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IUGR – The Role of Amino-acid Supplementation

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OBJECTIVES – To see the therapeutic efficacy of amino-acid supplementation in preventing intrauterine growth restriction among "at risk" mothers. **METHODS** – This prospective case control study compared fetal outcome following amino-acid supplementation of 220 mothers having different risk factors for intrauterine growth restriction and equal number of mothers with same risk factors without supplementation. **RESULTS** – The 14.5% incidence of intrauterine growth retardation (IUGR) in the study group was significantly low compared to that of 25.7% in the control group ($p<0.01$). Among the IUGR babies in both the groups, fetal outcome was better in the study group compared to that in the control group with reference to birth weight (2 – 2.4 kg vs. 1.2 – 2.2 kg.), intraterine fetal death (IUFD) / still birth (1 vs 3) and neonatal death (nil vs 2). **CONCLUSION** – Amino- acid supplementation in pregnancy can cause meaningful reduction in the incidence of IUGR in mothers having risk factors for delivering growth retarded fetus and thereby improve perinatal outcome.

Key words : IUGR, amino-acid, hyperalimentation

Introduction

Intrauterine growth restriction (IUGR) is defined in a number of ways though none of them is absolutely precise. The best definition of IUGR is failure of a fetus to reach its genetic growth potential[1]. Though the precise cellular and molecular mechanism by which normal fetal growth occurs is ill understood. Fetal genome is one of the major determinants of growth in early fetal life. As the pregnancy advances, environmental, nutritional and hormonal influences become increasingly important in the process of fetal growth[2]. Other ways of defining IUGR are babies whose birth weights are below 10th percentile for their gestational age. But these percentiles need considerations for variations due to maternal height, weight, race, socioeconomic status, sex and birth order. Prior to 38 weeks, the diagnosis of IUGR is best made by an index of body mass like the "Ponderal Index[3]".

The global incidence of IUGR varies from 3-10% and in India, the average incidence is about 11%. But the incidence of IUGR is several times higher among mothers who are having risk factors for delivering growth-restricted babies (20-30%). Fetal growth restriction is associated with substantive perinatal mortality and morbidity. Fetal demise, birth asphyxia, meconium aspiration, hypoglycemia, hypothermia etc. are all increased, as is the prevalence of abnormal neurological development. Therefore, various attempts are being made to predict and diagnose IUGR early. Various therapies are tried to prevent and treat IUGR so as to improve overall perinatal mortality and morbidity.

Inadequate maternal nutrition can restrict growth of the fetus as reported after the Dutch Famine[4]. Fetal growth is also below par if preconception nutritional status is poor. It is not very clear whether it is due to lack of overall calories or of a specific substrate that causes IUGR. Glucose, amino- acids and lactate are the major substrates for the fetus. There is relatively less information concerning the physiology of maternofetal transfer of amino-acids. In growth restricted fetuses, the serum amino acids were found lower than those in normally grown fetuses, a feature similar to the biochemical changes seen in postnatal protein starvation states[5]. Based on this fact, there has been a renewed interest to prevent and treat IUGR by maternal amino-acid supplementation and hyperalimentation.

The present prospective study was carried out to assers the efficacy of amino-acid supplementation in the form of commercial preparation capsule viz., alamin forte and alamin-SN infusion during pregnancy for prevention of IUGR in "at risk" mothers.

Material and Methods

This prospectie study was carried out during the period September 1998 to August 2001. Two hundred and twenty mothers who had predisposing or predicting factors that could lead to IUGR were taken up for the study. These mothers were given amino-acid supplementation in the form of one alamin forte capsule thrice daily. The therapy was started between 18-26 weeks of gestation and continued till term or delivery. Fetal growth was monitored closely clinically and also by repeated ultrasound scans. When early IUGR was detected the therapy was changed to alamin-SN infusion-

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one bottle every 4th day, and continued till delivery. Fetal outcome of this study group was compared with that of similar number of matched mothers with similar risk factors who did not receive amino-acid supplementation, and served as control.

Results

The numbers of mothers with different risk factors in both the study and the control group were the same. The perinatal outcome in the study group was quite encouraging with amino-acid therapy preventing IUGR. Table I depicts the fetal outcome in the study group. Out of 241 babies in the study group (220 mothers with 21 twin pregnancies) only 35 babies had features of IUGR (14.5%), weighing less than 2.5 kg. Birth weight of the babies varied from 2 kg to 3.5kg. No baby weighed less than 2 kg. There was no intrauterine fetal death (IUFD) and only one stillbirth due to multiple congenital malformations. Table II shows the perinatal outcome in the control group. As compared to the study group the number of IUGR babies viz., 62 (25.72%) was considerably higher in the control group and the birth weight ranged from 1.2.–3.1kg. There were three stillbirths and two neonatal deaths, one from jaundice, and another from birth asphyxia and neonatal septicemia. However no congenital malformation was found in the control group. This comparison clearly demonstrates that with amino-acid therapy there is a considerable reduction in the incidence of IUGR among high-risk mothers (14.5% vs 25.7%, $p<0.01$) and so also better perinatal outcome.

Discussion

Perinatal mortality and morbidity among babies with IUGR are manifold higher than those in normally grown fetuses of similar gestation. Though the exact mechanism of normal fetal growth is ill understood, the technique of fetal blood sampling in growth impaired fetuses and analysis for various substrates including $P0_2$, $PC0_2$, ph, lactate, amino-acids and glucose has permitted remarkable insight into the pathophysiology of IUGR[6]. Like insulin and insulin like growth factors (IGF-I and IGF – II), nutrients like fat, glucose and amino-acids also play an important role in fetal growth. Economides and colleagues[7] measured glycine / valine ratios in umbilical cord blood from growth restricted fetuses and found ratios similar to those observed in children with protein deprivation. From these observations it was postulated that adequate supplementation of amino-acids might prevent or treat intrauterine growth restriction. Charlton and Johengen[8] infused 5% glucose and 6.8% amino acids in fetuses of sheep where placentas were embolized. The supplemented fetuses maintained normal growth without development of hypoxemia. Inspired by this animal study Lampariello et al[9] found a favourable outcome with l-arginine supplementation in prevention and treatment of IUGR. Two similar studies were conducted by IDECG working group (1998) on definition, classification, causes and prevention of IUGR in Norway and in Italy with improved outcome[10,11]. In our study, there was a significant reduction (14.5% vs. 25.72%) in the incidence of IUGR in the supplemented

Table I : Fetal Outcome in the Study Group.

Risk Factors	No. of Babies	No. of IUGR Babies
History of abortion	27	3 (11%)
History of IUFD / Stillbirths	18	2 (11%)
History of IUGR / Small Baby	28	6 (21.4%)
Tobacco takers	20	3 (15%)
1st / 2nd trimester bleeding	25	2 (8%)
Twin Pregnancy	21+21	10 (23.5%)
Hypertension	48	5 (10.4%)
Heart Disease / COPD	15	2 (13.3%)
Proteinuric renal disease	6	1 (16.6%)
Diabetis	12	1 (8.3%)
Total	**241**	**35 (14.5%)**

Table II : Fetal Outcome in the Control Group

Risk Factors	No. of Babies	No. of IUGR Babies
History of abortion	27	5 (18.5%)
History of IUFD / Stillbirth	18	3 (16.6%)
History of IUGR / Small Baby	28	9 (32.1%)
Tobacco takers	20	7 (35%)
1st / 2nd trimester bleeding	25	4 (16%)
Twin Pregnancy	21 +21	13 (30.9%)
Hypertension	48	16 (33.3%)
Heart Disease / COPD	15	3 (20%)
Proteinuric renal disease	6	1 (16.6%)
Diabetis	12	1 (8.3%)
Total	**241**	**62 (25.7%)**

group as compared to that in the nonsupplemented group ($p<0.01$). Moreover, even among the IUGR babies, the perinatal outcome is better in the study group than in the control group. In India, Joshi and Sapre[12] found favorable role of amino-acid infusion in the treatment of IUGR with oligohydramnios.

Thus, amino acid supplementation commencing from the early second trimester of pregnancy among high risk mothers not only reduces the chance of intrauterine growth restriction but also improves the overall perinatal outcome.

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