

To Study The Effect of L-Arginine in Oligohydramnios To Improve Perinatal Outcome

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Abstract:

Background: Oligohydramnios is a common diagnosis in obstetrics and carries an increased risk of operative interference and perinatal mortality and morbidity. Administration of L-arginine (precursor of nitric oxide) has been suggested to improve amniotic fluid index (AFI) in Oligohydramnios.

Objective: To study the effect of L-Arginine in improving AFI and Perinatal outcomes in Oligohydramnios

Methods: A Retrospective study was conducted at Pacific Medical College And Hospital, Udaipur consisting of 50 antenatal patients with decreased liquor [AFI < 8 cm] remote from term. Patients started on L-arginine sachets (3 g, 3 sachets a day) after evaluation of risk factors. The treatment was continued till improvement in liquor was noted. However, patients were considered for delivery if the AFI remained < 5 cm. Further, mean increase in AFI, intervention delivery interval, and neonatal outcome were studied.

Results: The mean gestational age at the time of recruitment was 32.4 weeks. The mean AFI noted was 5.321 cm. These patients were delivered at 35 ± 1.1 weeks, and thus, pregnancy could be prolonged by 2.3 ± 1.1 weeks. The mean AFI at the end of therapeutic intervention was 8.553, and thus, an AFI increase of 3.232 cm could be obtained. There was no significant neonatal morbidity in these patients. Significant improvement in liquor volume was obtained in these patients after intervention with L-arginine sachets.

Conclusion: L-arginine supplementation is promising in improving volume of amniotic fluid in cases of oligohydramnios and prolonging pregnancy by a mean of 2.3 weeks, allowing fetal lung maturation thus benefiting the neonatal outcome.

Keywords: Amniotic fluid index (AFI), Fetal Growth Restriction (FGR) L-Arginine (Arg), Nitric Oxide (NO), Oligohydramnios

I. Introduction

Amniotic fluid provides a protected milieu for the growing fetus, cushioning the fetus against mechanical and biological injury, supplying nutrients, and facilitating growth. Decreased amniotic fluid is associated with placental insufficiency, impaired lung development in fetus, and fetal growth restriction (FGR). Long-term complications of oligohydramnios are cord compression and variation in fetal heart rate during labor and increased chance of operative deliveries. Amniotic Volume increases to about 800–1000 ml at 28 weeks, plateaus near term and declines to about 400 ml at 42 weeks.^[1] The amount of AF is most commonly evaluated by ultrasound using amniotic fluid index (AFI) or single largest pocket (SLP). An AFI of 8 cm and above is considered normal, between 5 cm and 8 cm is low normal, and < 5 cm is oligohydramnios. In chronic placental insufficiency, the fetus tries to acclimatize by redirecting blood flow to vital organs such as in reduction of available intrauterine space for adequate fetal growth. Subjected to pressure from all sides, the fetus assumes a peculiar appearance like potter facies (which includes prominent epicanthal folds, flattened nose, low-set ears) and abnormal position of hand and feet. Different medical interventional methods have been tried to treat oligohydramnios. This study was done to find out the effect of L-arginine on AFI, the mode of delivery, and the fetal outcome. L-Arginine (Arg), a nutritionally essential amino acid for the fetus (2), is a precursor for synthesis of nitric oxide (NO) and polyamines in cells (3). L-arginine is a semi-essential amino acid acting as a substrate for synthesis of NO (4). NO has a diverse role in obstetrics as it plays a vital role in labour, cervical ripening, preeclampsia and intrauterine growth restriction. (5). L-Arginine is also reported to improve growth hormone releasing hormone secretion, and as a consequence increase in plasmatic growth hormone influencing somatic growth (6). It is also suggested that it may play a significant role in fetal growth, by stimulating insulin secretion and as a precursor for both polyamine synthesis and NO production (7).

II. Materials and methods

It is a retrospective study of 50 patients diagnosed with oligohydramnios by ultrasound (AFI less than 5th percentile for gestational age, AFI<8 cm) carried out at Pacific Medical College And Hospital , Udaipur.

Inclusion Criteria

The inclusion criteria were: 26–36 weeks gestational age in singleton pregnancies with or without complications and initial AFI between 4 and 8 in presence of intact membranes.

Exclusion Criteria

Exclusion criteria were smoking and chronic illnesses , PROM, Patient not giving consent for the study, diagnosed major congenital anomalies, history of having received treatment for oligohydramnios. The amniotic fluid volume was estimated as AFI in accordance with the four-quadrant technique. The AFI was calculated by summing up the maximum vertical fluidpockets (measured in cm) in each of the four quadrants, All patients were supplemented with L-arginine 3 gm per sachet in oral form until delivery, and monitored according to standard procedure. The decision about the time and mode of delivery in each case depended on the conditions of the mother and fetus. Serial ultrasound monitoring at regular intervals was performed, and patients were followed-up till delivery .Effect of L-arginine on oligohydramnios and intrauterinegrowth was analyzed. As far as fetal well-being was observed spontaneous delivery was recommended. In case of fetal distress a cesarean section was performed. After delivery, following parameters were assessed: gestational age and mode of delivery, Apgar score in the 1st and 5th minute, birth weight,NICU admission Student's t test was used to find the statistical significanceof the observations. The differences were considered significant if the P value was<0.05 and highly significantif it was < 0.01.

III. RESULTS

Table 1 shows Data for parity, gestational age at recruitment, and mean liquor volume

Maternal characteristics

Total number of patients	50
Parity	Primigravida -37(74%) Multigravida -13(26%)
Mean gestational age	32.4weeks
Mean AFI BEFORE INTERVENTION	5.321cm

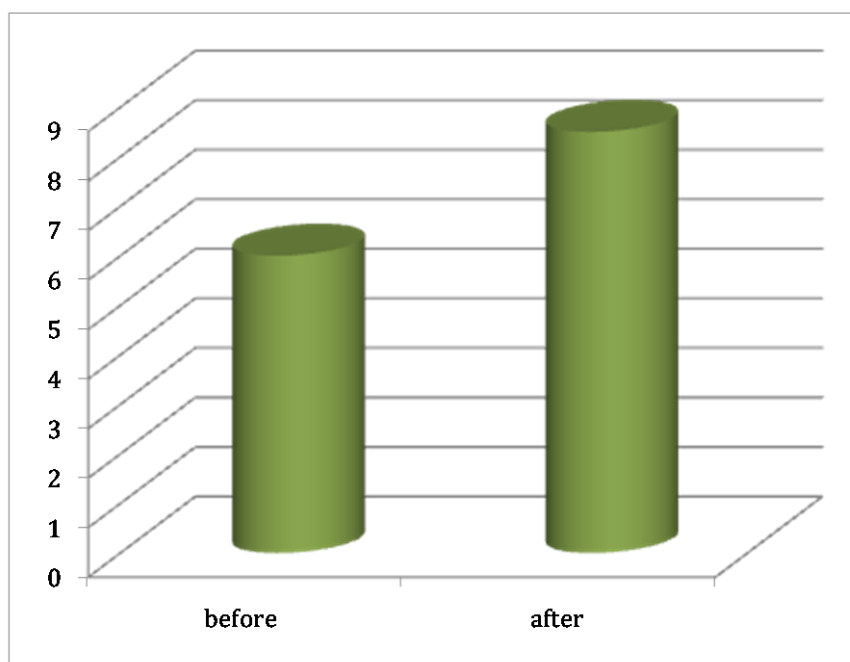
The majority of cases were primigravidae (74%). They were detected to have low liquor during their third trimester(range 29-35 weeks) scan for fetal growth and amnioticfluid estimation. We defined low normal liquor as AFI in the range of 5.1-8 cm and oligoamnios as AFI <5 cm. The mean value of AFI was 5.321 around 32.4 weeks in the patients we studied.

Table 2 shows Antenatal risk factors

	NUMBER OF PATEINTS
MILD IUGR	16(32%)
GESTATIONAL HYPERTENSION	14 (28%)
ANAEMIA	8 (16%)
THREATENED PRETERM	3(6%)
HYPOTHYROIDISM	1(2%)
GESTATIONAL DIABETES	1(2%)
PREVIOUS LSCS	3(6%)
ASTHMA	1(2%)
NO COMPLICATION	3(6%)

Mild intrauterine growth restriction (IUGR) was detected in 32% of patients. Mild IUGR was experienced by those fetuses with biometric parameters (mainly abdominalcircumference) falling below 10th percentile, but with noDoppler changes such as absent or reversed diastolic flow in umbilical arteries, cerebroplacental ratio >1.08, and no venous Doppler changes. The other major antenatal risk factors included gestational hypertension and anaemia.

The overall improvement in AFI is shown in Graph 1.



The overall increase in liquor was found to be 2.5cm [pretreatment AFI 6 (SD 1.205), post-treatment AFI 8.5(SD 1.042); <0.05]. The increase was statistically significant in all the classes. Rate of cesarean delivery noted is 70 %. Main indication is fetal distress as fetuses with less amount of liquor are likely to experience cord compression and variable deceleration.

Table 3: shows the overall obstetric outcome of these patients.

Mode of delivery	Frequency
Caesarean delivery	35(70%)
Normal delivery	15(30%)

Table 4 : shows neonatal outcome

Birth weight	2.3 -2.9 kg
Small for GA	17 (34%)
APGAR Score	
<4	Nil
4-6	3
>7	47
Still birth/ Neonatal death	Nil
NICU Admission	10(20%)

There were no perinatal deaths. There were 3 neonates who had 5-min APGAR score between 4 and 6. Two of them recovered in neonatal intensive care unit (NICU) with continuous positive airway pressure (CPAP) ventilation. One developed respiratory distress and required invasive mechanical ventilation; however, the babies recovered completely. Neonatal outcomes are shown in table 4. The end point of the intervention was to achieve reasonable gestational age of 36–37 weeks in our study. The average gestational age at the time of delivery was 35 ± 1.1 weeks, and thus, 2.4 weeks of prolongation period was noted with the therapy. Overall growth of the fetus and improvement was noted due to increased gestational period and gave time to administer inj betamethasone for lung maturity. There was no significant neonatal morbidity in the babies born.

IV. Discussion

With the easier availability of ultrasonography nowadays more cases of oligohydramnios are being identified. However the need for an effective, economical, easily available treatment modality remains unmet. Maternal dehydration has been always believed to cause oligohydramnios though it cannot be coined as the

cause in every case. Recently, serial ultrasound guided amnio-infusions have been tried but with varying success rates. Moreover it carries the inherent danger of fetal loss as it is an invasive procedure. L-arginine is a versatile amino acid with a wide range of biological functions. It serves as a precursor not only to proteins but also nitric oxide which has been identified as endothelium-derived relaxing factor. L-arginine increases uteroplacental blood flow through nitric oxide mediated dilatation of vessels thereby increasing the supply of nutrients to the fetus aiding its growth.

L-arginine promotes intrauterine growth of the fetus by increasing bioavailability of endothelial nitric oxide (NO) production and improving the umbilical artery flow in pregnant women with pregnancy-induced hypertension and IUGR. In a study by Dera et al, use of L-arginine was associated with lower rate of operative deliveries and higher Apgar scores at both 1 and 5 minutes (8) . Sreedharan et al. studied the effect of l-arginine in 100women diagnosed to have oligoamnios between 28 and 36 weeks of gestation.[9] 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.

Shripad Hebbar et al studied the effect of Maternal hydration and L-arginine supplementation in improving liquor volume in patients with decreased liquor and prolongs pregnancy[9] Treatment with l-arginine and fructodex resulted in significant improvement in liquor mean increase in AFI WAS found to be 2.4 and mean increase in gestational age was 2.9 weeks in their study . In our study the mean duration of treatment was 2.3 ± 1.1 weeks which was similar to study by Anita Soni et al in which duration of therapy in study was 2.4 ± 1.1 weeks (10) Therefore, studies recommend the supplementation of L-arginine and antioxidants in pregnancy to maintain the levels of NO so as to facilitate the requiredvasodilatation and have a beneficial role in the fetal growth.

IV. CONCLUSION

This study points towards the effectiveness of L-arginine in increasing amniotic fluid index in cases of oligohydramnios. Though evidences are accumulating on the possible benefits of L arginine ,however extensive long-term studies are required to demonstrate not only its efficacy but also its effect on maternal and perinatal outcome which would help in establishing its role as a potent non invasive treatment option in oligohydramnios.

Acknowledgements

The authors are thankful to the patient and her attendants for their consent to publish the case .

Conflict of interest

The authors declare no conflict of interest.

Source of funding

None

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