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Relationship between higher intra-amniotic pressures in polyhydramnios and maternal symptoms

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ABSTRACT

Objectives: Our study aimed to analyze the differences in intra-amniotic pressures in patients with polyhydramnios with and without symptoms.
Study design: We recruited patients with pregnancies in which amnioreduction was performed for polyhydramnios in the Department of Fetal-Maternal Medicine at Nagara Medical Center between April 2017 and August 2018. Amnioreduction was performed for severe polyhydramnios with maternal symptoms [symptomatic group] or polyhydramnios without maternal symptoms [asymptomatic group] such as abdominal distension, dyspnea, or threatened premature labor. We measured the intra-amniotic pressure after every 200 ml volume reduction during the amnioreduction.
Results: A total of 27 patients who underwent amnioreduction were classified into symptomatic (66.7%, 18/27) and asymptomatic (33.3%, 9/27) groups. Gestational age, amniotic fluid index at the time of amnioreduction, and the volume of amniotic fluid removed were not significantly different between the symptomatic and asymptomatic groups [median 32.4 weeks vs. 33.1 weeks, median 38.0 cm vs. 39.0 cm, and median 1500 ml vs. 2500 ml, respectively]. However; the intra-amniotic pressure before amnioreduction was significantly higher in the symptomatic group than in the asymptomatic group [median 15.0 mmHg (range, 10–27) vs. 10.0 mmHg (range, 6.0–13); $p < 0.005$]. After amnioreduction, these pressures decreased significantly to median 9.0 mmHg (range, 5.0–13) ($p < 0.001$) in the symptomatic and 7.0 mmHg (range, 4.0–11) ($p < 0.05$) in the asymptomatic group. The median intra-amniotic pressure gradually decreased and reached a plateau during the amnioreductions in both groups.
Conclusions: With polyhydramnios, the intra-amniotic pressure was significantly higher in the symptomatic group than in the asymptomatic group. Therefore, uterine pressure tolerance might vary according to the individual. In addition, intra-amniotic pressure monitoring might enhance the safety during amnioreduction procedures to avoid drastic and potentially harmful pressure changes.

Introduction

Polyhydramnios, defined by an amniotic fluid index (AFI) >25 cm, is reported to show a prevalence of 1–2%. Polyhydramnios, which is primarily idiopathic, is divided into mild (AFI, 25–29.9 cm), moderate (AFI, 30–34.9 cm) and severe (AFI > 35 cm) conditions [1] and is associated with morbidities such as perinatal death, fetal abnormalities, and preterm birth [2]. Patients with polyhydramnios are usually asymptomatic; however, occasionally they will have some symptoms. Interestingly, we have encountered both symptomatic and asymptomatic patients who had identical AFIs.

Normally, the intra-amniotic pressure during pregnancy is believed to decrease exponentially with the advancing gestation, going from 9 mmHg at 10 weeks to 5 mmHg at 30 weeks [3]; however, it has not been shown to be significantly elevated in twin pregnancies [4]. In pregnancies affected by polyhydramnios, the intra-amniotic pressure is high, which correlates positively with the depth of the deepest fluid quadrant [4]. Amnioreduction (AR) is often performed to prevent preterm delivery and relieve maternal symptoms by decreasing the intra-amniotic pressure [5].

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The purpose of this study was to clarify the difference in intra-amniotic pressures in pregnancies complicated by polyhydramnios by analyzing serial intra-amniotic pressures during AR in women with and without symptoms.

Materials and methods

We included 27 pregnancies in which AR was performed for polyhydramnios at the Department of Fetal-Maternal Medicine, at Nagara Medical Center between April 2017 and August 2018. For pregnancies with polyhydramnios, we performed a detailed ultrasound assessment of the fetus and placenta and screening for gestational diabetes mellitus, and considered amniocentesis for fetal karyotype if chromosomal anomaly was suspected and screening for infection if congenital infection was suspected. For cases with mild and moderate polyhydramnios without maternal symptoms, no intervention was performed. Although prostaglandin inhibitors, such as indomethacin, may reportedly improve polyhydramnios, we have not used these because the treatment has not been established [6]. Our indications for AR included severe polyhydramnios (AFI > 35 cm) without maternal symptoms and polyhydramnios with maternal symptoms such as abdominal distension, dyspnea, and threatened premature labor with a shortened cervix (cervical length <2.5 cm) and regular uterine contractions. Tocolysis was performed by administering ritodrine hydrochloride or magnesium sulfate during the AR procedure. In cases of abdominal distension and dyspnea, we considered maternal symptoms as those causing marked limitations in activity, even during sub-normal activities such as walking short distances. Many of these patients admitted that they were comfortable only at rest. After local anesthesia using subcutaneous lidocaine injection was induced, AR was performed using a 16-gauge needle (Safeletcass NIC*16 × 2 1/2, NIPRO, Japan) under ultrasound guidance to avoid transplacental insertion. The insertion needle was connected to extension tubing, which was connected to an electronic vacuum pump and a drainage bottle (VD-1000; TOITU Corporation, Tokyo, Japan). The amniotic fluid was removed at a rate of about 100–125 ml/min [2]. The volume of amniotic fluid removed was situation-dependent, according to the maternal and fetal conditions, fetal and placental positions, and presence or absence of uterine contractions. Women were continuously monitored for symptoms such as persistent abdominal pain and low blood pressure and impairment of consciousness, which would signal a halt to AR. In addition, continuous fetal monitoring was conducted to detect persistent bradycardia, which might be a sign of placental abruption or amniotic fluid embolism, and to monitor the location of the fetus and placenta in relation to the AR needle. Any such concerns with the fetus would also signal a halt to AR. However, none of the patients had such maternal or fetal conditions and no patient had more than 3000 ml removed.

Intra-amniotic pressures were measured after each 200 ml was removed during the procedure. A saline-filled line was attached at one end to the hub of the needle and at the other end to a silicone stain-gauge transducer (DX-300; Nihon Kohden Corporation, Tokyo, Japan). Pressures were measured at the needle tip level as in our previous report [7] once they were stable for 10 s.

Written informed consent was obtained from all patients. This study protocol was approved by the Institutional Review Board of Nagara Medical Center.

We collected data on maternal characteristics and perinatal outcomes including: maternal age, parity, body mass index, cause of polyhydramnios, number of AR sessions, time interval between AR sessions, gestational age (GA) at AR and at delivery, volume of amniotic fluid removed, mode of delivery, birthweight, umbilical artery pH, amniotic fluid index at AR, intra-amniotic pressure during AR, and complications of AR.

The Mann-Whitney *U*-test, Wilcoxon rank sum test and Fisher`s exact test were used to compare the data. A p-value of <0.05 was considered statistically significant. Statistical analyses were performed using Easy R (EZR, the R Foundation for Statistical Computing, Vienna, Austria) for Windows [8].

Results

A total of 27 AR cases were included and classified into symptomatic (66.7%, 18/27) and asymptomatic (33.3%, 9/27) groups. In the symptomatic and asymptomatic groups, the cause of polyhydramnios was classified as idiopathic in 33.3% (6/18) and 66.6% (6/9) of pregnancies, respectively; fetal structural anomalies were present in 38.8% (7/18) and 22.2% (2/9), respectively; fetal chromosomal abnormalities were present in 5.5% (1/18) and 11.1% (1/9), respectively; diabetes mellitus complicated 22.2% (4/18) and 0% (0/9) of the pregnancies, respectively (Table 1). No significant differences were observed in maternal age, parity, body mass index, cause of polyhydramnios, number of AR sessions, time interval between AR sessions, GA at delivery, mode of delivery, birthweight, or umbilical artery pH (Table 1).

The GA and AFI at AR and the volume of amniotic fluid removed were not significantly different between groups; however, the intra-amniotic pressure before AR was significantly higher in the symptomatic group than it was in the asymptomatic group [median 15.0 mmHg (range, 10–27) vs. median 10.0 (range, 6.0–13), respectively; $p < 0.005$]. After AR, these pressures decreased significantly to median 9.0 mmHg (range, 5.0–13) ($p < 0.001$) in the symptomatic and 7.0 mmHg (range, 4.0–11) ($p < 0.05$) in the asymptomatic group (Table 2). In the comparison of changes in the median pressure during AR, we judged that there was a plateau if there was no significant difference in two consecutive intra-amniotic pressure readings. The median intra-amniotic pressure gradually decreased and reached a plateau during AR in both groups (Fig. 1).

The complications of AR [9] were delivery within 48 h. after drainage in 6.2% (1/18) and transient bleeding from the insertion site in 27.7% (5/18) in the symptomatic group and transient bleeding from the insertion site in 12.5% (1/9) in the asymptomatic group. There was no significant difference

Table 1
Characteristics and outcomes in the symptomatic and asymptomatic groups.

Variables		Symptomatic group (n = 18)	Asymptomatic group (n = 9)	p value
Age (years)[a]		32 (22–44)	30 (28-33)	0.568
Primipara (%)[b]		33.3 (6/18)	33.3 (3/9)	1
BMI (kg/m^2)[a]		20.0 (18.1–26.6)	21.2 (21.2–22.7)	0.194
Cause of AR (%)[b]	Idiopathic	33.3 (6/18)	66.6 (6/9)	0.127
	Fetal structural anomaly	38.8 (7/18)	22.2 (2/9)	0.667
	Fetal chromosomal abnormality	5.5 (1/18)	11.1 (1/9)	1
	Diabetes mellitus	22.2 (4/18)	0 (0/9)	0.268
Number of AR sessions[a]		2.5 (1.0–5.0)	1.0 (1.0–3.0)	0.078
Time interval between sessions (days)[a]		14 (6.0–32)	21 (11–32)	0.514
GA at delivery (weeks)[a]		36.4 (29.3–40)	35.7 (35.7–38.4)	0.742
Cesarean delivery (%)[b]		33.3 (6/18)	22.2 (2/9)	0.676
Birthweight (g)[a]		2873 (1302–4190)	2393 (1689–2758)	0.115
Umbilical artery pH[a]		7.31 (7.29–7.35)	7.25 (7.21–7.27)	0.1

AR: amnioreduction; GA: gestational age; BMI: body mass index.
[a] Mann–Whitney *U* test was used to compare the data between groups – results are presented as medians (ranges).
[b] Fisher's exact test was used to compare the data between the groups.

Table 2
GA and AFI at AR, volume of amniotic fluid removed, and intra-amniotic pressure before and after AR in the symptomatic and asymptomatic groups.

Maternal symptoms		Symptomatic group (n = 18)	Asymptomatic group (n = 9)	p value[b]
GA at AR (weeks)		32.4 (23.1–37.0)	33.1 (29.0–34.4)	0.59
AFI before AR (cm)		38.0 (28.0–50.6)	39.0 (35.0–61.6)	0.401
Volume removed (ml)		1500 (800–2000)	2500 (1000–2800)	0.104
Intra-amniotic pressure (mmHg)	Before AR	15.0 (10–27)	10.0 (6.0–13)	0.001
	After AR	9.0 (5.0–13)	7.0 (4.0–11)	0.015
	p value[a]	<0.001	0.0139	

GA: gestational age; AFI: amniotic fluid index; AR: amnioreduction.
[a] Wilcoxon rank sum test was used to compare the data before and after AR – results are presented as medians (ranges).
[b] Mann–Whitney *U* test was used to compare the data between groups – results are presented as medians (ranges).

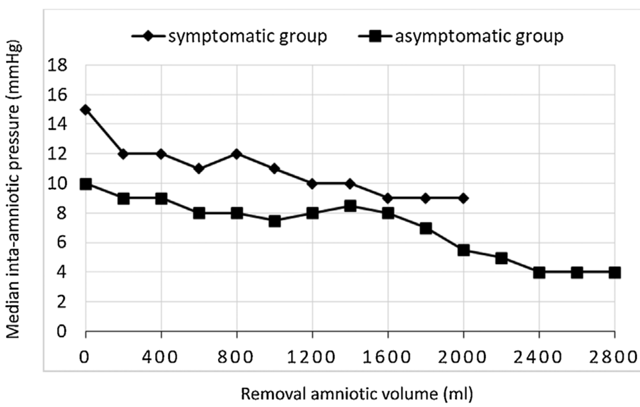

Fig. 1. Median intra-amniotic pressure changes during amnioreduction in the symptomatic (n = 18) and asymptomatic groups (n = 9).

Table 3
Complications of AR in the symptomatic and asymptomatic groups.

Complication	Symptomatic group (n = 18)	Asymptomatic group (n = 9)	p value[a]
PPROM ≦48 h after drainage (%)	0 (0/18)	0 (0/9)	1
Delivery ≦48 h after drainage (%)	6.2 (1/18)	0 (0/9)	1
Placental abruption (%)	0 (0/18)	0 (0/9)	1
Chorioamnionitis (%)	0 (0/18)	0 (0/9)	1
Fetal death ≦48 h after drainage (%)	0 (0/18)	0 (0/9)	1
Bleeding from the insertion site (%)	27.7 (5/18)	12.5 (1/9)	0.628
Peripheral organ injury (%)	0 (0/18)	0 (0/9)	1

AR: amnioreduction; PPROM: preterm premature rupture of membranes.
[a] Fisher's exact test was used to compare the data between the groups.

between the groups (Table 3). Regarding bleeding from the insertion site, one patient in the symptomatic group developed a hematoma; however, the other cases of bleeding stopped quickly and spontaneously. Chorioamnionitis was pathologically assessed in cases with maternal fever, elevated white blood cells and C-reactive protein, and fetal tachycardia. However, there were no cases of confirmed chorioamnionitis.

Comment

Polyhydramnios is defined as an excess of amniotic fluid that can lead to harmful symptomatology for the mother. In our patients with polyhydramnios, there were symptomatic and asymptomatic patients, which might suggest that uterine pressure tolerance is unique. No previous authors have provided a pathophysiological analysis of the relationship between the extent of polyhydramnios and maternal symptoms. Thus, we measured and analyzed the intra-amniotic pressures during AR and found that the intra-amniotic pressures before the ARs were high. The pressures were significantly higher in patients with symptoms compared to those without, when the groups were similar in GA and AFI. We concluded that the intra-amniotic pressure in polyhydramnios might reflect uterine pressure tolerance.

This study showed that uterine pressure tolerance might vary according to the individual. The uterus comprises smooth muscle. Leiomyoma and adenomyosis, which cause lesions that can exist within the myometrium, could have an effect on uterine pressure tolerance by limiting the extension of the uterus and altering maternal symptoms by their degeneration with pregnancy [10,11]. However, in this study, none of the patients had either of these conditions. Uterine pressure tolerance, therefore, might depend on individual constitutions and other factors. For example, even without an intra-amniotic pressure increases, the larger uterus might squeeze the surrounding organs and cause maternal symptoms, such as abdominal distension and dyspnea, particularly if the maternal physique is small. These could be the subject of a future study.

A previous report has also shown that in pregnancies with polyhydramnios, the intra-amniotic pressure was high and decreased after AR [4]. Our study confirmed that the pressure gradually decreased and reached a plateau during AR. It is possible that AR only needs to continue long enough to remove amniotic fluid volume until the reference intra-amniotic pressure for relieving maternal symptoms and improving threatened premature labor is reached. However, it is necessary to determine the reference intra-amniotic pressure while considering the individual differences in uterine pressure tolerance.

In this study, complications included delivery within 48 h. after AR and bleeding from the insertion site. Delivery was caused by an induction of labor and bleeding did not affect the subsequent pregnancies. AR is reportedly associated with a 1–3% complication rate, and includes problems such as preterm labor, premature rupture of membranes, placental abruption, and infection [12,13]. Although a previous report recommended restricting the volume removed to a maximum of 5000 ml, considering the potential for complications [12], there is no consensus regarding the maximum volume of amniotic fluid that can be removed. Our hypothesis is that sudden decreases in intra-amniotic pressure might lead to placental abruption. Therefore, intra-amniotic pressure monitoring might be a positive predictor of adverse events, and non-invasive monitoring of the speed and extent of pressure changes could enhance the likelihood of safely removing the excess amniotic fluid.

We acknowledge that this study had several limitations. First, the number of patients included was small. Second, we did not include a subgroup comparison in this study. Further detailed and thorough subgroup comparison studies might provide further insights into the pathophysiology of polyhydramnios, the factors that affect uterine pressure tolerance and the efficacy of intra-amniotic pressure monitoring during AR.

In conclusion, uterine pressure tolerance may vary according to the individual. Therefore, the indications for AR should be carefully selected, considering not only AFI but also maternal symptoms, the clinical risk of polyhydramnios, and the risk of the complications of AR. Well-trained experts should perform AR. In addition, intra-amniotic pressure monitoring might be valuable for predicting adverse events during AR and enhance the safety during the procedure because the technique is non-invasive and easily available.

Disclosure of potential conflicts of interests

The authors declare that there are no conflicts of interest regarding the publication of the article.

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