ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

EFFECT OF L-ARGININE IN OLIGOHYDROMNIOS TO IMPROVE PERINATAL OUTCOME

KEY WORDS:

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ABSTRACT

BACKGROUND: Oligohydramnios is associated with adverse perinatal outcomes like fetal distress, meconium staining, low APGAR, and increased perinatal morbidity and mortality. So assessment of amniotic fluid index with the help of L-Arginine is a helpful tool in determining the perinatal outcome. **AIMS AND OBJECTIVES :** To study the effect of L-Arginine in oligihydromnios to improve perinatal outcome **METHODS:** It is a prospective study conducted on 200 antenatal women in the Department of obstetrics and gynaecology, Narayana medical college and hospital, Nellore. The study group comprises of pregnant women between 28 to 36 weeks of gestation fulfilling the inclusion and exclusion criteria. The fetal APGAR score at 1 and 5 minutes was recorded. The outcome of the baby was studied in terms of NICU admission, birth weight. **RESULTS:** In our study, fetal distress (29%) was the most common indication for the Emergency cesarean section in the oligohydramnios group. 79% of babies in the oligohydramnios group were less than 2.5kg, APGAR was <7 at 5min in 45% of babies in the oligohydramnios group and 9% of babies were admitted to NICU. **CONCLUSION:** L-arginine supplementation shows an efficient increase in the volume of amniotic fluid in cases of oligoamnios and prolongs pregnancy by a mean of 2.5 weeks, allowing fetal lung maturation. Considering the cost of rearing preterm babies in the NICU, the administration of oral L-arginine can use as the best and feasible method in low resource countries.

INTRODUCTION

Amniotic fluid is essential to the well-being of the fetus. It serves several roles during pregnancy. Amniotic fluid volume is the sum of inflow and outflow of fluid into the amniotic space and, as such, reflects the fetal fluid balance. Clinical assessment of amniotic fluid volume is an integral part of the fetal assessment as variation in amniotic fluid amount has been relating to a variety of pregnancy complications. Diagnosis is generally made by measuring the amniotic fluid compartment using sonographic criteria. Oligohydramnios is diagnosed when ultrasonographically, the AFI is ≤ 5cm or a single deepest pocket of 2 cm1. It affects 3-5% of pregnancies2.

Oligohydramnios is associated with adverse perinatal outcomes like fetal distress, meconiumstaining, low APGAR, and increased perinatal morbidity and mortality.

So assessment of amniotic fluid index with the help of L-Arginine is a helpful tool in determining the perinatal outcome. This study is conducted to assess the effect of L-Arginine on Oligohydramnios and its correlation with perinatal outcome.

MATERIALS AND METHODS

It is a prospective study conducted on 200 antenatal women in the Department of obstetrics and gynaecology, NMCH. The study group comprises of pregnant women between 28 to 36 weeks of gestation fulfilling the inclusion and exclusion criteria. Data was collected using a pretested proforma meeting the objectives of the study by convenience sampling method. Selection of cases was considered based on detailed history like duration of amenorrhea, fetal movements, past obstetric history, medical history regarding hypertension, diabetes, and renal disease were noted. On clinical examination presence of anemia, pedal edema, blood pressure was recorded.

On per abdomen examination, the following points: Symphysiofundal height. Presentation and position of the fetus. Fetal heart sounds. Amount of liquor- decreased or increased clinically.

Per vaginal examination was done to observe the Bishop's score and adequacy of the pelvis for women.

All the cases subjected to routine blood investigations like blood grouping, Rh typing, HIV, HbsAg, VDRL, GTT, urine routine, and microscopy. A detailed ultrasound examination was done, and AFI was measured using Phelan's four-quadrant ultrasound technique. An AFI of 5.1 - 24cm is normal. AFI ≤ 5cm is considered Oligohydramnios. Written informed consent taken from the study group. 100 pregnant women with Oligohydramnios in controls and other 100 pregnant women with Oligohydramnios treated with L-arginine containing 3 grams of the active ingredient three times a day in cases included in the study. The following outcomes evaluated: 1. Mode of delivery 2. Improvement of AFI. 3. APGAR at 5 minutes. 4. Birth weight. 5. NICU admission. 6. Perinatal Outcome.

INCLUSION CRITERIA:

Pregnant women between gestational age 28 to 36 weeks with intact membranes, Singleton pregnancy.

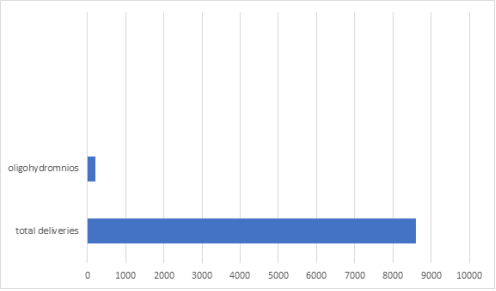
EXCLUSION CRITERIA: Pregnant women with gestational age less than 28 and more than 36 weeks excluded from the study,Pregnant women with ruptured membranes, Multiple pregnancies, Placenta previa,Smoking and chronic illnesses like hypertension, congenital heart disease, renal disease, diabetes mellitus fetal malformations, severe preeclampsia, severe FGR, preterm premature rupture of membranes (PPROM).

RESULTS

Incidence During the study period (octber 2018 to december 2019) total no of the deliveries conducted was 8600, of which 200 oligohydramnios cases were taken into the current study. A total of 200 oligohydramnios subjects were enrolled in this study. One hundred cases were administered L-arginine to improve perinatal outcome, and 100 oligohydramnios subjects kept as control without L-arginine treatment.

In the current study cases, 62% were primigravida, and 38% were multigravida. The incidence of oligohydramnios was more in primigravida, which was statistically significant (P <0.0001). In controls, 51% were primigravida, and 49% were

multigravida. The incidence of oligohydramnios was more in primigravida, which was statistically significant (P=0.001).



PARITY OF CASES

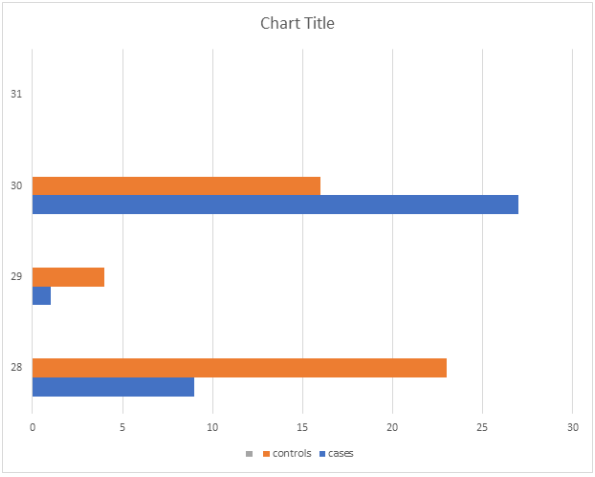
PRIMI GRAVIDA	62%
MULTIGRAVIDA	38%

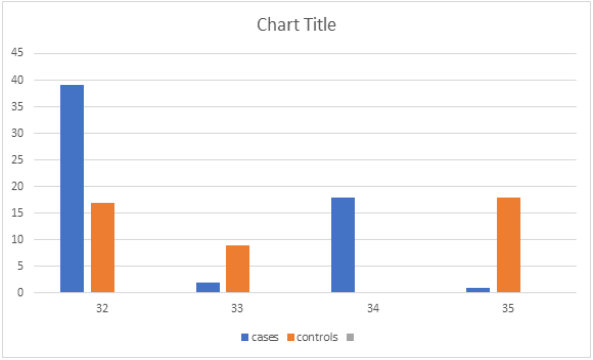
PARITY OF CONTROLS

PRIMIGRAVIDA	51%
MULTIGRAVIDA	49%

In cases, the mean gestational age (GA) at the time of diagnosis was 31.45 weeks. Among them, 39 participants were 32 weeks of gestation, and 27 participants were 30 weeks of gestation, and 18 participants were 34 weeks of gestation.

In controls, the mean gestational age (GA) at the time of diagnosis was 31.59 weeks. Among them, 23 participants were 28 weeks of gestation, and 16 participants were 30 weeks of gestation, and 17 participants were 32 weeks of gestation, and 18 participants were 34 weeks of gestation.

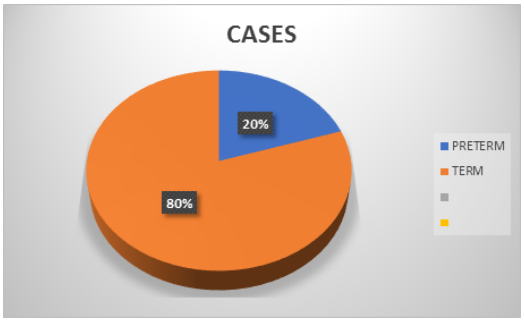




In cases, the mean AFI at the time of diagnosis and after treatment with L-arginine was 3.48 cm and 6.11 cm, respectively, with a mean duration of 2.87 wks. After a mean treatment duration (SD) of 2.87 weeks, a mean increase of AFI by 2.50195 ± 0.21891 cm was observed, which was statistically significant (P <0.0001). A statistically significant increase of AFI was noted cases (P<0.0001).

Gestational age	Difference in AFI	Difference in AFI	Difference in AFI
	2CM	3CM	4CM
28	1	6	2
29	1		
30	13	10	4
31	1	2	
32	26	10	3
33	10	3	5
34	10	3	5
35	1		
TOTAL	53	33	14

There are 80% and 54% of term pregnancies in cases versus controls. Only 66 participants required operational deliveries, whereas 34 participants delivered by normal vaginal delivery in cases, and 60 participants required operational deliveries, whereas 40 participants delivered by normal vaginal delivery in controls. There were no stillbirths or intrauterine deaths.



MODE OF DELIVERY

	CASES	CONTROLS
VAGINAL	34	40
CESAREAN	66	60

Neonatal Outcomes Mean (SD weight of the newborns was 2.59(0.372) kg in cases, which is best when compared to controls with a mean birth weight of 1.99 kilograms ± 0.7316. Mean APGAR score (SD) at 5 minutes was 7.816 ± 1.480 and 7.021 ± 1.047 in controls and cases, respectively. The details regarding the mean AFI of the women with the neonatal characteristics given (birth weight and NICU admissions) in the table.

APGAR at 5 min	cases	controls
4	4%	1%
6	22%	44%
8	41%	49%
9	20%	-
10	11%	-

Among 100 newborns, 9% required Neonatal Intensive Care Unit (NICU) admission whereas, 91% did not require NICU admission in cases who treated with L-arginine. In cases, the mean AFI (SD) of women whose babies needed NICU admission was 6.0161 (0.113)cm and who did not require NICU admission was 6.1225 (0.126)cm. The difference in AFI was not statistically significant (p=0.0025*).

DISCUSSION

Amniotic fluid is one of the vital requirements for proper fetal growth and good fetal outcome. Decreased amniotic fluid is associated with the most dreaded complications like placental insufficiency, defective lung formation, and reduced space for the fetus to grow and move. Amniotic fluid volume increases typically to about a litre between 32 and 34 weeks but decreases after that at term about 400 ml. An AFI of 8 and above is said to be normal, between 5 and 8 as below normal, and less than five is called oligoamnios. In chronic placental insufficiency, the fetus attempts to adapt by redirecting blood flow to vital organs such as the brain and heart at the cost of renal circulation. There is a significant

reduction in urine output, which results in a reduction of available intrauterine space for adequate fetal growth. The fetus has musculoskeletal deformities such as club foot, talipes, and wry neck noted. It is a known fact that severe oligohydramnios is associated with adverse perinatal outcome. On the other hand, it remains a poor predictor in detecting an outcome. But often oligohydramnios is used as an indication for operative delivery. Hence assessing amniotic fluid volume antenatally is essential in determining high and low-risk groups. With the quick availability of ultrasonography nowadays, more cases of oligohydramnios are being identified. The invasive treatment options like amnioinfusion not only had variable success rates but also can lead to fetal loss.

L-Arginine is thus promising alternative as diverse physiological functions such as improving amniotic fluid index, promoting intrauterine growth of the fetus, prolonging period of gestation, and decreasing operative deliveries. L-arginine, a semi-essential amino acid, is an endogenous precursor of nitric oxide (NO).NO plays a vital role in the regulation of blood flow in vascular beds4 and placental perfusion, vasodilatation, and platelet aggregation3. This mechanism increases the volume and viscosity of blood in the maternal-fetal circulation4. L-arginine promotes the growth of the fetus in utero by increasing its bioavailability of endothelial nitric oxide (NO) production, thus improving the umbilical artery flow in pregnant women with pregnancy-induced hypertension and IUGR.L-arginine is a semi-essential amino acid acting as the substrate for the synthesis of Nitric oxide (NO)5.

. Nitric oxide is synthesized from the physiologic precursor L-arginine by the stereospecific enzyme Nitric oxide synthase and is called as L-arginine/NO pathway, and L-arginine is the only substrate for Nitric oxide6. Nitric oxide diffuses through the underlying vascular smooth muscle cells and mediates the vasodilatation and platelet stabilization by cyclic GMP-dependant process 7.

L-Arginine also suggested that it may play a major role in fetal growth, by stimulating insulin secretion, and as a precursor for polyamine synthesis and nitric oxide production8. The L-arginine treatment enhances fetal weight gain and improves biophysical profile 9. Gene expression and protein tissue content of arginase II (an enzyme that degrades arginine to ornithine) were found to be more in preeclamptic villi than in normotensive pregnancy10.

The combination of a deficiency of nitric oxide and a raise in peroxynitrite is associated with placental dysfunction, increased thromboxanes and endothelins, and a decrease in prostacyclins. Therefore, the study recommends the supplementation of L-arginine and antioxidants in pregnancy to retain the levels of Nitric oxide so as to facilitate the required vasodilatation and have a beneficial role in fetal growth. The amniotic fluid volume measured with the four-quadrant technique done by ultrasound. It is the sum of the maximum vertical fluid pockets (measured in cm) in each of the four quadrants. Quantitatively oligohydramnios is described as the amniotic fluid index (AFI) <5 cm or <5th percentile for the gestational age or 5-10 cm as borderline or single deepest pocket (SDP) <2 cm. Though there is no specific treatment for oligohydramnios, the use of L-arginine seems to be promising. In our study, a total of 200 oligohydramnios subjects was taken into consideration. In these, 100 patients were administered L- arginine to improve the perinatal outcome in comparison to the control subjects of oligohydramnios without L-arginine treatment. The mothers were prescribed sachets of L-arginine containing 3 grams of the active ingredient three times a day for periods varying between 1 and 4 weeks. Sreedharan et al25 studied the effect of L-arginine in 100 women who were diagnosed to have oligohydramnios between 28 and 36 weeks of gestation. This is a prospective study conducted from Oct 2018 to dec 2019. The total no of deliveries during the study period was 8600, of which 200 oligohydramnios cases were taken into the current study.

CONCLUSION

L-arginine supplementation shows an efficient increase in the volume of amniotic fluid in cases of oligoamnios and prolongs pregnancy by a mean of 2.5 weeks, allowing fetal lung maturation, thus benefiting the neonatal outcome by preterm deliveries and operative intervention.

Considering the cost of rearing preterm babies in the NICU, the administration of oral L-arginine can use as the best and feasible method in low resource countries. Though data shows the benefits of L arginine, however, long-term, extensive studies are required to demonstrate its effect on the maternal and perinatal outcome, which would help in establishing its role as a potent non-invasive treatment option in oligohydramnios.

REFERENCES

1. Cunningham, Leveno, Bloom Hauth, Rouse, Spong, Williams Obstetrics-23rdedition, chapter 21,490-499.
2. D K James, P J Steer, C P Weiner, B Gonik-High risk pregnancy and management options, 4th edition, chapter 12, 197-207.
3. RCOG. Nitric oxide, the endothelium, pregnancy and preeclampsia. Br J Obstet Gynaecol. 1996;103:4–15
5. Appleton J. Arginine: clinical potential of a semi essential amino acid. Altern Med Rev. 2002;7:512–22.
6. Mittal R, Satwant K, Mittal N, et al. L-arginine supplementation in intrauterine growth retardation. Int J Pharm Chem Sci. 2013;2(3):1569–72. (ISSN: 2277–5005).
7. Viviana DP, Giuseppe C, Fabio F. Clinical use of nitric oxide donors and L-arginine in obstetric. J Mater Fetal Neonatal Med. 2007;20(8):569–79.
8. Lampariello C, De Blasio A, Merenda A, et al. Use of L-arginine in intrauterine growth retardation (IUGR): authors' experience. Minerva Ginecol. 1997;49:577–81.
9. Staff AC, Berge L, Haugen G, et al. Dietary supplementation with L-arginine or placebo in women with pre-eclampsia. Acta Obstet Gynecol Scand. 2004;83:103–7.70
10. Thureen PJ, Baron KA, Fennessey PV, et al. Ovine placental and fetal arginine metabolism at normal and increased maternal plasma arginine concentrations. Pediatr Res. 2002;51:464–71.
11. Xiao XM, Li LP. L-Arginine treatment for asymmetric fetal growth restriction. Int J Gynecol Obstet. 2005;88:15–8. 38. Myatt L, Rosenfield RB, Eis ALW, et al. Nitrotyrosine residues in placenta evidence of peroxynitrite formation and action. Hypertension. 1996;28:488–93.