ejpmr, 2021,8(9), 311-313

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

EFFECTS OF L- ARGININE IN OLIGOHYDRAMNIOS: A REVIEW

***Dr. Nabajyoti Baishya and Dr. Clarinda Khongwar**

Department of Obstetrics & Gynaecology, Bethany Hospital Shillong, Meghalaya, India.

***Corresponding Author: Dr. Nabajyoti Baishya**

Department of Obstetrics & Gynaecology, Bethany Hospital Shillong, Meghalaya, India.

Article Received on 14/07/2021 **Article Revised on 03/08/2021** **Article Accepted on 23/08/2021**

ABSTRACT

Amniotic fluid is an essential liquid that provides cushioning of the fetus against mechanical and biological injury, facilitating the growth of the fetus and supplying nutrients. Oligohydramnios is a decreased amount of amniotic fluid which is associated with placental insufficiency, impaired lung development in fetus and fetal growth restriction. Long term complications may result in cord compression, fetal heart rate variation in labour, and increased chance of operative deliveries. L-arginine have been used in various studies to find out the effect on AFI, the mode of delivery and the fetal outcome.In this article, required information was collected through few case studies done on effects of L-arginine on oligohydramnios. L-arginine is an endogenous sole precursor of nitric oxide which is an important regulator of placental perfusion and plays a vital role in placental vascular endothelial function. L-arginine increases uteroplacental blood flow through nitric oxide, thereby, increasing the supply of nutrients to the fetus aiding its growth. With administration of L-arginine, there is increased in amniotic fluid index and prolongation of gestational period.

KEYWORDS: Amniotic fluid, L-arginine in Oligohydramnios, Oligohydramnios.

INTRODUCTION

Amniotic fluid is the protective liquid contained by the amniotic sac of a gravid amniote. It serves as a cushion for the growing fetus protecting against mechanical and biological injury, supplying nutrients and promoting growth of the fetus. Oligohydramnios is the decreased amount of amniotic fluid seen in about 3-5% of pregnancies associated with placental insufficiency, impaired lung development in fetus, fetal growth restriction and long-term complications like cord compression, variation in fetal heart rate during labour and increased chances of operational deliveries.[1] L-Arginine and maternal hydration has been found to increase the amniotic fluid index in cases of oligohydramnios and improved perinatal outcome.

Amniotic Fluid

Amniotic fluid is a clear, slightly yellowish liquid that surrounds the fetus during pregnancy. The amniotic fluid is the protective liquid contained by the amniotic sac of a gravid amniote. This fluid serves as a cushion for the growing fetus, but also serves to facilitate the exchange of nutrients, water and biochemical products between mother and fetus. The source of amniotic fluid in early pregnancy is unclear but it is present from the formation of the gestational sac. The similarity in osmolality between maternal plasma and amniotic fluid suggests that amniotic fluid is an ultrafiltrate of maternal plasma. There are two possible ways on how amniotic fluid reaches amniotic cavity, i.e., through placental surface and through non-keratinised fetal skin. Keratinisation of the skin however occurs at 24 weeks of gestation and then mucosal surfaces of oral and nasal cavities play the role. [1] In the first 20 weeks of gestation, lung secretions with hydrostatic and osmotic transport of maternal plasma through fetal membranes, make up majority of the production. Around 16 weeks when the kidneys begin to function, fetal urine contributes as a principal source of amniotic fluid production till termed gestation hence proved as evidence by lack of amniotic fluid in fetuses with bilateral renal agenesis. Adequate amniotic fluid volume is maintained by a balance of fetal fluid production (lung liquid and urine) and resorption (swallowing and intramembranous flow). Even though different hypotheses have been advanced on the mechanisms regulating this turnover, the inflow and outflow mechanism that keeps amniotic fluid volume within the normal range is not entirely clear.[2]

In Initial stage, the amniotic fluid mainly contains of water and electrolytes, and by around 12-14 weeks, the liquid also contains of protein, lipids, urea and carbohydrates all of which promotes the growth of the fetus.

The volume of the amniotic fluid varies with the growth of fetus. It increases to about 800-1000ml between 32 and 34 weeks of gestation and thereafter decreases to around 400ml till term gestation.[1,3,4,5]

The volume of amniotic fluid is evaluated by Ultrasound using Amniotic Fluid Index (AFI) or Single Largest Pocket (SLP). An AFI of 8cm or more is considered as normal, between 5cm and 8cm is considered as low normal, and less than 5cm is considered as oligohydramnios.[3,4,5]

Oligohydramnios

Oligohydramnios is defined as decreased amniotic fluid volume (AFV) for gestational age and Amniotic Fluid Index (AFI) less than the 5th centile for gestational age. AFI less than 5cm is considered as oligohydramnios. Oligohydramnios is seen in around 3-5% of pregnancies.[1,4]

Oligohydramnios is associated with many medical and obstetric conditions including Chronic hypertension, Vascular disease, Thrombophilia, Pre-eclampsia, Gestational Diabetes, Preterm Premature Rupture of Membranes (PPROM) in second and third trimester (37% of oligohydramnios cases), Genitourinary tract abnormalities (renal agenesis, obstructive nephropathy), Post term pregnancies, Fetal demise, Abruptio placenta (8.6% of oligohydramnios cases) and Twin-twin transfusion.[6]

Decreased amniotic fluid is associated with:

- Placental insufficiency
- Impaired lung development in fetus
- Intrauterine fetal growth retardation

Oligohydramnios may result in long term complications like

- Compression of the cord
- Variation in fetal heart rate during labor
- Increased chances of operative deliveries.

The surviving infants may present with anatomical and physiological consequences such as contractures, skeletal deformities and pulmonary hypoplasia.[1,4]

In chronic placental insufficiency, the fetus tries to acclimatize by redirecting the blood flow to the vital organs such as the brain and the heart at the cost of renal circulation. There is significant reduction in the urine output, which is the primary source of amniotic fluid, resulting in decreased availability of intrauterine space for adequate fetal growth. Subjected to pressure from all sides, the fetus attains a peculiar appearance like potter facies (including low set of ears, flat nose, prominent epicanthal folds) and musculoskeletal deformities of hands and feet such as club foot, talipes and wry neck. Lack of movement of amniotic fluid around the tracheobronchial tree may result in lung underdevelopment.[3,4,5]

L-Arginine

L-arginine is a nutritionally essential amino acid, the endogenous precursor of nitric oxide (NO) synthesis. NO is a ubiquitous mediator that is formed by a family of enzymes called NO synthases. In the brain it acts as a neurotransmitter; in the immune system it acts as a mediator of host defense; in the cardiovascular system, it mediates the protective effects of the intact endothelium, acting as a vasodilator and endogenous, antiatherogenic molecule. L- arginine is an important regulator of placental perfusion. It leads to vasodilatation and causes aggregative effect on platelets which increases the volume and viscosity of blood in the fetomaternal circulation.[1,4] NO- induced vasodilatation in renal vessels and improve Glomerular Filtration Rate and thereby promote urine production in fetus which is the main source of amniotic fluid. L-arginine enhances the intrauterine fetal growth by increasing the bioavailability of endothelial nitric oxide synthesis and improving the umbilical artery flow during gestational hypertension and fetal growth retardation.[5] Nitric oxide has a vital role in obstetrics in labor, cervical ripening, preeclampsia and intrauterine growth restriction. L-arginine is reported to promote secretion of growth hormone and as a result, increase in plasmatic growth hormone influencing somatic growth.[3] L-arginine treatment accelerates fetal weight gain and improves the biophysical profile.

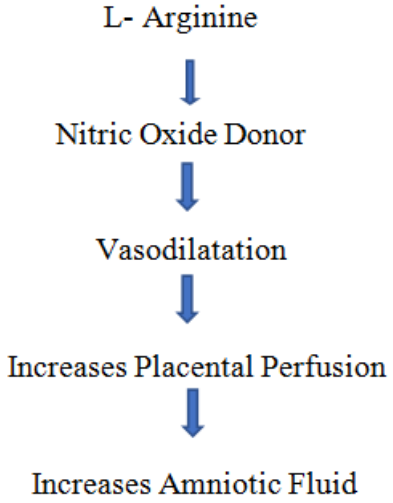

Figure 1: Mechanism of action of L-arginine.

METHODOLOGY AND RESULTS

In this review article, required information was collected through articles and keywords (Amniotic fluid, L-arginine in oligohydramnios, oligohydramnios) where case studies have been performed on selected numbers of pregnant women with decreased amniotic fluid and treated with L-arginine for a certain amount of period and the perinatal outcome was analysed.

Majority of cases were noted to occur in primigravidae (74%) and decreased amniotic fluid index (AFI<8cm) is usually detected around 26 and 36 weeks of gestation by ultrasound for scan of fetal growth and amniotic fluid estimation. All patients were administered with L-arginine 3gm per sachet in oral form till delivery and serial ultrasounds monitoring at regular intervals. Patients were then followed up till delivery. Effect of L-

arginine on oligohydramnios and intrauterine growth was analysed.

All patients were monitored and were found to have good compliance with no injurious side effects. The treatment was continued till improvement in the liquor was noted significantly. All patients were monitored with Non-Stress Test (NST)and Biophysical Profile (BPP) till delivery. [4][5] If Amniotic liquor remained less than 5cm, patients were considered for delivery irrespective of the gestational age. These patients were administered with two doses of injection Betamethasone 12mg intramuscularly 24hrs apart for acceleration of fetal lung maturity. Similarly, when the amniotic liquor remained low normal (5cm-8cm) beyond 36 weeks of gestation, patients were also considered for delivery.

As far as fetal well-being was observed, spontaneous normal delivery was recommended. In case of fetal distress, a cesarean delivery was performed. The rate of caesarean delivery was noted to be around 70-72% and the main indication was found to be fetal distress, as with less amount of liquor, fetuses are likely to experience cord compression and variable decceleration.[3,4]

The overall increase in liquor was found to be 2.5cm-2.6cm and the prolongation of gestational period was noted to be 2.4 -2.9 weeks with this therapy. The prolongation of gestation was beneficial as it improved the fetal intrauterine stay and growth. There was no significant neonatal morbidity in the babies born.[3,4,5]

There were no perinatal deaths reported in any of the studies. However, around 34% of neonates presented with birth weight SGA (small for gestational age) were reported; 14-20% of NICU admission where neonates with APGAR score between 4 and 6 at 5th-min were being treated with Continuous Positive Airway Pressure (CPAP) and recovered. Very few neonates developed respiratory distress and required invasive mechanical ventilation. However, all the babies recovered completely. There were no incidence of hypoxic ischemic encephalopathy, necrotizing enterocolitis, or sepsis in any of the babies.[3,4,5].

DISCUSSION

Amniotic fluid plays a multiple role in fetal development. Its main function is to promote development of fetal lungs by two-way movement of fluid into fetal bronchioles and severe oligohydramnios in early stage is associated with pulmonary hypoplasia. Amniotic fluid allows growing fetus to move freely and prevents contractures, adhesions between fetus and protects the fetus from mechanical injury. With easier availability of transabdominal ultrasound, more cases of oligohydramnios are being detected. Oligohydramnios is decreased amniotic fluid volume with Amniotic Fluid Index less than 5cm.

L-arginine is a versatile amino acid with a wide range of biological functions. It serves as a sole precursor to nitric oxide which is identified as endothelium-derived relaxing factor. Nitric oxide mediates vasodilatation and causes aggregative effect on platelets which increases the volume and viscosity of blood in the fetomaternal circulation, thereby increasing the supply of nutrients to the growing fetus. Nitric oxide plays a vital role in labor, cervical ripening, preeclampsia and intrauterine growth retardation. L-arginine promotes intrauterine growth by increasing bioavailabilty of endothelial nitric oxide production and improving the umbilical artery flow in pregnant women with pregnancy induced hypertension and fetal growth retardation. L-arginine treatment accelerates fetal weight gain and improved fetal well-being.

Therefore, studies recommend the supplementation of L-arginine in pregnancy especially in oligohydramnios to maintain the level of nitric oxide so as to facilitate the vasodilatation and obtained a beneficial for fetal growth.

CONCLUSION

Based on the various studies performed and the evidences of effectiveness of L-arginine in increasing the amniotic fluid index in cases of oligohydramnios and promoting the fetal growth, this article supports use of supplementation of L-arginine in oligohydramnios.

REFERENCE

1. Matrood AlKhazraji RH, Abdulhussain AS, Hachim MH. The Effect of L-Arginine on Amniotic Fluid Index in Pregnant Women with Oligohydramnios. Indian Journal of Forensic Medicine & Toxicology, 2019 Oct 1; 13(4).
2. Modena AB, Fieni S. Amniotic fluid dynamics. Acta bio-medica: Atenei Parmensis, 2004 Jan 1; 75: 11-3.
3. Sharma A, Dashora S, Sharma R, Chandra K, Gunawa MS. To Study The Effect of L-Arginine in Oligohydramnios To Improve Perinatal Outcome. IOSR J Dental Med Sci (IOSR-JDMS), 2017; 16(4): 16-9.
4. Soni A, Garg S, Patel K, Patel Z. Role of l-Arginine in Oligohydramnios. The Journal of Obstetrics and Gynecology of India, 2016 Oct; 66(1): 279-83.
5. Hebbar S, Rai L, Adiga P. Maternal hydration and L-arginine supplementation improves liquor volume in patients with decreased liquor and prolongs pregnancy. Medical Journal of Dr. DY Patil University, 2014 Jul 1; 7(4): 429.
6. Keilman C, Shanks AL. Oligohydramnios. StatPearls [Internet], 2020 Sep 15.