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The Effect of Maternal Lower Limb Compression on Amniotic Fluid Index, Uteroplacental Perfusion, and Fetal Blood Flow in Isolated Oligohydramnios

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Mini-Summary

What does this study add to current knowledge?

- Only a few investigational therapies have aimed to increase amniotic fluid volume in oligohydramnios. This preliminary study demonstrated that the application of a sequential compression device on maternal lower limbs could increase the amniotic fluid index in pregnancies with isolated oligohydramnios in the third trimester. Moreover, the increment in amniotic fluid index was coupled with changes in certain parameters of fetal blood circulation that could be related to the pneumatic compression mechanism of action.

What are the main clinical implications?

- The findings of this study suggest that pneumatic compression of the maternal lower limbs could improve amniotic fluid volume in oligohydramnios. Future studies could examine whether this improved amniotic fluid index persists long term and whether it is associated with improved obstetrical and neonatal outcomes.

Keywords

Oligohydramnios · Amniotic fluid index · Pneumatic compression · Lower extremities · Doppler

Abstract

Introduction: The aim of this study was to examine the efficacy of pneumatic compression of the maternal lower extremities in increasing the amniotic fluid index (AFI) in pregnancies complicated by isolated oligohydramnios. ***Methods:*** Women with isolated oligohydramnios (AFI <5 cm) at 32–41 weeks of pregnancy were connected to a sequential compression device for 60 min. Prior and after the application, AFI and the pulsatility index (PI) of a number of arteries were measured. ***Results:*** The median (interquartile range) maternal age of the 21 women included was 29 years (26.50–32.00), the median parity was 1 (1–2), and the median

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gestational age at intervention was 37.60 weeks (37.00–39.40). The median AFI increased after the application from 4.00 (3.62–4.50) to 6.08 cm (4.90–7.03) ($p < 0.001$). The median PI of the fetal renal artery decreased from 2.30 (2.01–2.88) to 2.26 (1.68–2.71) ($p = 0.01$). The hourly fetal urine production did not increase. Changes were not significant in the PI of the umbilical artery, the middle cerebral artery, and the bilateral uterine arteries. ***Conclusion:*** Short-term activation of pneumatic compression on maternal lower extremities could increase the AFI in women with isolated oligohydramnios.

Introduction

Oligohydramnios, defined as decreased amniotic fluid volume for gestational age, complicates 3–5% of pregnancies [1]. Oligohydramnios is associated with adverse pregnancy outcome [2]. A systematic review by Rabie et al. [3] evaluated adverse pregnancy outcomes in singleton pregnancies diagnosed with oligohydramnios. The review included 8,067 high risk pregnancies and 27,526 low-risk pregnancies. Among women with isolated oligohydramnios compared to normal AFI, the rates were higher for meconium aspiration syndrome, cesarean delivery for fetal distress, and admission to the neonatal intensive care unit.

A few investigational therapies have aimed to increase amniotic fluid volume, by means of maternal hydration, serial amnioinfusion, and administration of sildenafil citrate [4–7]. Maternal oral hydration has demonstrated more effectiveness than intravenous hydration, and hypotonic solutions have shown superiority to isotonic solutions [4]. A systematic review and meta-analysis concluded that maternal hydration could be a useful long-term strategy to increase amniotic fluid volumes [8]. It has been speculated that maternal hydration improves fetal urination by increasing maternal plasma volume and uteroplacental blood [4].

Pneumatic compression is commonly used to facilitate circulation in the lower extremities and thus prevents deep vein thrombosis. Activation of pneumatic compression increases venous return and leads to increased cardiac preload. Compression of the ankle and the calf of 50 mm Hg has been estimated to increase venous return by 107 mL of blood [9]. The improvement in venous return is reflected in increased central venous pressure, pulmonary artery pressure, and stroke volume [10]. The aim of this study was to examine the efficacy of pneumatic compression of the maternal lower extremities in increasing amniotic fluid volume in pregnancies with isolated oligohydramnios. We hypothesized that the use of pneumatic compression of the lower extremities would lead to increased maternal venous return and stroke volume, which would improve uteroplacental blood flow. Enhancement in fetal oxygenation would result in improved fetal renal blood flow and increased urinary output.

Methods

This prospective study was conducted in the Department of Obstetrics and Gynecology at the Galilee Medical Center from August 2022 to March 2023. The study was approved by the Local Helsinki Committee (NHR-21-151). All the women gave their consent after receiving information from the investigators. Our study protocol was prospectively registered at ClinicalTrials.gov; NCT05474326.

Women with a diagnosis of isolated oligohydramnios (AFI <5 cm) after 32 weeks of gestation were invited to participate. The exclusion criteria were fetal renal abnormalities, major fetal malformations, multiple pregnancy, fetal growth restriction, and rupture of membranes. Data regarding maternal and pregnancy characteristics were collected, including maternal age, gravity, and parity, and gestational age at the diagnosis of oligohydramnios. The pneumatic compression device (Kendall SCD™ 700 Smart Compression™ System) was applied to both the lower extremities and sequentially inflated for 1 h. On successive cycles, the controller automatically adjusts its operating parameters to maintain a set pressure of 45 mm Hg. Study variables, including AFI and Doppler studies, both maternal and fetal, were measured before and after application of a sequential compression device (SCD), such that each woman served as her own control. The same investigator assessed AFI and performed all the Doppler studies.

Several parameters were measured immediately before and after the utilization of SCD. Pulsed wave high-resolution color Doppler ultrasonography (Samsung Co., HERA W10, South Korea) was used to identify and to obtain blood flow velocity waveforms from the following vessels: maternal uterine arteries, a free loop of the umbilical cord, the middle cerebral artery, and the renal artery. Regarding the maternal uterine arteries, the sample volume was positioned 1 cm downstream from the apparent crossover of the uterine and external iliac arteries. Regarding the free loop of the umbilical cord, the sample volume was equivalent to the width of the vessel and was located at its center. Regarding the middle cerebral artery, the sample volume was placed immediately after its origin, at the center of the vessel. As for the renal artery, the sample volume was located immediately after its origin from the descending aorta. For all the vessels, the pulsatility index was calculated with the mean of at least four consecutive waveforms used for analysis.

During the application of the SCD, fetal urinary production was measured. For volume calculation, we used the rotational virtual organ computer-aided analysis method. Bladder volume was measured at an interval of 5–10 min. An increase in fetal bladder volume was considered as fetal urine production. The following

Table 1. Background data of the study participants ($N = 21$)

Maternal age, years, median (IQR)	29 (26.5–32.0)
Gravity, median (IQR)	1 (1–2.5)
Parity, median (IQR)	1 (1–2)
Gestational age at intervention, weeks, median (IQR)	37.6 (37.0–39.4)
Gestational age at delivery, weeks, median (IQR)	39.4 (38.8–40.2)
Birthweight, g, median (IQR)	3,132.0 (2,835.0–3,382.5)
Intrauterine growth restriction, *n* (%)	2 (9.5)
1-min Apgar score, median (IQR)	9 (8–10)
5-min Apgar score, median (IQR)	10 (9–10)
Male fetus, *n* (%)	13 (61.2)
Cesarean delivery, *n* (%)	5 (23.8)

IQR, interquartile range.

formula was used to determine hourly fetal urine production: (second larger bladder volume – first smaller bladder volume)/(time interval in minutes between the 2 measurements) × 60. Fetal urine production was compared between the first and last 30 min of SCD application.

Statistics

Statistical analysis was performed using SPSS version 26 (SPSS, Chicago, IL, USA). Continuous variables are presented as means and standard deviations, or as medians and interquartile ranges. Qualitative variables are presented as frequencies and percentages. The paired sample *t* test and Wilcoxon signed rank test were used, as appropriate, to evaluate the significance of the mean and median changes in study parameters before and after activation of the SCD.

For study sample determination, we assumed that SCD application in women with oligohydramnios would result in an increase in the mean AFI, from 4.3 to 6.3 cm, following the application of SCD [4]. Based on these estimates, using a 2-sided alpha of 0.05% and a beta of 0.10 (power of 90%), we calculated that a sample size of 19 women with isolated oligohydramnios would be needed to show the expected change in AFI.

Results

The study included 21 women with isolated oligohydramnios. All of them had normal second trimester fetal scan and normal repeated fetal anatomy scans due to the emergence of oligohydramnios. Moreover, rupture of membranes was ruled out by characteristic findings regarding both the women's histories and physical examinations. These included a history of leaking fluid, pooling of amniotic fluid on sterile speculum examination, and AmniSure immune-chromatography methods to detect trace amounts of placental alpha microglobulin-1 protein in vaginal fluid. Furthermore, serological tests for toxoplasma, cytomegalovirus, herpes virus, parvovirus, and syphilis revealed no recent infections for any of the women. The median maternal age was 29 years (26.50–32.00). The median parity was 1 (1–2). The women were recruited at a median gestational age of 37.60 weeks (37.00–39.40). Their characteristics are presented in Table 1.

After the application of SCD, the median AFI increased from 4.00 (3.62–4.50) to 6.08 (6.08–7.03) cm ($p < 0.001$). Figure 1 demonstrates changes in AFI of all the women. The changes in the median values of PI were not statistically significant for the bilateral uterine arteries, the umbilical artery, and the middle cerebral artery. The median PI of the renal artery decreased from 2.30 to 2.26, $p = 0.01$. Figure 2 shows median values of PI, before and after SCD, of the bilateral uterine, umbilical, middle cerebral, and renal arteries. No significant change was observed in the systolic to diastolic ratio or peak systolic velocity of the vessels. The change in fetal urine production between the first and last 30 min of the SCD application was not statistically significant: median of 25.61 versus 22.15 mL/h/kg, $p = 0.92$.

Table 2 shows all the uteroplacental and fetal blood flow parameters that were examined, before and after the SCD was applied to the lower legs for 1 h. All the women tolerated the SCD application well, and no adverse effects were reported.

Discussion

This preliminary study demonstrated that the application of SCD on lower limbs can increase the AFI in pregnancies with isolated oligohydramnios in the third trimester. Furthermore, the increment AFI was coupled with changes in certain parameters of fetal blood circulation that could be related to the SCD mechanism of action.

SCD compresses intermittently the lower limbs from the foot upward, followed by a decompression cycle. SCD has been shown to increase venous return from the lower limbs, leading to increased cardiac preload. Bickel et al. [11] investigated the underlying cardiovascular mechanism induced by the activation of intermittent sequential pneumatic compression in healthy persons. They reported significant increases in cardiac output, stroke volume, and ejection fraction and a decrease in the total

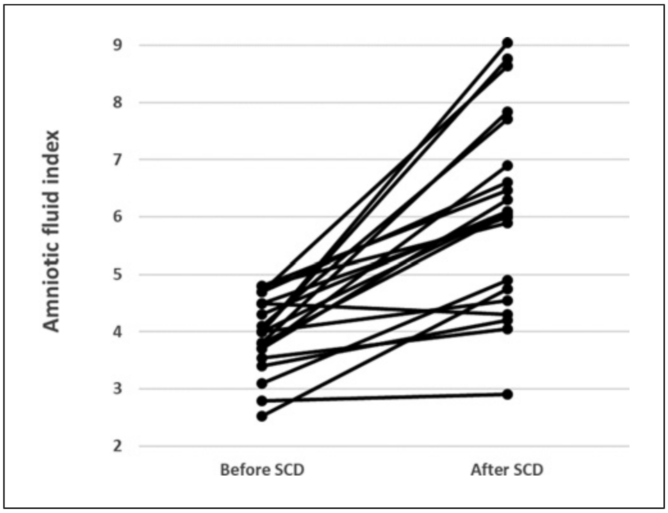

Fig. 1. The amniotic fluid index before and after application of the SCD on lower limbs. SCD, sequential compression device.

peripheral resistance. Therefore, it was concluded that pneumatic compression of the lower limbs increases cardiac output by raising preload and decreasing cardiac afterload. Another study of individuals with congestive heart failure showed similar findings, of improved cardiac output during SCD activation. Moreover, toward the end of SCD activation, cardiac function returned to baseline [12].

In our cohort, SCD activation did not result in a significant change in the median PI of the bilateral uterine arteries. A study by Flack et al. [4] on maternal hydration in 10 women with oligohydramnios reported increased uterine artery mean velocity after oral hydration of 2 L, over 2 h. Nevertheless, similar to our results, the median PI of the uterine artery did not change. During SCD activation, the median PI of the fetal renal artery decreased, while fetal urine production did not change. Nevertheless, after maternal hydration, no change was observed in the median PI of the renal artery nor in the fetal hourly urine production rate. In Flack et al.'s study [4], seven of 10 fetuses were small for gestational age (SGA) (defined as estimated fetal weight of <5th). In our cohort, only 2 of 20 newborns were SGA (both had actual birthweights of 5th percentile). A previous study showed that the median PI of the renal artery was higher for SGA than appropriate-for-gestational-age fetuses. A significant correlation was found between fetal blood oxygen deficit (as determined by cordocentesis) and increased renal artery pulsatility index [13]. Possibly, SGA fetuses differ from appropriate-for-gestational-age fetuses in their responses to techniques that attempt to improve uteroplacental blood flow, such as maternal hydration and lower limb compression. We calculated the sample size for our study by considering the expected alterations in AFI before and after application of the SCD. Our hypothesis was that an increase in AFI could be related to improvement in uterine and fetal renal blood flow. To detect significant changes in maternal and fetal Doppler, larger studies are needed, with an adequately powered sample size. Although SCD is commonly used to prevent deep vein thrombosis in pregnant women, lower limb compression by SCD was previously shown to decrease the incidence of maternal hypotension in women receiving epidural anesthesia during term labor [14]. A Cochrane Review that included 11 studies concluded that lower limb compression is a safe and effective option in preventing maternal hypotension after spinal anesthesia for cesarean section (relative risk of 0.61, 95% CI 0.47–0.78) [15].

Several experimental interventions have been reported as increasing amniotic fluid volume in oligohydramnios. In a meta-analysis of 16 studies including 1,121 pregnancies, maternal hydration was found to be a potential long-term strategy for increasing AFI in cases of idiopathic oligohydramnios. No reported harms were noted, but the impact on perinatal outcomes could not be evaluated. Improved outcomes were noted when the treatment approach involved a combination of intravenous hydration for 1 day and oral hydration for at least 14 days with hypotonic fluids [8]. A randomized controlled study by Vahid Dastjerdi et al. [6] compared the effectiveness of fluid therapy versus fluid therapy and sildenafil administered during 6 weeks in women with borderline oligohydramnios. After the intervention, no change in AFI was found, nor did pregnancy outcomes differ between the arms of the study. Laboring women with oligohydramnios are at risk of cesarean delivery for fetal distress; and their infants are at risk for low Apgar score, admission to the neonatal intensive care unit and meconium aspiration syndrome [3]. Prophylactic interventions during labor in women with oligohydramnios are limited. Future studies should examine, in women with oligohydramnios, the effect of SCD activation during labor, on maternal and neonatal outcomes. This intervention could have a double role: prevention of deep vein thrombosis during prolonged immobility and increasing amniotic fluid volume in laboring women with oligohydramnios.

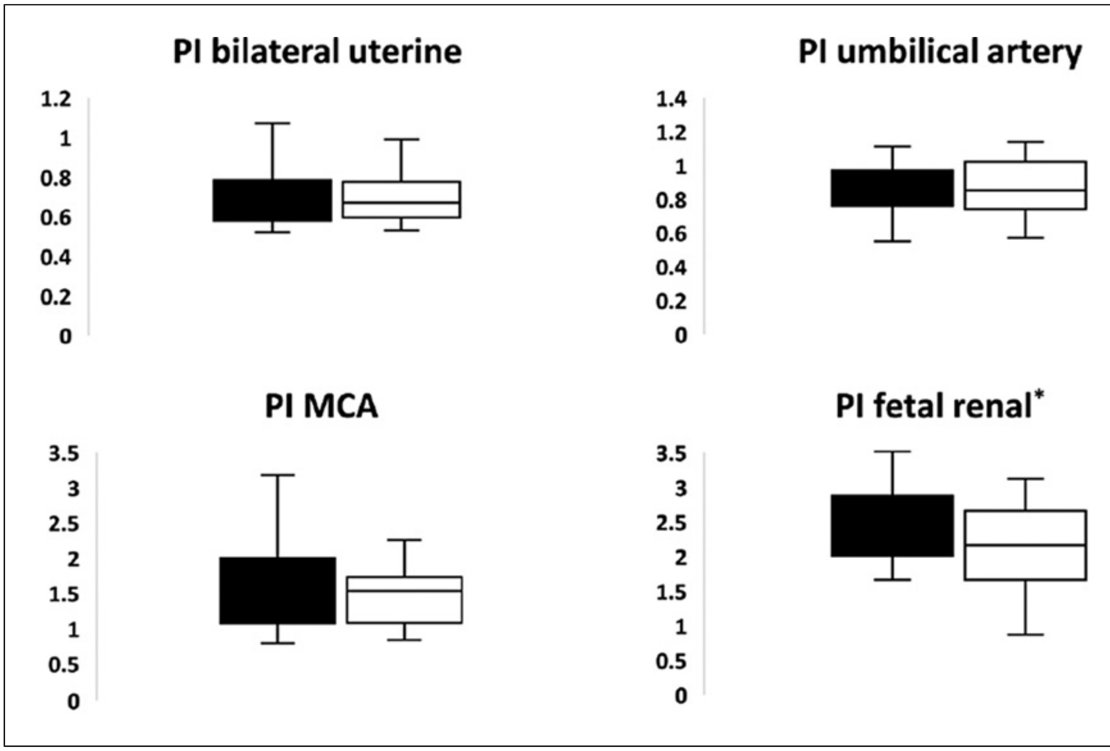

Fig. 2. The box plot depicts the median and IQR for uteroplacental and fetal blood flow parameters before (black boxes) and after (white boxes) the application of a SCD on maternal lower legs. *$p < 0.05$. SCD, sequential compression device; PI, pulsatility index; MCA, middle cerebral artery.

Table 2. Amniotic fluid index, uteroplacental, and fetal blood flow parameters before and after the application of a SCD on the lower legs

	Pre SCD	Post SCD	*p* value
AFI, cm, median (IQR)	4.00 (3.62–4.50)	6.08 (6.08–7.03)	<**0.001**
Fetal urine production, mL/h/kg, median (IQR)	25.61 (13.66–32.62)	22.15 (16.44–37.14)	0.922
Bilateral uterine arteries (average)			
PI	0.70 (0.70–0.79)	0.67 (0.59–0.78)	0.55
S/D	1.90 (1.78–2.02)	1.92 (1.76–2.07)	0.64
PSV	118.19 (79.15–15.49)	103.90 (91.55–145.90)	0.64
Umbilical artery			
PI	0.86 (0.76–0.97)	0.85 (0.74–1.02)	0.75
S/D ratio	2.42 (2.11–2.50)	2.38 (2.06–2.76)	0.89
PSV	47.92 (42.14–55.07)	45.96 (39.95–55.61)	0.72
Middle cerebral artery			
PI	1.37 (1.08–2.00)	1.53 (1.11–1.76)	0.44
S/D ratio	3.84 (2.89–5.50)	3.96 (2.96–5.96)	0.82
PSV	61.03 (45.57–68.66)	58.46 (58.46–66.39)	0.86
Renal artery			
PI	2.30 (2.01–2.88)	2.26 (1.68–2.71)	**0.01**
S/D ratio	5.37 (5.24–10.17)	6.05 (4.47–13.04)	0.32
PSV	49.00 (40.89–54.51)	45.05 (36.15–50.80)	0.15

SCD, sequential compression device; AFI, amniotic index; PI, pulsatility index; PSV, pulsatility index; S/D, systolic/diastolic.

Strengths and Limitations of the Study

To our knowledge, this is the first study to examine the effect of lower limb compression by the application of a sequential pneumatic compression device on oligohydramnios. Several maternal and fetal variables were measured using Doppler studies to investigate the effect of such intervention on hemodynamics. Our study suggests novel findings of short-term improvement in amniotic fluid volume. Nevertheless, several limitations must be acknowledged. Due to the small number of women, the study was not powered to examine changes in all the maternal and fetal Doppler parameters assessed. Moreover, we did not include a control group of women with normal AFI.

To conclude, short-term activation of pneumatic compression on lower extremities could increase the AFI in women with isolated oligohydramnios. Larger studies are needed to confirm our results and to investigate the hemodynamic effects, both of the mother and the fetus in such intervention. Such studies should explore the durability of our findings and determine the optimal frequency of compressions, pressure levels, and intervals required for the treatment.

Statement of Ethics

Our study was performed in compliance with the Declaration of Helsinki. The protocol of the study was approved by the Local Institutional Review Board (Helsinki Committee) of the Galilee Medical Center, Nahariya, Israel (date of approval November 24, 2021, number of approval NHR-21-151). The study was registered prospectively at ClinicalTrials.gov (NCT05474326). Written informed consent was obtained from all the participants.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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This study did not receive funding from any source, commercial, or otherwise.

Author Contributions

Inshirah Sgayer: study design, acquisition of data, drafting the manuscript, and critical review of the manuscript. Maya Frank Wolf: data analysis and drafting the manuscript. Susana Mustafa Mikhail: interpretation of data and critical review of the manuscript. Lior Lowenstein: substantial contribution to study design and critical review of the manuscript. Marwan Odeh: study design, acquisition of data, and drafting the manuscript. All authors agree for all aspects of the work and have approved the final version for publication.

Data Availability Statement

All data analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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