Intravenous Amino Acids in Third Trimester Isolated Oligohydramnios

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Abstract

Objective: To determine the efficacy of maternal administration of intravenous amino acid solution in improving amniotic fluid volume in cases of isolated oligohydramnios and to observe its impact on mode of delivery and neonatal outcome.
Study Design: A prospective case series.
Place and Duration of Study: Lady Willingdon Hospital, Lahore from Jun, 2008 to May, 2010.
Methodology: Forty two women with singleton pregnancy, well established gestational age and clinically and sonographically proven isolated oligohydramnios in the third trimester before 36 weeks were administered amino acid solution intravenously after excluding cases of premature rupture of membranes, congenital anomaly of fetus, maternal pulmonary, cardiovascular and hypertensive disorders, and severe placental insufficiency (raised S/D ratio). Pre-infusion and post-infusion Amniotic fluid Index (AFI) was measured and repeated weekly. Women were followed till delivery.
Results: According to repeated measurement analysis of variance, mean pre-infusion AFI was 4.7 cm, mean one week post-infusion AFI was 5.8 cm, mean two week post-infusion AFI was 6.2 cm and mean three week AFI was 6.3 cm (p-value 0.029, significant). Cesarean section became a predominant mode of delivery in this group without a firm evidence of associated fetal compromise.
Conclusion: Amino acid infusion is an effective therapy for raising AFI in isolated oligohydramnios in this case series. Liberal use of cesarean section in this selected group should be carefully re-evaluated.
Key words: Oligohydramnios, amino acid infusion, amniotic fluid index, cesarean section rate.

Introduction

Amniotic fluid surrounds the fetus and provides the protective low resistance environment suitable for growth and development of fetus. In oligohydramnios, volume of amniotic fluid may fall below the normal limits. Oligohydramnios encountered in 3 – 5% of the pregnancies.[1] Most cases are due to premature rupture of membranes, fetal growth restriction, fetal abnormallities, such as urinary tract malformations, chromosomal disorders and drugs e.g. NSAID's. Isolated oligohydramnios refers to 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.[2] Objective measurement of amniotic fluid volume is done sonographically and denoted to as 'Amniotic Fluid Index' (AFI).[3] Oligohydramnios of mild entities (AFI 5 – 10 cm) is often associated with preterm birth and fetal growth restriction. Neonatal prognosis is often disastrous in cases with severe oligohydramnios (AFI < 5 cm) when it may also result in meconium staining, fetal heart conduction abnormalities, poor

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tolerance of labour which often requires caesarean section could lead to increase in both maternal and perinatal morbidity and mortality.[4] 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.[5] However no such studies are done in pregnancies complicated by isolated oligohydramnios with normal umbilical artery Doppler velocimetry. 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 mode of delivery and neonatal outcome.

Methodology

A prospective case series is being reported here for 42 women at Lady Willingdon Hospital, Lahore from Jun, 2008 to May, 2010, to determine the efficacy of maternal administration of intravenous amino acid solution in improving amniotic fluid volume in isolated oligohydramnios and its impact on mode of delivery and neonatal outcome.

Forty two women with singleton pregnancy well established gestational age and clinically and sonographically proven isolated oligohydramnios in third trimester of pregnancy were selected from the antenatal clinic of the Department of Obstetrics and Gynecology at Lady Willingdon Hospital, Lahore. Gestational ages ranged from 28 weeks to 35 weeks. Cases of premature rupture of membranes, congenital fetal anomaly, maternal pulmonary, cardiovascular and hypertensive disorders, and severe placental insufficiency (raised S/D ratio) 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 uterus. The sum of all the measurements gave AFI. AFI from 6 – 10 cm was labeled 'mild' and less than or equal to 5 cm was considered '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. Symphysio – fundal height was measured in centimeters. Fetal movements and fetal heart rates were recorded serially. Blood investigations i.e. Hemoglobin, ABO grouping, Rh factor and Cell counts were carried out. Urinalysis and microscopy followed by culture / sensitivity was done when required. Initial obstetric sonography was followed by estimation of umbilical artery blood flow velocity and calculation of S/D ratio, thereby excluding severe placental insufficiency. After taking informed consent, women were administered 500 ml of amino acid infusion intravenously. It is a commercially available, sterile aqueous solution and a well – balanced mixture of L-Amino acids optimally proportioned for maximum protein synthesis. The infusion was administered daily for three consecutive days. Fetal kick counts and non-stress tests were performed as and when indicated. AFI measurements were repeated weekly. Iron, calcium and multi – vitamin supplements were continued orally as before. These women were followed till delivery. A pre-designed study proforma was filled for each case.

Outcome variables analyzed were Age, Parity, Gestational age at entry into the study, Pre-infusion AFI, Post-infusion AFI at week 1, week 2 and week 3, Gestational age at delivery, mode of delivery, neonatal APGAR scores, birth weight and admission in Neonatal intensive care unit (NICU).

Results

Forty two women were found eligible for the study. Two women did not show up for delivery. Forty women completed the study and their mean age was 26 years, among which 70% (28) were multigravida. Thirty six (90%) of women entered into the study at less than or equal to 34 weeks of gestation and 60% (24) were perceiving normal fetal movements. On admission 65% (26 out of 40) had AFI < 5 cm. This frequency decreased to 47.4% (18 out of 38) one week after the infusion. Out of 16 women who entered the second week after infusion, AFI improved in eight pregnancies. All eight women completed third week as well with no deterioration in AFI. In pregnancies where no improvement in AFI was observed at the end of second week, only two progressed into third week and had repeat AFI < 5 cm. After repeated measurement analysis of variance, mean pre-infusion AFI was 4.7 cm, mean one week post-infusion AFI was 5.8 cm, mean two week post-infusion AFI was 6.2 cm and

mean three week AFI was 6.3 cm (Table 1) p-value 0.029, significant (Graph 1).

The gestational age up to which half (21 out 0f 40) of the women were delivered was < / = 35 weeks and all the rest were delivered by 37 completed weeks. Majority (85%) (34) had cesarean section due to abnormal fetal heart patterns (50%) with added indication of scanty liquor (20%) in about half of the cases. Other indications were breech presentation, placenta previa, previous 2 or more cesarean deliveries and premature onset of labor in various combinations.

Table 1:

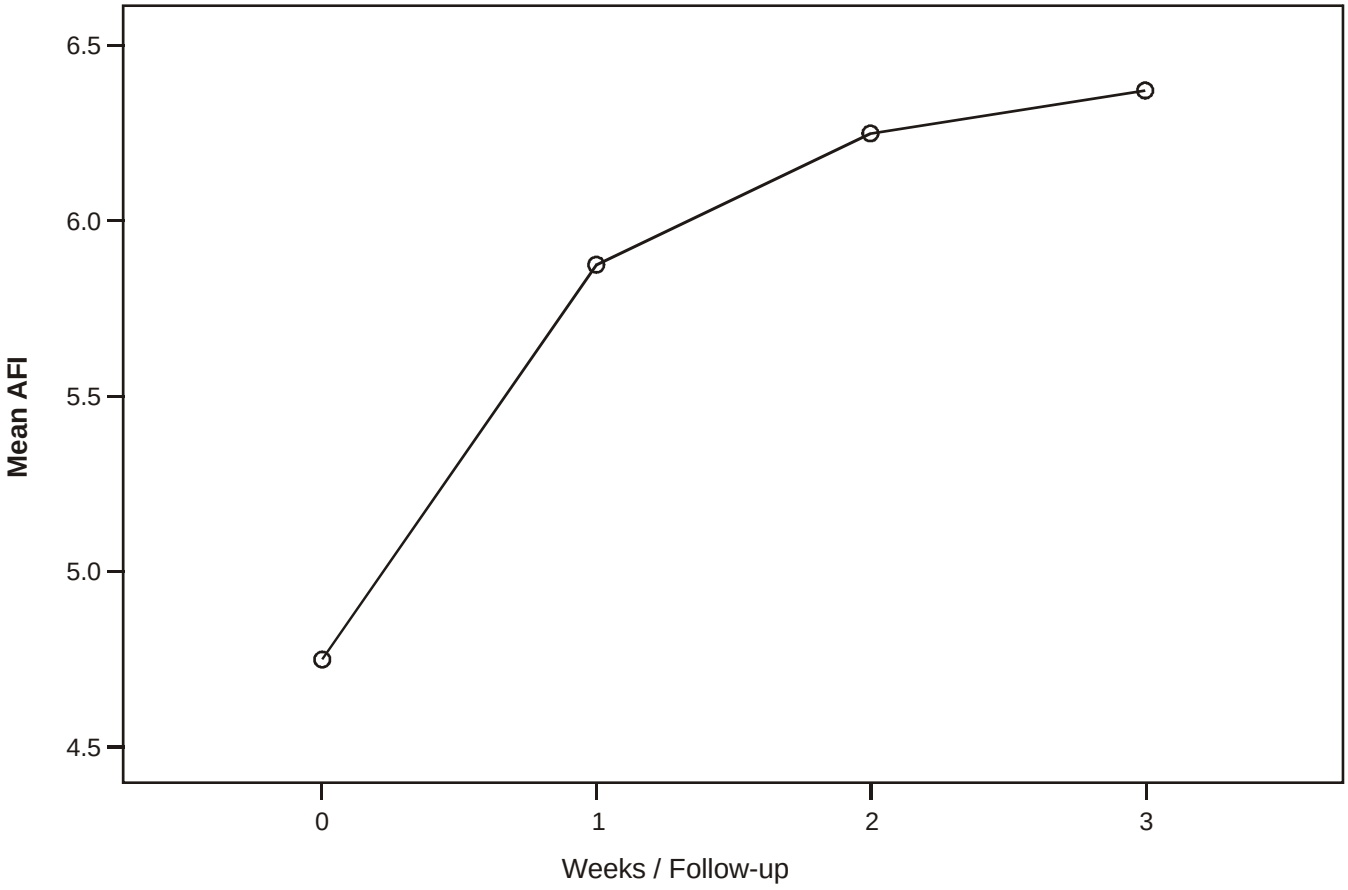
	Mean	Std. Deviation
Pre-infusion AFI	4.7500	1.58114
1 week post-infusion AFI	5.8750	2.16712
2 week post-infusion AFI	6.2500	1.75255
3week post-infusion AFI	6.3750	1.84681

About three quarter of infants (75%) (30) weighed between 2 – 2.6 kg, majority (68%) (26 out of 38) had APGAR scores > 5 at 10 minutes after birth. No meconium staining was observed in 80% neonates and didn't require admission to neonatal ICU. One antepartum death occurred at 30 weeks in a multigravida with severe oligohydramnios (< 5 cm) despite equivocal test results of fetal well – being during the second week after infusion.

Discussion

Amino acids form an important nutrient component of amniotic fluid. Maternal caloric consumption may profoundly alter amino acid concentration in amniotic fluid.[6] The rise in mean AFI seen in this series after maternal intravenous infusion of amino acids is indicative of possible intrauterine nutrient deficiency.

Prematurity increases the risk of adverse neonatal outcome and oligohydramnios is significantly increased in both spontaneous and indicated preterm deliveries compared to term controls.[7] In the present study



Graph 1: P-value = 0.029 (significant).

all preterm births were associated with oligohydramnios irrespective of the indication for delivery.

There is a continuing search for suitable therapies for pathologies that alter the amniotic fluid. Various studies have tried antenatal infusions of large amounts of glucose and amino acids intravenously. Oligohydramnios has also been treated with 10% maltose[8] and amino acids infusion[9] for improvement of fetal outcome. One of the available methods in the active management of pregnancies affected by second – term and incipient third – term oligohydramnios is trans abdominal amnioinfusion.[10] Salvia miltiorrhiza is a Chinese medicine studied for the treatment of oligohydramnios.[11] Simple maternal hydration appears to increase amniotic fluid volume transiently[12] and may be beneficial in the management of oligohydramnios during labor or before external cephalic version.[13,14] Most recent case report is to implant a catheter into the umbilical vein (UV) by cordocentesis, and then connected to a subcutaneously implanted port system. The treatment course involved daily infusions of amino acid solution and 10% glucose into the UV. Daily intravascular fetal nutrition may significantly improve both fetal condition and fetal weight gain.[15] In the present case series an improvement in AFI which lasted longer, is observed with a relatively simpler technique.

Fetal heart rate abnormalities were frequently seen in this study and in fact became the most common indication for preterm delivery. Similar findings are being reported by other studies determining significance of low AFI in predicting adverse perinatal outcome.[4,16,17] An AFI of 5.0 cm or less is significantly associated with an abnormal ante / intra-partum fetal heart rate,[18] meconium – stained fluid,[19] Apgars less than 7, or NICU admission. Subjects with an AFI of 5.0 cm or less have a higher rate of cesarean for fetal distress.[20,21] Although in present series < / = 5 cm AFI is not predictive of adverse perinatal outcome as measured by low Apgars and NICU admissions, which may be reflective of the aggressive antepartum and intrapartum management that these patients received, probably at the expense of a very high rate of cesarean section.

Despite the fact that growth – restricted fetuses with normal umbilical artery Doppler velocimetry appear to be at a lower risk than those with abnormal velocity waveforms[22] proper monitoring and treatment during pregnancy for all subsets of small for gestational age infants (premature and growth – restricted fetuses) cannot be overemphasized.[23] Pregnancies with oligohydramnios and normal umbilical artery Doppler velocimetry are significantly less likely to experience an abnormal perinatal outcome as compared to those with abnormal Doppler indices.[24,25] Although in the present series comparison with abnormal Doppler group is lacking but it is suggested by the author that keeping a high threshold for surgical intervention in parturients with oligohydramnios and normal umbilical artery Doppler velocimetry may decrease the rate of cesarean section without raising adverse perinatal outcome. Another proposed direction for future research could be to combine intravenous amino acids to raise AFI with another therapeutic intervention like ante / intrapartum amnioinfusion to minimize the risk of fetal feart rate abnormalities in third trimester isolated oligohydramnios.

Conclusion

From the study conducted it can be suggested that intravenous amino acid solution is an effective therapy for raising AFI in isolated oligohydramnios in this case series. This improvement may not have been achieved with diet alone because of non-compliance and socioeconomic status in a developing country like Pakistan. However, larger studies with controlled trial are required. Liberal use of cesarean section in this selected group should be carefully re-evaluated.

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Conflict of Interest

There is no conflict of interest.

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