The Effect of Co-bedding Premature Multiple-birth Infants on Growth and Physiological Stability: A randomized clinical trial

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Received: November 8, 2021, Accepted: April 9, 2022, ePublished: October 31, 2022

Introduction
Over the past three decades, the rate of twin or higher-order multiple births has shown a rising trend (1). In studies conducted all around Iran, the prevalence of twin or higher-order multiple pregnancies has been 6.2-14 cases per 1000 live births (2). Growth in the number of such pregnancies as well as preterm delivery has also resulted in an increase in the number of premature infants admitted to neonatal intensive care units (NICUs) (3). The stress of coping with the environment outside the uterus in premature twin or multiple birth infants can also bring about problems by itself such as growth and neurodevelopmental defects (4). These infants hospitalized in NICUs are often dealing with numerous therapeutic challenges and their neurodegenerative development is not completely able to overcome postpartum-induced infections compared with term neonates (5). In this regard, support for evolutionary care of twin or multiple birth infants whose populations are rapidly growing as well as support of their families should be taken into consideration. Co-bedding has been considered as one of the evolutionary care strategies being implemented in many NICUs throughout the world (6).

Co-bedding means the placement of twins for sleeping together in a shared crib and bed or an incubator (3). The purpose of this method is to regulate and stimulate the intrauterine environment for these neonates to continue physical contact with each other instead of sudden exclusion of this stimulus. Obviously, retaining skin-to-skin contact between twins or multiple birth infants can...
help them to cope with the surrounding environment and subsequently increases their compatibility mechanism (3). Co-bedding also allows infants to be adjacent to each other and skin-to-skin contact between them correspondingly provides opportunities to recognize familiar stimuli of hearing, and smell and continue neonatal bonds that began during fetal age (7). By adjusting the body temperature and the sleep-wake cycle of twins or multiple birth infants, co-bedding also helps them to adapt to the environment outside the uterus and leads to their better growth and development (8). Besides, co-bedding of these infants increases co-regulation and physiological stability, reduces the required oxygen, improves growth and development, and shortens the length of hospitalization and number of admissions (9).

Elsewhere, Chin et al, in a randomized controlled trial reported a greater increase in mean weight gain in the co-bedded group compared to the control group (10). Moreover, there are manifestations of improvement in heart rate, respiratory rate, and sleep-wake cycle in premature twin or multiple infants with unstable conditions placed in the same incubators (11).

According to Campbell-Yeo et al study, co-bedding premature twin or multiple birth infants could boost physiological stability following heel blood sampling but did not reduce their pain scores (12). Reduced apnea, improved bonds between infants, as well as higher levels of satisfaction in parents and, NICU staff had been included among co-bedding advantages (13). Findings from preliminary clinical studies of neonates have also shown that disconnection from incubators and discharge of this group of infants have been performed earlier (14). Common concerns about co-bedded neonates have been mentioned the risk of infections, medication errors, no correct control of incubator temperature, reduced quality of sleep, physical harm, as well as increased risk of sudden infant death syndrome (4). According to a study by LaMar and Dowling, no significant difference was observed in the rates of sepsis and pneumonia in both groups of infants receiving traditional and co-bedding care services (15). It should be noted that research studies on the co-bedded twin or multiple birth infants are limited (9,10,12,16-18) and the advantages and disadvantages of co-bedding have not been fully understood; so far, there is a need to evaluate them in the different clinical settings (19). Recently, Lai et al in a Cochrane systematic review concluded that evidence on the benefits and harms of co-bedding for stable preterm twins was insufficient to permit recommendations for practice. Further studies with the powered design are warranted to detect clinically important differences in these infants’ growth and neurodevelopment and researchers should evaluate disadvantages such as infection, along with medication errors and, caregiver satisfaction (20).

Accordingly, the main purpose of this study was to determine the effect of co-bedding premature twin or multiple birth infants on their growth, physiological stability, and short-term prognosis in NICUs in order to provide a positive step towards improving care services for this specialized cohort of patients.

Methods

This study was a randomized clinical trial aimed to determine the effect of co-bedding premature twin or multiple birth infants on their growth and physiological stability in the NICU of Shahid Akbar-Abadi Hospital in the city of Tehran affiliated with Iran University of Medical Sciences from January 2018 to January 2019. The study population included all infants hospitalized in the NICU with a weight of fewer than 2000 grams, stable general health status, with no umbilical catheters and chest tube as well as no mechanical ventilation. The exclusion criteria were the infant’s need for mechanical ventilation or aggressive interventions and presence of sepsis or asphyxia.

A simple random sampling method was also performed using block randomization by a researcher not included in the study from all the infants admitted to the NICU of this hospital. After dividing the samples into the two intervention and control groups, the neonates in the intervention group were co-bedded using a predefined checklist derived from valid Persian and English articles, protocols and, instructions, as well as neonatal nursing and pediatric reference books. At first, the NICU nurses received the required training on how to perform co-bedding and to use the checklists within three training sessions on three consecutive days. The teaching method was in the form of providing pamphlets, practical training, discussion, as well as questions and answers.

The data collection instrument was a demographic questionnaire containing items such as age, gender, weight, and height, head circumference at birth, underlying illnesses, heart rate, arterial oxygen saturation, and respiratory rate, as well as weight, height, and head circumference measured during the intervention. The infants were also co-bedded under a radiant warmer or inside an incubator or on a shared crib or bed and received care services by trained nurses as needed according to the ward protocols. The infants’ weight in both groups was measured on a daily basis, their height and head circumferences were determined twice weekly, and their physiological stability was assessed every 3 hours during the interventions. Normal weight gain was defined as an increased weight of at least 20 gr per day. Increasing one centimeter per week in height and head circumference was considered normal. Normal neonatal heart rate (120-160 per minute) and normal respiratory rate (40-60 per minute) were clarified. Normal arterial O₂ saturation was determined as arterial O₂ saturation above 90% without external oxygen supplementation. The heart
and respiratory rates and arterial oxygen saturation were collected from electronic medical records.

The sample size was determined by a statistical consultant based on the incidence rate of twin or higher-order multiple pregnancies in previous studies through replacing the following cases as $\beta = 0.8-1$, $\text{Rep} = 4$, $P = 0.5$, and effect size $= 0.142$, and $\alpha = 0.05$ on the specific formula was calculated by 70 infants in each group; i.e. 35 pairs of neonates in each group. Considering the probability of sample loss in this center and in order to control this problem, the sample size increased by 5% and, finally 40 pairs of infants were allocated to each group. In order to analyze the data, the SPSS Statistics software (version 21) was used. The statistical tests including chi-square for categorical variables and Student’s $t$ test for quantitative variables were applied as appropriate.

**Ethical considerations**
The study was approved by the Ethics Committee, Iran University of Medical Sciences (approval ID: IR.IUMS.REC.1395.95-03-208-28921). Written consents have been obtained from the infants’ parents. The study was also registered in the Iranian Registry of Clinical Trials (identifier: IRCT2017010926115N3, http://www.irct.ir/).

**Results**
In total, one hundred and five pairs of premature twin infants were evaluated and 26 pairs of them were excluded due to lack of the inclusion criteria ($n = 15$) and dissatisfaction of parents to participate in the study ($n = 10$). There was no case of dropout in both groups. Therefore, the data of 40 pairs of premature twin infants in each group were analyzed (Figure 1).

Demographic characteristics of 160 neonates divided into the two groups of co-bedding (40 pairs of twins) and standard care group (40 pairs of twins) were recorded and compared. In the co-bedding group, 52 (65%) neonates were born 28-34 weeks and 28 (35%) were born 34-37 weeks and in the standard care group, 56 (70%) of neonates were born 28-34 weeks of gestation and 24 (30%) were born 34-37 weeks, with no statistical difference between the two groups ($P = 0.7$). In terms of infants’ gender, 46 (57.5%) and 37 (42.5%) of infants were male in co-bedding and control group, respectively ($P = 0.2$). Mean ± SD of neonates’ birth weight was $1460 \pm 496$ g in the co-bedding group, and $1393 \pm 474$ g in the standard care group with ($P = 0.2$). Mean ± SD of birth length in the co-bedding and control group were $45.40 \pm 3.89$ cm and $44.54 \pm 3.91$ cm, respectively ($P = 0.3$). Head circumference mean ± SD were $33.40 \pm 2.83$ and $32.76 \pm 2.91$ respectively in the case and control group ($P = 0.2$). The analysis showed that there were no significant differences between the two groups in terms of infants’ gender, gestational age, weight, height and head circumference at birth ($P > 0.05$). The results revealed that the rate of weight gain in the co-bedded group ($P < 0.001$) was significantly different.
compared with the standard care infants. However, no significant difference was observed in terms of increased height \( (P=0.9) \) and head circumference \( (P=0.4) \) between two study groups. There was also no significant difference between the two groups \( (P=0.32) \) in terms of heart rate, arterial oxygen saturation \( (P=0.12) \), and respiratory rate \( (P=0.68) \). Moreover, there was a significant difference in the mean number of NICU hospitalization days between the study groups \( (P<0.01) \) in a way that the mean of hospitalization days of the co-bedded neonates was lower than that of the control group. No medication or medical equipment incidents or infection transmission was reported in the two groups (Table 1).

**Discussion**

The findings of this study demonstrated that the given strategy had only affected weight gain among the growth parameters and length of NICU hospitalization with no influence on other physiological criteria. Among the studies performed on co-bedded premature neonates, the results of investigations have indicated physiological and behavioral changes due to neonatal co-bedding (10,14,17,21). In co-bedding strategy, twin or multiple birth infants are placed in one bed so that parents are not forced to pay much more attention to one of them, and thus the bond between parents and such infants progresses (22). In this respect, Byers et al suggested that co-bedding twin or multiple infants might be an effective preventive intervention to avoid negative emotions by parents during their hospitalization in NICUs (17). Moreover, previous studies had reported better weight gain and growth in co-bedded groups which were consistent with the results of the present study; however, these investigations had their own limitations specifically small sample sizes (10,14,16,17).

In Byers et al study on 37 preterm infants, the heart rate of neonates co-bedded in incubators compared to those with separate hospitalization had increased during the first and second days of the study and then dropped off (17). In a similar way, Lutes and Altimier compared the weight gain and changes in head circumference and height among 62 co-bedded neonates and 59 separately bedded infants and found no significant difference between the intervention and control groups (16). In agreement with them, Hayward et al found no significant difference between physiological variables in co-bedded and separately hospitalized groups (23).

The gender of 51.5% of the neonates in this study was female of which, 28.7% belonged to the co-bedded group. According to a previous study, cardiac and respiratory stability is lower in male neonates than female ones (21). Also, in the study by Casey et al boys had a more significant growth rate until 36 months of age in terms of weight, height, and head circumference than girls of the same age (24).

The fetal age of 40% of the neonates in this study was between 31 and 34 weeks, and 40% of the neonates were between 34 and 37 weeks. In the study by Campbell-Yeo et al, a total number of 67 pairs of neonates examined had a fetal age between 28 and 36 weeks (3). Elsewhere, Chin and colleagues evaluated 39 pairs of neonates who had a gestational age of fewer than 34 weeks (10). The results of the study by LaMar and Dowling also showed no significant relationship between the fetal age and infection rates of neonates in the co-bedded group and those hospitalized separately (15). However, the authors in the *Williams Obstetrics textbook* had stated that neonatal age is an important determinant of the chance of survival as well as natural growth and development (25).

Furthermore, in the present study, the mean number of hospitalization days in the co-bedded neonates was smaller. However, there was a difference in the number of days of stay in the incubator as well as completion of breastfeeding and weight gain, and the number of hospitalization days of the neonates in the NICU between the two groups. So, the number of days of admission of twin or higher-order multiple birth neonates was two days shorter than that of traditional care services (26). Moreover, Hayward and colleagues found no significant difference in terms of length of hospitalization between

### Table 1. Comparison of developmental status of infants between co-bedding and standard care groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Co-bedding group (n = 80)</th>
<th>Standard care group (n = 80)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight gain (yes), n (%)</td>
<td>72 (90)</td>
<td>47 (58.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Increased height (yes), n (%)</td>
<td>68 (85)</td>
<td>66 (82.5)</td>
<td>0.9</td>
</tr>
<tr>
<td>Increased head circumference (yes), n (%)</td>
<td>38 (47.5)</td>
<td>40 (50)</td>
<td>0.4</td>
</tr>
<tr>
<td>Normal heart rate, n (%)</td>
<td>18 (22.5)</td>
<td>20 (25)</td>
<td>0.32</td>
</tr>
<tr>
<td>Normal arterial O₂ saturation, n (%)</td>
<td>23 (28.7)</td>
<td>20 (25)</td>
<td>0.12</td>
</tr>
<tr>
<td>Normal respiratory rate, n (%)</td>
<td>15 (18.75)</td>
<td>17 (21.25)</td>
<td>0.68</td>
</tr>
<tr>
<td>Number of NICU hospitalization days, mean ± SD</td>
<td>21.7 ± 9.1</td>
<td>28.7 ± 9.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Infectious transmission &amp; material/medication accidents, n (%)</td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

Normal weight gain was defined as increased weight at least 20 gr per day. Increasing one centimeter per week in height and head circumference were considered as normal. Normal neonatal heart rate was considered as 120-160 per minute. Normal respiratory rate was considered as 40-60 per minute. Normal arterial O₂ saturation was determined as arterial O₂ saturation above 90% without external oxygen supplementation.
the co-bedded groups and those hospitalized separately (18). In a recent randomized clinical trial, Legrand et al evaluated 32 sets of twins and concluded that co-bedding had no significant impact on the weight gain trajectories in the preterm twins, as shown in previous studies (10,16); however, it does highlight potential benefits in terms of birth weight recovery delays, decreased parenteral weaning delays and reductions in the length of hospital stay (27). In accordance with the previous studies (28, 29), the present study failed to demonstrate clear cardio-respiratory benefits of co-bedding.

The strength of the present study was the relatively high sample size compared to the previous studies. It is suggested that future studies on neurodevelopment and oral maturation be performed during the first 2 years of life with long-term follow up in preterm newborn infants.

Conclusion
It was concluded that co-bedding twin infants is a safe practice and could lead to weight gain among them and consequently accelerate their recovery and discharge. It is hoped that this study will lead to more research on co-bedding and the development of policies specific to co-bedding for preterm multiples.

Acknowledgements
This research was supported by grant No.28921 from Iran University of Medical Sciences (IUMS) and the authors would like to thank the Shahid Akbarabadi Clinical Reserch Development Unit (ShACRDU), IUMS, Tehran, Iran for their cooperation and to thank the Shahid Akbarabadi Clinical Reserch Development Unit (ShACRDU), IUMS, Tehran, Iran for their cooperation and assistance throughout the period of study.

Conflict of Interests
The authors declare that they have no competing interests.

References


