Effects of three methods of breast milk expression on breastfeeding initiation, breast milk extraction and proportion of exclusive breastfeeding—an open label, randomized controlled trial

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Research

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Abstract

Background Direct breastfeeding has multiple health benefits. However, in certain circumstances direct breastfeeding is not possible immediately after delivery, yet provision of infants with their mother's milk is important. There is insufficient evidence regarding an effective method of breast milk expression in the absence of an infant's suction. Therefore, we undertook a trial to investigate the effects of different methods of breast milk expression on breastfeeding initiation, efficacy of breast milk extraction, and on the rate of exclusive breastfeeding at 6 months.

Methods The participants of mother-infant dyads separated immediately after birth for at least 6 hrs were recruited and randomly assigned (1:1:1) into three groups: (1) hand expression of breast milk; (2) sequential and (3) simultaneous electrical breast pumping. The two primary outcome measures were the time required for initiation of breastfeeding and the milk volume expressed in a 10-minute session (direct breastfeeding in hand expression group) at 3 days and at 6 weeks; a secondary outcome was the proportion of exclusive breastfeeding at 4 and 6 months. The data were analysed according to intention-to-treat.

Results Between 2018 and 2019, we recruited 226 participants, of whom 154 were randomized. The median time (in hours) of breastfeeding initiation of the sequential (46.5, 95% CI 36.1-50.5) and simultaneous (45.6, 95% CI 34.2-53.0) breast pumping groups did not differ from those of hand expression group (46.7, 95% CI 40.8-50.0) ($p=1.000$). At 3 days the breast milk volume (10 min per breast) through simultaneous pumping (13.1 ± 10.9 ml), but not sequential pumping (16.7 ± 11.6 ml) ($p=0.560$), was significantly less than hand expression (23.8 ± 26.2 ml through direct sucking) ($p=0.007$). At 6 weeks the breast milk volume through sequential pumping (64.7 ± 51.0 ml), but not simultaneous pumping (71.6 ± 50.8 ml) ($p=0.670$), was significantly less than hand expression (89.8 ± 67.3 ml through direct sucking) ($p=0.035$). The breast milk volume obtained through sequential breast pumping was 37.9 ml less than that obtained by those of simultaneous pumping ($p<0.001$). The rate of exclusive breastfeeding at 4 months was 21.0%, and at 6 months 10.6%, and did not differ between the three methods of breast milk expression. **Conclusions** Hand expression, sequential breast pumping, or simultaneous breast pumping in absence of immediate infant suction after birth did not show differences on the time required to initiate breastfeeding, or on the rate of exclusive breastfeeding at 4 and 6 months.

Trial registration This trial was registered with www.chictr.org.cn (ChiCTR1800018193) on 4 September 2018.

Background

Breastfeeding is considered unequivocally to provide the optimal nutrition for infants.^{1,2} Indeed, the World Health Organization (WHO) recommends exclusive breastfeeding for at least the first six months of life and that breastfeeding is continued with appropriate introduced supplement food for “up to two years and beyond”.³

There are a number of circumstances in which initiating breastfeeding soon after birth (<1 hr) and sustaining exclusive breastfeeding are not possible. First, premature infants have difficulties in latching-on, sucking and digestion,^{4,5} yet provision to these infants with their own mothers' milk is important². Compared with full-term mothers, mothers of preterm infants find it more difficult to establish and sustain lactation;⁶ it has been reported that only about 50% of them are able to express sufficient milk for their infants.⁷ Breast pumping within the first hour after delivery in mothers of premature babies, shortens the time of lactogenesis.⁸⁻¹⁰ Second, mothers who deliver by cesarean section are usually prevented from putting their infants to the breast in the first hour after birth, and hence have a delay in lactation initiation and reduced lactation duration.¹¹⁻¹⁹ The cesarean delivery rates increased from 28.8% in 2008 to 34.9% in 2014 in China,²⁰ Third, China has a high level of female participation in the workforce and a short period (14 weeks) of paid maternal leave,²¹ which may be a barrier to direct breastfeeding. It has been reported that mothers with established breastfeeding believe that any excessive breast milk after direct breastfeeding should be squeezed out and that breast milk should be expressed regularly even in the absence of the infant's sucking, in order to maintain the breast milk production. As a result, manual or pump-aided breast expression, has become a common practice in nursing mother.^{5,13,22-24}

In a survey of infant feeding practices in the US in the period 2005-2007, 85% of women had expressed breast milk in the first 4 months since their babies' birth²⁵. Apart from scenarios that necessitate expression of breast milk, there is evidence that many women with full-term, healthy infants also express breast milk regularly. Among Australian women with healthy term infants 60% had a breast pump within two days postpartum and 40% of them expressed several times a day in the following two weeks.²⁶ Among Chinese women with healthy term infants 64% used a breast pump and 22% expressed exclusively at 6 weeks postpartum.²⁷ The high frequency of breast milk expression has even influenced the definition of exclusive breastfeeding by including both at the breast and exclusively pumped milk, though its potential consequence is unknown.^{28,29} On the other hand, bottle-feeding the full-term, healthy infants with expressed milk (exclusively pumped in this case) did not contribute to the rate and duration of exclusive breastfeeding.^{9,27,30,31} Breast pumping should not be used in full-term, healthy birth as stated in the fourth step of the revised "Ten steps to successful breastfeeding" guidance that "*Facilitate immediate and uninterrupted skin-to-skin contact and support mothers to initiate breastfeeding as soon as possible after birth*" [<https://www.who.int/nutrition/bfhi/ten-steps/en/>]. With regard to methods of breast expression, a systematic review concluded that hand expression may be as effective as electric pumping but there was considerable diversity in the interventions used and the trials were small, limiting assessment of effectiveness. Further bias may have arisen because of commercial involvement in about half of the included studies.³² Thus, the effectiveness of different methods of breast pumping remains unclear.

We therefore undertook a randomized controlled trial of the effect of alternative methods of breast pumping on time required to initiate lactation, volume of milk production and rate of direct breastfeeding in otherwise healthy mother-infant pairs in which the neonates had been separated from their mothers

immediately after birth for at least 6 hours to undergo medical observation or examination. Three typical methods in breast milk expressing were included in this trial, namely hand expression (different from vacuum sucking, usually positive pressure without any extra gadget), sequential and simultaneous suction (electronic pump).

Methods

Aim

To investigate the effects of different methods of breast milk expression on breastfeeding initiation, efficacy of breast milk extraction, and as a consequence, on the rate of exclusive breastfeeding at 6 months.

Design and setting of the study

In this open-label, randomized controlled trial, the participants were recruited at Xinhua Hospital affiliated to Shanghai Jiaotong University, certified as a Baby Friendly Hospital. This is a tertiary general hospital with a 75-bed obstetrics unit and approximately 3300-3500 deliveries annually. Being the Shanghai Critical Maternal Transfer Center, Shanghai Prenatal Diagnosis Center, and Shanghai Premature Birth Center, it is also a referral centre for high-risk pregnancies from other hospitals in Shanghai City and surrounding provinces.

Participants

The participants were recruited from April 2018 to September 2019 through posters at an Obstetrics unit and in a delivery room of the hospital. Mother-neonate dyads were potentially eligible if the mother was aged 20-40 years, had attended antenatal education course in the hospital, committed to direct breastfeeding for at least 4 months in her maternity leave and were willing to express breast milk if required. The neonates had to have been delivered at gestational age ≥ 34 weeks and body weight ≥ 2000 grams with a 1-minute Apgar score ≥ 7 . Dyads in which the woman had a history of smoking or regular alcohol drinking, or contraindications (such as human immunodeficiency virus or other infectious diseases) to direct breastfeeding, or the infant had congenital anomalies or was otherwise unsuitable for direct breastfeeding, were excluded. Ethical approval of this trial was obtained from the Institutional Review Board of Xinhua Hospital Ethics Committee Affiliated to Shanghai Jiaotong University School of Medicine on 25th Dec. 2017 (XHEC-C-2017-108-2). All participants provided written informed consent before any trial-related procedures, first during antenatal preparation classes during 30-37 weeks of gestation, and then if the mother-infant dyads matched the eligibility criteria, either just before delivery or within 2 hours after delivery, depending on the clinical situation of the baby. From recruitment onwards, the principles of good clinical practice were followed. This trial is registered with Chinese Clinical Trial Registry (<http://www.chictr.org.cn>), code ChiCTR1800018193. The reporting of the trial is guided by the extension to the CONSORT statement for multi-arm parallel-group randomized trials.³³

Randomization and masking

Participants were randomly assigned into three groups (1:1:1) through a simple “lottery drawing” process without replacement. The information on group assignment, was pre-sealed in 155 opaque envelopes which were opened in the presence of two investigators. The three groups were defined according to the methods of breast milk expression in the absence of infant sucking, namely hand expression, sequential pumping (Avent SCF902/11 single electric breast pump, Philips Invest, China) and simultaneous pumping (Avent SCF303/01 bilateral electric breast pumps, Philips Invest, China) in the first 6 months after birth.

Hand expression means no vacuum sucking. The sequential Avent SCF902/11 single electric breast pump system provided five-gear vacuum pressure (5 to 1) labeled from -250 to -130 mmHg. The simultaneous pumping Avent SCF 303/01 system provided two mode of suction: Stimulation and Expression, both in four-gear mode. Vacuum pressure in Stimulation mode was from -150 to -80 mmHg, and from -250 to -170 mmHg in Expression mode. The suction frequency was 1.0-2.5 Hz in Stimulation mode and 0.71-1.05 Hz in Expression mode accordingly, while the single electric breast pump only provided constant vacuum pressure.

This was an open-label trial with blinded outcome assessment. Nurses collecting the data and questionnaire information, and statisticians conducting the analysis were blinded to group allocation.

Procedures

Recruitment and randomization occurred immediately (within 30 mins) after birth in the delivery/recovery room if a decision was made based that the neonates should be separated from their mothers for ≥ 6 hours. The common causes of mother and infant separation include preterm birth, neonatal asphyxia, maternal or neonatal suspicious infections (such as maternal fever before delivery, meconium-stained amniotic fluid) and complications of delivery. Physical examination and laboratory tests in pregnancy were carried out and demographic data were obtained.

All participants were trained in manual expression of breast milk during mother-baby separation according to guidelines for initiating milk supply in the absence of infant suction.³⁴ Women were asked to begin breast milk expression at 2 hours after birth and continue with an interval of 2-3 hours between subsequent sessions (each comprising 10 min of pumping per breast per session) until initiation of direct breastfeeding. After the infants were able to suck, the usage of breast pumping was restricted to remove excessive breast milk, to alleviate the fullness of breast milk, to donate breast milk, or to discard breast milk likely to be contaminated with medications. The number of sessions of breast pumping per day was expected to decrease gradually as lactation became established in healthy mother-infant dyads.

The 10-minute expression volume of breast milk per breast at 3 days and at 6 weeks postpartum were recorded, and the mother-infant dyads were followed up at 4 and 6 months after birth (Figure 1).

All women in this study stayed in the hospital for more than 48 hrs after delivery and were discharged at the 3rd day. On the 3rd day, the two breasts were sequentially or simultaneously pumped for 10 minutes per breast. This was repeated 2-3 hours later, using the same type of pumping (Figure 1).

At 6 weeks postpartum, the mothers were followed-up and asked to breastfeed directly first, and one hour later each breast was pumped for 10 minutes per breast with one of the two types of electric pump. After a clinical review, the mothers were asked to breastfeed their infants directly again, and one hour later had milk pumped with the other type of electric breast pump (crossed over trial).

The participants also joined an online trial member group through WeChat (Tencent, China), a mobile phone App that facilitates instant communication between participants and investigators. One investigator was assigned to answer questions from the trial group and provide professional advice. The information on breastfeeding at 4 and 6 months was collected through online questionnaire.

Outcomes and data collection

The two primary outcomes were (1) Time for lactation initiation: also known as time for breastfeeding initiation, defined as the time of the infant was provided successfully direct breastfeeding or with expressed breast milk between delivery and hospital discharge and (2) Volume or weight of expressed breast milk in 20 min (10 min per breast) at three days or six weeks postpartum. To assess the effects of manual breast expression, milk transfer was measured at 3 days and at 6 weeks postpartum. The infants were weighed just before and after breastfeeding to determine milk transfer to the infant in the obstetrics ward. This method had been validated and was used in lactogenesis research.^{9,35} Test weights of infants were obtained in duplicate using an electronic scale (accuracy=0.1 g). Each weight was recorded when the measurement was stable for 10 seconds. A density factor of 1.03 g/ml was used in conversion between weight and volume of breast milk.

The secondary outcomes were the rates of exclusive breastfeeding at 4 and 6 months. The mode of feeding was divided into seven categories: direct breastfeeding, direct breastfeeding plus expressed breast milk, direct breastfeeding plus expressed breast milk and formula milk powder, direct breastfeeding plus formula milk powder, merely expressed breast milk, expressed breast milk plus formula milk powder, total formula milk powder. The data on self-reported mode of feeding were collected online.

The reported adverse events during breast pumping include those reported by mothers and from device. General adverse events are those, which patients or trial participants reported other than during breast pumping or were observed by clinicians.

Sample size and Statistical analysis

According to unpublished data from a pilot comparison between two groups of lactation-established women that each applied one of the two types of breast pumps, there was a difference in breast milk

volume of around 15 ml with a standard deviation of 40 ml. To detect a difference of this magnitude, with a statistical power of 0.8 and significance level of 0.05, the sample size was estimated to be 90 participants in each group. Considering the limited number of potentially eligible participants, the target sample size was revised to 50 participants in each group, and a cross over design of breast pump types used at 6 weeks was incorporated in the trial design.

The data were analysed according to intention-to-treat (ITT). The continuous data were presented as mean $\pm$ SD and the categorical data were presented as counts and percentages. To compare baseline characteristics, two-tailed one-way ANOVA was conducted for variables with a normal distribution and for other variables the Wilcoxon signed rank (Mann-Whitney U) test. For comparisons between the three trial groups, the nonparametric Kruskal-Wallis rank sum test and the chi-square test were applied for continuous and categorical data, respectively. Tukey honest significant differences were calculated in multiple comparisons adjusted with *p* values. The paired student's *t* test was applied to compare the milk volumes between left and right breasts or between the two types of breast pump. The log-rank test was applied to compare the time required for breastfeeding initiation (event=1). Linear mixed-effect modelling (lme4 package) was used to analyze the association between the expressed milk volume and co-variables. *p*<0.05 was considered statistically significant. Statistical analyses were done using R (version 3.3.3).³⁶

Results

Study participants

Following prenatal examination 226 participants returned written informed consent. After delivery 2/3 of them (*n*=154) were randomized into the three trial groups of breast expression. Six participants withdrew between hospital discharge and review at 6 weeks. Meanwhile 2 participants stopped breastfeeding prematurely due to maternal health problems. Later, over 20% participants declined feedback at 4 months though they remained in contact. At 6 months less than half of participants in total remained in contact. More participants were lost to follow-up during the last 2 months than in previous 4 months, especially in group of sequential breast expression (Figure 1). The three groups were well balanced at baseline (Table 1).

Table 1. Baseline Characteristics

	Hand (n=51)	Sequential (n=52)	Simultaneous (n=51)	pooled (n=154)	p value
Maternal factors					
Maternal age at giving birth, yr	31.7(3.6)	31.0(3.3)	31.9(3.6)	31.5(3.5)	0.358
Gestational age at enrollment, wk	30.8(2.6)	30.7(2.3)	32.1(3.9)	31.2(3.1)	0.125
Gestational age at delivery, wk	39.0(1.0)	39.1(1.3)	38.7(0.8)	38.9(1.1)	0.070
Prepregnancy BMI, kg/m ²	21.7(3.3)	21.2(3.1)	22.6(4.0)	21.8(3.5)	0.103
Education level college or higher, %(n)	94.1(48)	90.4(47)	84.3(43)	89.6(138)	0.267
Monthly income $\geq$ 5000 RMB, %(n)	80.4(41)	82.7(43)	74.5(38)	79.2(122)	0.594
Social insurance, %(n)	90.0(45)	90.0(45)	84.0(42)	88.0(132)	0.698
Natural implant, %(n)	94.1(48)	92.3(48)	92.2(47)	92.9(143)	1.000
Nullipara, %(n)	88.2(45)	82.7(43)	74.5(38)	81.8(126)	0.208
Family support of direct breastfeeding, %(n)	41.2(21)	63.5(33)	56.0(28)	53.6(82)	0.072
Know benefit of direct breastfeeding, %(n)	41.2(21)	63.5(33)	56.0(28)	53.6(82)	0.069
Feel confident in direct breastfeeding, %(n)	39.2(20)	61.5(32)	54.0(27)	51.6(79)	0.064
Prepared formula milk before delivery, %(n)	70.6(36)	71.2(37)	72.5(37)	71.4(110)	1.000
Prepared breast pump before delivery, %(n)	39.2(20)	42.3(22)	33.3(16)	38.4(58)	0.638
Self-reported risk factors, %(n)					0.996
Age >35 yr	24.4(11)	10.4(5)	25.0(11)	19.7(27)	
Gestational diabetes	24.4(11)	14.6(7)	34.1(15)	24.1(33)	
C-section indication	2.2(1)	0(0)	4.5(2)	2.2(3)	
Other risk factors	0(0)	0(0)	2.3(1)	0.7(1)	
Delivery mode, %(n)					0.896
Vaginal delivery (including anesthesia)	45.1(23)	48.1(25)	43.1(22)	45.5(70)	
C-section (including emergency)	54.9(28)	51.9(27)	56.9(29)	54.5(84)	
Planned maternal leave, m	4.4(1.4)	5.4(2.8)	5.0(2.7)	5.0(2.4)	0.145
Times of breast expression in first day postpartum	2.5(2.2)	3.6(2.7)	4.1(2.7)	3.5(2.6)	0.0345
Time interval of breast expression in first day postpartum, hr	3.8(6.8)	3.9(2.9)	4.9(5.1)	4.2(5.1)	0.004
Breast milk production increased significantly, day	7.5(7.4)	6.0(4.7)	7.4(6.8)	7.0(6.4)	0.323
Neonatal factors					
Male, %(n)	40.0(20)	49.0(25)	51.0(26)	46.7(71)	0.509
Body weight, g	3308.7(371.5)	3332.2(383.2)	3330.9(475.7)	3323.9(410.2)	0.943
Body length, cm	49.6(1.3)	49.5(1.6)	49.6(1.6)	49.6(1.5)	0.944
Apgar score (1 min)	9.9(0.5)	9.9(0.3)	9.9(0.1)	9.9(0.3)	0.555
First breast suckling by neonate, hr	18.5(14.4)	18.6(16.1)	17.0(12.3)	18.0(14.3)	0.858
Infant body weight at 6 weeks, g	5120.0(640.3)	5113.4(602.5)	5189.9(608.6)	5141.3(614.5)	0.789
Infant body length at 6 weeks, cm	56.7(2.2)	57.2(2.3)	57.3(2.1)	57.1(2.2)	0.401
Times of breastfeeding (directly or indirectly) in 24 hs at 6 wks	6.3(2.9)	5.5(3.6)	5.4(3.4)	5.7(3.3)	0.485
Time of breastfeeding per session at 6 weeks, min	23.5(11.7)	23.0(12.7)	20.1(12.4)	22.3(12.3)	0.280
Plan to breastfeed, month	10.2(3.5)	10.0(2.4)	9.8(3.3)	10.0(3.1)	0.480
Plan to supplement food, month	6.5(1.6)	6.2(0.9)	5.9(1.3)	6.2(1.3)	0.141

Notes: summary statistics for continuous variables presented as mean (SD), categorical as %(n); BMI: body mass index;

Primary outcomes

The estimated median times required for breastfeeding initiation of hand expression, sequential breast pumping, and simultaneous breast pumping were 46.7 (95% CI 40.8-50.0), 46.5 (95% CI 36.1-50.5) and 45.6 (95% CI 34.2-53.0) hours, respectively. In each of the three groups, around 10% participants initiated breastfeeding after 3 days (i.e., >72 hr). Compared with hand expression, sequential and simultaneous breast pumping did not promote earlier initiation of breastfeeding (log-rank test, $p=1.000$) (Figure 2A). For

dyads with vaginal delivery, the median time to breastfeeding initiation with simultaneous breast pumping was 34.2 (95% CI 26.9-53.0) hours, with sequential pumping is 45.3 (95% CI 20.3-49.0) hours, and with hand expression 45.7 (95% CI 31.4-51.8) hours. For dyads in which cesarean section had been used, the median times to initiation with breast pumps were somewhat longer - 49.3 (95% CI 38.9-66.8, $p=0.096$) hours for simultaneous pumping and 50.5 (95% CI 40.2-67.1, $p=0.086$) hours for sequential pumping. However, the differences were not statistically significant (Figure 2B). With regard to mode of delivery, the time required for breastfeeding initiation in women with vaginal delivery was significantly less (median 45.1 (95% CI 31.4-48.0) hours) than for women who had cesarean section (median 48.2 (95% CI 43.5-53.0) hours; $p=0.002$) (Figure 2C).

The efficacy of breast expression in the early and mature stages of lactation was measured through expressed breast milk volume. The breast milk volume was estimated from weight, either of test weighing in the hand expressing group at 3 days or 6 weeks, or of weights in two breast pump groups at 3 days when the milk volume was <10 ml. At 3 days after birth the infants in hand expression group were breastfed directly and weighed right before and after feeding. Averaged breast milk volumes were 23.8 ± 26.2 ml for hand expression, 16.7 ± 11.6 ml for sequential pumping and 13.1 ± 10.9 ml for simultaneous pumping. Averaged breast milk volume in simultaneous pumping was less than that in hand expression group through direct breastfeeding ($p=0.007$). However, it was not different from that for sequential pumping ($p=0.560$). There was no difference between two delivery modes (vaginal delivery vs cesarean section) and no difference in subgroups of delivery mode in three groups (Figure 3A).

At 6 weeks the averaged breast milk volumes in a 10-minute session were 89.8 ± 67.3 ml for hand expression, 64.7 ± 51.0 ml for sequential pumping and 71.6 ± 50.8 ml for simultaneous pumping.. The average breast milk volume in the sequential pumping group was statistically significantly less than that of the hand expression group ($p=0.035$) but was not different from that of the simultaneous pumping ($p=0.670$). The averaged breast milk volume at 6 weeks were 72.8 ± 55.1 ml in participants with vaginal delivery and 71.8 ± 55.0 ml in these who underwent cesarean section; the difference was not statistically significant ($p=0.834$). Further subgroup analysis of breast milk volume of delivery modes in three groups did not show any statistical difference (Figure 3B). The average milk volume from the left breast was about 2 ml less than that from the right breast ($p=0.012$).

To minimize random effect from individual woman, cross over of the two breast pump types by two periods (2×2) was applied at 6 weeks. In the 1st period (before breast pump cross over) the average breast milk volumes of sequential and simultaneous pumping groups were 40.4 ± 25.3 ml and 76.5 ± 52.5 ml ($p=0.001$), respectively. In 2nd period (after breast pump cross over) the averaged breast milk volumes of sequential and simultaneous pumping groups were 88.6 ± 58.3 ml and 67.0 ± 49.7 ml ($p=0.167$), respectively. Total breast milk volume pumped in 1st period (59.3 ± 45.0 ml) was less than that in 2nd period (79.0 ± 55.1 ml) ($p=0.009$). The increase in breast milk volume associated with transition from sequential to simultaneous pumping was statistically significant ($p<0.001$), while the converse transition from simultaneous to sequential pumping was not (Figure 4). A linear mixed effects model was fitted for this cross over design by using breast milk volume at 6 weeks as the dependent variable (Table 2).

Table 2 The estimated coefficients in fitted linear mixed effects model for breast milk volume at 6 weeks

	Estimate	Std Error	t value	df	p value
Intercept	93.36	10.587	8.818	112	<0.0001
Breastfeeding initiation	-0.380	0.181	2.105	90	0.038
Groups/sequential	-37.94	9.717	3.905	144	0.000
Period/2nd period	-9.672	7.167	1.349	91	0.181
Sequential:2nd period	58.41	9.946	5.873	90	<0.0001

Note: Group/sequential stands for sequential pumping compared with simultaneous pumping; Period/2nd period stands for the period 2 in cross-over (2x2) compared with the first period; Sequential:2nd period stands for the effect of sequential pumping (1st period) change into simultaneous pumping (2nd period)

Secondary outcomes

At 4 months, among women who completed the online questionnaire, the median count of self-reported direct breastfeeding sessions was 5.5 (interquartile range, IQR 2-8) per day, the median count of using breast pumps was 2 (IQR 2-4) sessions per day, and the averaged breast milk volume expressed at each session was 172.4±95.7 ml. In the following two months infant body weight increased by about 800 grams ($p<0.0001$) and body length increased by 3 cm ($p=0.030$) on average. The baby's body weights differed between the three groups at six months ($p=0.016$) while their body lengths differed between the three groups at four months ($p=0.033$). In both breast pumping groups, 80% of mothers reported using the breast pumps frequently. Among participants who responded, 80.0% used breast pumps at 4 months and 71.9% at 6 months. The proportions were not different among three groups at 4 and 6 months ($p=0.079$, $p=0.436$), or by delivery modes ($p=0.737$). The paired student t test on expressed milk volume of mothers showed no difference ($p=0.787$) between 4 and at 6 months (pairs=41). The expressed breast milk volume in mothers who responded only once (at 4 months, $n=35$) was 136.8 ml, less than the 202.6 ml expressed by mothers who responded both (at 4 and at 6 months, $n=41$) ($p=0.002$). At 4 months, the maternity leave of 50.4% nursing mothers had ended, and this increased to 80.0% at 6 months ($p<0.001$). About 90% mothers provided complementary food to their infants at 6 months. The rate of introduction of formula milk was 40%- at 4, and 50% at 6, months. In terms of breastfeeding mode, the proportion of exclusive breastfeeding dropped from 21% at 4 months to 10% at 6 months. The rates of exclusive breastfeeding did not differ between the three groups either, at 4 months ($p=0.109$) or at 6 months ($p=0.459$) (Table 3).

Table 3 Breastfeeding mode at 4 and 6 months

	Time point	Hand	Sequential	Simultaneous	pooled
EBF, %(n)	4m	32.4 (12/37)	12.8 (5/39)	18.6 (8/42)	21.0 (25/118)
	6m	8.7 (2/23)	20.0 (3/15)	7.1 (2/28)	10.6 (7/66)
	p value	0.072	0.812	0.296	0.103
BF+, %(n)	4m	67.6 (25/37)	59.0 (23/39)	58.1 (24/42)	61.3 (73/118)
	6m	52.2 (12/23)	40.0 (6/15)	39.3 (11/28)	43.9 (29/66)
	p value	0.358	0.342	0.222	0.021
+milk powder, %(n)	4m	40.5 (15/37)	41.0 (16/39)	39.5 (17/42)	40.3 (48/118)
	6m	47.8 (11/23)	33.3 (5/15)	57.1 (16/28)	50.0 (33/66)
	p value	0.775	0.835	0.224	0.278
solely milk powder, %(n)	4m	2.7 (1/37)	7.7 (3/39)	7.0 (3/42)	5.9 (7/118)
	6m	0 (0/23)	0 (0/15)	3.6 (1/28)	1.5 (1/66)
	p value	1.0	0.658	0.645	0.262

Note: EBF, exclusive direct breastfeeding; BF+, breastfeeding directly or with sucked milk plus other food including milk powder; +milk powder, supplemented with milk powder; p value, of Fisher's exact test;

Adverse events

No serious or severe adverse events episodes were reported in follow-up to six months. The proportion who reported any type of local breast adverse events was 11.5% and for any types of systemic adverse events of mild to moderate severity 2.9%. Eleven participants (one from the hand expression group, two from the sequential breast pump and eight from the simultaneous pump group) reported 12 local (breast) adverse events with mild to moderate severity. These local adverse events, which included breast skin rash, breast pain, breast lump or swelling, cracked nipple and slightly peeling of the areola, resolved without treatment. Three cases (one from the hand expression and two from the sequential breast pump group) reported fever, mastitis and antibiotics for high fever with moderate severity, all of which resolved after medical treatment.

Discussion

In this open-label, randomized control trial, we studied different methods of breast expression immediately after birth in the absence of infant sucking. The time required for breastfeeding initiation in the three groups - hand expression, sequential electric pumping, and simultaneous electrical pumping was not statistically different. The 10-minute breast milk volume extracted through breast pumps was less than that yielded in direct breastfeeding. Compared with participants with vaginal delivery, the time required for breastfeeding initiation was delayed in those with cesarean section, but there was no significant difference in breast milk volume either at 3 days or at 6 weeks. Further analysis indicated that the time required for breastfeeding initiation may inversely predict expressed breast milk volume at 6 weeks. The effectiveness of breast pumps was differed by birth outcome (premature birth vs full-term birth) or starting time(e.g. <1 hr or >2 hrs after birth). Based upon these inconsistent results, we suggest that any stimulating effect of the suction of breast pumps on the production of breast milk is likely to be

very weak. The efficacy of sequential pumping was inferior to that of simultaneous pumping in the 10 min per breast test. The rates of exclusive breastfeeding at 4 and 6 months did not differ between the three groups.

Comparison with other studies

Breastfeeding initiation within 1 hr after birth may facilitate the appearance of copious breast milk^{8-10,37} and reduce risk of infant death in first 28 days.³⁸ Early skin-to-skin contact, mode of delivery, and maternal illness are associated with early breastfeeding initiation.^{39,40} In our trial participants who required immediate mother-and-infant separation after birth also had other conditions necessitating medical care. This made introduction of breast expression within 1 hr impractical. We introduced breast expression as soon as possible after birth to promote early breastfeeding initiation for the dyads who were separated more than 6 hrs,⁸ as it has been reported that breast expression at 24-72 hrs after cesarean section does not improve milk transfer.⁹ Antenatal breast expressing (twice daily at convenient time) after 37 weeks of gestational age has been recommended⁴¹⁻⁴⁵. In the present trial, the time for breastfeeding initiation ranged from 17 hrs before delivery to 95 hrs after delivery, with a median time greater than 45 hrs in all six subgroups of expression methods and delivery mode. This suggests some common underlying causes influenced on both the mother-infant separation after birth and the timing of lactation initiation. In line with this delayed breastfeeding initiation, the median time between delivery and sudden copious breast milk (self-reported data to indicate start of lactogenesis stage II) ranged from 4.0 to 7.5 days. Usually, the lactogenesis stage II starts at 30-48 hrs after birth, and delayed lactogenesis stage II (>72 hrs) occurs in about a quarter of mothers.^{46,47}

Clinical relevance

Breast milk transfer in the hand expression group under specified conditions, such as maternal-baby separation by delivery complications, could be viewed as comparable to that received by healthy infants from direct breastfeeding in the general population. At 3 days, the averaged breast milk volume through electric pumping was less than that from hand expression. At 6 weeks the breast milk volume pumped simultaneously in a 10-minute period was much closer to that obtained through direct breastfeeding than to that pumped sequentially. Nevertheless, the average milk volume pumped was 18 ml less than that of direct breastfeeding in the same period. Therefore, direct breastfeeding is undoubtedly the optimal option for breast milk extraction. Compared with sequential pumping, the simultaneous breast pump introduced a cyclic expressing mode accompanied with different vacuum pressures (80-150 mmHg) and an extra stimulation step (1.0-2.5 Hz) before expression. However, we have no data to support whether this design improved the total breast milk production in mothers with established lactation. The inconsistency in the apparent efficacy of breast pumps in different study populations and timing of use suggests that the role of feedback control of breast milk extraction, if any, is limited.^{8,11,31,48,49} The electric breast pumps should be viewed as a tool solely for breast milk expression when other methods are not available.

Comparison among the three methods of breast expression

Low rates and durations of exclusive breastfeeding often result from factors such as planned cesarean section delivery,⁵⁰ gestational age at delivery, breast refusal, sore nipple, lack of access to breast pumps, use of free formula milk,^{23,27,49,51} insufficient support for breastfeeding, self-perceived inadequacy of milk supply, having to leave infants to go to work or school^{5,25,26,52,53} and medical conditions³¹. In women who provided self-reported data in our trial, 80.0% used breast pumps at 4 months and 71.9% at 6 months. The proportions did not differ between the three groups at 4 or 6 months, or by mode of delivery modes. Although the length of maternity leave of nursing mothers in our trial was short (ending for half at 4 months and for 80% at 6 months), the proportion of breast pump usage during maternity leave was not different from that of mothers not on maternal leave. We do not know the reasons for application of breast pumps before 6 months, however, the high rate of breast pump usage could potentially inversely match the proportion of exclusive breastfeeding.

Limitations of the study

This trial was conducted in nearly healthy mother and infants who were healthy other than for, the mother-infant separation immediately after birth specified in the eligibility criteria, so the external generalizability may be limited. Women in trial groups with an adequate breast milk supply may have been more likely to provide self-reported data respond at 4 and 6 months. The high rate of breast pumping among nursing women, instead of laborious hand expressing, would lead to biased estimation of breast milk volume as the effect of breast pump on breast milk production has yet to be justified.

Conclusions

Introducing breast expression (hand expressing, sequential and simultaneous pumping) in the period of mother-infant-separation later than 2 hours postpartum did not affect the time for breastfeeding initiation. Simultaneous breast pumping was more effective than sequential pumping in women with established breastfeeding both in volume and time, while the direct breastfeeding resulted in the greatest volume of breast milk extraction both at 3 days and at 6 weeks. The time for breastfeeding initiation could predict the volume of pumped breast milk at 6 weeks inversely. The rates of exclusive breastfeeding at 4 and 6 months did not differ between the three methods of breast expression.

List Of Abbreviations

WHO: World Health Organization; CONSORT: Consolidated Standards of Reporting Trials; ITT: Intention-to-treat; one-way ANOVA: One-factor Analysis of Variance; IQR: Interquartile range; BMI: Body mass index; EBF: Exclusive direct breastfeeding; BF+: Breastfeeding directly or with sucked milk plus other food including milk powder.

Declarations

Ethics approval and consent to participate

All participants in this study provided written informed consent before recruitment, and the Institutional Review Board of Xinhua hospital approved this project (XHEC-C2017-108-2).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributors

LZ and JYN designed the study. LZ coordinated the study. YZ and JYN enrolled the participants and arranged informed consent from the participants and drafted of the manuscript. LJW and CCZ provided care for participants and checked the questionnaires. YC and CCZ conducted the test weighing and checked the breast milk volume and conducted the breast pump types cross over. LZ and YZ did the data analyses including statistical analyses. All authors critically reviewed the report. LZ had full access to all of the data in this study and take responsibility for the integrity of the data and accuracy of the data analyses.

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Figures

Figure 1

Participants flowchart Hand stands for hand expression if required and the infants were breastfed directly; sequent stands for sequential breast pumping; simult stands for simultaneous breast pumping; an inset graph for detailed cross over of breast pumps was also provided.

Figure 2

Time for breastfeeding initiation in survival analysis Breastfeeding initiation, also known as colostrum appearance in this study, was viewed as an event; successful breastfeeding initiation defined as events=1; VD, vaginal delivery; C-sect, cesarean section; (A) breastfeeding initiation in hand expression, sequential and simultaneous pumping; (B) breastfeeding initiation in subgroups of delivery mode (VD vs C-sect) of three groups; (C) comparison between two delivery mode across all three groups;

Figure 3

Breast milk volume expressed at 3 days and 6 weeks Breast milk volume in hand expression group was estimated through test weighing of transferred milk through infants' sucking, strictly speaking it was not expressed; the mere difference in three groups were the methods of breast expression without infant sucking, the infant should be direct breastfed or indicated otherwise;

Figure 4

Breast pumps cross over at 6 weeks. The upper panel displayed the breast milk volume in two periods of pumping in individual in two different pattern of shift, namely from sequential to simultaneous pumping or vice versa; the green dots represented the sequential pumping, the orange dots for simultaneous pumping; the lower panel provided the averaged levels of each groups in each period; sim, simultaneous pumping; seq, sequential pumping;

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