Effects of Self-Regulated Physical Activity in Premature Infants on Bone Density and Length of Stay: A Pilot Study

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Importance: Premature infants are not prepared developmentally, physically, or cognitively with the multiple survival skills of the typical newborn.

Objective: To determine whether physical activity generated spontaneously by premature infants stretching against the resistance of "prepod" garments is as effective as exercises provided by therapists in slowing bone density loss.

Design: Preterm very low birth weight infants were placed in two nonrandomized parallel groups according to birth age.

Setting: Infants routinely started in a traditional intense intervention setting and graduated to a special care section with private rooms that allowed parents to remain with their child.

Participants: Healthy infants without medical complications, born between 28 and 32 wk postmenstrual age.

Intervention: The control group received traditional exercises. The experimental group wore a prepod almost 24 hr a day.

Outcomes and Measures: An ultrasound of the tibia was obtained at 31 to 32 wk and 4 wk later. Weight gain, head circumference growth, and length of stay (LOS) were also measured.

Results: Although not statistically significant, the ultrasound results showed that the prepod group had less loss of bone density than the traditional therapy exercise group. The desired outcome was for pods to be as effective at reducing bone loss as traditional exercise, so the results exceeded expectations. The unexpected, and more notable, finding was a striking drop in LOS for the prepod group.

Conclusions and Relevance: Spontaneous exercise by premature infants decreases bone loss and LOS. Better bone health and increased developmental maturity increase the chances of a positive developmental outcome and save the hospital significant expense.

What This Article Adds: The prepod is a simple, cost-effective, noninvasive treatment tool occupational therapy practitioners can use to support a premature infant's development. This study has considerable potential to affect how infants are served, both developmentally and financially.

Premature infants born before 34 wk postmenstrual age experience considerable challenges with bone growth health after birth. They are at risk for developing osteopenia and subsequent fractures (Chan et al., 2008). Multiple studies have shown that even when provided calcium supplements, premature infants have difficulty metabolizing needed compounds at the rate their fetal counterparts are able to do (Hovi et al., 2009). These premature infants have significantly lower mineral bone content at age 1 yr, and many go on to have smaller bones and shorter stature as adults (Hovi et al., 2009).

Exercise stimulates bone formation and mineral absorption (Moyer-Mileur et al., 2000). Exercise programs evolved as early as 1995 that offered a simple range of motion and joint compression routine for the infant, usually once per day (Moyer-Mileur et al., 1995). Most programs are 10 to 15 min long, designed around the infant's care routine, and administered by trained therapists or a parent under the therapist's training (Moyer-Mileur et al., 2000, 2008;

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Vignochi et al., 2008). A review of the available literature shows that most older studies measured results by dual-energy X-ray absorptiometry. In the past decade, most results have been measured by ultrasound (UTS) because it is a less invasive measurement system (Litmanovitz et al., 2003, 2016). Interestingly, although all available studies tended to show value in preventing bone density loss by providing exercise, the variety of results—some showing dramatic results in short periods with others showing minimal results with more involved intervention—is thought provoking.

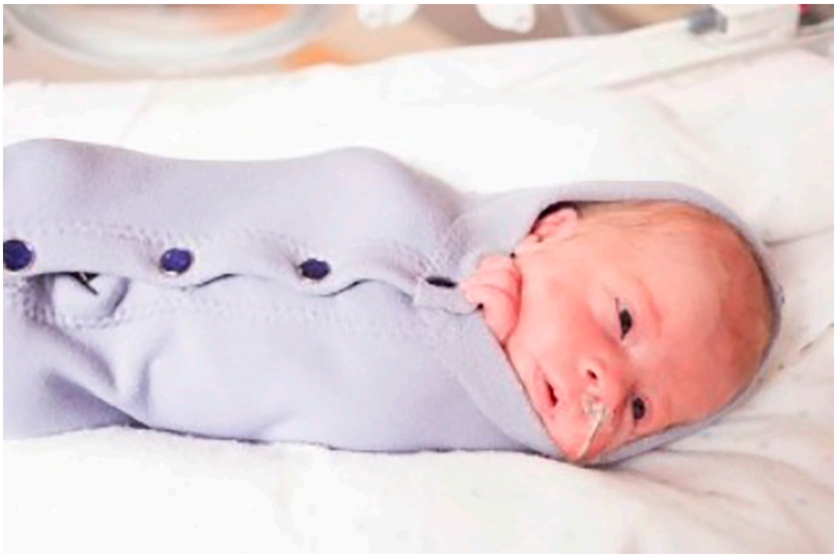
At Rogue Valley Medical Center, a bone stimulation exercise program began in 2012. On the basis of Moyer-Mileur et al.'s (2000) traditional protocol, occupational and physical therapists worked with the infants' care schedule, providing exercise one time per day, 5 days per week. Each exercise consisted of gentle passive range of motion (PROM) of all four extremities and then joint compression of each shoulder, elbow, wrist, hand, hip, knee, ankle, and foot. Each exercise session lasted about 10 min.

In an effort to create a more "infant-driven" neonatal intensive care unit (NICU) environment, the concept of the *prepod* was conceived: a fabric artificial womb where infants could provide their own exercise when they felt like it. The pod had several theorized advantages over therapist-provided sessions. Theoretically, the infants could get more exercise because they could push against the elastic fabric at will. Second, infants might experience less stress because one more imposed procedure was removed from the infant's ongoing multitude of challenges. In addition, by removing the need for specific exercise sessions, the therapist was then free to do other tasks.

Prototypes were initially created on the author's own sewing machine; seamstress assistants were added in 2016. The garment design was reviewed by the U.S. Food and Drug Administration and the supervising institutional review board.

After several prototypes, the final prepod was developed (Figure 1). The prepod's design had to incorporate the following features: It had to loosely maintain the infant in physiological flexion (the fetal position), but the fabric had to allow the infant to fully extend arms and legs at will. Fabric content was also a factor because overheating in an isolette is a constant concern. Four sizes were created to allow for growth, ranging from approximately 800 g to 3,000 g. The purpose of this study was to test the following question: Would the prepod be as effective as a traditional bone stimulation program in decreasing bone density loss?

Figure 1. Infant in prepod.



Method

Participants were infants born at or admitted to the NICU between 28 and 32 wk of gestational age. They needed to be in good general health, have no medical complications or syndromes, be size appropriate for postmenstrual age, have no ongoing supplemental oxygen requirement, and have no medications other than vitamins or caffeine. They were tolerating enteral feeds at >110 ml/kg of body weight per day on entrance into the study at between 31 and 32 wk postmenstrual age.

Infants were assigned to the prepod or control group largely on the basis of birth age. The examiners attempted to keep the two groups as balanced as possible. For example, if the prepod group was overall slightly older than the control group, and the next available infant was slightly older, then that infant would automatically be considered for the control group.

Infants were also matched for weight and head circumference to ensure that the two groups were as equally healthy and robust as possible. We had no concern regarding ethnicity or gender because work by Pereda et al. (2003) documented no significant differences in bone density growth patterns in these groups.

Infants were measured for changes in bone density, weight, and head circumference, and length of stay was calculated. Bone density was measured with the Sunlight Omnisense Premier Ultrasound (BeamMed, Plantation, FL), which has software data measuring typical bone density in premature infants (Pereda et al., 2003). Two measurements were taken at the left midtibia after entrance into the study at 31 to 32 wk gestational age and at exit from the study 4 wk later. If the infant was fussy and moving during the measurement or the examiner was concerned about validity, then three measurements were taken, and the most discordant was discarded. Weight and head circumference data were retrieved from routine registered nurse growth recordings. LOS was a simple comparison of admission date versus discharge date.

The control group received bone stimulation exercises based on Moyer-Mileur et al.'s (2000) protocol provided by a trained occupational or physical therapist 5 days per week. The infant was usually seen just before feeding and frequently awakened with a slow, gentle PROM program to all four extremities followed by joint compression of each extremity toward the trunk (hand, wrist, elbow, and shoulder or foot, ankle, knee, and hip). This exercise routine usually took approximately 10 min. The prepod group received no exercise program but wore their pod 24 hr a day, having it removed only for bathing or for skin to skin time with parent (sometimes parents only opened the pod snaps for skin to skin, not removing it entirely).

After entry into the study, each infant's statistical information (age, weight, head circumference) was entered into the study database. The initial ultrasound (UTS) speed of sound (SOS), the speed at which a sound wave travels through the midpoint of the tibia bone, was entered. The SOS percentage, comparing their score with other infants their age, and the resulting standard deviation for postmenstrual age of the infant were also entered. After 4 wk, another UTS was performed, and SOS and percentile and standard deviation for age were recorded. Change was then recorded and compared between the two groups, as was overall LOS.

Table 1. Developmental Measures for All Participants

Variable	Total Study (N = 54)	
	Prepod Group (n = 27)[a]	Control Group (n = 27)[b]
Birth age		
M	30 wk, 5 days	30 wk, 0 days
Range	28 wk, 4 days–31 wk, 4 days	28 wk, 2 days–31 wk, 6 days
Study exit age		
M	36 wk, 6 days	38 wk, 0 days
Range	35 wk, 2 days–40 wk, 6 days	35 wk, 1 day–42 wk, 3 days
Head circumference, cm		
M at birth	28.62	27.81
M at discharge	33.05	33.25
Growth per hospital day	0.10	0.10
Infant weight, g		
M birth weight	1,550.74	1,463.28
M discharge weight	2,737.62	2,852.14
Growth per hospital day	27.66	26.20

[a]The prepod group was composed of 16 male infants and 11 female infants. [b]The control group was composed of 15 male infants and 12 female infants.

Results

The study period lasted from 2013 through 2017, and 54 infants completed the study (Table 1). Unfortunately, late in 2014 a discrepancy was discovered in the UTS data (the antitheft anklets produced a sound wave that interfered with the machine readings), and bone density data had to be discarded for the first 33 participants, leaving only 21 with valid completed bone density values. Therefore, we included only the 21 participants with valid SOS data in the bone density analysis (Table 2). For the secondary measurements of LOS, head circumference growth, and weight gain, we were able to review all participants. The original goal was to have 30 matched participants.

Table 2. Developmental Measures for Participants Completing the Bone Density Study

Variable	Prepod Group (n = 10)[a]		Control Group (n = 11)[b]	
	M	Range	*M*	Range
Age				
Birth age	29 wk, 6 days	28 wk, 4 days–31 wk, 4 days	29 wk, 6 days	28 wk, 2 days–31 wk, 4 days
Initial UTS age	32 wk, 2 days	30 wk, 5 days–32 wk, 5 days	32 wk, 3 days	31 wk, 2 days–32 wk, 5 days
Exit UTS age	36 wk, 1 day	34 wk, 4 days–37 wk, 1 day	36 wk, 2 days	35 wk, 2 days–36 wk, 5 days
SOS, m/s				
Initial SOS	2,911	2,705–3,032	2,918	2,756–3,045
Exit SOS	2,848	2,755–2,934	2,803	2,653–2,973
SD	95.48		79.99	
t		−3.5		
df		10		
p		.27		
Weight gain, g				
Birth weight	1,426	1,145–1,825	1,472	1,080–1,975
Discharge weight	2,556	2,085–3,255	2,811	2,481–3,295
Gain (range)	1,132 (567–1,770)		1,339 (826–1,780)	
Daily growth	26.28		25.26	
SD	372		273	
t		−1.40		
df		10		
p		.09		
Head circumference, cm				
At birth	27.9	24.5–31.8	28.9	25.0–31.5
At discharge	32.2	30.5–35.5	33.4	31.5–35.5
Growth per day (range)	0.10 (0.20–6.50)		0.10 (2.00–8.80)	
SD	2.03		2.02	
t		−1.43		
df		10		
p		.09		

Note. SOS = speed of sound; UTS = ultrasound.
[a]The prepod group was composed of 5 male infants and 5 female infants. [b]The control group was composed of 7 male infants and 4 female infants.

However, in 2017 the institutional review board felt that the evolving data regarding LOS were compelling and that despite the small size, the study should be concluded because the data were not likely to statistically change significantly.

The 21 infants who were able to complete the bone density project were divided into uniformly well matched groups for the research project, closely controlled for entrance age and weight. The only imbalance between the two groups was in gender ratio. The control group had a greater percentage of male infants (7 male infants and 4 female infants compared with 5 male infants and 5 female infants in the prepod group). The prepod group had slightly higher weight gain (26.28 g per day) than the control group (25.26 g per day). Head circumference growth was identical for the two groups (0.10 cm per day). We then examined the entire experimental group and discovered similar results. The prepod group had slightly better weight gain (27.66 g per day) than the control group (26.20 g per day). Again, head circumference growth was identical. On our primary outcome, bone density, the prepod group had slightly less bone density loss than the control group, not a statistically significant difference.

Interestingly and unexpectedly, in both the larger sample and the bone density subsample, the prepod group had a reduced LOS compared with the control group. In the whole group, LOS was reduced in the prepod group by 10 days, whereas in the bone density group, LOS was reduced by 16 days (Table 3).

Table 3. Length of Stay

Variable	Bone Density Group (N = 21) Prepod Group (n = 10)	Bone Density Group (N = 21) Control Group (n = 11)	Total Group (N = 54) Prepod Group (n = 27)	Total Group (N = 54) Control Group (n = 27)
M (SD), days	48 (7.76)	64 (10.11)	43 (12.03)	53 (14.67)
Range, days	40–58	44–90	24–65	29–90
t	−3.40		−2.59	
df	20		53	
p	.002		.006	

Discussion

The purpose of our research was to see whether an infant-driven form of exercise that used a stretch-resistant garment could decrease bone loss of prematurity as well as programs that used exercise regimens provided by a trained therapist. The prepod actually did a slightly (nonsignificant) better job of decreasing bone density loss than traditional exercise provided 10 min per day, as hypothesized. Because our hope was that the pods would work as well as, not necessarily better than, traditional exercise programs, we felt that the pods were a successful therapeutic tool, offering a cost-effective way of providing important physical exercise to infants.

Theoretically, an infant with a means to experience passive resistance at any time during the day or night is most likely going to execute more exercise than the child who is bundled, restrained, or left “hanging free” for the great majority of the day. Increased exercise contributes to both physical and neurological growth (Als, 1982).

The unexpected finding was the considerable decrease in LOS. In the completed study group of 21 infants, the LOS difference between the prepod group (48 days) and the control group (64 days) is 16 days. This finding has significant implications neurodevelopmentally for infants and financially for hospitals. When we looked for supporting data by examining our total group of study infants (N = 54), including those with unreliable bone density data, we found a difference of 10 days (prepod group = 43 days vs. control group = 53 days).

No single explanation was obvious for the significant difference in LOS. Anecdotally, nurses commented that the infants in pods appeared calmer and slept better. Very quickly into the study, therapists were approached about using pods for nonstudy infants for the calming effects, and it became standard protocol on the unit to have pod babies identified as “study babies” (not to be removed from pods) or “nonstudy babies” (pods to be used as needed for calming). Nursing requests for pods were usually for intrauterine drug-exposed infants, and occasionally for infants with hypoxic ischemic encephalopathy or intrauterine growth restriction.

A third-trimester fetal brain grows extremely rapidly (approximately 800 million neurons per day), and it has to organize all the new growth in patterns conducive to later learning. Premature infants are significantly challenged to match this growth when they have to learn to breathe, digest, and cope with gravity, pain, and aversive tactile and sensory input. When babies are stressed, they produce cortisol, the stress hormone, which can interfere with growth and, especially, brain development. The goal of all developmental therapists is to provide an environment designed to be as supportive and stress free as possible to promote growth. Earlier discharge from a NICU occurs as a result of infants reaching a threshold maturity level more quickly.

The prepod group could have matured faster for several possible reasons. Probable factors include (1) less stress from decreased handling by therapists; (2) less stress by avoiding clothing changes, which involve manipulating arms and legs in and out of garments (the pod, used with no clothing under it, simply slips over the child; in addition, rompers may become twisted or ill fitted, causing discomfort and stress—the infant cannot self-correct or complain, except by generalized crying); (3) increased spontaneous exercise; (4) maintenance of desired fetal position; (5) increased proprioceptive feedback similar to the contact of the womb not only from arms and legs but the entire body, including head and spine during stretches; and (6) increased tactile input, again of the entire body.

Questions still exist about the degree of bone density loss because the literature is so varied. Although the pod group was better than the exercise group in this study, the exercise group was about the same as a regular no-exercise control group in two other studies (Litmanovitz et al., 2003, 2016). The existing UTS bone density studies we reviewed were conducted in Israel and in Tampa, Florida, essentially sea-level areas. Other studies have shown that humans lose bone density with gains in altitude (Basu et al., 2013; Tanaka et al., 1992). These studies were of adults but were based on the understanding that humans need oxygen for good bone metabolism. Thus, an infant who graduates to room air at 32 wk at 1,600 ft does not necessarily have the same bone support system as an infant who graduates to room air at 32 wk at sea level. This study was conducted at an elevation of 1,600 feet. Therefore, elevation may be an important factor to consider in interventions to promote premature infants' bone health.

Limitations

This study has several limitations. The sample for which we were able to obtain bone density information is small. The creator of the prepod is also an author of this report, a potential conflict of interest. The results of this small study, however, provide good preliminary data that the prepod is a promising tool for greater prevention of bone loss compared with traditional therapist-provided exercise sessions. More important, it shows potential as an extraordinarily effective developmental tool for decreasing an infant's LOS in the NICU. Beside the benefit to the infant, a decrease of 10 or more hospital days per premature infant younger than age 32 wk would save even modest-sized NICUs millions of dollars per year. Carl Sagan said that "extraordinary claims require extraordinary evidence." The probability scores would seem to qualify our findings as extraordinary evidence, but because this study is small, the results still need to be interpreted cautiously. Further research is needed to confirm these results.

Implications for Occupational Therapy Practice

The results of this study have the following implications for occupational therapy practice:

- Therapists in NICUs have become increasingly aware of the importance of incorporating awareness of the infant's developmental needs into the care plan. They are often the leaders in developmentally appropriate care. This study supports the effectiveness of these practices.
- Because decreased LOS has significant financial savings potential for hospitals, use of the pod can reflect very positively on the occupational therapist and therapy department.
- The prepod has great potential for assisting infants to develop a higher level of integration of sensory systems and resulting brain development. More study is needed.

Conclusion

Our initial goal was to determine whether self-administered exercise (via stretching against a prepod) was as effective as traditional therapist-administered exercise programs. We gathered evidence through a small study that the pods were actually slightly more effective. More dramatic, however, was the unanticipated sharp decrease in LOS for pod infants compared with exercise infants. This secondary finding has important implications both neurodevelopmentally and financially.

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