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Research Article

ANTEPARTUM TRANSABDOMINAL THERAPEUTIC AMNIOINFUSION FOR IDIOPATHIC OLIGOHYDRAMNIOS

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ABSTRACT

Introduction: Severe oligohydramnios can cause fetal pulmonary hypoplasia, cord compression and hence poor pregnancy outcome. Theoretically antepartum therapeutic amnioinfusion can prevent the complication.

Materials and methods: It is a prospective case control study conducted from July 2015 to December 2018. Women with unexplained oligohydramnios from 16weeks to 34weeks of pregnancy were included the study. Therapeutic transabdominal amnioinfusion (TAI) was offered to them. Patients who opted for amnioinfusion were recruited as cases (n=45) and patients who opted for conservative management were recruited as controls (n=50).

Results: Three women in case group were detected to have fetal malformations and hence were excluded from further analysis. Mean gestational age at presentation was significantly earlier in cases than controls (25.78±4.86 weeks vs 33.36±3.48 weeks, p<0.001). One TAI was done in 40(88.9%) patients, two in four (8.9%) women and three in one (2.2%) woman. Volume of infused fluid ranged from 22ml to 650ml. Mean latency period was significantly more in cases as compared to controls (6.39±6.05weeks vs 3.19±3.09 weeks, p=0.013). Mean gestational age at delivery was significantly earlier in cases than controls (32.18±6.18weeks vs. 36.44±1.72weeks, p=0.001). Vaginal delivery occurred in 29(69%) cases as compared to 19(38.1%) in control group (p=0.003). There was no statistically significant difference in perinatal mortality in both groups.

Conclusion: Transabdominal amnioinfusion during pregnancy in idiopathic severe oligohydramnios can be done as early as sixteen weeks. This may help in diagnosing fetal malformation. It may prolong pregnancy from six to twelve weeks and aid in vaginal delivery.

INTRODUCTION

Amniotic fluid plays a vital role in normal development of fetus at all stages of pregnancy. Volume of amniotic fluid increases gradually from 12weeks till 34-36 weeks of gestation, remains constant till 40 weeks and then starts decreasing[1]. It contains growth factors and antimicrobial factors which help in optimal growth of fetus in a sterile environment. Normal volume of amniotic fluid is also important for fetal pulmonary maturity, visualisation of fetal anatomy by ultrasound and for cushioning the fetus to prevent umbilical cord compression[2].

Oligohydramnios has been defined as a decrease in volume of amniotic fluid surrounding the fetus with amniotic fluid index (AFI) measuring less than 5cm or deepest vertical pocket (DVP) measuring less than 2cm on ultrasound [3, 4]. Its incidence has been variably reported as 1-5%. Various causes of oligohydramnios are uteroplacental insufficiency, maternal conditions like vascular diseases and chronic hypertension, intake of drugs like NSAIDS, leaking per vagina, poor maternal water intake, summer season, certain ethnic groups, fetal renal agenesis or bladder outlet obstruction [5]. In a subset of women with oligohydramnios, no identifiable causative factors can be identified thereby eluding prevention and treatment. If untreated, oligohydramnios can lead to pulmonary hypoplasia, compression deformities, meconium aspiration syndrome in neonate and still birth.

Our aim was to study the effect of transabdominal therapeutic amnioinfusion in idiopathic oligohydramnios during pregnancy, excluding labor.

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Experimental Section

The study was randomised control trial conducted from July 2015 to December 2018 in the Department of Maternal and Reproductive Health, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow. Women with unexplained oligohydramnios were included in the study. Therapeutic transabdominal amnioinfusion (TAI) was offered to them after detailed counselling by a team of obstetrician paediatrician and geneticist. Patients who opted for amnioinfusion were recruited as cases and patients who opted for conservative management were recruited as controls.

All patients were screened for genitourinary infections before the procedure and were treated before TAI. Nitroglycerine patch (10mg) was applied 30minutes prior to the procedure in all cases. After informed consent, TAI procedure was done under continuous ultrasound guidance using 20gauge spinal needle with aseptic precaution in cases. No anesthesia was used for the procedure. After the initial aspiration of 1 ml and discarding, 10-20 ml of amniotic fluid was aspirated initially and sent for fetal karyotype and toxoplasma, cytomegalovirus and rubella PCR analysis. Injection Cetriaxone 500mg was added to 500ml of ringer lactate solution just prior to the procedure. Subsequently, ringer lactate solution at 37.4 degree centigrade was infused using 50ml syringe and three way tap. All patients were given Capsule Amoxycillin 500mg thrice a day for five days from the day of procedure. Aim of infusion was to achieve deepest vertical pocket of 4cm. Care was taken not to exceed volume of infusion beyond 50th centile for POG and rate of infusion was maintained between 25 to 30ml/minute. Detailed ultrasound was done subsequently to look for congenital malformations in the fetus. Women with fetal or placental abnormalities were subsequently excluded from further analysis. USG was repeated at interval of 24hours, one week and subsequently fortnightly to look for recurrence of oligohydramnios. Repeat TAI was done if oligohydramnios was observed till 34weeks. Complications, if any, were noted.
In controls, women were followed up at weekly interval. Fetal surveillance measures like daily fetal kick count, non stress test and biophysical profile were used where applicable. 6mg intramuscular injection dexamethasone was given 12hours apart for four doses for fetal lung maturity after 28weeks and injection Magnesium sulphate was given for fetal neuroprotection when delivery occurred between 26 to 34weeks. All the mothers were followed up and delivered at our hospital. Placenta was sent for histopathological examination in all cases. Maternal and neonatal outcome was noted in both the groups.

Exclusion criteria were presence of PPROM, abruptio placentae, fetal growth restriction with or without umbilical artery doppler abnormalities, twin gestation, chorioamnionitis, prolonged use of NSAIDS, fetal renal malformations or aneuploidy.

Statistical Analysis

Normality of the continuous variable was assessed and a variable was considered normally distributed when Z value of the skewness was ±3.29. Continuous variables were presented in mean ± standard deviation (if normally distributed) and median "inter-quartile range" (if non-normally distributed) while categorical variables in frequency (%). Means was compared between cases and controls using independent samples t test while non normal distribution were compared using Mann Whitney U test. To compare the proportions between cases and controls, Fisher exact test was used. A p value <0.05 was considered as statistically significant. Data were analyzed using statistical package for social sciences version 23 (SPSS-23, IBM, Chicago, USA).

RESULTS AND DISCUSSION

Total of 95 participants with 45 cases and 50 controls were included in the study. Table 1 shows the distribution of the demographic and clinical parameters of both cases and controls. Mean and median age of the participants was 26.51±4.36 years and 25.0 years with equal distribution between cases and controls (p>0.05). Two cases conceived following in vitro fertilisation technique. Medical disorders encountered in mothers were gestational diabetes mellitus in 3(6.7%) cases and 15 (30%) controls, hypothyroidism in 1(2.2%) case and 6(12%) controls and intrahepatic cholestasis of pregnancy in 7(14%) controls while none in cases.

Mean gestational age at presentation was significantly earlier in cases than controls (25.78±4.86 weeks vs 33.36±3.48 weeks, p<0.001). Total 51 sittings of trans-abdominal amnioinfusions were done with one TAI in 40(88.9%) patients, two in four (8.9%) and three in one (2.2%) patient. Pre-infusion mean DVP was 1.6cm which rose to mean DVP of 3.9cm post-infusion. Volume of infused fluid ranged from 22ml to 650ml. Out of 45 cases, three cases were diagnosed to have fetal malformations, one each of unilateral multicystic kidney with contralateral shrunken kidney, unilateral renal agenesis with contralateral shrunken kidney and multiple amniotic band syndrome and hence were excluded from further analysis. None of the foetuses had abnormal karyotype or fetal infections of TORCH group.

Mean latency period i.e. period of TAI to delivery was significantly more in cases as compared to controls (6.39±6.05weeks vs 3.19±3.09 weeks, p=0.013). Mean gestational age at delivery was significantly earlier in cases than controls (32.18±6.18weeks vs. 36.44±1.72weeks, p=0.001). Vaginal delivery occurred in 29(69%) cases as compared to 19(38.1%) control group (p=0.003). Most common indication of LSCS was catergory III CTG (4/15) followed by meconium stained liquor (1/9) in study groups (case/control).

Mean birth weight was significantly less in cases as compared to controls (1.87±1.01kg vs 2.72±0.41kg, p<0.001). 5(11.9%) neonates in case group and 6(12%) in control group required admission in NICU. 2(4.8%) neonates from case group and one (2%) from control group had pulmonary hypoplasia. One neonate requiring three sittings of TAI was diagnosed to have renal failure at birth. There were 2(4.8%) perinatal mortalities in case group, one due to renal failure at birth and another due to extreme prematurity and early onset sepsis. There was no perinatal mortality in control group. There were two cases of compression deformity (congenital talipes equino varus) in control group.

Complications observed were leaking per vaginum within 7 days of procedure (3, 7.14%), intrauterine demise (3, 7.14%) and chorioamnionitis (1,2.4%).

Table 1 Distribution of clinical variables between the study groups

	Study Groups				
	Treatment (n=42)		Controls (n=50)		P Value
	Mean ±SD	Median (Range)	Mean ±SD	Median (Range)	
Mothers Age (years)	26.13± 4.60	24.9 (20-30)	26.78± 3.72	24.2 (18-32)	0.514
Fetal age at presentation (in weeks)	25.78 ±4.86	27 (17-32.5)	33.36 ±3.48	34 (25-38)	**<0.001**
#Latency period (weeks)	6.39 ±6.05	4.6 (0.43-20)	3.19 ±3.09	2 (0.29-12)	**0.013**
POG at delivery (weeks)	32.18 ±6.18	34 (18-39)	36.44 ±1.72	37 (32-40)	**0.001**
Birth weight (Kg)	1.87 ±1.01	2.1 (0.3-3.6)	2.72 ±0.41	2.8 (1.3-3.6)	**<0.001**

#Independent samples t test / #Mann Whitney U test used, SD =Standard deviation, Range =Minimum –Maximum. **p<0.05 significant**

DISCUSSION

Procedure of amnioinfusion has been described in published English literature since last four decades[6]. However its utility was limited to labour by transcervical route for dilution of amniotic fluid in cases of meconium stained liquor[7]. Antepartum use of transabdominal amnioinfusion has also been described for optimisation of fetal visualisation in cases of oligohydramnios[8]. Antepartum therapeutic amnioinfusion in cases of oligohydramnios has been postulated to decrease the risks associated with pulmonary hypoplasia thereby improving perinatal survival.

In our study, only cases with idiopathic oligohydramnios were included similar to Kozinsky *et al* [9].TAI was done earliest at 17weeks in our series. Kozinsky *et al*, Hsu *et al* and Chen *et al* also reported the earliest infusion in the range of 16 to 19weeks gestation[9, 10, and 11]. But the maximum POG at which they did the procedure was 26weeks because the foetuses had reached the period of viability after that. In our study, maximum POG at which TAI was done was 32weeks 3days which is similar to that reported by Turhan *et al* and Gramellini D *et al* [12,13]. The rationale was to prolong the period of gestation beyond 34weeks after which neonatal morbidity and mortality reduces significantly. The mean gestational age at presentation was significantly later in the control group than in cases. Women who presented in third trimester were more likely to opt for expectant management than women who presented in second trimester with oligohydramnios.

Time interval between TAI and delivery (latency period) was statistically significantly prolonged in cases as compared to controls. Similar findings have been reported by other authors[12, 13]. Maximum latency period reported by Gramellini *et al* was 98days and Miyazaki *et al* was 103 days[14]. Maximum latency period achieved in our study was 140 days which is maximum in the published literature. Hence therapeutic amnioinfusion significantly prolonged the pregnancy in women who opted for it in our study as compared to those who opted out of it. 88.9% of women required single TAI which apart from prolonging pregnancy also helped in excluding fetal structural malformations, aneuploidy and infections. 40% of women who required more than one TAI for persistent oligohydramnios were diagnosed to have fetal renal failure at birth in our study. Similar finding has been reported by Hsu *et al* who also suggest that if TAI works well for the first time, it indicates favourable neonatal outcome in contrast to women who require more TAI. In latter cases chances of severe fetal renal disease is more and neonatal outcome is guarded. We observed bilateral CTEV in one fetus in control group.

TAI also aided in vaginal delivery in cases as compared to controls. Similar findings have been reported by Chhabra S *et al* who reported need of caesarean section in 18% of cases and 46% of controls[15]. Mean gestational age at delivery was earlier in our cases than controls. This could be due to early enrolment of cases than controls. Mothers who presented in second trimester with oligohydramnios had an inclination to chose TAI as compared to controls as they were far from term. Perinatal outcome was however similar in both the groups in terms of admission in NICU. Chhabra *et al* have reported perinatal mortality rate (PNMR) of 4% in cases and 18% in controls. Butt *et al* have reported a higher PNMR of 88% and neonatal mortality rate of 35% because most of their cases had multiple fetal abnormalities [15].

Incidence of chorioamnionitis was 2.4% in our study which is comparable to the study published by Fisk *et al* and Hsu *et al* [10, 16]. Incidence of fetal loss secondary to leaking PV and spontaneous abortion was 21.4%in our study which is lesser as compared to Kozinsky *et al* who reported 66.7% of their patients having spontaneous abortion.

This was a prospective case control study in which the patients were given the option of choosing the category of cases and control group. Hence, selection bias could have skewed the results. A randomised case control trial may provide more power to the study.

CONCLUSION

Antepartum transabdominal therapeutic amnioinfusion is an effective procedure for increasing the amniotic fluid index in patients with idiopathic oligohydramnios. Patients can be reassured that if a single TAI is successful in them, neonatal outcome is favourable. And for the women requiring multiple TAI, chances of fetal severe renal disease is high though the same may not be visible on antenatal ultrasound. Diagnosing and treating genitourinary infections prior to the procedure can reduce the risk of leaking per vaginum and spontaneous abortion in such cases. Prolonging pregnancy not only helps in preventing short term complications like pulmonary hypoplasia in newborn but also decreases the long term risks associated with prematurity.

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