投稿論文

Comparison of Salivary Cortisol, Heart Rate, and Oxygen Saturation Between Early Skin-to-Skin Contact with Different Initiation and Duration Times in Healthy, Full-Term Infants

The transition from intrauterine to extrauterine life represents one of the most dynamic and potentially dangerous events in the human life cycle. Therefore, in caring for newborn infants after birth, one should not underestimate the importance of preventing heat loss, facilitating the adaptation of the infant to the outside world, and the mother-infant interaction.

Skin-to-skin contact (SSC) is a well-known caregiving method to facilitate breastfeeding[1-5] and maintain newborn temperature.[5-11] SSC may be a method to promote the neurobehavioral self-regulatory responses of the infant after delivery.[12] According to studies investigating the effect of SSC physiologically, reduced crying, heart rate (HR), oxygen saturation (SpO_2), and temperature regulation remain stable during SSC. [5-11, 13] However, there are few studies that examine the effect of early SSC after birth on infants biochemically, particularly among full-term infants.

Early SSC is the placing of the naked baby prone on the mother’s bare chest at birth or soon afterward.[9] The American Academy of Pediatrics, in its 2005 policy statement[14] regarding breastfeeding, states that “Healthy infants should be placed and remain in direct SSC with their mothers immediately after delivery until the first feeding is accomplished.” In most hospitals, however, the infant is moved to a separate triage area for assessment temporarily after birth. Additionally, the duration of SSC is different between institutions. Futhermore, the duration of SSC is different between institutions though SSC is recommended to last for at least an hour.[15-17] The characteristics of SSC also varied In SSC intervention studies.[16] In their review article on early SSC for mothers and their healthy newborn infants, Moore et al. [18] in 2007 divided early SSC into 3 subgroups (Birth SSC, Very early SSC, and Early SSC). However at that time not enough studies were available for subgroup analysis. They also stated that in the future these groups may be analyzed separately and that studies should make explicit SSC initiation time, frequency, and duration in order to investigate a possible dose-response relationship.

Our interest is whether the difference in the initiation time of SSC or the in duration of SSC influences the stress reduction for the infant soon after birth. When the infant attempts to cope with a stressful situation, the hypothalamic-pituitary-adrenal axis is activated. Salivary cortisol levels show a close correlation with plasma cortisol levels.[19-21] Salivary cortisol level is markedly influenced by physiologic and psychologic stress.[19] In a few previous studies on full-term infants, the salivary cortisol level has been reflected as an index of distress/ comfort responses to stressors.[22-25] Salivary cortisol is known as a useful and noninvasive measure of a neonate's immediate stress response to both physical and environmental stimuli.

Finally, we used three indexes to evaluate the efficacy of SSC. HR and SpO_2 were the indexes to evaluate circulatory and respiratory adaptation, respectively. Salivary cortisol was used as a physiologic and psychological stress marker since its level was low in the comfortable condition. Moreover, to evaluate the effectiveness of SSC on infant stress postbirth, one must control the influence of gestation age. Preterm infants are more likely to have physiologic stress in utero and at birth than full-term infants. Therefore, we selected healthy full-term infants as study subjects to minimize the influences of various confounding factors.

We pursued two themes among healthy full-term infants. The first was to determine whether or not the difference in the initiation time of SSC influences the time to stability of HR and SpO_2 for 30 min after birth (STUDY I). The second was to assess whether or not the difference in the duration of SSC influences salivary cortisol levels over the first 2 hours after birth (STUDY II).

METHODS

Study Subjects

This study protocol was approved by the Ethics Review Committee of the Nagoya University School of Medicine, Nagoya, Japan. We conducted a non-experimental study of 147 consecutive newborn infants who were born spontaneously at two maternity hospitals in Aichi Prefecture, Japan, from January to October in 2009. The parents gave written informed consent to participate in this study and the use of individual information concerning pregnancy and delivery in Medical records and laboratory data when mothers were admitted to the hospital.

Figure 1 shows the recruitment of study infants in this analysis. The subjects were healthy full-term infants who were selected according to the following criteria: Maternal inclusion criteria were spontaneous vaginal delivery, singleton full-term infant, and uncomplicated pregnancy and delivery courses. Maternal exclusion criteria were dysfunctional labor, dystocia, sign of fetal distress during labor, general anesthesia during delivery, multiple birth, and cesarean section. In addition, infants had to be healthy and full-term. Infant exclusion criteria were any congenital anomaly, and obvious birth asphyxia as assessed by either 1- or 5-minute Apgar of seven or less. Furthermore, the 79 infants for whom the salivary cortisol levels were obtained at 1 min, 60 min, and 120 min were eligible for this study. Finally, STUDY I included 68 subjects from whom both HR and SpO_2 were obtained, and 79 subjects were in STUDY II.

Procedure

In both maternity hospitals, immediately after birth, infants were routinely examined by experienced midwives and obstetricians. The face, trunk, and extremities of each newborn infant were dried, and the umbilical cord was cut on the delivery bed by the midwife within the first minute of life. The subsequent procedure was different between the two hospitals. In the Birth SSC hospital, soon after the assessment of the 1-min Apgar score, the infant was placed prone skin-to-skin on the mother's abdomen. To prevent heat loss, midwives put a diaper on the infant, covered the infant's back with a prewarmed towel and blanket, and the infant's head was covered with a dry cap. After SSC was finished, the infant was placed on an infant warmer (Atom Medical, Infa Warmer V-505, Tokyo, Japan), an examination table with a radiant heater above, and then cared for according to the hospital routine including weighing and anthropometric measurements. The infant was then placed beside their mother soon after routine examination and rest or drank the mother's breast milk until 2 hours postbirth. In the Very Early SSC hospital, the infant was placed on an infant warmer (Atom Medical, Infa Warmer V-505, Tokyo, Japan) and then cared for according to the hospital routine including weighing and anthropometric measurements. After completion of the routine newborn examination and completion of the suturing of spontaneous rupture and/or episiotomies for the mother, the infant was placed prone skin-to-skin on the mother's abdomen. Prevention of heat loss was performed in the same way in both hospitals.

STUDY I

Study Plan and Statistical Analysis

The first theme was to determine whether or not the difference in the initiation time of SSC influences the time to stability of HR and SpO_2 for almost 30 min after birth. The time to stability of HR and SpO_2 were defined as the first of 3 consecutive HR readings of 120-160 beats per minute (bpm) and SpO_2 reading of 96% or more, respectively. The first of 3 consecutive SpO_2 readings of 92% or more was also evaluated.

In HR and SpO_2 analyses, study infants were divided into two groups; those who began SSC 5 min or less (*n*=32) after birth and those who did so more than 5 min (*n*=36) after birth. In the present study, the former group was defined as 'birth SSC' and the latter group as 'Very early SSC' based on the classification of early SSC by Moore et al.[18] Kaplan-Meier curves were generated for time to HR and SpO_2 stability. The difference between groups was assessed with log-rank test. Next, we used Cox proportional hazard model to relate the time of HR or SpO_2 stability to a number of explanatory variables including SSC initiation time category, umbilical artery pH, labor induction, meconium staining, birth weight, and total length of first and second-stage labor in minutes. The exponent of the parameter estimate of SSC initiation time category [EXP(parameter estimate)] indicates the efficacy for the Birth SSC group compared with the reference category (Very early SSC group). Additionally, mean HRs were calculated at 1-min intervals from 3 to 30 min after birth.

Data were analyzed using the SPSS statistical package for Windows Version 17.0 (SPSS, Chicago, USA). Differences were considered significant when $P<0.05$ for the two tails.

Heart Rate and Oxygen Saturation

Pulse oximetry measurements were carried out using a NELLCOR Oxisensor N-25 and a NELLCOR™ OxiMax™ N-600™ Pulse Oximeter (Covidien-Nellcor and Puritan Bennett, Boulder, USA). We placed a pulse oximetry probe over the newborn's right sole as soon as possible after birth. The pulse oximeter recorded arterial SpO_2 and HR every 10 seconds for 120 min after birth.

STUDY II

Study Plan and Statistical Analysis

The second theme was to assess whether or not the difference in the duration of SSC influences salivary cortisol levels over the first 2 hours after birth.

SSC is recommended to last for at least an hour in some endorsements.[15-17, 26] Therefore, we divided the subjects into two groups; those who underwent SSC for 60 min or less (*n*=18) and those who did so for more than 60 min (*n*=61). As we measured salivary cortisol levels a total of 3 times for 120 min after birth, the general linear model (GLM) in SPSS that is used in repeated measures designs (two-way repeated measures ANOVA) was used to compare the effect on salivary cortisol levels between the two groups and calculate each mean cortisol level 3 times by 2 groups while adjusting for the initiation time of SSC, umbilical artery pH, labor induction, meconium staining, birth weight, and total length of first and second-stage labor in minutes.

Salivary Cortisol

Saliva specimens were collected a total of 3 times; at 1 min after checking 1-min Apgar score, and 60 min and 120 min after birth, respectively. Saliva was collected from infants using the Sorbette (Salimetrics, LLC, Pennsylvania, USA) without any stimulation. All infant's mouths were checked gently for any contaminating components before saliva collection. After collection, the saliva was stored at - 83°C. Salivary cortisol concentration was determined using a commercial high sensitivity EIA kit (Salimetrics, LLC, Pennsylvania, USA).

RESULTS

STUDY I

Study Group Comparability in Analysis of SSC Initiation Time after Birth

The characteristics of study infants and their mothers according to the SSC initiation time after birth are shown in Table 1. The mean (standard deviation: SD) times until SSC started in birth and very early SSC groups were 1.60 (1.10) and 26.3 (4.97) min, respectively. All SSCs for the study infants began less than approximately 30 min postbirth [mean (SD) 14.7 (13.0) min]. The duration of SSC was significantly shorter in the birth SSC group than the very early SSC group ($P<0.001$), but the mean duration time of SSC was over 60 min even in the birth SSC group. Both body temperatures at 60 min and 120 min were significantly lower in the birth SSC group than the very early SSC group ($P<0.001$, $P<0.05$, respectively). However, all measured body temperatures kept within the normal range. The only significant difference related to mothers is the mode of delivery. In addition, no tachycardia, bradycardia or dyspnea was observed during examination.

Association of SSC Initiation Time with HR Stability

Table 2 demonstrates HR changes for 60 min after birth. Sixty-five of 68 subjects had HR stability within 30 min postbirth. HRs showed a lower tendency among the birth SSC group than the very early SSC group. There were significant differences at 5, 10, 15, and 20 min ($P<0.05$, $P<0.01$, $P<0.01$, $P<0.05$, respectively). As shown in Figure 2, Kaplan–Meier analysis showed a significant difference in the cumulative probability of HR stability of 120-160 bpm between the subgroups ($P=0.001$). In Cox model analysis, the birth SSC group showed 2.52 times the efficacy of HR stability compared with the very early SSC group [EXP(0.925)=2.52 (95% CI: 1.41-4.51), P=0.002].

Association of SSC Initiation Time with SpO_2 Stability

Figure 3 shows the cumulative probability of the SpO_2 stability of 92% or more (Fig 3A), and 96% or more (Fig 3B), using Kaplan-Meier analysis. Sixty-seven of 68 subjects had SpO_2 stability of both 92% and 96% within 30 min postbirth. No significant difference was found in cumulative probabilities of either 92% or more nor 96% or more between the subgroups (P=0.69 and 0.39, respectively). Cox model analysis also showed no significant associations between initiation time of SSC and SpO_2 stability [SpO_2 stability of 92% or more as dependent variable; EXP (parameter estimate)=EXP(0.062)=1.06 (95% confidence interval: 0.609-1.86), P=0.872 and SpO_2 stability of 96% or more as dependent variable; EXP(0.111)=1.12 (95% CI: 0.652-1.92), P=0.652].

STUDY II

Study Group Comparability in Analysis of SSC Duration

The characteristics of study infants and their mothers according to the duration of SSC are summarized in Table 3. There were no significant differences in infant-related variables except for the time until SSC starts after birth, which was significantly later among the infants who underwent SSC for more than 60 min than those who did so for 60 min or less (P<0.05). The variables related to mothers were not significantly different between subgroups.

Change of Salivary Cortisol Levels

Crude means (standard error: SE) and adjusted means of salivary cortisol were shown in Table 4. The cortisol level for 1 min was not significantly different between the subgroups (*P*=0.824). Salivary cortisol levels showed decreasing trends in both groups and no significant difference between the two groups (*P*=0.429). After multivariate adjustment, there was no significant difference in salivary cortisol levels within two hours after birth between the two groups (*P*=0.179) (Table 4, Fig 4A). We also compared the effects of the two SSC groups on the salivary cortisol levels at 60 min and 120 min after multivariate adjustment including salivary cortisol level at 1 min (Table 4, Fig 4B). Salivary cortisol levels decreased about 2 μg/dl in both groups. Salivary cortisol levels were significant lower between 60 and 120 min after birth in the SSC group continuing for more than 60 min compared with the SSC group for 60 min or less (P=0.046), under the condition that SSC began by 30 min at the latest in this study.

No infants had medical problems requiring their withdrawal from the study while they underwent SSC and some examinations.

DISCUSSION

In our study of healthy full-term infants, we found that birth SSC led to the stability of HR earlier than very early SSC. In addition, SSC continuing for more than 60 min significantly decreased salivary cortisol levels as a marker for stress between 60 min and 120 min postbirth compared with SSC for only 60 min or less. The present study provided further evidences of early SSC for full-term infants.

As for the basic efficacies of SSC, some previous studies showed strong evidences of increasing body temperature, keeping the normal range, [1, 6-8] and reducing the amount of crying or crying time.[6,7,12] In a few studies examining the efficacy of SSC physiologically during the early period after birth, HR and respiratory rate have been used as study outcomes.[1, 6-8,13] Christensson et al.[7] reported that SSC full-term infants had significantly higher skin temperature but also cried significantly less than control infants who were separated from their mothers. SSC infants also had a lower mean HR and respiratory rate at 90 min postbirth. An increase in body temperature and reducing crying may lead to a decrease in HR and respiratory rate. Interestingly, we found further evidence that HR became stable significantly earlier in full-term infants with birth SCC than those who underwent very early SSC. However, both rectal and axillar temperatures were lower in the birth SSC group within the normal range. Besides increasing temperature, many other beneficial effects may be associated with HR stability immediately after birth.

So we paid due attention to salivary cortisol. Many investigators have pointed out the advantages of using salivary cortisol concentration as a stress marker in adults and children.[19-21, 23-30] There is good experimental evidence that salivary cortisol levels reflect the free, biologically active plasma fraction.[19-21] In addition, the sampling procedure is performed easily, painlessly, and noninvasively. Therefore, salivary cortisol is a suitable marker to assess the degree of stress in infants. However, few studies have shown the salivary cortisol concentration immediately postbirth. Klug et al.[23] reported that the salivary cortisol levels obtained from full-term infants between 18 and 24 hours postbirth ranged 0.22 to 4.95 μg/dl. Our finding that the salivary cortisol ranges at 60 min and at 120 min were 0.21 to 9.91 μg/dl and 0.25 to 9.65 μg/dl, respectively, were reasonable, since the salivary cortisol level is thought to decrease gradually after birth. To the best of our knowledge, only a few studies have reported the effects of SSC on salivary cortisol in preterm infants. Gitau et al.[27] compared salivary cortisol levels between 20 min before and after a 20-min intervention of SSC among 14 infants (mean gestational week: 29 weeks) who were clinically stable and no longer required intensive care support. They found that a 20-min SSC period caused a consistent and significant reduction in salivary cortisol levels. On the other hand, Mörelius et al.[28] observed the changes of salivary cortisol levels before, during, and after at least 1-hour SSC among 17 infants (25-33 weeks) requiring intensive care support. They found that their salivary cortisol either increased or decreased, but showed no significant change. We found that salivary cortisol levels immediately after birth were significantly lower in the infants with SSC of 60 min or less than those with more than 60 min. Considering the results of the two previous studies, the efficacy of SSC in our study may be more pronounced because our study subjects were healthy and full-term, suggesting the natural situation after birth and normal stress response based on the hypothalamic-pituitary-adrenal axis.

The initiation and duration times of SSC have differed even among many randomized control studies on SSC. Most of the studies also compared the infants with SSC with control infants who were separated from their mothers. To our knowledge, only a few randomized control studies have compared behavioral and physiological change of infants or mothers between dyads with different initiation times and/or duration of SSC. Hales et al.[30] examined the effects of different initiation times of SSC among 3 groups consisting of 60 healthy full-term infants: 1) Early contact group: 45 min of SSC immediately postbirth. 2) Delayed contact group: 45 min of SSC 12 hours postbirth. 3) Control group: glance at babies immediately after birth and the nurse brought the wrapped infants to their mothers' beds approximately 12 hours later. The early contact group showed significantly more affectionate behavior than the delayed contact group or control group. Unfortunately, study outcomes included no infant factor. In the study by Christensson et al.[6], 44 healthy full-term infants were observed during the first 90 min after birth in terms of duration of crying when infants were cared with: 1) 76-85 min of SSC with mother. 2) In a cot next to the mother's bed for the first 45 min of 90 min observation period, and then SSC with the mother for 45 min. 3) In a cot for 76-85 min. The cumulative amount of crying during the first 90 min after birth was significantly less in the SSC group than in the mixed cot/SSC group. The findings of these two previous studies appeared likely to corroborate ours.

It is difficult to explain the unitary mechanism underlying the various efficacies of SSC. SSC is suggested to facilitate the first phases of neurobehavioral self-regulatory responses of the infants who persist in more labile imbalance and fluctuation of autonomic, motor, state, and attention/interaction subsystem. Our findings are supposed to be due to the postbirth development of self-regulation of each subsystem by SSC. Self-regulation is considered as infant adaptation to various internal and external stimuli and to unstable situations, and is in great demand immediately after delivery. Early SSC may be a 'natural way' of antagonizing the 'stress of being bone' as in the other mammals. Therefore, 'When should SSC start after birth?' and 'How long should SSC be undergone?' are the important issues in establishing effective SSC. Additionally, it is also necessary to establish the most effective dose of SSC and the safety of the SSC.

There are both strengths and limitations in our study. One strength is the larger sample size compared to other earlier studies evaluating the physiological and biochemical effects of SSC. Moreover, since data on many kinds of exposure during pregnancy and delivery known or suspected to modify infant's HR, SpO_2, and salivary cortisol were collected, we could elucidate the independent effects of SSC by multivariate adjustment. There is, to our knowledge, no previous study evaluating the effect of SSC after adjusting the potential confounding factors. The first limitation was that our study was a non-experimental study. Thus, subjects must be randomized to confirm our results, though the characteristics of SSC groups were almost comparable and multivariate adjustment was performed. The second limitation was that salivary cortisol was obtained only 3 times for 2 hours postbirth. Time of separation and examination was not determined for each infant. The pattern of the cortisol following separation and the subsequent examination of the infant should be studied further. The third limitation arises from the fact that healthy and full-term infants were the subjects of our study. Hence, our results may not apply to preterm infants and infants with any complication.

CONCLUSIONS

We found physiological and biochemical evidences that earlier SCC beginning within 5 min postbirth and longer SSC continuing for more than 60 min until 2 hours postbirth are both beneficial for the reduction of stress during the early period after birth. Moreover, no subjects had medical problems in the course of this study. Our results thus further underscore the importance of early SSC, particularly in healthy full-term infants.

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CONFLICT OF INTEREST STATEMENT

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REFERENCES

1. Bystrova K, Ivanova V, Edhborg M, et al. Early contact versus separation: effects on mother-infant interaction one year later. *Birth* 2009;36:97-109.
2. Moore ER, Anderson GC. Randomized controlled trial of very early mother-infant skin-to-skin contact and breastfeeding status. *J Midwifery Womens Health* 2007;52:16-125.
3. Carfoot S, Williamson P, Dickson R. A randomised controlled trial in the north of England examining the effects of skin-to-skin care on breast feeding. *Midwifery* 2005; 21:71-79.
4. Mikiel-Kostyra K, Mazur J, Bołtruszko I. Effect of early skin-to-skin contact after delivery on duration of breastfeeding: a prospective cohort study. *Acta Paediatr* 2002;91:1301-1306.
5. Ransjö-Arvidson AB, Matthiesen AS, Lilja G, et al. Maternal analgesia during labor disturbs newborn behavior: effects on breastfeeding, temperature, and crying. *Birth* 2001;28: 5-12.
6. Christensson K, Cabrera T, Christensson E, et al. Separation distress call in the human neonate in the absence of maternal body contact. *Acta Paediatr* 1995;84:468-473.
7. Christensson K, Siles C, Moreno L, et al. Temperature, metabolic adaptation and crying in healthy full-term newborns cared for skin-to-skin or in a cot. *Acta Paediatr* 1992;81:488-493.

8. Marín Gabriel M, Llana Martín I, López Escobar A, et al. Randomized controlled trial of early skin-to-skin contact: effects on the mother and the newborn. *Acta Paediatr* 2009;1-5.
9. Bergström A, Okong P, Ransjö-Arvidson AB. Immediate maternal thermal response to skin-to-skin care of newborn. *Acta Paediatr* 2007; 96:655-668.
10. Walters MW, Boggs KM, Ludington-Hoe S, et al. Kangaroo care at birth for full term infants: a pilot study. *MCN Am J Matern Child Nurs* 2007;32:375-381.
11. Bystrova K, Widström AM, Matthiesen AS, et al. Skin-to-skin contact may reduce negative consequences of "the stress of being born": a study on temperature in newborn infants, subjected to different ward routines in St. Petersburg. *Acta Paediatr* 2003; 92:320-326.
12. Ferber SG, Makhoul IR. The effect of skin-to-skin contact (kangaroo care) shortly after birth on the neurobehavioral responses of the term newborn: a randomized, controlled trial. *Pediatrics* 2004;113:858-865.
13. Michelsson K, Christensson K, Rothgänger H, et al. Crying in separated and non-separated newborns: sound spectrographic analysis. *Acta Paediatr* 1996;85:471-475.
14. American Academy of Pediatrics Section on Breastfeeding. Breastfeeding and the use of human milk. *Pediatrics* 2005;115:496-506.
15. DiGirolamo AM, Grummer-Strawn LM, Fein S. Maternity care practices: implications for breastfeeding. *Birth*.2001;28:94-100.
16. World Health Organization, Dept. of Child Health and Development. Evidence for the ten steps to successful breastfeeding. *Geneva*, 1998.
17. Baby-Friendly USA. The ten steps to successful breastfeeding final report. Massachusetts.

18. Moore ER, Anderson GC. Bergman N. Early skin-to-skin contact for mothers and their healthy newborn infants. *Cochrane Database of Systematic Reviews* 2007;Issue 3.

19. Francis SJ, Walker RF, Riad-Fahmy D, et al. Assessment of adrenocortical activity in term newborn infants using salivary cortisol determinations. *J Pediatr* 1987;111:129-133.

20. Gunnar MR, Hertsgaard L, Larson M, et al. Cortisol and behavioral responses to repeated stressors in the human newborn. *Dev Psychobiol* 1991;24:487-505.

21. Riad-Fahmy D, Read GF, Walker RF, Griffiths K. Steroids in saliva for assessing endocrine function. *Endocr Rev* 1982;3:367-395.

22. Chang HP, Anderson GC, Wood CE. Feasible and valid saliva collection for cortisol in transitional newborn infants. *Nurs Res*. 1995;44:117-9.

23. Klug I, Dressendörfer R, Strasburger C, et al. Cortisol and 17-hydroxyprogesterone levels in saliva of healthy neonates: normative data and relation to body mass index, arterial cord blood ph and time of sampling after birth. *Biol Neonate* 2000;78:22-26.

24. Nelson N, Arbring K, Theodorsson E. Neonatal salivary cortisol in response to heelstick: method modifications enable analysis of low concentrations and small sample volumes. *Scand J Clin Lab Invest* 2001; 61:287-291.

25. White-Traut RC, Schwertz D, McFarlin B, et al. Salivary cortisol and behavioral state responses of healthy newborn infants to tactile-only and multisensory interventions. *J Obstet Gynecol Neonatal Nurs* 2009;38:22-34.

26. World Health Organization, Dept. of Reproductive Health and Research. Kangaroo mother care: a practical guide. Geneva, *WHO*: 2003.

27. Gitau R, Modi N, Gianakoulopoulos X, et al. Acute effects of maternal skin-to-skin contact and massage on saliva cortisol in preterm babies. *J Reprod Infant Psychol* 2002; 20: 83-88.

28. Mörelius E, Theodorsson E, Nelson N. Salivary cortisol and mood and pain profiles during skin-to-skin care for an unselected group of mothers and infants in neonatal intensive care. *Pediatrics* 2005;116:1105-1113.

29. Bettendorf M, Albers N, Bauer J, et al. Longitudinal evaluation of salivary cortisol levels in full-term and preterm neonates. *Horm Res* 1998;50:303-308.

30. Hales DJ, Lozoff B, Sosa R, et al. Defining the limits of the maternal sensitive period. *Dev Med Child Neurol* 1977;19:454-461.

Fig.1

Flow of the recruitment of study infants

Fig.2

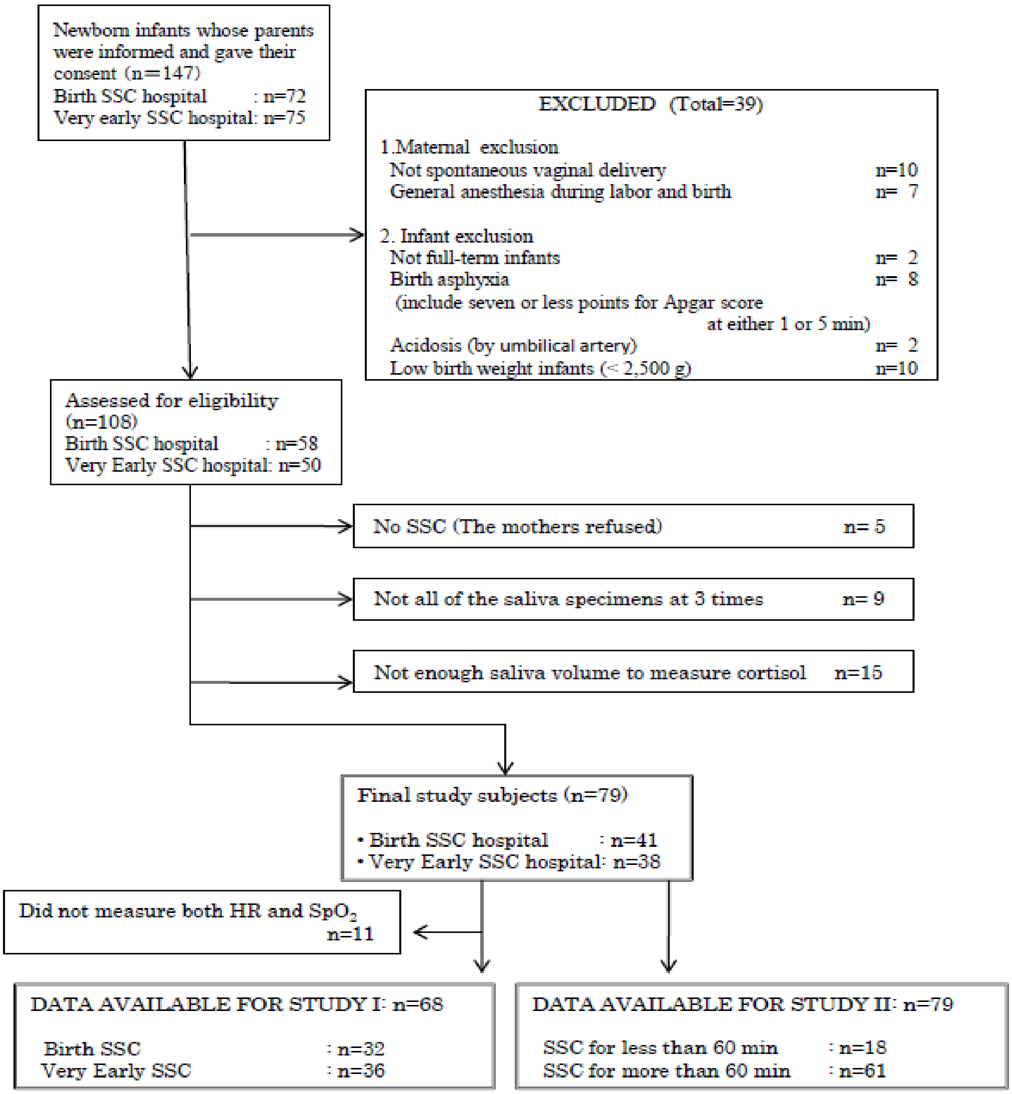
Cumulative probability of HR stability of 120-160 bpm by the initiation time of SSC after birth using Kaplan-Meier analysis. log-rank = 10.6, *P*=0.006.

Fig.3

Cumulative probability of SpO2 stability of more than 92% (A) and more than 96% (B) by the initiation time of SSC after birth using Kaplan-Meier analysis. (A): log-rank = 0.168, *P*=0.68, (B): log-rank = 0.385, *P*=0.56.

Fig.4

Mean values of salivary cortisol levels at 1min, 60 min, and 120 min by the duration of SSC after multivariate adjustment (A). Mean values of salivary cortisol levels at 60 min and 120 min by the duration of SSC after further adjustment for salivary cortisol level at 1 min after birth. (B).



Newborn infants whose parents were informed and gave their consent (n=147)
Birth SSC hospital : n=72
Very early SSC hospital: n=75
EXCLUDED (Total=39)
1.Maternal exclusion
Not spontaneous vaginal delivery n=10
General anesthesia during labor and birth n= 7
2. Infant exclusion
Not full-term infants n= 2
Birth asphyxia n= 8
(include seven or less points for Apgar score at either 1 or 5 min)
Acidosis (by umbilical artery) n= 2
Low birth weight infants (< 2,500 g) n=10
Assessed for eligibility (n=108)
Birth SSC hospital : n=58
Very Early SSC hospital: n=50
No SSC (The mothers refused) n= 5
Not all of the saliva specimens at 3 times n= 9
Not enough saliva volume to measure cortisol n=15
Final study subjects (n=79)
• Birth SSC hospital : n=41
• Very Early SSC hospital: n=38
Did not measure both HR and SpO2 n=11
DATA AVAILABLE FOR STUDY I: n=68
Birth SSC : n=32
Very Early SSC : n=36
DATA AVAILABLE FOR STUDY II: n=79
SSC for less than 60 min : n=18
SSC for more than 60 min : n=61

Fig. 1

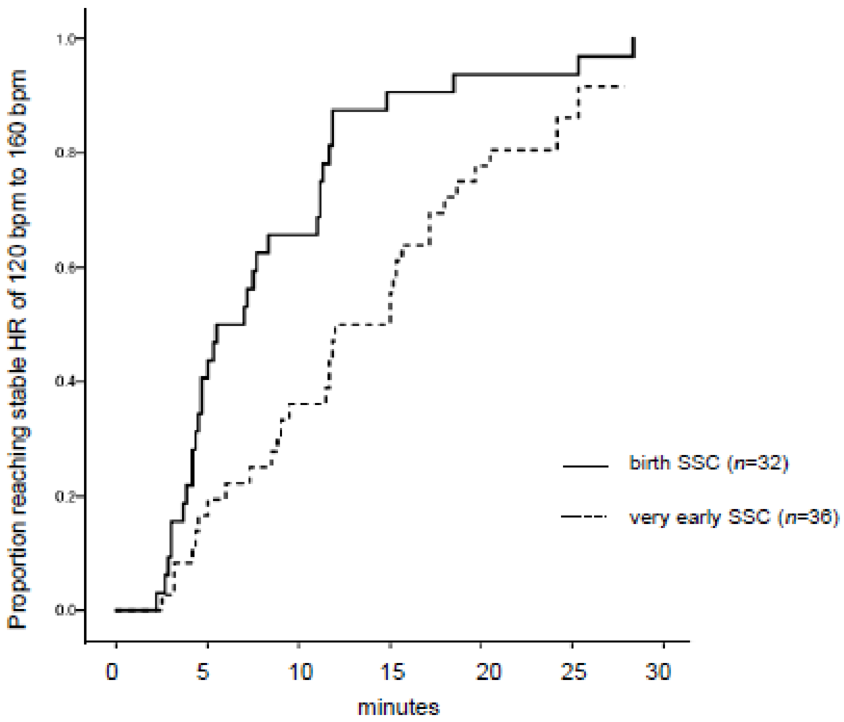
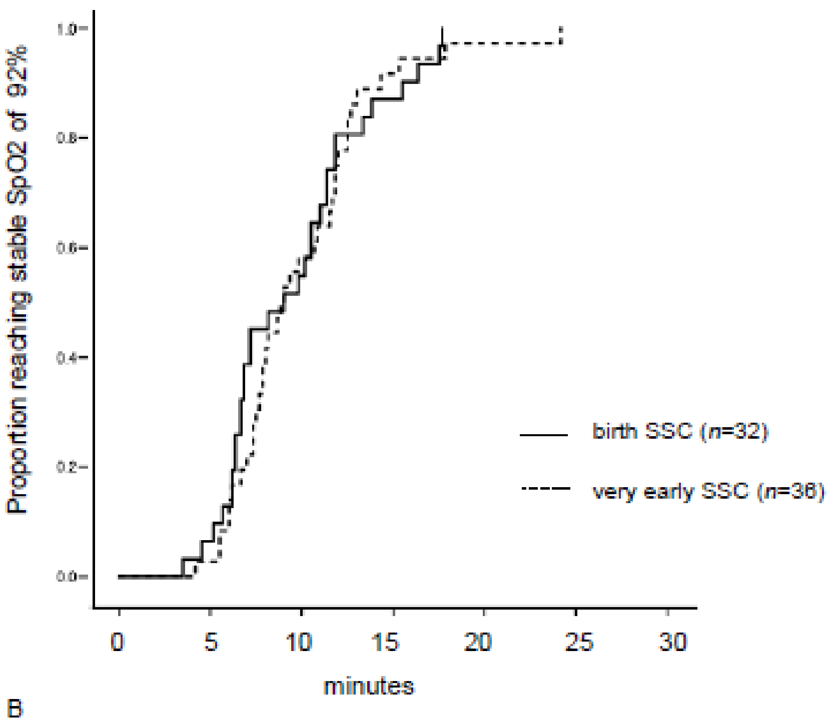

Proportion reaching stable HR of 120 bpm to 160 bpm
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
minutes
birth SSC (n=32)
very early SSC (n=36)

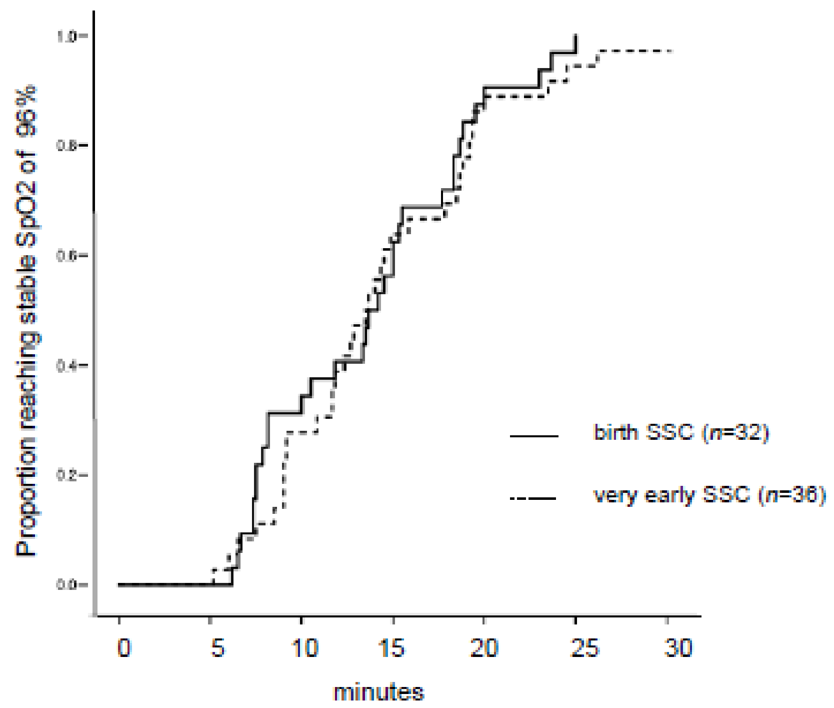
Fig.2

A



Proportion reaching stable SpO2 of 92%
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
minutes
birth SSC (n=32)
very early SSC (n=36)

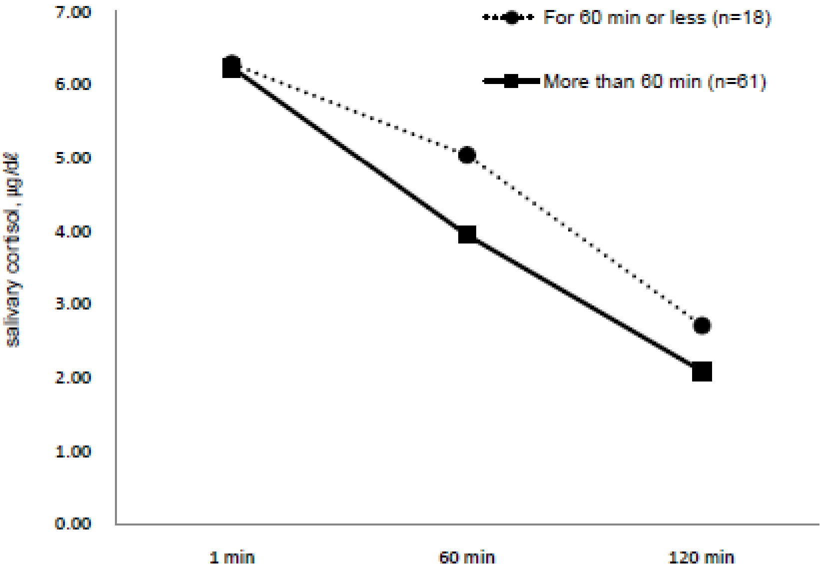
B



Proportion reaching stable SpO2 of 96%
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
30
minutes
birth SSC (n=32)
very early SSC (n=36)

Fig.3

A


7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
salivary cortisol, µg/dℓ
1 min
60 min
120 min
For 60 min or less (n=18)
More than 60 min (n=61)

B

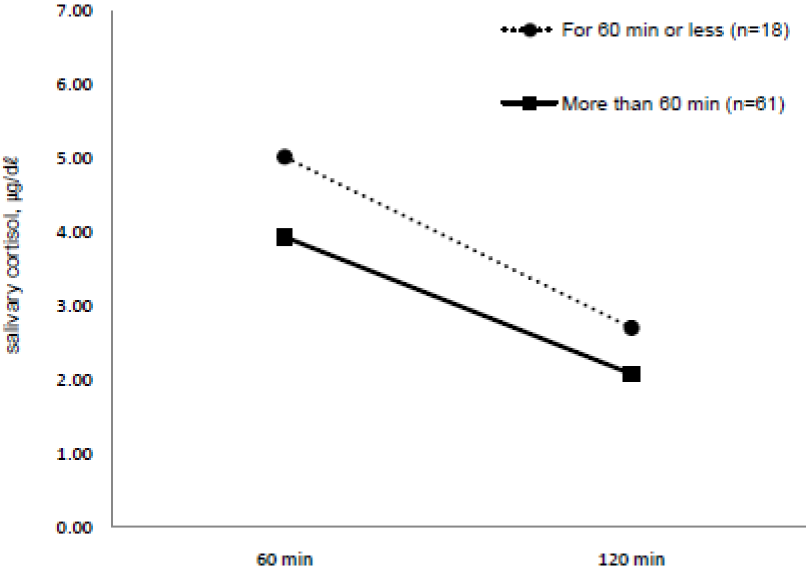

7.00
6.00
5.00
4.00
3.00
2.00
1.00
0.00
salivary cortisol, µg/dℓ
60 min
120 min
For 60 min or less (n=18)
More than 60 min (n=61)

Fig.4

TABLE 1 Characteristics of Study Subjects According to SSC Initiation Time after Birth

Variable	Birth SSC (n=32) Mean ± SD	Very Early SSC (n=36) Mean ± SD	*P value*
Infants			
Birth weight, g	3083.6 ± 326.3	3056.4 ± 293.8	0.72
Gestational age at birth, wk	39.9 ± 1.0	39.7 ± 0.8	0.39
Apgar score at 1 min	9.1 ± 0.5	9.0 ± 0.3	0.13
Apgar score at 5 min	9.5 ± 0.5	9.5 ± 0.5	0.82
Umbilical cord pH at birth	7.31 ± 0.07	7.31 ± 0.06	0.92
Boys / Girls	12/20	15/21	0.81
Initiation time of SSC, min	1.6 ± 1.1	26.3 ± 5.0	<0.01
Duration of SSC, min	60.3 ± 12.5	89.6 ± 14.3	<0.01
Rectal temperature at 60 min, ℃	36.6 ± 0.3	37.1 ± 0.3	<0.01
Axillar temperature at 120 min, ℃	36.9 ± 0.4	37.2 ± 0.3	<0.05
Maternal			
Maternal age, yr	28.1 ± 4.9	30.5 ± 4.9	0.05
Number of previous live birth	0.9 ± 0.8	0.7 ± 0.7	0.33
Number of previous abortion or stillbirth	1.1 ± 1.1	1.1 ± 1.4	0.89
Length of first-stage labor, minutes	444.8 ± 366.9	438.2 ± 435.7	0.95
Length of second-stage labor, minutes	44.5 ± 51.5	27.2 ± 22.5	0.09
Total length of labor, minutes	495.0 ± 382.2	470.6 ± 444.9	0.81
Meconium staining of amniotic fluid (%)	3(9.4%)	7(19.4%)	0.31
Mode of delivery			<0.01
Spontaneous vaginal delivery (%)	20 (62.5%)	35 (97.2%)	
Labor Induction (%)	12 (37.5%)	1 (2.8%)	

TABLE 2 Heart Rate Values According to SSC Initiation Time after Birth

	HR (bpm) Birth SSC (*n*=32)	HR (bpm) Very early SSC (*n*=36)	*P value*
1 min			
2 min			
3 min	156.8 ± 11.6	176.5 ± 33.7	0.13
4 min	161.1 ± 18.7	169.7 ± 16.0	0.11
5 min	157.0 ± 21.8	171.1 ± 20.6	<0.01
6 min	159.7 ± 14.7	172.2 ± 19.3	<0.01
7 min	154.9 ± 22.7	173.7 ± 19.7	<0.01
8 min	156.3 ± 14.7	175.8 ± 18.3	<0.01
9 min	154.7 ± 14.5	172.9 ± 16.7	<0.01
10 min	153.8 ± 13.4	171.6 ± 17.0	<0.01
11 min	152.4 ± 12.7	169.4 ± 17.2	<0.01
12 min	151.0 ± 13.1	167.9 ± 15.3	<0.01
13 min	150.8 ± 12.2	164.9 ± 15.3	<0.01
14 min	152.0 ± 11.7	165.3 ± 13.8	<0.01
15 min	151.6 ± 13.4	161.9 ± 15.1	<0.01
16 min	152.6 ± 14.0	164.6 ± 20.1	<0.01
17 min	150.7 ± 13.4	162.0 ± 14.0	<0.01
18 min	151.5 ± 11.4	158.1 ± 14.4	<0.05
19 min	150.1 ± 10.9	157.5 ± 15.2	<0.05
20 min	149.8 ± 11.5	156.7 ± 13.7	<0.05
21 min	150.3 ± 11.0	153.7 ± 11.3	0.22
22 min	150.2 ± 9.3	152.9 ± 12.9	0.33
23 min	151.1 ± 11.5	153.4 ± 12.2	0.42
24 min	149.1 ± 9.9	152.2 ± 13.3	0.28
25 min	150.3 ± 10.8	151.2 ± 12.9	0.76
26 min	149.0 ± 11.9	151.1 ± 11.7	0.46
27 min	148.5 ± 11.0	152.2 ± 12.6	0.21
28 min	148.7 ± 11.1	151.2 ± 13.6	0.42
29 min	148.0 ± 11.0	151.8 ± 13.2	0.22
30 min	149.3 ± 12.4	150.6 ± 13.6	0.68

Data are mean±SD

TABLE 3 Characteristics of Study Subjects According to SSC Duration

Variable	SSC was 60 min or less (*n* =18)			SSC was more than 60 min (*n* =61)			*P value*
	Mean	±	SD	Mean	±	SD	
Infants							
Birth weight, g	3152.1	±	315.3	3056.8	±	291.4	0.23
Gestational age at birth, wk	39.7	±	1.0	39.8	±	1.0	0.78
Apgar score at 1 min	9.1	±	0.4	9.0	±	0.4	0.71
Apgar score at 5 min	9.4	±	0.5	9.5	±	0.5	0.64
Umbilical cord pH at birth	7.31	±	0.06	7.31	±	0.06	1.00
Boys / Girls	9/9			23/38			0.42
Initiation time of SSC, min	7.5	±	12.2	15.2	±	12.5	<0.05
Duration of SSC, min	51.1	±	13.5	81.0	±	14.9	<0.01
Rectal temperature at 60 min, ℃	36.8	±	0.4	36.9	±	0.4	0.62
Axillar temperature at 120 min, ℃	36.9	±	0.4	37.1	±	0.4	0.05
Maternal							
Maternal age, yr	29.1	±	5.6	29.5	±	5.1	0.79
Number of previous live birth	0.8	±	0.7	0.8	±	0.8	0.89
Number of previous abortion or stillbirth	1.2	±	1.2	1.1	±	1.2	0.79
Length of first-stage labor, minutes	463.7	±	394.8	442.7	±	390.8	0.84
Length of second-stage labor, minutes	37.4	±	33.5	35.0	±	39.6	0.82
Total length of labor, minutes	506.4	±	401.5	483.1	±	404.1	0.83
Meconium staining of amniotic fluid (%)	1 (5.6 %)			10 (16.4 %)			0.44
Mode of delivery							0.29
Spontaneous vaginal delivery (%)	13 (72.2 %)			51 (83.6 %)			
Labor Induction (%)	5 (27.8 %)			10 (16.4 %)			