit from immediate and continued skin-to-skin contact (SSC) for term and moderately preterm infants and their parents but there is a knowledge gap on its effect on unstable very preterm infants when initiated immediately after birth.

Methods and analysis In this ongoing randomised controlled trial from Stavanger, Norway and Stockholm, Sweden, we are studying 150 infants born at 28+0 to 32+6 gestational weeks, randomised to receive care immediately after birth in SSC with a parent or conventionally in an incubator. The primary outcome is cardiorespiratory stability according to the stability of the cardiorespiratory system in the preterm score. Secondary outcomes are autonomic stability, thermal control, infection control, SSC time, breastfeeding and growth, epigenetic profile, microbiome profile, infant behaviour, stress resilience, sleep integrity, cortical maturation, neurodevelopment, mother-infant attachment and attunement, and parent experience and mental health.

Ethics and dissemination The study has ethical approval from the Swedish Ethical Review Authority (2017/1135-31/3, 2019–03361) and the Norwegian Regional Ethical Committee (2015/889). The study is conducted according to good clinical practice and the Helsinki declaration. The results of the study will increase the knowledge about the mechanisms behind the effects of SSC for very preterm infants by dissemination to the scientific community through articles and at conferences, and to the society through parenting classes and magazines.

Study status Recruiting since April 2018. Expected trial termination June 2021.

Trial registration number NCT03521310 (ClinicalTrials.gov).

Strengths and limitations of this study

- ► To our knowledge, this will be the first randomised controlled trial to study the physiological effects of skin-to-skin contact (SSC) initiated immediately after birth for unstable preterm infants in a high-income setting.
- ► The high quality of care settings makes it possible to separate the effects of immediate SSC per se from other powerful co-interventions such as surveillance of the infant and breastfeeding support, which will provide novel mechanistic information.
- ► We will follow infants and their parents (primarily mothers) over a time course of 2 years in order to study possible long-term effects of the intervention.
- ► There is an ongoing shift towards earlier SSC for all infants in clinical practice, including very preterm infants, based on experience rather than scientific evidence. This may change the characterisation of conventional care throughout the course of the study, make the differences between intervention and control smaller, and the effects of SSC more difficult to define.

INTRODUCTION

Background

Care of the preterm infant

Preterm birth is defined as birth before 37 gestational weeks. Birth before 28, 32 or 37 gestational weeks is classified as extremely, very or moderately preterm, respectively.[1] For preterm infants, maturation, behavioural organisation and neurodevelopment continue in a hospital environment instead of in-utero. These first weeks to months of an infant's life contain many unexpected experiences, both physiologically and psychologically challenging. To maintain basic homeostatic regulation, supportive interventions for respiration, thermal control, fluid balance, nutrition and infection control are needed.[2] In our setting, very preterm infants or infants with a birth weight under 1500 g are mainly cared for in an incubator and moderately preterm infants in a cot with intermittent skin-to-skin contact (SSC) with the parents during the first days or weeks after birth. Neonatal care in Scandinavia is often considered state of the art.[3] Still, the adverse environment that the neonatal unit represents to a preterm infant may have a negative impact on health outcomes.[4] Of special importance are the first hours in life, when the transition from intra- to extra-uterine life takes place, as any instability may lead to a cascade of negative effects in the infant, causing morbidity and mortality.[5] The incubator provides the warmth and humidity that the infant needs but also implies an abrupt physical and psychological separation of the mother and infant. Separation can be avoided by the use of SSC between parent and infant.[6]

Socioeconomic perspective

Globally, around 12% of all infants, 15 million annually, are born preterm.[7] In Sweden and Norway, the corresponding number is approximately 6%, 8000 infants annually.[8 9] Preterm birth and low birth weight are the largest contributors to global mortality under the age of 5 years[10] and two-thirds of neonatal deaths occur within the first 3 days of life.[11] Survivors face short-term and long-term morbidity including neurobehavioural, socio-emotional and cognitive challenges.[12–16] Preterm birth affects families' lives, with higher perceived levels of stress, feelings of loneliness and isolation.[17] These challenges also have economic consequences, including the high costs for the intensive care during the hospital period and for the post-discharge morbidities: both for the individual family and the society at large.[18 19]

Skin-to-skin contact

Studies on non-human primates and mammals use maternal-infant separation paradigms as a standard procedure to induce severe stress.[20] They show immediate dysregulation of autonomic and physiological functions, and an adverse impact on stress neurobiology.[21] Our hypothesis is that this also applies to human infants. In our setting, stable infants born at term age are placed directly on their mother's chest after birth, at the sensitive time of transition from fetal to extra-uterine life.[22] This method is motivated by the observation that SSC between parent and term infant regulates the transition.[23] SSC may be even more vital for preterm babies. The WHO recommends that all stable low-birthweight infants be cared for in SSC with their mother and states that the first postnatal hour is of special importance.[6]

SSC involves placing the naked infant, covered with a warm blanket, prone on the parent's bare chest.[6] Globally, and also in the literature, the expression Kangaroo mother care (KMC) is often incorrectly used synonymously with SSC. KMC, however, is a wider term, including breastfeeding and early discharge from the hospital and is traditionally used as a step-down way of care for growing infants before discharge to home. In popular language and in practice globally, KMC can be the concept of caring for the infant together with the mother. We use the abbreviation iSSC for SSC provided immediately after birth, to emphasise that this is an intervention other than the routine intermittent SSC that is part of the conventional care in our setting.

Healthy infants born at term show enhanced breastfeeding behaviours, better temperature control and better glucose homeostasis, when cared for in SSC.[23] SSC decreases procedural pain in term and preterm infants.[24] Electroencephalography studies on KMC in stable term infants have shown a different activity in the prefrontal regions of the brain, known to be responsible for attachment.[25] Stable preterm infants cared for in SSC also have better temperature control[26] and cardiorespiratory stability.[27] They show a better self-regulation and sleep-wake cyclicity in the neonatal period,[28] a sleep-pattern more similar to infants born at term,[29] a better neurodevelopment at 6 months[30] and behavioural organisation throughout childhood.[31] Stress as measured by cortisol levels decrease in response to SSC in the stable preterm infant.[32] Research on moderately preterm infants has shown that they can safely be cared for in SSC even during the first hours in life, with regards to blood glucose levels and body temperature.[33 34] Positive maternal outcomes of SSC include higher rates of exclusive breastfeeding[23] and better maternal mental health.[30 35] The parent-infant bonding process and maternal-infant interactions are strengthened in the short-term[30 35 36] and long-term.[37 38]

In a Cochrane review from 2016, a 40% mortality reduction was reported among infants with birth weight below 2000 g when cared for in KMC as compared with conventional care. These infants also showed a lower rate of sepsis, a shorter hospital stay and a higher prevalence, and duration and degree of breastfeeding.[39] In almost all the studies in the review, KMC was commenced once the infant was stabilised, which in general meant the infant no longer needed respiratory support or intravenous fluids. The median age for initiation of KMC was 3.2 to 24.5 days. In one study only, KMC was initiated before 10 postnatal hours. Since most neonatal deaths occur within the first 3 postnatal days,[11] these results indicate that more than two-thirds of deaths in preterm infants would have

occurred before the infant was considered stable enough for KMC.

Data on SSC and physiological stabilisation from higher-income settings is limited. In a South African randomised controlled trial (RCT) on infants with birth weight of 1200 to 2199 g, improved stability during the first 6 postnatal hours according to a composite score called Stability of the cardiorespiratory system in the preterm (SCRIP) was reported in the group allocated to iSSC compared with incubator care. The infants cared for in an incubator also had a significantly lower body temperature.[40] In a similar study from Vietnam, children with birth weights of 1500 to 2500 g similarly had significantly better SCRIP scores in the iSSC group. Moreover, they had less need for respiratory support, intravenous fluids and antibiotics during the hospital stay.[41] Our own work on 50 infants in Stockholm between 2014 and 2016 showed that iSSC could safely be provided for very preterm infants during the first postnatal hour but that in contrast to in previous studies, attention needs to be paid to prevent hypothermia.[34]

There are indications that experiences early in life have implications on health and disease over the lifespan, partly governed by epigenetic mechanisms.[42] To our knowledge, no studies have explored the epigenetic consequences of SSC. A systematic review describes the impact of the neonatal intensive care unit environment on the infant microbiome[43] but it is not known whether SSC affects the infant's microbiome.

Currently, SSC initiation time and hours per day depend on the gestational age and medical condition of the infant but also on ward routines and facilities for the parents.[44] Few very preterm infants are cared for in uninterrupted iSSC during the first postnatal hours in our setting. For this group of infants, evidence is lacking for when SSC should be initiated, how many hours of SSC per day is necessary to exert positive effects and if there is a difference in effects of SSC provided during the first hours of transition and later in the neonatal period. Furthermore, it is concluded that there is a knowledge gap concerning the efficacy and safety of SSC in unstable preterm infants when initiated immediately after birth.[45]

Objectives

The overall aim of this trial is to compare iSSC for very preterm infants initiated immediately after birth and continued during the first 6 postnatal hours to current conventional care in incubator or cot. The purpose of conducting the study in a high-income setting is to explore the mechanisms behind the effects of iSSC in a manner that cannot easily be done in a low-resource setting where the effects of breastfeeding and the mother's surveillance of the infant when in SSC are difficult to separate from the effects of SSC per se. Our study will complement the recently closed international Immediate KMC study in low-income countries.[46] Our proposed study is the first, to our knowledge, to bring together variables in a generalisable population of very preterm infants. The *primary outcome* is cardiorespiratory stability during the first 6 postnatal hours as per the SCRIP score. The *secondary outcomes* are physiological, epigenetic, psychological and neurodevelopmental effects of iSSC on very preterm infants, including short-term and more long-term effects on parent-infant dyads. Potential biological processes that may mediate these outcomes are studied.

Hypotheses

Immediate and continued SSC between the unstable preterm infant and parent during the first 6 postnatal hours

- improves cardiorespiratory stabilisation during the transition from fetal to extra-uterine life
- improves autonomic control as measured by heart rate variability during the transition to extra-uterine life and at follow-up
- improves thermal control during the transition
- improves infection control during the hospital stay
- increases SSC time between parent and infant during the hospital stay
- improves breastfeeding, nutrition and growth
- is associated with a different infant epigenetic profile in the short-term and long term
- improves microbiome maturation and diversity in the short-term and long term
- improves behavioural organisation
- improves stress reactivity and resilience
- improves sleep integrity and maturation
- improves local and global cortical maturation
- improves neurodevelopment
- improves mother-infant attachment and cortisol attunement in the short-term and long term
- improves parental experience and mental health in the short-term and long term

METHODS AND ANALYSIS

Study design

The Immediate parent-infant skin-to-skin study (IPIS-TOSS) is a Scandinavian superiority RCT with a parallel two-arm non-blinded multicentre design. The trial is registered in ClinicalTrials.gov.

The two arms compared are skin-to-skin contact between either parent and their very preterm infant initiated immediately after birth (iSSC group) and conventional care under a radiant warmer, in an incubator or cot (control group). These arms differ only with respect to *place of care*, with all monitoring, nursing and medical care as per defined guidelines and routines being identical in both groups.

Procedures

In the iSSC group, the infant immediately after birth is placed in SSC with a parent and remains so continuously for at least the first 6 hours. To maintain normothermia, the infant is dried before being placed in iSSC and covered with pre-heated textiles. Mobile respiratory support and equipment for monitoring enables stabilisation in SSC in the birth unit. Placement of nasal

continuous positive airway pressure (CPAP), peripheral line and nasogastric tube is done during SSC. If stabilisation, including mask ventilation, placement of CPAP, saturation probe and electrocardiography electrodes, is likely to take more than 5 min to accomplish, the infant may first be placed under a radiant warmer in order not to lose heat before being placed in SSC and covered with textiles. iSSC is interrupted for procedures such as endotracheal intubation and placement of umbilical catheters, and the infant is returned to SSC as soon as the procedure is completed. The infant in the control group is, as per standard care, separated from the mother and cared for in an incubator or cot with intermittent SSC initiated after 6 hours.

The study settings

The study is conducted at Karolinska University Hospital (neonatal units at Danderyd and Huddinge) in Stockholm, Sweden, and at Stavanger University Hospital, Norway.

Danderyd is a level two neonatal unit with 15 beds serving a birth unit of 11 000 births per year, Huddinge is a level three neonatal unit with 15 beds serving a birth unit of 5000 births per year and Stavanger is a level three neonatal unit with 16 beds serving a birth unit of 4400 births per year.

Recruitment

Screening is performed among women admitted to obstetric units for threatening preterm labour at 28+0 to 32+6 gestational weeks+days. Informed consent is obtained from prospective parents. The timing of study information is a delicate matter as it is not easily predicted when these women will give birth. Some women will be hospitalised for risk of preterm birth but may be discharged and readmitted depending on their condition. Our procedure of choice is to inform about the study as soon as the parents to be have had a routine antenatal consultation about preterm care with the paediatrician. The routine antenatal consultation covers the conventional care including later intermittent SSC. The consent form describes the objectives of the study and all the outcomes measured. Parents to be are informed that they can consent to participation overall but decline participation in outcomes and they can also withdraw their consent from participation in all or parts of the study at any time. See figure 1 for a flow chart describing the recruitment.

Eligibility criteria

Inclusion and exclusion criteria are presented in table 1.

Allocation

Randomisation is performed electronically at www.randomize.net. The Karolinska Trial Alliance has set up the sequence generation using two strata, 28+0 to 30+6 and 31+0 to 32+6 each, with randomisation in uneven block sizes.

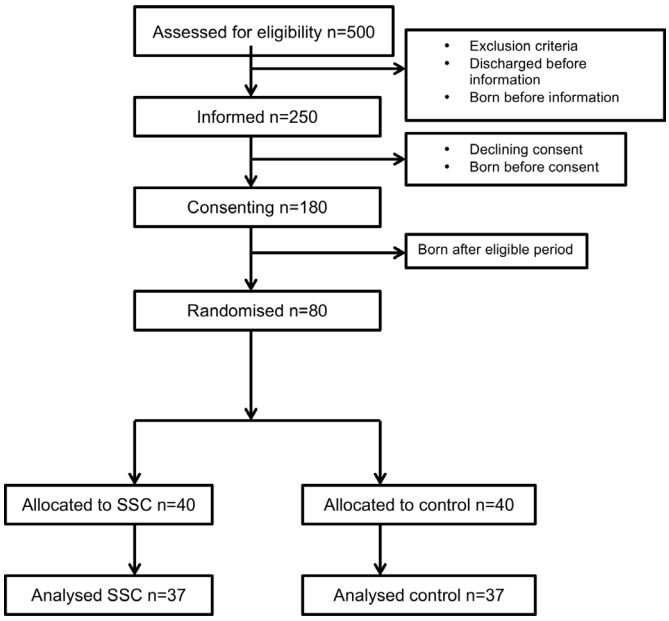

Figure 1 Flow chart showing estimated annual numbers of parents screened, informed, consenting, randomised, allocated and analysed. SSC, skin-to-skin contact.

Patient and public involvement

No patients or parents have been involved in the study design.

Outcome measurements

Primary outcome: cardiorespiratory stability

Cardiorespiratory stability is scored with the SCRIP score, a composite score including heart rate; respiration: respiratory support and respiratory rate; and oxygenation: fraction of inspired oxygen and oxygen saturation in the infant. This score was elaborated by Bergman in our team and used in previous versions in studies similar to ours.[40 47] SCRIP data is collected during close observation of the infant by members of the research team for 5 min periods during every quarter of an hour the first hour, every half an hour during the second to fifth hour and again every quarter of an hour during the sixth hour. During each period, the highest and the lowest value observed for each parameter is recorded. The least favourable value for each parameter gives a score of 0 to 2, where 0 represents instability and 2 represents stability, adding up to a composite score of 0 to 6 as a proxy for cardiorespiratory stability. See table 2 for a description of the parameters.

Secondary outcomes

The secondary outcomes are collected at different time points up to 24 months corrected age from the infant, the mother and, for some outcomes, the father as presented in table 3. Some members of our research team are involved in both intervention delivery and outcome assessment and are for logistic reasons unblinded. Whenever feasible, as in assessment of biological samples and films of mother-infant interaction and neurodevelopment, the researchers are blinded to the allocation.

Table 1 Eligibility

Inclusion criteria	Exclusion criteria
► Inborn infants regardless of mode of birth ► Gestational age 28+0 to 32+6 weeks ► Mother/other caregiver prepared to start skin-to-skin contact in the first 60 min after birth ► Informed consent provided by both parents, with the help of an interpreter if needed	► Triplets or higher-order births ► Major congenital malformations (life-threatening or needing immediate surgery) ► Known congenital infection ► Other reason contraindicating study participation according to physician in charge

Parent and infant inclusion and exclusion criteria for participation in the Immediate parent-infant skin-to-skin study (IPISTOSS).

Sample size calculation

Sample size for the primary outcome has been calculated based on the difference in proportion of full SCRIP score in the study by Luong *et al*[41] where with a two-sided test, with p<0.05 and a power of 90%, 100 infants were needed, half in each arm. Given a different control care in our setting and to compensate for attrition, a sample size of 150 has been estimated to be adequate. For the secondary outcomes heart rate variability, epigenetics, microbiota and functional brain maturation subsamples of about 50 infants will be analysed.

Data management

Data is collected at birth and during the time the infant is admitted at the neonatal unit and at follow-up visits at term equivalent age, at 3 to 4, 12 and 24 corrected months, according to routine time points in the Swedish and Norwegian national neonatal follow-up programmes. In Sweden, very preterm infants are routinely followed to 12 corrected months and moderately preterm infants are not followed after discharge, which means that, for infants included in this study, they will receive additional follow-up visits.

Prospective collection of data is performed from the clinical notes in paper and electronic patient files. Personal data is managed initially but coded and kept under code. All analyses will be done by exporting a coded data set to statistical software. Data collection and management follow the policy of Karolinska Institutet, Stavanger University Hospital and the General Data Protection Regulation (GDPR). An electronic logbook is used for the project. Data is currently collected under code in paper case report forms (CRF) and an electronic CRF is under construction. Swabs, blood, saliva and stool samples are stored under code in a biobank. Films of mother-infant interaction are kept in a safe cloud server provided by the Karolinska Institutet and Stavanger University Hospital.

Data analysis and statistics

We will use descriptive statistics, χ^2 statistics for categorical variables, and Student's t-test (unpaired) for continuous data to describe participant characteristics and to compare the intervention and control group at baseline. We will also use regression analyses, and mediation and moderation models. For example, to determine whether the intervention has effects on SCRIP scores, breastfeeding duration and scores of the Bayley scales, we will conduct regression analyses with the above as dependent variables and allocation as predictor. Covariates will include accumulated time spent in SSC during the first days or weeks, maternal age, parent socioeconomic status, parity, birth weight and gestational age etc.[48]

ETHICS AND DISSEMINATION

Ethical approval

The study has ethical approval from the Swedish Ethical Review Authority (2017/1135-31/3, 2019–03361) and the Norwegian Regional Ethical Committee (2015/889).

The study is conducted according to good clinical practice (GCP) and the Helsinki declaration. The research staff is GCP trained. All infants must receive the best available care and it is the responsibility of

Table 2 Stability of the cardiorespiratory system in the preterm (SCRIP) score

Score variable		2	1	0
Heart rate		120 to 160	100 to 119 or 161 to 180	<100 or >180
Oxygenation	If on room air	95% to 100% and	90% to 94% or	<90% or
	If on oxygen	FiO_2 0.21	FiO_2 0.22 to 0.30	FiO_2 >0.30
Respiration	If no respiratory support	40 to 60/min and	30 to 39 or 61 to 70/min or	<30 or >70/min or
	If respiratory support	None	CPAP/HFNC	MV

The Stability of the cardiorespiratory system in the preterm (SCRIP) score. Each of the parameters heart rate, oxygenation and respiration are graded 0 to 2 and summed up to 0 to 6.
CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen; HFNC, high-flow nasal cannula; MV, mechanical ventilation.

Table 3 Secondary outcomes

Domain	Description	Tool/analysis	Time point
Respiration	Need for surfactant. Time on invasive ventilation, CPAP and nasal cannula.	Medical records	During hospital stay
HRV	HRV as a proxy for autonomic stability	Propaq (Zoll, USA)	During intervention, at 48 to 72 hours, discharge and 3 to 4 months
Thermal control		Infant and parent axillary temperature	During intervention
Infection	Clinical sepsis, positive blood cultures and days on antibiotics	Medical records	During hospital stay
Skin-to-skin contact	Skin-to-skin contact duration per day with a parent	Parental diaries	During hospital stay
Breastfeeding and growth	Postnatal age at first feed, time to full enteral feeds and time to full non-gavage feeds. Breastfeeding initiation, and duration and maternal self-efficacy. Breastfeeding status. Weight trajectory.	IBS[51] BSES[52] Medical records	During hospital stay, at discharge, at term, 3 to 4, and 12 months
Epigenetics	Methylation status	Blood and buccal cells. Whole genome and locus-specific methylation analysis of stress-related genes[53 54]	Birth, after intervention, at 48 to 72 hours, 3 to 4, and 24 months
Microbiota	Characteristics: maturation and diversity of the microbiome	DNA analysis from paternal skin and from maternal skin, and stool and vaginal swabs	Birth, 72 hours, 3 to 4, 12 and 24 months
Functional brain maturation	EEG sleep and awake patterns, local and global maturation	EEG Galileo NT (EB Neuro, Italy)[29]	4 to 10 days
Neurodevelopment		HINE,[55] APIB,[56] AIMS,[57] ASQ,[58] IBQ,[59] MCHAT[60] Bayley scales,[61] General motor scales[62]	Term, 3,12 and 24 months
Mother-infant interaction and stress response	Assessment of emotional and interactive behaviours in the mother-infant dyad	Still Face Paradigm,[63] PCERA[64] for infant and mother (films)	4 and 12 months
Neuroendocrine response system	Salivary cortisol levels of mother and infant	Salivary cortisol trajectories in relation to a stressor and in normal daytime activity for infant and mother[65]	Discharge, 4 and 12 months
Parental well-being and mental health		EPDS,[66] STAI,[67] SPSQ[68] for mother and partner	7 days, term, 3 and 12 months

The secondary outcomes, tools and time points for data collection. Note: All times for follow-up are corrected ages calculated from the expected date of birth.
AIMS, Alberta infant motor scale; APIB, assessment of preterm infant behaviour; ASQ, ages and stages questionnaire; BSES, breastfeeding self-efficacy scale; CPAP, continuous positive airway pressure; EEG, electroencephalography; EPDS, Edinburgh postnatal depression scale; HINE, Hammersmith infant neurological exam; HRV, heart rate variability; IBQ, infant behaviour questionnaire; IBS, index of breastfeeding status; MCHAT, modified checklist of autism in toddlers; PCERA, parent-child early relational assessment scale; SPSQ, Swedish parenthood stress questionnaire; STAI, Spielberg state-trait anxiety inventory.

researchers to adhere to best practice. We are aware of the challenges in the consent process involving pregnant and parturient mothers and partners and their unborn infants, and have an elaborate parent information material and a pre-defined structure of how and when to inform parents-to-be about the study. Members of staff may think that infants in the control group are not receiving the best care, extrapolating the evidence from stable term infants. Trainings are held in the basics of clinical research and equipoise in RCTs. We have

discussed the following potential risks with this study's intervention:

Hypothermia

Data from our group has indicated that infants at this gestational age may have slightly lower body temperatures when cared for in SSC during the first postnatal hour.[34] Neonatal hypothermia is a risk factor for many morbidities.[49] In the methods section, we have described our strategy to maintain normothermia.

Sudden unexpected postnatal collapse

Sudden unexpected postnatal collapse (SUPC) has been described to occur in postnatal units in apparently well term infants. SUPC has been associated with unsafe SSC and breastfeeding in primiparous mothers and infant sleeping in prone position.[50] We see no risk of SUPC in our study as infants will be cared for by neonatal staff in a safe SSC position and monitored with at a minimum pulse oximetry.

Discomfort

Blood sampling in the study coincide with sampling for clinical purposes except at 3 to 4 months and 2 years when study participation necessitates additional blood tests which may cause pain. Collection of buccal and saliva swabs can be disturbing but not painful. Parents will need support from the staff and it must be made clear that monitoring and medical care is staff responsibility. Otherwise, staying in iSSC with an unstable preterm infant may make a parent feel left alone with many responsibilities.

Integrity

Research staff and external staff who are monitoring the study have access to patient files. Staff is screening maternal files to identify eligible study participants. When data is collected, it is kept, analysed and presented under code in an unidentified form.

Management of adverse events

Any unexpected medical event or deterioration is considered as an adverse event (AE), whether it is related to the study or not. An AE is classified as mild, moderate or severe. Examples are cardiorespiratory deterioration with escalated intensive care, such as repeated apnoea with need for mechanical ventilation, invasive ventilation or circulatory deterioration with need for volume expansion or inotropes, withholding feeds because of suspected necrotising enterocolitis, transport to facilities with higher level of care for any reason or prolonged hospital stay. Life-threatening events or those risking disability such as intraventricular haemorrhage, necrotising enterocolitis, deaths and any reason for re-admission to the hospital are defined as serious adverse event (SAE). AEs are classified in relation to the study intervention as likely, possible or unlikely. Within 24 hours after notification of a SAE, researchers report this to the sponsor. Non-serious AEs are reported monthly to the sponsor. Reporting is done under code on AE forms describing the event and actions taken. The original document is stored in the patient folder. Monthly and individual registries of AEs are kept. The sponsor is reporting SAEs within a week and AEs within 6 months to the Data Safety Monitoring Board (DSMB).

Monitoring and study safety

The Karolinska Trial Alliance has initially helped in study design, design of CRF and initial monitoring visits. An independent DSMB will review and evaluate the study data for participant safety, study conduct and progress, and make recommendations concerning continuation, modification or termination of the trial. An interim analysis evaluating a selection of data on parental health, temperature and SCRIP scores is currently being done after the first 60 recruited patients.

Dissemination

To the scientific community, the results of the trial will be distributed through articles and at conferences. Clinical staff will be educated about the study results. The findings will increase the knowledge about the mechanisms behind the effects of SSC and contribute to updated guidelines on care of the preterm infant. To the society, including parents-to-be, information will be distributed through parenting classes, social media, magazines and newspapers.

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