

Effect of intravenous amino acid infusion in cases of oligohydramnios in terms of mean gain in AFI

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ABSTRACT

Background: 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.

Objectives: To see the effect of intravenous amino acid infusion in cases of Oligohydramnios in terms of mean gain in AFI.

Study design: Quasi experimental study

Settings: Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore.

Study duration: 4th May 2019 to 3rd November 2019

Materials & Methods: A total of 80 females diagnosed with AFI is < 7 cm gestational age 28-37 weeks, 18 to 40 years of age of any parity were included. Patients having hypertension, diabetes

mellitus or other medical disorders and fetal anomalies were excluded. All patients were undergone on admission test for fetal wellbeing. All cases were given I.V. amino acid drip (200 ml)-6 drips (1drip/day). AFI was measured at the end at the time of delivery. As per the findings patient was discharged after the last drip and advised regarding proper diet, adequate oral hydration and weekly follow up. Patients were followed till delivery and mean gain in amniotic fluid index was calculated.

Results: Age range in this study was from 18 to 40 years with mean age of 29.50 ± 3.78 years. Majority of the patients i.e. 43 (53.75%) were between 31 to 40 years of age. Mean gestational age at the time of inclusion was 30.95 ± 1.96 weeks. Mean gestational age at the time of delivery was 39.15 ± 1.10 weeks. In my study mean AFI before therapy was 5.25 ± 0.75 cm and after therapy was 7.68 ± 0.94 cm with mean gain in AFI was 2.43 ± 0.82 . **Conclusion:** This study concluded that intravenous amino acid infusion is very effective in cases of Oligohydramnios in terms of mean gain in AFI.

Keywords: oligohydramnios, amino acid, amniotic fluid index.

INTRODUCTION

Pregnancy is a unique experience in every woman's life. The thought of a growing fetus with adequate amniotic fluid volume (according to gestational age) in the mother's womb, indeed is nature's way of expressing the attributes of motherhood, so adequate amniotic fluid volume is essential for the normal growth and well-being of the fetus.¹ Amniotic fluid surrounds the fetus in uterus and protective cushion around it. The amniotic fluid increases about a liter between 32 to 36 weeks gestation but decreases thereafter till term up to 400 ml. Oligohydramnios is defined as AFI (amniotic fluid index) less than 8 on

ultrasonography(USG). Between 5 and 7 considered as moderate

Oligohydramnios.^{2,3} Nearly 1% of pregnancies are affected by some type of midtrimester Oligohydramnios.⁴

Many factors may affect the amniotic fluid index. The mothers' blood volume plays an important role in maintaining the amniotic fluid volume.⁴ Hydration status and maternal plasma osmolality can also alter amniotic fluid volume.⁵ Amino acids form an important nutrient component of amniotic fluid. Maternal caloric consumption may profoundly alter amino acid concentration in the amniotic fluid. The rise in mean AFI seen in a series after maternal intravenous infusion of amino acids is indicative of possible intrauterine nutrient deficiency.⁶ Oligohydramnios in the absence of major congenital anomalies may be a marker for prior fetal adjustment to chronic uteroplacental insufficiency or partial cord occlusion, as well as a predisposing factor for cord compression. Therefore, it is generally recommended that, depending on gestational age, these patients be either followed closely with serial antenatal testing (nonstress test, biophysical profile) including assessment for the presence of variable decelerations, or else delivered. However, when oligohydramnios is present, there is no consensus at this time about a critical diagnosis-to-delivery interval.

Oligohydramnios in early pregnancy is attended by serious consequences to the fetus. Various conditions associated with Oligohydramnios increase perinatal mortality and morbidity. Different medical and interventional methods have been tried to treat Oligohydramnios.⁵ Amniotic fluid is one of the essential requirements for appropriate fetal growth and good fetal outcome. Decreased amniotic fluid (Oligohydramnios) leads to increase in danger of caesarean/operative delivery because of fetal distress.²

Amniotic fluid is a 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.^{6,7}

A current study in 2017 reported that the average gain in amniotic fluid index at time of delivery was 2.57 ± 0.68 cm in infusion group.⁵ A local study measured AFI at 3rd week of infusion, so they reported mean AFI before infusion was 4.75 ± 1.58 and at 3rd week of treatment it was 6.37 ± 1.84 . They did not

report AFI at time of delivery.⁷ This study is designed to see role of intravenous amino acid infusion in cases of Oligohydramnios in our local females. As a local study is available on lower sample size (n=42) in which AFI was not measured at time of delivery ⁷. So in this study we will measure AFI at time of delivery by taking larger sample size (80 overall). If through this study we find gain in AFI then in future amino acid infusion will be ensured in all cases to gain AFI. By increasing AFI we can improve fetal weight and thus can gain beneficial effect to both mother and fetus in case of Oligohydramnios.

MATERIALS & METHODS STUDY

DESIGN:

Quasi experimental study.

SETTING:

Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital Lahore.

DURATION OF STUDY:

4th May 2019 to 3rd November 2019.

SAMPLE SIZE:

The sample is estimated is 80, the sample size is estimated abusing an average gain in amniotic fluid index at time of delivery was 2.57 ± 0.68 cm using infusion. ⁵ We used 95% confidence level and d = 1%.

SAMPLE TECHNIQUE:

Non-probability, consecutive sampling.

SAMPLE SELECTION:

- **Inclusion Criteria:**
- Pregnant females aged 18-40 years
- Any parity
- Singleton pregnancy (on USG)

- Females diagnosed with AFI is < 7 cm gestational age 28-37 weeks (on USG)
- Intact membranes (was assessed clinical).
- **Exclusion Criteria:**
- Associated fetal anomalies (it was seen on USG)
- Patients having hypertension, diabetes mellitus or other medical disorders on antenatal examination.
- Cases in which delivery of baby is mandatory due to severe fetal distress.

DATA COLLECTION PROCEDURE:

After approval from ethical review committee and taking informed consent, a total of 80 females fulfilling the inclusion criteria were admitted after obtaining detailed history and thorough examination. They were investigated and subjected for USG in view of measurement of AFI. AFI 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. All reading was taken by the same sonographer to minimize any inter observer variation. A baseline color Doppler was done to rule out any element of foetal growth restriction. All patients were undergone on admission test for fetal wellbeing. All cases were given I.V. amino acid drip (200 ml)-6 drips (1drip/day). AFI was measured at the end at the time of delivery. As per the findings patient was discharged after the last drip and advised regarding proper diet, adequate oral hydration and weekly follow up. Patients were followed till delivery and mean gain in amniotic fluid index was calculated as per operational definition. All data was kept by researcher herself on attached proforma.

STATISTICAL ANALYSIS:

SPSS version 23 was used to analyze and enter the data using mean \pm S.D for age, gestational age (at time of inclusion and delivery) and AFI (before and after therapy). Parity was presented in form of frequency and percentage.

To address effect modifiers data was stratified for age, parity, BMI, gestational age at time of delivery and time since receipt of infusion. Post stratification independent sample t-test was applied taking p-value ≤ 0.05 as significant.

RESULTS

Age range in this study was from 18 to 40 years with mean age of 29.50 ± 3.78 years. Majority of the patients i.e. 43 (53.75%) were between 31 to 40 years of age as shown in Table III.

Mean gestational age at the time of inclusion was 30.95 ± 1.96 weeks

(Table IV). Mean gestational age at the time of delivery was 39.15 ± 1.10 weeks

(Table V). Distribution of patients according to parity is shown in Table VI. Mean BMI was 28.36 ± 2.76 kg/m² (Table VII). Mean time since receipt of infusion was 6.20 ± 2.01 weeks (Table VIII).

In my study mean AFI before therapy was 5.25 ± 0.75 cm and after therapy was 7.68 ± 0.94 cm with mean gain in AFI was 2.43 ± 0.82 as shown Table IX.

Stratification of mean gain in AFI with respect to age groups and gestational age at delivery shown in Table X & XI respectively. Table XII & XIII have shown the stratification of mean gain in AFI with respect to parity and BMI respectively. Stratification of mean gain in AFI with respect to time since receipt of infusion is shown in Table XIV.

Table-III: Distribution of patients according to Age (n=80).

Age (in years)	No. of Patients	%age
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18-30	37	46.25
31-40	43	53.75
Total	80	100.0

Mean ± SD = 29.50 ± 3.78 years

Table-IV: Distribution of patients according to gestational age at the time of inclusion (n=80).

GA (weeks)	No. of Patients	%age
28-32	61	76.25
33-37	19	23.75

Mean ± SD = 30.95 ± 1.96 weeks

Table-V: Distribution of patients according to gestational age at the time of delivery (n=80).

GA (weeks)	No. of Patients	%age
35-37	49	61.25
38-40	31	38.75

Mean ± SD = 39.15 ± 1.10 weeks

Table-VI: Distribution of patients according to parity (n=80).

Parity	No. of Patients	%age
0-3	35	43.75
>3	45	56.25

Table-VII: Distribution of patients according to BMI (n=80).

BMI (kg/m²)	No. of Patients	%age
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≤27	30	37.50
>27	50	62.50

Mean ± SD = 28.36 ± 2.76 kg/m²

Table-VIII: Distribution of patients according to time since receipt of infusion (n=80).

time since receipt of infusion (weeks)	No. of Patients	%age
≤5	37	46.25
>5	43	53.75

Mean ± SD = 6.20 ± 2.01 weeks

Table-IX: AFI before and after therapy and mean gain in AFI after intravenous amino acid infusion in cases of Oligohydramnios (n=80).

AFI (cm)	Mean ± SD
Before therapy	5.25 ± 0.75
After therapy	7.68 ± 0.94
Gain	2.43 ± 0.82

Table X: Stratification of mean gain in AFI with respect to age groups

Age groups	mean gain in AFI		P-value
	Mean	SD	
18-30	2.84	0.73	0.0001
31-40	2.07	0.74	

Table XI: Stratification of mean gain in AFI with respect to gestational age at time of delivery

age at time of	mean gain in AFI	P-value
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Gestational delivery	mean gain in AFI		P-value
	Mean	SD	
35-37	2.35	0.95	0.289
38-40	2.55	0.57	

Table XII: Stratification of mean gain in AFI with respect to parity

Parity	mean gain in AFI		P-value
	Mean	SD	
0-3	2.94	0.68	0.0001
>3	2.02	0.69	

Table XIII: Stratification of mean gain in AFI with respect to BMI

BMI (kg/m ²)	mean gain in AFI		P-value
	Mean	SD	
≤27	2.43	0.77	0.945
>27	2.42	0.86	

Table XIV: Stratification of mean gain in AFI with respect to time since receipt of infusion

	mean gain in AFI	P-value

time since receipt of infusion (weeks)	Mean	SD	
≤5	2.03	0.83	0.0001
>5	2.77	0.65	

DISCUSSION

DISCUSSION

Amino acids cross the placenta by active transport systems, and their concentrations in the fetus are higher than in the mother. A significant reduction in amino acid fetal – maternal gradients and in umbilical veno-arterial differences has been demonstrated in intrauterine growth-restricted (IUGR) pregnancies. In growth restriction associated with oligohydroamnios, serum amino acids were found lower than those in normally grown fetuses.⁸⁰ I have conducted this study to see the effect of intravenous amino acid infusion in cases of Oligohydramnios in terms of mean gain in AFI.

Age range in this study was from 18 to 40 years with mean age of 29.50 ± 3.78 years. Majority of the patients i.e. 43 (53.75%) were between 31 to 40 years of age. In my study mean AFI before therapy was 5.25 ± 0.75 cm and after therapy was 7.68 ± 0.94 cm with mean gain in AFI was 2.43 ± 0.82 . A current study in 2017 reported that the average gain in amniotic fluid index at time of delivery was 2.57 ± 0.68 cm in infusion group.⁵ A local study measured AFI at 3rd week of infusion, so they reported mean AFI before infusion was 4.75 ± 1.58 and at 3rd week of treatment it was 6.37 ± 1.84 . They did not report AFI at time of delivery.⁷

Mesaki and Cetin et al also concluded from their study that 10% Dextrose and 12% amino acid increases fetal weight effectively.⁸¹ Tayade S et al in their study on the role of intravenous hydration

and amino acid infusion in intrauterine growth restriction and oligohydramnios concluded that fetal weight gain of more than 500 grams was seen more significantly in group 2 and 3 who were receiving amino acids proving that it not only increases AFI but also increases foetal weight

which is the need of present hour to reduce perinatal mortality indirectly.^{82,83} Lampariello C et al administered L – Arginine to 43 pregnant women whose fetuses had been diagnosed with fetal growth restriction by ultrasonic examination and by Doppler evaluation of velocimetry value.⁸⁴

In a local study⁸⁵, twenty-five women with third trimester oligohydramnios (AFI < or = 5.0 cm) and 25 controls with normal amniotic fluid volume (AFI 8-24 cm) were prospectively recruited. Maternal hydration (5% dextrose) increased amniotic fluid volume (AFV) in women with oligohydramnios (mean change in amniotic fluid index 4.5 cm, 95% confidence interval 4.02 to 5.06; p-value<0.01); as well as in women with normal amniotic fluid volume (mean change in amniotic fluid index 2.7 cm, 95% confidence interval 2.23 to 3.21; pvalue<0.01). The percentage increase in mean AFI was 58.6% in the oligohydramnios group, which was significantly greater (p<0.05) than the percentage increase of 28.4% in control group.⁸⁵

A study was done to see whether maternal nutrition plays any role in maintaining the foetal environment in the Department of Obstetrics & Gynaecology at Srinagar where 20 clinically and sonographically proven cases of oligohydramnios in third trimester were selected. Maternal nutrition was improved by parenteral amino acid infusion. A significant improvement was observed subsequently as the AFI was seen to increase and less operative intervention was needed. A lesser perinatal mortality was as well seen. An important cause of IUGR and its associated complications are said to be to inadequate nutrition to mother. So improving the maternal nutritional status during pregnancy shall improve the pregnancy outcome.⁸⁶ Various studies have tried intravenous infusion of large amounts of glucose and aminoacids to the mothers. Mothers carrying IUGR babies have been infused with 10% Fructodex and aminoacid solutions Pregnant patients with oligohydramnios also have been infused with

aminoacids for improvement of foetal outcome. Improved maternal nutritional status by intravenous aminoacid infusion appears to improve the AFI. This improvement may not have been achieved with diet alone because of non-compliance and socioeconomic status.⁸⁷

According to Suzuki et al 10% Maltose can be used as an intravenous solution for increasing the amniotic fluid volume and there was significant increase in AFI with one week therapy. American pregnancy association states clearly that maternal intravenous infusion is known to increase amniotic fluid volume.⁸⁸ Mesaki also concluded from their study that 10% Dextrose and 12% AA increases fetal weight effectively. Cetin et al also observed that aminoacids are essential for fetal growth specially valine, leucine isoleucine varieties. IV Aminoacid infusion in Oligohydramnios helps In Improving perinatal outcome Joshi, Sapre.⁸⁹

Significant improvement in amniotic index was observed at the time of delivery. Sreedharan et al. studied the effect of l-arginine in 100 women diagnosed to have oligoamnios between 28 and 36 weeks of gestation.⁹⁰ The expectant mothers were prescribed sachets of l-arginine containing 3 g of the active ingredient for periods varying between 1 and 4 weeks. There was significant improvement in AFI (by 2.03 ± 0.39 cm), and they opined that l-arginine can be used as a cheaper alternative to ultrasound-guided amnioinfusion in pregnancy complicated by low liquor remote from term. Improved maternal nutritional status by intravenous amino acid appear to improve the AFI. This improvement may not have been achieved with diet alone because of non-compliance and socioeconomic status.

CONCLUSION

This study concluded that intravenous amino acid infusion is very effective in cases of Oligohydramnios in terms of mean gain in AFI. So, we recommend that amino acid infusion should be used as primary method in managing oligohydramnios in order to reduce morbidity and mortality of both mother and fetus.

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