

Research Article

# Comparison of Therapeutic Efficacy of Dydrogesterone with Conventional Treatment in Idiopathic Intrauterine Growth Restriction

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## ABSTRACT

**Background:** IUGR is an important health problem. It is associated with perinatal morbidity and mortality. In Pakistan, its prevalence is 25%. Few studies had been conducted on idiopathic IUGR. In previous study, effect of dydrogesterone (study group) and conventional treatment (control group). In idiopathic IUGR on mean neonatal birth weight was evaluated showing an improvement of birth weight with dydrogesterone. Thus, dydrogesterone provide promising results in management of this disease.

**Objectives:** Comparison of dydrogesterone and conventional management in terms of mean neonatal birth weight in idiopathic IUGR.

**Study design and Setting:** Randomized Controlled Trial was conducted at Gyneacology Department of Tertiary Care Hospital, Wah Cantt.

**Duration of Study:** 1<sup>st</sup> July 2023 to 31<sup>st</sup> December 2023

**Methodology:** Women were erratically assigned to dydrogesterone and control group by using processor created erratic order. The controller set was treated with conventional management including bedrest and amino acid rich food while study group received dydrogesterone (Duphaston) 10mg BD. Women got treatment and followed fortnightly until birth of neonate. On every follow up visit, a questionnaire was filled by patient regarding diet and intensive care was accomplished by using medical and sonography inspection. Patients were followed in outdoor till delivery. Upon delivery neonatal birth weight was noted and recorded.

**Results:** Over-all 60 women satisfying selection standards were registered for comparison of dydrogesterone with control group receiving conventional treatment in terms of mean newborn weightiness in idiopathic Intra Uterine Growth Retardation. Comparison of mean neonatal birth weight in idiopathic IUGR shows that neonatal weight at presentation in study group was  $1.39 \pm 0.20$  grams and  $1.36 \pm 0.20$  grams in control group, p value was 0.62, natal weightiness in research group was  $2.23 \pm 0.18$  and  $1.83 \pm 0.21$  in control group, p value was 0.0001, average variation in study group was  $0.84 \pm 0.24$  and  $0.047 \pm 0.15$  in control group, p value was 0.0001.

**Conclusion:** Dydrogesterone is effective in improving neonatal birth weight than conventional regime in idiopathic IUGR.

**Keywords:** Conventional Treatment, Dydrogesterone, Idiopathic Intrauterine Growth Restriction.

## INTRODUCTION

Intra uterine growth retardation is an important health problem.<sup>1</sup> It is associated with perinatal morbidity and mortality. It is observed in 3-7% of neonates and approximately 30 million newborns are affected with IUGR every year, out of which 75% are born in Asia mainly in south central Asia. In Pakistan, the prevalence of IUGR is 25%.<sup>2</sup>

IUGR is defined as estimated natal weightiness fewer than tenth centile for gestational age at

the time of delivery.<sup>3</sup> It is multifactorial; motherly, embryonic and placental aspects could affect the standard growing mechanism.<sup>4</sup> In most of cases, no cause is identified termed as Idiopathic IUGR.<sup>5</sup> The utmost usual origin of Intra uterine growth retardation is reduced nutritional stream towards the embryo. It can be due to impaired transfer of maternal nutrients, decrease blood stream towards womb. It might necessitate nutritious supplement, motherly hyper oxygenation or pharmacologic treatment to

Increase blood flow.<sup>6</sup> Different treatment strategies have been tried 'Including gut decompressing, bedrest, increased amino acids intake, parenteral hyperalimentation fish oils, beta androgenic drugs, ritodrine, theophylline, Arginine, allylestrenol Viagra etc. Many studies have shown that there is a decrease level of progesterone in IUGR. Progesterone in this condition might be related with

Increase in blood flow towards womb. It acts on uterine musculature and cause vasodilatation of small arteries. It produces immunomodulatory effect on progesterone hindering aspect that might cause enhancing the product of gravidity in IUGR.<sup>6</sup>

Few studies had been conducted on idiopathic IUGR. In previous study, effect of dydrogesterone (study group) and conventional treatment (control group) In idiopathic IUGR on mean neonatal birth weight was evaluated showing an improvement of neonatal weightiness in kgs ( $1.17 \pm 0.37$  and  $2.03 \pm 0.41$ ,  $p=5$ ) in control and study group respectively. Thus, dydrogesterone provide promising results in treatment of idiopathic IUGR.<sup>6</sup> It is an oral analogue of progesterone and has high affinity for progesterone receptors. It does not have any androgenic, anabolic, and estrogenic and corticoid properties.<sup>7</sup>

The objective of my research is to compare the efficiency and effectiveness of dydrogesterone from conventional regime (rest and high protein diet) as there is no local data available for its use while international study shows beneficial effects in Idiopathic IUGR. The outcomes of this research would support in better management of IUGR patients in future to reduce the neonatal morbidity and mortality.

## METHODOLOGY

This Randomized Controlled Trial conducted in Gyneacology Department of Tertiary Care Hospital, Wah Cantt from 1<sup>st</sup> July 2023 to 31<sup>st</sup> December 2023. Sample size is calculated by WHO sample calculator with Significant level (%) =5%, Power of test (%) =90%, Standard deviation=0.38<sup>6</sup>, Variance=0.1444<sup>6</sup>, Average test value =1.71<sup>6</sup>, Anticipated average=2.03<sup>6</sup>. I took 30 females in respective group, Group-A (Control group) receiving conventional treatment while Group-B (study)=receiving dydrogesterone along with Conventional treatment. Non-probability consecutive sampling is used in this study. Woman at 20 to

35 years diagnosed with idiopathic IUGR at gravidity age of 28 or >28 weeks and Singleton pregnancies remained included in this study while women with diabetes, cardiac, renal and connective tissue diseases, twin pregnancy, congenital fetal and chromosomal diseases, premature rupture of membranes and severe PIH stayed out of this research work.

Afterwards consent of the ethical board of hospital. Duration of pregnancy being confirmed by last menstruation or sonography in initial three months of gestation. Females were erratically assigned to both groups using processor produced erratic numerals. The control group was provided conservative management in terms of bedrest and increased amino acid intake (4 oz beef=28g proteins, 1 large egg=6g proteins, 8oz or 16 table spoon of milk=8g proteins, 3 table spoon of yogurt =5g proteins, 1 cup lentils which is 250 gram in weight =18g proteins, 1 cup chickpeas which is 250 gram in weight=12g proteins per day).

The study group was given dydrogesterone (Duphaston) 10mg BD along with conservative management in terms of bedrest and increased amino acid intake and patients were treated and followed fortnightly till delivery. On every follow up visit, a questionnaire was filled by patient regarding diet and intensive care being provided using medical and sonography checkup. Medical checkup involved physical inspection especially vitals, increase in weightiness, Abdominal inspection for symphysiofundal height. On ultrasound fetal weight by Had lock formula was calculated. Patients were followed in outdoor till delivery. Upon delivery neonatal birth weight was noted and recorded along with demographic details of the patient. All the patients were managed by a single resident and the weight measurement was done by a single staff nurse on a single machine to eliminate bias and confounding variables were controlled by exclusion.

The statistics was endorsed and evaluated by SPSS version 16. Graphics were used to analyze quantitative data. For measurable factors (age, gravida/parity and birth weight) mean and standard deviation was designed, for qualitative factors (occupation, socioeconomic status, education) frequency was calculated. Mean change in weights were evaluated using nondependent sample t test. P value <0.05 was taken as significant. Result converters including age, gravitational age,

socioeconomic status, education and occupation was precise using stratification.

## RESULTS

A sum of 60 females gratifying the inclusion standards were registered for comparison of dydrogesterone with control group receiving conventional treatment in terms of mean neonatal birth weight in idiopathic IUGR.

Age distribution shows that 73.33%(n=22) in Study and 73.33%(n=22) in Control group were from 20-30 years of age while 26.67%(n=8) in study group and 26.67%(n=8) were from 31-35 years of age, mean $\pm$ sd was analyzed as 28.2 $\pm$ 3.43 years in Study and 28.67 $\pm$ 3.11 years in Control group. (Table No.

1) Mean parity in study group was 2.73 $\pm$ 1.14 and 2.7 $\pm$ 1.21 in control group. (Table No. 2) Mean gestational age in study group was 31.97 $\pm$ 2.89 weeks in and 31.17 $\pm$ 2.78 weeks in control group. (Table No. 3)

Comparison of mean neonatal birth weight in idiopathic IUGR shows that neonatal weight at presentation in study group was 1.39 $\pm$ 0.20 grams and 1.36 $\pm$ 0.20 grams in control group, p value was 0.62, neonatal weightiness in study group was 2.23 $\pm$ 0.18 and 1.83 $\pm$ 0.21 in control group, p value was 0.0001, mean variation in study group was 0.84 $\pm$ 0.24 and 0.047 $\pm$ 0.15 in control group, p value was 0.0001. (Table No. 6)

Table. 1 Age Dispersal (n=60)

| Age (in years) | Study group(n=30) |       | Control group(n=30) |       |
|----------------|-------------------|-------|---------------------|-------|
|                | No. of females    | %     | No. of females      | %     |
| 20-30          | 22                | 73.33 | 22                  | 73.33 |
| 31-35          | 8                 | 26.67 | 8                   | 26.67 |
| Total          | 30                | 100   | 30                  | 100   |
| Mean $\pm$ SD  | 28.2 $\pm$ 3.43   |       | 28.67 $\pm$ 3.11    |       |

Table. 2 Parity Dispersal (n=60)

| Parity        | Study group(n=30) |       | Control group(n=30) |     |
|---------------|-------------------|-------|---------------------|-----|
|               | No. of females    | %     | No. of females      | %   |
| 1-3           | 23                | 76.67 | 24                  | 80  |
| >3            | 7                 | 23.33 | 6                   | 20  |
| Total         | 30                | 100   | 30                  | 100 |
| Mean $\pm$ SD | 2.73 $\pm$ 1.14   |       | 2.7 $\pm$ 1.21      |     |

Table. 3 Gestational Age (n=60)

| Gestational age (in weeks) | Study group(n=30) |     | Control group(n=30) |       |
|----------------------------|-------------------|-----|---------------------|-------|
|                            | No. of females    | %   | No. of females      | %     |
| 29-33                      | 18                | 60  | 19                  | 63.33 |
| >33                        | 12                | 40  | 11                  | 36.67 |
| Total                      | 30                | 100 | 30                  | 100   |
| Mean $\pm$ SD              | 31.97 $\pm$ 2.89  |     | 31.17 $\pm$ 2.78    |       |

Table. 4 Comparison of Mean Neonatal Birth Weight in Idiopathic IUGR (n=60)

| Neonatal weight (grams) | Study group(n=30) |      | Control group(n=30) |      | P value |
|-------------------------|-------------------|------|---------------------|------|---------|
|                         | Mean              | Sd   | Mean                | Sd   |         |
| At presentation         | 1.39              | 0.20 | 1.36                | 0.20 | 0.62    |
| Birth weight            | 2.23              | 0.18 | 1.83                | 0.21 | 0.0001  |
| Mean change             | 0.84              | 0.24 | 0.47                | 0.15 | 0.0001  |

## DISCUSSION

Intrauterine growth restriction (IUGR) is related to augmented death rate in pre, intra and postnatal period,<sup>8</sup> along with delayed comorbidity and tendency towards progress of long-lasting ailments in grown-ups.<sup>9</sup> Amongst females with inexplicable natal demise, a large number of fetuses are below gravidity age.<sup>10</sup>

Likewise, amongst large for date gravidities with opposing consequences, small for gravidity age fetuses dominate.<sup>11</sup> Therefore, the aim for obstetrical supervision of gravidities with small for gravidity age fetuses must focused upon identification of fetuses that might underwent extreme natal decreased oxygenation and unwanted results.

The females in which intrauterine growth retardation is connected with motherly ailments like eclampsia, the obstetrical supervision could be verbalized in relation to the maternal illness. Many other conditions where retardation of development is due to natal cause, it could be addressed with the obstetrical care. A lot of other situations the developmental abnormality is related with the weak anatomical connection of fetus and uterus, in such conditions patient might be asymptomatic.

In a number of research papers, it has been established that the congenital parameters play role in development of fetus and the proportion is approximately thirty to fifty percent, while the rest of proportions were owing to ecological parameters.<sup>12-15</sup> Mother genetics effect on development of fetus more than father genetics. Precise allelomorphic related to development of fetus are, transmutations in GCK and HNF1beta, ultimately causes decreased developmental rate of the fetus, while transmutations in HNF4 alpha might cause increase in developmental rate of fetus. Other alleles like ADCY5 and loci near CCNL1 proved to be related with decreased development rate of fetus.<sup>16</sup> The vulnerability of decreased development of fetus is also inherited.<sup>17,18</sup>

Numerous management options have been experienced to overcome this developmental abnormality which causes decreased growth of fetus. Multiple research work has shown a strong bonding between low levels of maternal steroid hormones and decreased developmental rate of fetus.<sup>19-20</sup> These hormones like progesterone supplements might be associated with improved uteroplacental circulation.<sup>21-22</sup>

The mechanism behind the effect of dydrogesterone is that it decreases the production of maternal steroidal hormones during gestation.<sup>23</sup> Moreover, it might play an important role in increasing the blood supply of uterus by inducing vasodilatory effects of maternal uterine wall vasculatures which ultimately increases the blood flow towards the uterine wall and the fetus. Elahieh Zarean and others<sup>24</sup> reveals that dydrogesterone enhances the development of the fetus without causing any adverse effects in both maternal and fetus.

#### **Limitations of Study:**

Dydrogesterone supplement might be the most unpretentious and financially acceptable way in avoiding growth retardation of fetuses.

But in forthcoming researches with greater number of patients, several clinical parameters, cord and uteroplacental specimen, and evaluation of natal outcomes are reasonable to approve the consequences of their research work.

#### **CONCLUSION**

Dydrogesterone is effective in improving neonatal birth weight than conventional regime in idiopathic IUGR. Dydrogesterone supplement might be the most unpretentious and financially acceptable way in avoiding growth retardation of fetuses.

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