The role of amino acid infusion in isolated Oligohydramnios

Satyaprabha Siripurapu [1], Achanta Vivekanand [2], A Sarojini [3], Sethi Pruthwiraj [3]

[1]Assistant Professor, Department of Obstetrics and Gynecology, [2] Professor, Department of Obstetrics and Gynecology, [3]Associate Professor, Department of Obstetrics and Gynecology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

Address for Correspondence: Dr. Satyaprabha Siripurapu, Assistant Professor, Department of Obstetrics and Gynecology, Prathima Institute of Medical Sciences, Karimnagar, Telangana, India.

Email: siripurapu.satyaprabha@gmail.com

ABSTRACT

Introduction: Oligohydramnios is defined as a single pocket of amniotic fluid measuring < 2 cm in both vertical and horizontal planes in the ultrasound or AFI < 5cm. Isolated oligohydramnios refers to the absence of significant growth restriction, normal umbilical artery doppler velocimetry (absence of maternal and fetal risk factors) and failure to identify a recognizable underlying etiology. This study aims at determining the efficacy of maternal administration of amino acid infusion in improving the amniotic fluid volume in cases of isolated oligohydramnios and observes its impact on the neonatal outcome.

Materials and Methods: A prospective study was conducted among women attending antenatal clinic of the Obstetrics and Gynecology department, Prathima Institute of Medical Sciences, Karimnagar from July 2014 to February 2015. The infusion was administered on alternate day along with 10% dextrose in between. The significance of changes in AFI was tested using paired t test and the relation between neonatal outcome was interpreted using an unpaired t test.

Results: The mean age of the participants in this study group was 23±2.54 years. The majority 42 (51.2%) of the women were primigravida and 44 (53.7%) women were having a gestational age less than 34 weeks. The baseline AFI at the time of enrollment was 5.720 ± 1.0889 and there was improvement in mean AFI score at the end of the first week (6.341±1.7265) second week (6.806 ± 1.7332) and third week (7.44 ± 1.593). The difference in the AFI scores were statistically significant (p=0.000). There was no statistically significant difference in weight of the baby, Apgar score at 5 minutes and admission in the NICU with AFI at the time of delivery (p=0.219, 0.332, 0.599 respectively).

Conclusion: Infusion of amino acids improved the AFI and its supplementation might be beneficial in the management of isolated oligohydramnios.

Keywords: Amino acid infusion, Isolated oligohydramnios, Amniotic fluid index

Please cite this article as: Satyaprabha S, Vivekanand A, Sarojini A, Sethi P. The role of amino acid infusion in isolated Oligohydramnios. Perspectives in medical research 2015;3: 1-5.

Source of Support: Nil, Conflict of interest: None Declared

INTRODUCTION

The fluid that collects within the amniotic cavity surrounding the embryo is called amniotic fluid (AF).[1] Amniotic fluid is marvelously dynamic milieu that changes as pregnancy progresses. The amniotic fluid contains nutrients and growth factors that facilitate fetal growth, provides mechanical cushioning and antimicrobial effect that protects the fetus and allows assessment of fetal maturity and disease. In the early fetal period AF volume and fetal size are related in linear fashion. AF volume increases from about 25 ml at 10 weeks to about 400 ml at 20 weeks. During this period AF composition is similar to fetal plasma. There is a rapid bi-directional diffusion between the fetus and AF across the not yet keratinized fetal skin and the surfaces of the amnion, placenta and umbilical cord. When keratinization of fetal skin completes at around 25 weeks, the relationship between fetal size and AF volume is no longer linear. By 28 weeks of gestation, AF volume reaches around 800 ml, where it plateaus near term and declines to about 400 ml at 42 weeks.[2] After 25 weeks of gestation, AF volume is determined by: a)

Predominantly by excretion of fetal urine (300ml/kg fetal weight/day).[3] b) By secretion of oral, nasal, tracheal and pulmonary fluids (60 to 100 ml/kg fetal weight/day).

While volume changes with each fetal breath are small, < 5 ml per breath, and fetal breathing occurs only for 20 to 30 minutes of each hour in late gestation, the overall contribution to fetal breathing to AF volume is insignificant. Removal of fluid depends on fetal swallowing and intra membranous transport via the skin, placenta and cord surfaces. The trans-membranous pathway, the movement of AF across the fetal membranes and into maternal circulation is estimated to be equal to 10 ml /day at term. The incidence of oligohydramnios is estimated to be 3-5% of total pregnancies.[4]

According to Manning, Oligohydramnios is defined as a single pocket of amniotic fluid measuring < 2 cm in both vertical and horizontal planes in ultrasound, whereas Phelan defined Oligohydramnios when the amniotic fluid index (AFI) < 5cm. A cutoff value of 8 cm was proposed by Jeng et al as AFI < 8 cm showed an increased incidence of meconium staining, cesarean delivery, fetal distress, APGAR 7 or less in one minute. Most cases are due to premature rupture of membranes, fetal growth restriction, fetal abnormalities such as urinary tract malformations, chromosomal disorders and drugs, eg. NSAIDS. Isolated oligohydramnios refers to the absence of significant growth restriction, normal umbilical artery doppler velocimetry (absence of maternal and fetal risk factors) and failure to identify a recognizable underlying etiology. [5]

Amino acids cross the placenta by an active transport system and their concentration in the fetus are higher than in the mother. In growth restriction associated with oligohydramnios, serum amino acids were found to be lower than those in normally grown fetuses. [6] However, no such studies are done in pregnancy complicated by isolated oligohy dramnios. This study aims at determining the efficacy of maternal administration of amino acid infusion in improving the amniotic fluid volume in cases of isolated oligohydramnios and observes its impact on the neonatal outcome.

MATERIALS AND METHODS

A prospective study was conducted among women attending antenatal clinic of the Obstetric and Gynecology department, Prathima Institute of Medical Sciences, Karimnagar from July 2014 to February 2015 to determine the efficacy of maternal administration of intravenous amino acid solution in improving AF Volume in isolated oligohydramnios and its impact on the neonatal outcome. The purpose of the study was explained to them and informed consent was taken. A total of 82 women with singleton pregnancy, well established gestational age and clinically and sonographically proven isolated oligohydramnios in the 3rd trimester of pregnancy were included in the study. The gestational age ranged from 28 weeks to 36 weeks. Cases of premature rupture of membranes, congenital fetal anomaly, maternal pulmonary, cardiovascular and hypertensive disorders and severe placental insufficiency (raised S/D ratio of umbilical artery) were excluded from the study. Amniotic fluid volume was measured with four quadrant technique which consisted of measuring the largest pool of fluid devoid of cord and fetal parts found in each of the four quadrants of the uterus. The sum of all measurements gave AFI. The AFI from 6-10 cm was labelled "mild" and less than or equal to 5cm was considered as "moderate to severe" oligohydramnios. All readings were taken by a single sonographer to minimize inter observer variation. A detailed past medical, obstetric, personal and family history was taken. Obstetrical and systemic physical examinations were conducted. Symphysis-fundal height was measured in centimeters. Fetal movements and fetal heart rates were recorded serially.

Blood investigations i.e. hemoglobin estimation, ABO grouping, Rh factor and cell counts were carried out. Urine analysis and microscopy was done. Initial obstetric sonography was followed by estimation of umbilical artery blood flow velocity and calculation of S/D ratio, thereby excluding severe placental insufficiency. Women were administered with 500 ml of amino acid fluid randomly on alternate days. It is a commercially available sterile aqueous solution and a well balanced mixture of L-amino acid optimally proportioned for maximum protein synthesis.

The infusion was administered on alternate day along with 10% dextrose in between, fetal kick counts and non stress test were performed as and when indicated. AFI measurements were repeated weekly. Iron, calcium and multivitamin supplements were continued orally as before. These women were followed till delivery. A predesigned study proforma was filled for each case. The outcome variables analyzed were age, parity, socioeconomic status, gestational age at entry into the study, pre-infusion AFI, post infusion AFI at 1 week, week 2 and week 3,

mode of delivery, neonatal Apgar score, birth weight, and admission in NICU (Neonatal Intensive Care Unit). Data was analyzed using Epi Info Version 7. The baseline characteristics and obstetrics characteristics were expressed as numbers and percentages. The significance of changes in AFI was tested using paired t test and the relation between NICU admission, the weight of the baby and Apgar score with AFI at the time of delivery was interpreted using an unpaired t test.

Results

Table 1: Baseline characteristics of the participants

Variable		No.	Percent
Age in (Years)	<20	16	19.5
	21-25	52	63.4
	>25	14	17.1
Socioeconomic status	Lower	6	7.3
	Upper Lower	28	34.1
	Middle Lower	40	48.8
	Upper Middle	8	9.8
Total		82	100

Table 1 describes the baseline characteristics of the participants. The mean age of the participants in this study group was 23±2.54 years and the majority of them, 52 (63.4%) were between the age of 21-25 years. A total of 40 (48.8%) women belonged to middle lower socioeconomic status as per the modified Kuppuswamy's Socioeconomic Status Scale.

Table 2: Obstetrics characteristics of the participants

Variable		No.	Percent
Gravida	Primigravida	42	51.2
	Gravida 2	24	29.3
	Gravida 3 ≥	16	19.5
Gestational Age	< 34 Weeks	44	53.7
	≥34 Weeks	38	46.3
Total		82	100

Table 2 reveals the obstetrics characteristics of the participants. The majority 42 (51.2%) of women were primigravida followed by 24 (29.3%) were gravida 2. A total of 44 (53.7%) women were having a gestational age less than 34 weeks, whereas 38 (46.3%) were having a gestational age more than or equal to 34 weeks.

Table 3: AFI Score of the participants

Variable		No.	Percent
Baseline AFI	< 5	30	36.6
	5-10	52	63.4
Total		82	100
AFI After 1 Week	< 5	26	31.7
	5-10	56	68.3
Total		82	100
AFI After 2 Weeks	< 5	16	19.5
	5-10	56	68.3
Total	72	87.8	
AFI After 3 Weeks	< 5	6	7.3
	5-10	44	53.7
Total		50	61

Table 3 depicts the baseline AFI Score and changes in the AFI scores of the participants at first, second and third weeks. It has been observed that out of total 82 pregnant women, 10 women delivered at the end of the second week and another 22 women at the end of third week, hence the final analysis was restricted to 72 women at the end of second week and 50 women at the end of the third week. A total of 30 women were having baseline AFI less than 5. The AFI improved marginally at the end of the first week, with 26 women showing AFI less than 5. At the end of second week 16 women were having AFI less than 5, whereas the AFI improved further with only 6 women scoring AFI less than 5 at the end of the third week.

Variable		Mean	N	SD	T	Significance
Pair 1	Baseline AFI	5.720	82	1.0889	-3.613	0.001
	AFI after 1 Week	6.341	82	1.7265		
Pair 2	Baseline AFI	5.681	72	1.0424	-5.640	0.000
	AFI after 2 Weeks	6.806	72	1.7332		
Pair 3	Baseline AFI	5.780	50	1.0698	-7.027	0.000
	AFI after 3 Weeks	7.44	50	1.593		

Table 4 showed the mean increase in AFI scores by paired sample t test. The baseline AFI at the time of enrollment was 5.720±1.0889 and there was a marginal improvement in mean AFI score at the end of one week which was 6.341±1.7265. The difference in the AFI was statistically significant (p=0.001). Similarly, a total of 72 women entered in the second week intervention and the mean AFI was 6.806 ± 1.7332 at the end of the second week. There was marked improvement observed at the end of the third week with total 50 women having mean AFI 7.44 ± 1.593. The difference in the AFI scores at the second week and the third week were statistically significant (p=0.000).

Table 5: Neonate related characteristics and AFI

Variable		Numbers	Mean AFI±SD	F	Significance
Weight of baby	< 2.5 Kg	26	6.62±1.909	3.224	0.219
	>2.5 Kg	56	7.11±1.551		
Apgar scores at 5 minutes	< 7	4	7.75±1.443	4.9	0.332
	>7	78	6.91 ±1.686		
NICU admissions	Admitted	8	7.25±1.439	.169	0.599
	Not Admitted	74	6.92±1.706		

Table 5 describes the neonate related characteristics and its correlation with AFI at the time of delivery. The predominant mode of delivery was LSCS (66) and 42 were female babies. It has been observed that 26 were weighing less than 2.5 kg with mean AFI 6.62±1.909 and 56 weighing more than 2.5 kg with mean AFI 7.11±1.551. Although AFI was higher in the latter group, the difference was not statistically significant. In contrast, in the context of Apgar score at 5 minutes, only 4 babies were having scores less than 7 and the mean AFI score was higher (7.75±1.443) whereas 78 babies were having an Apgar score more than 7 with mean AFI of 6.91 ±1.686. A total of 8 children required admission in the NICU and their mean AFI score was 7.25±1.439 and 74 children who did not require admission in NICU, the mean AFI score was 6.92±1.706. There was no statistically significant difference in weight of the babies, Apgar score at 5 minutes and admission in the NICU with AFI at the time of delivery (p=0.219, 0.332, 0.599 respectively).

DISCUSSION

In isolated oligohydramnios, there are various studies that have tried the infusion of large amounts of glucose and amino acids intravenously. Patients with oligohydramnios have also been treated with 10% maltose and amino acid infusion to improve the fetal outcome.[8]

Amino acids, an important component of amniotic fluid, their concentration in AF can be improved with good maternal nutrition by intravenous amino acid infusion. The rise in mean AFI in this study after maternal intravenous amino acid infusion indicates the possibility of intrauterine nutrient deficiency as a cause of oligohy dramnios.[9]

There was marked improvement observed in AFI after the infusion of amino acids. Our findings are consistent with the findings obtained by Qureshi et al. In his study, the mean preinfusion AFI was 4.7 cm, mean one week post infusion AFI was 5.8 cm, mean two weeks post infusion AFI was 6.2 cm and mean three weeks AFI was 6.3 cm. An increase in AFI was found to be statistically significant.[10]

Oligohydramnios itself increased the incidence of pre-term deliveries.[11] Oligohydramnios, AFI <5 with non re-assuring fetal heart rate pattern is the predominant indication for cesarean section. In the present study, by improving AFI we prolonged the gestational age at delivery thereby improving the neonatal outcome. Our findings are consistent with Hebbar et al study.[12]

There is continuous search for alternate suitable therapies to improve AFI in oligohydramnios. Salvia miltiorrhiza is a Chinese medicine studied for the treatment of oligohydramnios.[13] The effect of maternal hydration on AFI rise is only transient [14] and may be useful in the management of oligohydramnios during labor or before external cephalic version.[15,16] Most recent case reports are implanting a catheter into the umbilical vein by cordocentesis, then connected to subcutaneously placed port system. The daily infusions of amino acids and 10% glucose are given into the umbilical vein.[17]

To minimize the cesarean section rate, combining intravenous amino acids to raise AFI with intrapartum amnioinfusion to decrease the cord compression could be a possible approach in future.

CONCLUSION

Infusion of amino acids improved the AFI and its supplementation might be beneficial in the management of oligohydramnios to prolong the pregnancy resulting in better neonatal outcome. In developing countries like India, because of the socioeconomic constraint and non compliance the improvement is difficult through dietary approach. However, large scale controlled trials are required to understand the mechanism and to determine the safe dose of amino acids.

REFERENCES

1. Mudaliar AL, Krishna Menon MK , Sarala Gopalan, Vanitha Jain, editors. Mudaliar and Menon's clinical obstetrics. Tenth edition. Chennai;Orient longman pvt ltd;2007. ISBN-13;9788125028703.
2. Ian Donald, Renu Misra MS, editor. Ian Donald's practical obstetric problems. Sixth edition. New Delhi; BI publications pvt ltd; 2012 ISBN-13; 978-81-7225-238-0.
3. Gilbert WM and Brace RA. Amiotic fluid volume and normal flows to and from the amniotic cavity. semin perinatol 1993; 17; 150-157.
4. Volante E, Gramellini D, Moretti S, Kaihura C, Bevilacqua G. Alteration of the amniotic fluid and neonatal outcome. Acta Biomed. 2004 ; 75 suppl.1;71-5.
5. Sherer DM. A review of amniotic fluid dynamics and the enigma of isolated oligohydramnios. Am J Perinatol 2002 ;19[5];253-66.
6. Regnault TR, Friedman JE, Wilking RB, Anthony RV, Hay WW Jr. Feto placental transport and utilization of aminoacids in IUGR- a review. placenta 2005;26 suppl A; S52-62.
7. Kumar N, Shekhar C, Kumar P, Kundu AS. Kuppuswamy's socioeconomic status scale-updating for 2007. Indian J Pediatr 2007 ;74:1131-2.
8. Suzuki S, Mine K, Sawa R, Yoneyama Y, Araki T. 10% Maltose infusion therapy for oligohydramnios. Australian and Newzealand Journal of Obstetrics and Gynecology 1999; 39; 373-5.
9. Under wood M, Sherman. Nutritional characte ristics of amniotic fluid. Neo Reviews, 2006;7;e 310.
10. Qureshi FU, Yusuf AW. Intravenous Amino Acids in Third Trimester Isolated Oligohydramnios. ANNALS 2011;17:140-144.
11. Yuan W, Duffner AM, Chen L, Hunt LP, Sellers SM, Bernal AL. Analysis of preterm deliveries below 35 weeks' gestation in a tertiary referral hospital in the UK. A case-control survey. BMC Res Notes. 2010 Apr 28;3:119.
12. Hebbar S, Rai L, Adiga P. Maternal hydration and L-arginine supplementation improves liquor volume in patients with decreased liquor and prolongs pregnancy. Med J DY Patil Univ 2014;7:429-34.
13. Chu HN,Shen MJ. Treating oligohydramnios with extract of Salvia miltirrhiza; A randomized control trial. Ther Clin Risk manag 2008 Feb;4[1];287-90.
14. Malhotra B, Deka D, Duration of the increase in amniotic fluid index [AFI] after acute maternal hydration. Arch Gynecol Obstet.2004 Mar;269[3];173-5.
15. Hofmeyr GJ, Gulmezoglu AM. Maternal hydration for increasing amniotic fluid volume in oligohydramnios and normal amniotic fluid volume. Cochrane Database Syst Rev 2000[2];CD000134.
16. Umber A, Chohan MA. Intravenous maternal hydration in third trimester oligohydramnios; effect on amniotic fluid volume. J Coll physicians Surg pak 2007 jun;17[6];336-9.
17. Tchirikov M, Kharkevich O, Steetskamp J, Beluga M, Strohner M. Treatment of Growth-Restricted Human Fetuses with Aminoacids and Glucose Supplementation through a Chronic Fetal Intravascular Perinatal port System. Eur Surg Res. 2010 Aug 20;45[1];45-9.