

A COMPARATIVE STUDY OF THE EFFECT OF ORAL AMINO ACID SUPPLEMENTATION VS INTRAVENOUS AMINO ACID INFUSION ON AMNIOTIC FLUID INDEX AND PERINATAL OUTCOME IN PREGNANCIES COMPLICATED BY OLIGOHYDRAMNIOS AND FOETAL GROWTH RESTRICTION.

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ABSTRACT:

BACKGROUND: *The primary function of amniotic fluid is protection of the growing foetus while providing nutrition. A considerable amount of research has been conducted to evaluate interventions to improve amniotic fluid index and the subsequent impact on foetal growth restriction and oligohydramnios. However, there isn't any conclusive evidence hence this study aims to compare the effect of oral amino acid supplements and intravenous infusions in pregnancies with oligohydramnios and foetal growth restriction.*

AIM: *To compare the effect of oral amino acid supplementation vs intravenous amino acid infusion on amniotic fluid index and perinatal outcome in pregnancy complicated by oligohydramnios and foetal growth restriction*

OBJECTIVES: *To compare the effectiveness of oral amino acid supplementation vs intravenous amino acid infusion in pregnancy having oligohydramnios and foetal growth restriction. To study the increase in amniotic fluid index in pregnancy with foetal weight gain. To study the interval growth rate of baby after two weeks and four weeks of therapy.*

MATERIAL AND METHOD: *This Semi experimental study will be conducted in Department of Obstetrics and Gynaecology, AVBRH, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha. A total of 104 clinically and sonographically proven cases of foetal growth restriction & Oligohydramnios in third trimester attending antenatal clinic or admitted in wards, fulfilling the exclusion and inclusion criteria will be comprise the study groups. After providing oral supplements or intravenous infusions arbitrarily, repeat ultrasonography will be done after two weeks and four weeks of therapy.*

EXPECTED RESULTS: *We compare from our results the effect of oral amino acid supplementation vs intravenous amino acid infusion on amniotic fluid index and perinatal outcome in pregnancies complicated by oligohydramnios and foetal growth restriction.*

KEYWORDS: *Pregnancy, Amniotic fluid index, Amino acid supplementation, Foetal Growth Restriction, Oligohydramnios*

INTRODUCTION

Amniotic fluid is alkaline, watery content which fills amniotic cavity during gestation. Amniotic fluid provides protection for the growing foetus. It supplies nutrients to the foetus while providing a cushion against mechanical and biological injury as well as a barrier against infection. Regulation of amniotic fluid is balanced by the production lung fluid and foetal urine, and it's absorption by intramembranous flow and foetal swallowing (1) . Amniotic fluid plays an important role in foetal growth and orderly development of the foetal musculoskeletal, respiratory, genito-urinary tracts and digestive system and in a controlled sterile environment, throughout the period of gestation. (1)

Amniotic fluid gradually increases from 25 ml at 10 weeks to around 400 ml at 20 weeks and further rises to about 800-1000 ml at around 28 weeks, achieves plateaus near term and them gradually reduces to 400 ml at 42 weeks of gestation .There are various ultrasound techniques for the measurement of amniotic fluid such as amniotic fluid index, two-diameter pocket, deepest single vertical pocket. The largest pocket in each quadrant free of foetal parts and cord are measured and added to give the value of amniotic fluid index. Normal amniotic fluid ranges from 5 to 24 cm (2).

Table 1: Diagnostic criteria for AFI (Jeng et al. 1992).²

AF volume	AFI values
Oligohydramnios	≤5cm
Borderline oligohydramnios	5.1 – 8 cm
Normal	Normal 8.1 – 24 cm

Oligohydramnios has been defined as amniotic fluid index equal to less than 5 cm or a single pocket of amniotic fluid less than 2 cm(3). An insufficient quantity of amniotic fluid hampers lung maturation and can cause foetal demise.

Oligohydramnios is also correlated with placental insufficiency and foetal growth restriction in utero (4). Foetal growth restriction is the inability to acquire the genetically predetermined growth potential and can be attributed to by foetal, maternal, external or placental factors. It impacts 5-10% of pregnancies and is considered the second most common reason for perinatal mortality. There is increased association with meconium stained liquor, still birth. Studies show 5 times higher rate stillbirth and 3-times rise in neonatal mortality and morbidity (4). Foetal growth restriction infants can exhibit long-term neurological deficits such as attention and learning disability, school failure, behavioural problems, epilepsy, cerebral palsy and psychiatric disorders (5).

Foetal growth restriction is recorded affecting about 24% of newborns affecting about 30 million infants annually. Majority cases predominantly found in Asia accounting for approximately 75% of all affected infants.(6) In developing countries foetal growth restriction is observed in around 8 – 10 % of total pregnancies and almost 40 – 45 % are associated with oligohydramnios.

Amino acid supplementation and infusion is often prescribed for the treatment of oligohydramnios. Amino acids constitute the carbon and nitrogen requirement for the placenta and foetus. Amino acid acts as regulators of the development of the foetus and placenta. They are a source of protein building blocks in the foetus and they also influence metabolic cyclic pathways between placenta and foetus. These are shown to improve vascularity through nitric oxide and also stimulate insulin secretion leading to foetal growth (7) .

An essential amino acid L Arginine is a prerequisite for synthesizing polyamines and nitric oxide in foetal cells. NO is an important factor for labour and cervical ripening and plays a role in foetal growth restriction and preeclampsia. L-Arginine is considered to influence somatic growth by enhancing growth hormone releasing hormone secretion and a subsequent rise in plasmatic growth hormone. (3)

Various research has analysed various forms treatment of foetal growth restriction and oligohydramnios. Amniotic fluid index appears to be influenced by enhanced maternal nutritional status by oral and IV amino acid supplementation. Diet alone may not provide such improvement due to non-compliance and poor maternal nutrition. Various research points towards the beneficial role of oral and IV amino acids in pregnancies complicated with oligohydramnios and foetal growth restriction (8). Also, in growth restricted foetuses, the serum amino acids were found lower than those in normally grown foetuses. So to prevent and treat foetal growth restriction and oligohydramnios maternal amino acid supplementation is used. In pregnancies with foetal growth restriction with concurrent increase in uterine resistance, L-arginine infusion impacts utero-placental circulation (9).

RATIONALE:

Undernutrition of various nutrients such as amino acids and fatty acids ultimately leads to foetal growth restriction owing to shift in amino acid uptake and transport mechanisms in the fetoplacental unit. It is further complicated by oligohydramnios. There have been various studies regarding interventions to improve amniotic fluid index and consequent impact on foetal growth restriction and oligohydramnios, some of which are : bed rest, high protein diet, alamine infusion, transabdominal and transvaginal amnioinfusion, vesicoamniotic shunt, 10% maltose infusion and oral and intravenous hydration therapy. Most oral and intravenous therapies though proven to be effective, there haven't been many conclusive studies as to the guaranteed effectiveness of any one particular modality. This study is an attempt to compare on the effectiveness of oral amino acid supplementation and intravenous amino acid infusion in improving perinatal outcome

AIM:

To compare the effect of oral amino acid supplementation vs intravenous amino acid infusion on amniotic fluid index and perinatal outcome in pregnancy complicated by oligohydramnios and foetal growth restriction

OBJECTIVES:

1. To compare the effectiveness of oral amino acid supplementation vs intravenous amino acid infusion in pregnancy having oligohydramnios and FGR.
2. To study the increase in amniotic fluid index in pregnancy having oligohydramnios and FGR.
3. To study the interval growth rate of baby after 2 weeks and 4 weeks of therapy.
4. To study the effect on foetal weight gain and weight of newborn at the time of delivery.
5. To study APGAR score at the time of birth.

MATERIALS AND METHOD

Ethical approval: Ethical approval will be obtained from Institutional Ethics Committee (IEC)

Duration of Study: 2 years

Study design: Semi experimental study

Study Site: Department of Obstetrics and Gynaecology, AVBRH, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe), Wardha.

Study Population – Pregnant women in IPD unit of Obstetrics & Gynaecology, in the AVBRH hospital, Sawangi, Meghe, fitting into inclusion and exclusion criteria of study.

Sample size-

Two study group, each study group will include 52 proven cases of foetal growth restriction & oligohydramnios by clinical and sonographical assessment in third trimester attending antenatal clinic and those admitted in wards.

Sample size formula with desired error of margin (9) :

$$n = Z_{\alpha/2}^2 \times p(1-p) / d^2$$

where,

$Z_{\alpha/2}$ is the level of significance at 5% i.e. 95%

Confidence interval= 1.96

p = prevalence of oligohydramnios in 3rd trimester (10) = 5% = 0.05

d = desired error of margin= 6% = 0.06

$$n = 1.96^2 \times 0.05 \times (1 - 0.05) / 0.06^2$$

$$= 50.68$$

=52 patients needed in each group

Inclusion criteria

- singleton pregnancy
- Amniotic fluid index less than or equal to 8 cm
- Gestational age more than 28 weeks
- Intact foetal membrane
- Foetal growth restriction

Exclusion criteria

- Multifoetal gestation
- Patients with foetal congenital abnormalities
- Patients with premature rupture of membranes
- Patient with cardiovascular, abdominal and respirator pathology
- Known case of allergies to amino acid/ proteins
- women not willing to consent

Methodology

Ethical clearance from the institutional ethical committee will be taken. After taking consent, every woman will be explained the type and nature of the study, the need of supplementation & infusion and effects associated with the infusion and informed consent will be taken. We shall be applying for funding from intramural grant/ICMR/concession for synopsis

A total of 104 patients full-filling the exclusion and inclusion criteria will be admitted and monitored in the ward. Detailed menstrual, obstetric, past, personal & family history will be taken. General, systemic and obstetric examination to be done. All blood & urine investigation related to ANC profile will be done.

The patients will be segregated into two groups:

- Group A: Fifty two pregnant women in third trimester admitted in the institution who are clinically and sonologically proven cases of oligohydramnios and/or foetal growth restriction in third trimester of pregnancy admitted at our institution

Oral amino acid supplementation will be given

L- Arginine granules 5 grams sachet TDS for two consecutive weeks

- Group B: fifty two pregnant women who are clinically and sonologically proven cases of oligohydramnios and/or foetal growth restriction in third trimester of pregnancy

In group B: Usage of the pure crystalline essential amino acid IV infusion:-

Route of administration: IV infusion

Dosage: Amino acid IV infusion 200ml thrice in a week for two consecutive weeks

Drip rate: initial drip rate 15-20 drops/min, followed by 20-40 drops/min

Oral iron, calcium and multivitamins will also be given in both study groups. Other advices like bed rest in left lateral position, plenty of fluid intake will be given. Women will be followed up till their delivery. Foetal weight will be assessed clinically. Clinically and sonological assessment of liquor will be done. Repeat ultrasonography will be done after two weeks and four weeks of therapy. Outcome will be noted in the form of mode of delivery, foetal outcome, apgar score, foetal birth weight, maturity, admission to neonatal care unit and postnatal complication, if any.

EXPECTED OUTCOME:

Foetal outcome will be assessed with respect to

- Foetal weight gain
- Weight at the time of birth
- One and five minutes of birth apgar score

DISCUSSION:

Oligohydramnios and foetal growth restriction have been widely researched since no distinct therapeutic options have been developed for their treatment. Oligohydramnios and foetal growth restriction causes foetal heart abnormalities, meconium staining of amniotic fluid, lower apgar scores, foetal acidosis and poor tolerance of labour. Foetal growth restriction is associated with placental insufficiency which causes shallow trophoblast invasion during the early stages of gestation which results in perinatal morbidity and mortality. A significant number of studies published on morbidity and mortality proved major determinant of cardiovascular disease and glucose intolerance in adult life (11). Various studies have been documented without satisfactory evidence for the ideal treatment modalities. Inadequate maternal nutrition is an important cause attributed to foetal growth restriction. Thus, a considerable amount of research focuses on improving the maternal nutrition so as to improve the perinatal outcome. Attempts to improve maternal nutrition have been made by several methods: diet alone, intravenous fluids, glucose, oral supplementation of amino acids, intravenous infusion of amino acids among many others. Improvement can't be achieved with only diet because of and low socio-economic standing and non-compliance. Improvement of foetal out-come in pregnant patients with oligohydramnios is done by infusion or supplementation of amino acids.

In a study conducted in the Department of OBGY at Sher-I- Kashmir institute of medical sciences, Soura, Shrinagar parenteral amino acid infusion was used(12). Similarly, in a study by Umber, parenteral amino acid supplementation was provided to the participants (13). In both the studies, a significant improvement in amniotic fluid index was noted as compared to the control groups, resulting in overall better perinatal outcome and reduced need for operative procedures. In another study conducted by Ahmad A, intravenous amino acid supplementation with glucose was found to have improved results in the cases. American Pregnancy Association also advocates the positive co relation between maternal intravenous infusion and increase in amniotic fluid index (12).

Bioavailability of endothelial NO production and the umbilical artery flow improvement in fetal growth restriction is affected by L arginine. A research consisting of 100 antenatal patients diagnosed with oligohydramnios from term was done at Dr. Hiranandani hospital. L-arginine sachets were started for the patients. The study concluded that L-arginine supplementation is promising in improving amniotic fluid index in pregnancies complicated by oligohydramnios (14). Few of the related studies were reviewed (15,16). A number of evidences reflect on similar problems(17-20).

According to the report conducted at Acharya Shri Chan-der College of Medical Sciences from Oct 2017 to Sept 2018 in the Dept. of OBGY, the study consisted of 50 clinically and sonographically proven cases of foetal growth restriction and oligohydramnios in third trimester. It was noticed that there was significant improvement in amniotic fluid

index in the groups who received amino acid infusion as compared to the control group proved after a week by repeat ultrasound. Gupta R et al in their study observed decrease in the incidence of low APGAR scores and lowering in the number of neonatal deaths at birth when amino acids were infused to the patients. This study concluded that parenteral amino acid transfusion in cases of foetal growth restriction and oligohydramnios considerably increases the amniotic fluid index of the patients and lowers incidence of neonatal care admissions, low APGAR scores, meconium stained liquor (7).

LIMITATIONS: An important obstacle arises in the study, regarding the affordability and availability of the oral as well as intravenous supplements.

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