The Changes in Doppler Indices of Fetal Ductus Venosus and Umbilical Artery After Amnioinfusion for Women With Preterm Premature Rupture of Membranes Before 26 Weeks' Gestation

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SUMMARY

Objective: To investigate the changes in Doppler indices of the fetal ductus venosus (DV) and umbilical artery (UMA) after amnioinfusion in pregnant women with preterm premature rupture of membranes (pPROM). Pregnancies with pPROM and severe oligohydramnios cause sequelae in newborns and mothers.

Materials and Methods: This cross-sectional study included a group of 25 patients with pPROM before 26 weeks' gestation. Color Doppler imaging was used to measure the impedance index and quantitative blood flow in the DV and systolic/diastolic ratio (S/D) of the UMA before and 30 minutes after the end of amnioinfusion. The following velocity parameters were measured: (1) DV peak systolic velocity; (2) DV time-averaged velocity; (3) DV maximum forward velocity during atrial contraction; (4) DV S/D; (5) DV pulsatility index (PI); (6) DV Pourcelot's resistance index (RI); (7) fetal heart rate; and (8) UMA S/D.

Results: Twenty-one of the 25 patients underwent a total of 27 amnioinfusions. The mean PI and RI of the DV, and S/D of the DV and UMA decreased significantly after amnioinfusion (PI, 0.75 ± 0.24 *vs.* 0.60 ± 0.18, $p = 0.009$; RI, 0.60 ± 0.15 *vs.* 0.50 ± 0.13; DV S/D, 3.07 ± 1.81 *vs.* 2.13 ± 0.66, $p = 0.008$; UMA S/D, 3.58 ± 0.87 *vs.* 2.88 ± 0.62, $p = 0.001$).

Conclusion: Amnioinfusion increases the space for the fetuses and reduces the impedance of the fetoplacental circulation. Improvements in DV and UMA flow may benefit fetuses suffering severe oligohydramnios in mid-pregnancy. [*Taiwan J Obstet Gynecol* 2009;48(3):268–272]

Key Words: amnioinfusion, Doppler, ductus venosus, preterm premature rupture of membranes

Introduction

Pregnancies with preterm premature rupture of membranes (pPROM) before 26 weeks and severe oligohydramnios are at significant risk of neonatal pulmonary hypoplasia, extremity abnormalities, perinatal morbidity and mortality, and maternal infectious morbidity. Severe oligohydramnios, defined as an amniotic fluid index

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(AFI) of 5 cm or less, is associated with a shorter pPROM-to-delivery interval, a higher risk of chorioamnionitis, and infectious neonatal outcomes, especially if detected during the second trimester. Conversely, adequate residual amniotic fluid volume connotes a better chance of a favorable perinatal and neurologic outcome.

Whether or not oligohydramnios in the second trimester affects fetal and fetoplacental blood flow is uncertain. Few studies have been published to date addressing this question. It has been suggested that cord compression in oligohydramnios may impair fetoplacental perfusion. Fisk et al [1] suggested that restoring amniotic fluid volume in human pregnancies complicated by severe oligohydramnios does not acutely alter the umbilical artery (UMA) pulsatility index (PI). However, acute changes in amniotic fluid volume which alter uterine artery PI have been demonstrated [2]. In post-term pregnancies, it has been suggested that oligohydramnios is not associated with a major redistribution of blood flow [3].

Severe oligohydramnios can potentially be ameliorated. Strategies have been devised to improve amniotic fluid volume in patients with second trimester pPROM and oligohydramnios. These include serial amnioinfusion, intracervical tissue sealants, gelatin sponge embolization, and an amniopatch. In 1983, Miyazaki and Taylor [4] described a technique of intra-amniotic saline instillation that was originally used in the treatment of repetitive variable decelerations in labor. Amnioinfusion seemed to be a safe and effective technique to improve the intrauterine milieu [5].

A preliminary study in 1978 concluded that the ductus venosus (DV) is a main distributor of oxygenated blood in fetal lambs [6]. A decrease in end-diastolic DV blood velocity has been reported during hypoxia in a fetal lamb model. The DV may, therefore, play an important role in maintaining a stable supply of oxygen to the fetal vital organs. Abnormal UMA blood flow waveforms indicate increased fetoplacental circulation impedance. Absent or reversed blood flow is indicative of severe placental insufficiency and, in conjunction with gestational age, may indicate the need for immediate delivery [7]. One could claim that the UMA is the most studied vessel in obstetrics. In fetal growth restriction resulting from impaired placentation, chronic fetal hypoxia is associated with centralization of blood flow to the vital organs, such as the brain, heart and adrenal glands, in order to maintain oxygenation.

The purpose of the study was to investigate whether acute alteration of amniotic fluid volume (amnioinfusion) affects the fetal DV and UMA parameters in women with pPROM and severe oligohydramnios lasting more than 4 days.

Materials and Methods

Between December 1998 and May 2000, 25 patients with singleton pregnancies and severe oligohydramnios arising from pPROM at < 26 weeks and lasting 4 days or longer were admitted to the perinatal unit at Kaohsiung Chang Gung Memorial Hospital and enrolled as the study group. Patients with fetal anomalies, twin gestation, maternal hypertensive disorders and diabetes were excluded. The diagnosis of rupture of the membranes was made by observing persistent vaginal pooling during sterile speculum examination, the nitrazine test, and serial ultrasonographic observation. Gestational age was established by the last menstrual period and confirmed by an ultrasonographic examination before 20 weeks. All patients were placed on hospital bed rest during the first week and received an initial 7-day course of antibiotic prophylaxis. Vaginal cultures were obtained and positive results were treated. Consenting women with persistent (> 7 days) oligohydramnios received an amnioinfusion to maintain an AFI > 10 cm.

Prenatal histories and delivery records were reviewed. The study was approved by the institutional review board at Chang Gung Memorial Hospital. In all cases, the AFI was < 5 cm before the infusion and > 10 cm without leaking after the infusion. All amnioinfusions utilized a transabdominal approach which required the insertion of a 20-gauge needle into the amniotic cavity under sonographic guidance. Warmed normal saline (37°C) was used as a liquid substitute. The speed of the infusion was about 25–40 mL/min.

An ultrasound color-coded Doppler machine (128XP; Acuson Mountain View, CA, USA) with a 3.5-MHz transabdominal probe was used to examine each patient before and after the amnioinfusion. A two-dimensional color flow mapping was combined with continuous Doppler velocimetry. For the pulsed Doppler mode, the spatial peak temporal average power output was less than 94 mW/cm. The specific audio cut-off filter was set at 125 Hz.

The following parameters were measured: (1) DV peak systolic velocity (DVP); (2) DV time-averaged velocity (TAMX); (3) DV maximum forward velocity during atrial contraction (DVM); (4) DV systolic/diastolic ratio (S/D); (5) DV pulsatility index (PI); (6) DV Pourcelot's resistance index (RI); and (7) fetal heart rate (FHR; beats per minute). Measurements were performed before and within 30 minutes of the end of the amnioinfusion. UMA S/D Doppler indices were also determined.

The results were recorded. The conditions of fetal breathing or body movement were excluded. All Doppler measurements were made by only one operator (T.Y.H.) and measured twice. The difference between the two

measurements was calculated with the use of the Cronbach α reliability coefficient. Paired sample *t* tests were used for statistical analysis. A two-tailed *p* value < 0.05 was considered to be statistically significant.

Results

All Doppler measurements were recorded before and within 30 minutes of the end of each amnioinfusion. The intraobserver variation, which was calculated with use of the Cronbach's reliability coefficient, was 0.908. Twenty-one subjects met the inclusion criteria for the study, and the four pregnancies with failed restoration of the AFI > 10 cm were excluded. The amnioinfusion was made at a median gestational age of 23.23 weeks (range, 17–26 weeks; Table 1).

In total, 27 amnioinfusions were performed. The median amnioinfusion time and volume were 15 minutes and 355 mL, respectively. The mean DV PI and RI, and the S/D ratio of DV and UMA (Figure) decreased significantly after amnioinfusion (PI, 0.75 ± 0.24 *vs.* 0.60 ± 0.18, $p = 0.009$; RI, 0.60 ± 0.15 *vs.* 0.50 ± 0.13; DV S/D, 3.07 ± 1.81 *vs.* 2.13 ± 0.66, $p = 0.008$; UMA S/D, 3.58 ± 0.87 *vs.* 2.88 ± 0.62, $p = 0.001$; Table 2). No changes in DVP (0.39 ± 0.13 *vs.* 0.34 ± 0.10 cm/s), DVM (0.16 ± 0.08 *vs.* 0.17 ± 0.08 cm/s), TAMX (0.32 ± 0.11 *vs.* 0.29 ± 0.09 cm/s), or FHR (153.47 ± 17.50 *vs.* 158.21 ± 16.23 beats per minute) were observed after the procedure (Table 2). There were no complications relating to amnioinfusion, such as uterine hypertonia, uterine rupture, or maternal cardiac/respiratory failure.

Discussion

The etiologies underlying severe oligohydramnios include fetal renal tract abnormalities or damage, placental insufficiency associated with impaired fetal growth, acute or chronic amniotic fluid leakage, or adverse effects of drugs such as prostaglandin synthetase inhibitors [8]. pPROM may account for 30% of premature births and is often the cause of oligohydramnios. It is further complicated by an increased risk of chorioamnionitis, pulmonary hypoplasia, unpredicted fetal distress, fetal demise or abruptio placenta. In the first or early second trimester, an absence or a severe lack of amniotic fluid may be associated with the compression triad.

Table 1. Summary of patient history, number and volume of amnioinfusion, and outcome

Patient	Age (yr)	GA at first amnioinfusion (wk)	Amnioinfusion, *n*	Median volume (mL)	GA at delivery (wk)	Outcome		
						Birth weight (g)	Apgar score at 1 min/ 5 min	Others
1	30	23	1	250	25	600	1/1	Chorioamnionitis
2	34	26	1	350	27	800	2/5	Chorioamnionitis
3	20	26	1	350	28	943	2/5	Chorioamnionitis
4	18	26	2	425	30	1,420	6/7	
5	27	22	2	350	28	1,213	6/9	
6	35	25	2	475	32	1,780	7/9	
7	33	17	3	370	37	2,164	3/6	
8	20	18	1	250	20	264	2/0	
9	28	26	2	450	40	1,730	7/8	
10	29	23	1	250	25	600	1/1	
11	30	24	1	300	27	1,000	2/5	
12	26	19	1	250	24	423	0/0	Chorioamnionitis
13	29	22	1	250	27	1,280	5/7	
14	22	21	2	300	27	1,240	4/7	
15	28	26	1	450	38	2,440	9/10	
16	30	26	1	560	33	1,840	2/6	
17	26	25	1	400	32	1,740	3/7	
18	27	25	1	400	27	880	2/0	Chorioamnionitis
19	34	17	1	250	38	3,480	9/10	Amniocentesis
20	36	26	1	350	31	1,520	6/7	
21	37	25	1	500	32	1,690	6/8	

GA = gestational age.

Pregnancy with oligohydramnios during labor is associated with early and variable decelerations. These variable decelerations are believed to result from umbilical cord compression. Severe oligohydramnios may result in umbilical cord compression, especially following pPROM. The presumed mechanism is that there is an obstruction of the umbilical vein after a short pause, during which placental pressure compliance is taken up and the pressure increase is transmitted back to the umbilical arteries, causing increased peripheral resistance.

Doppler ultrasonography allows the obstetrician to assess blood flow in both maternal and fetal vessels under various conditions in a minimally invasive way. Despite this, the hemodynamic condition of the fetus during severe oligohydramnios remains largely unknown. The findings of this study disclosed the changes in DV and UMA Doppler parameters in mid-trimester pregnancies with severe oligohydramnios before and after amnioinfusion. The DV is a main distributor of oxygenated blood in the fetus and is an important regulator of fetal circulation [9]. An increase in the S/D and the percentage of reverse flow with atrial contraction in the inferior vena cava, absence of end-diastolic flow in the UMA and umbilical vein pulsations have been described in fetuses with intrauterine growth retardation [10].

The effects of short-term changes in amniotic fluid volume on DV and UMA hemodynamics were studied in this research, and the results showed improvements in DV and UMA flow. Amniotic fluid volume plays an important role in pregnancy outcomes. Severe oligohydramnios in mid-pregnancy results in poor perinatal outcomes, including pulmonary hypoplasia, chorioamnionitis, and neonatal infection. Conversely, an adequate residual amniotic fluid volume is predictive of better perinatal and neurologic outcomes. Locatelli et al [11] reported pregnancies with pPROM-related oligohydramnios at <26 weeks' gestation in which serial amnioinfusions successfully alleviated oligohydramnios; this lead to a better perinatal outcome [11]. The median time between the onset of severe oligohydramnios and the amnioinfusion was 9.6 days (range, 2–21 days). The changes in flow observed with the amnioinfusion were less clinically relevant, since the procedure was generally diagnostic. This study aimed

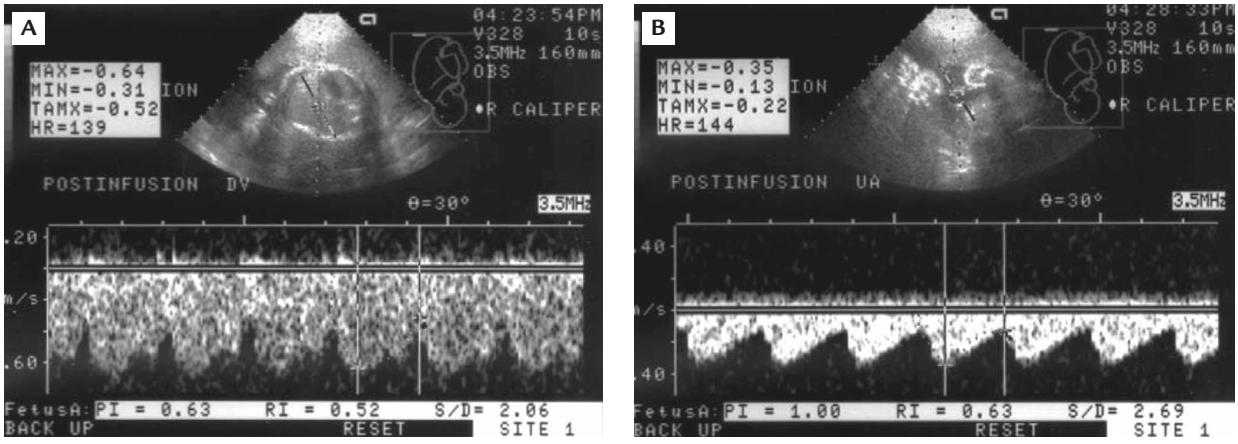

Figure. (A) Ductus venosus Doppler flow velocity. (B) Umbilical artery Doppler flow velocity.

Table 2. Ductus venosus (DV), umbilical artery (UMA) Doppler flow velocity measurements before and after amnioinfusion*

	Study		$p^{\dagger}$
	Before	After	
DVP (cm/s)	0.39±0.13	0.34±0.10	0.485
DVM (cm/s)	0.16±0.08	0.17±0.08	0.136
TAMX (cm/s)	0.32±0.11	0.29±0.09	0.617
DV PI	0.75±0.24	0.60±0.18	0.009
DV RI	0.60±0.15	0.50±0.13	0.003
DV S/D	3.07±1.81	2.13±0.66	0.008
FHR (beats/min)	153.47±17.50	158.21±16.23	0.213
UMA S/D	3.58±0.87	2.88±0.62	0.001

**Results are expressed as mean ± standard deviation; †paired sample t test, $p<0.05$ was statistically significant. DVP=DV peak systolic velocity; DVM=DV maximum forward velocity during atrial contraction; TAMX=time-averaged velocity; PI=pulsatility index; RI=Pourcelot's resistance index; S/D=systolic/diastolic ratio; FHR=fetal heart rate.*

to evaluate fetal DV and UMA hemodynamics before and after amnioinfusion. It was found that the PI of the DV, and the S/D of the DV and the UMA, decreased significantly after amnioinfusion. These results may reflect the fact that decreased venous flow velocity ratios in oligohydramnios-compromised fetuses are associated with decreased placental resistance and arterial redistribution after amnioinfusion. Dramatic changes in the fetoplacental circulation occurred in jeopardized fetuses, especially in venous vessels that are indicative of fetal deterioration. No statistical analysis of perinatal outcome in our pPROM group was performed because of the small sample size.

In conclusion, short-term hemodynamic changes in the DV and UMA have been demonstrated in response to the correction of amniotic fluid volume. Improvement of DV and UMA blood flow following serial amnioinfusion may be advantageous to fetuses suffering severe oligohydramnios after pPROM in mid-pregnancy.

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