Intrauterine growth restriction type 0: A comparison between deliveries at 37 weeks versus spontaneous labor

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Abstract

Objective: The objective of the study was to evaluate obstetric outcomes in patients diagnosed with intrauterine growth restriction (IUGR) type 0 on termination of pregnancy at 37 weeks of gestation (WOG) compared with weekly flowmetry and spontaneous evolution or termination at 40 WOG. **Materials and methods:** An experimental, ambispective, longitudinal, comparative study carried out in a third level hospital in Northeast Mexico over a 1 year period. It included 80 patients forming two groups: patients diagnosed with IUGR type 0 with interruption of pregnancy at 37 WOG, or if older, at diagnosis, and patients with diagnosis of IUGR 0 with weekly monitoring and interruption at 40 WOG. **Results:** The demographic characteristics were similar. Gestational age at the time of termination of pregnancy was lower in Group A (38 vs. 39.2 WOG $p < 0.001$), and a higher frequency of labor induction was shown ($p = 0.007$). No significant difference was found in the number of cesarean sections between groups ($p = 0.160$). Neonatal results: weight of the newborn in Group A was lower ($p = 0.017$), the rest of the results were similar between groups. **Conclusion:** Continued pregnancy after week 37, with weekly monitoring, in patients diagnosed with IUGR type 0, decreases the number of patients undergoing induction of labor, the cesarean section index. It also allows greater weight gain of fetuses, without increasing the risk of disease progression.

Key words: Small for gestational age. Intrauterine growth restriction. Acute fetal distress. Induction of labor.

Introduction

Intrauterine growth restriction (IUGR) is the inability of the fetus to achieve its genetic potential growth, due to a lack of nutrition or, less commonly, due to genetic, toxic or infectious causes¹. Most fetuses with low weight are normal children with low genetic growth potential by statistical range. Although this potential is difficult to determine, some definitions are based on clinical variables and the measurement of fetus placental Doppler flowmetry²⁻⁵.

IUGR increases morbidity and mortality in newborns regardless of gestational age at birth⁶. It is estimated that about 30 million patients diagnosed with IUGR are born annually in the world. The prevalence in developed countries is close to 6.9% and in developing countries is up to 23.8%; in Latin America and the Caribbean, the estimate is about 10%^{7,8}. Therefore, the socioeconomic aspect must be considered to implement public health policies. However, it is noteworthy that the previous data do not differentiate between small for gestational age (SGA) and IUGR⁸⁻¹⁰.

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Low birth weight is associated with alterations in childhood development. Reports suggest that more than 50% of chronic neurological morbidity can be attributed to this disorder. Recently, it has been associated with some adult disorders, such as coronary heart disease, high blood pressure, and obesity^{11,12}. Therefore, it represents a huge burden for the patient, their family, and society.

To date, multiple definitions, classifications, and management guidelines have been developed, generating wide discussion and controversial opinions around some specific questions about the disease. Great emphasis has been placed on the correct diagnosis of IUGR because it has shown to decrease fetal morbidity and mortality and its complications such as prematurity, hypoxic-ischemic encephalopathy, necrotizing enterocolitis, intraventricular hemorrhage, meconium aspiration, and other metabolic complications¹³⁻¹⁵. On the other hand, the identification of a small fetus for gestational age without IUGR allows the reduction of unnecessary obstetric interventions and the morbidity caused by these entities.

The classification accepted by most Mexican hospitals is the recommendation by the Centro Nacional de Excelencia Tecnológica en Salud (CENETEC) published in 2011¹⁶. A new classification has been proposed for the main purpose of a correct management and identification of these products with major perinatal risk¹⁵. In this proposal, fetuses between the 3rd and 10th percentiles with a normal Doppler flowmetry are classified as SGA and it is not recommended to interrupt at 37 weeks of gestation (WOG) but to continue the pregnancy with a weekly surveillance and induction of labor at 40 WOG; this has shown a better perinatal outcome in this group, with early interventions being unnecessary¹⁷⁻¹⁹.

The main objective of this paper is to evaluate obstetric outcomes in patients diagnosed with IUGR type 0 on termination of pregnancy at 37 WOG compared to weekly flowmetry and spontaneous evolution or termination at 40 WOG.

Materials and methods

An ambispective, experimental, longitudinal, comparative study was carried out at the Obstetrics and Gynecology Department at the "Dr. José Eleuterio González" University Hospital between December 2016 and December 2017. The study was approved by the Ethics Committee of the Hospital under the following register number: GI15-016. Patients were divided into two

groups: Group A: patients who had delivery at 37 WOG (or at time of diagnosis if older) as indicated in the CENETEC guidelines (Table 1) by collecting information of clinical records retrospectively and Group B: patients recently diagnosed with type 0 IUGR who had weekly appointments at the high-risk pregnancy clinic, maintaining close surveillance through obstetric ultrasound and Doppler flowmetry and, in case of no exacerbations, pregnancy was terminated at 40 WOG with a trial of labor as the first option, prospectively. The number of patients included in the study was calculated with a formula for a hypothesis test for differences in proportions, with a α value of 1.96 with a 95% significance level in a two-tailed set and $z\beta$ value of 0.84 with a power of 80% and a difference of proportions of 0.3. A sample of 40 participants per group was obtained.

Gestational age was verified according to the first ultrasound examination: if the classification using the crown-rump length (CRL) differed by more than 1 week from the last menstrual period (LMP), the gestational age was dated by CRL; if the CRL did not differ by more than 1 week, the pregnancy was dated by LMP. If LMP was not reliable, gestational age was dated by the earliest ultrasound. Estimated fetal weight (EFW) was calculated according to an algorithm that included biparietal diameter, cephalic circumference, abdominal circumference, and femoral length. The adjusted fetal size percentile was determined using the gestational age and EFW.

Those fetuses with a percentile equal to or > 3 but < 10 were evaluated through Doppler ultrasound, including uterine arteries, umbilical artery, and the middle cerebral artery. Those who had normal blood flow were classified as IUGR type 0. In these products, a follow-up at the high-risk pregnancy clinic was monitored through weekly Doppler flowmetry, and fetometry every 2 weeks.

The variables that were evaluated in this study were age, gestational age at diagnosis (with IUGR), parity, delivery practice, and cesarean delivery indications. After birth, the following variables were analyzed: delivery practice, asphyxia, and acute fetal distress if present, meconium aspiration, fetal weight, Fenton growth charts, and APGAR score.

The inclusion criteria were age ≥ 14 years, pregnancy with a product between percentiles $\geq 3\%$ but < 10%, normal fetal Doppler flowmetry corroborated by the measurement of the umbilical artery, middle cerebral artery, and uterine arteries, terminating the pregnancy at the labor and delivery department of our hospital. Exclusion criteria: age ≤ 13 years, patients without a

Table 1. CENETEC and Figueras-Gratacos classification comparison

Type	Percentile	Ecographic features	Follow-up	Delivery	Type	Ecographic features	Management
0	> 3 < 10	Normal	Every 2 weeks	37 weeks; Vaginal	1	EFW < 3% CPR < 5% UA PI > 95% Mean UtA PI > 95%	Weekly surveillance Interruption at 37 weeks Consider risk of CTG during labor
1	< 3	Normal	Weekly	37 weeks; Vaginal	2	Absent diastolic flow of the umbilical artery above 50% of the cycles in both arteries in two occasions. Reverse diastolic flow in aortic isthmus	Twice a week surveillance Interruption at 34 weeks Consider elective C-section
2	< 10	CPR < 5% or UA PI > 95%, UtA PI > 95%	Weekly	37 weeks; Vaginal	3	Reverse diastolic flow in umbilical artery venous duct PI > 95%	Surveillance every 24-28 h Interruption at 30 weeks C-section as first choice
3	< 10	Absent diastolic flow of the umbilical artery	Every 2 weeks	34 weeks; C-section	4	Absent variability without sedative medication to explain it and/or spontaneous decelerations Reverse diastolic flow in the venous duct	Surveillance every 12-24 h Spontaneous decelerations can justify emergency C-section Absent variability or reverse flow in the venous duct Interruption at 26 weeks with 2 cycles of steroids
4	< 10	CPR < 5%, MCA PI < 5% In two measurements with a difference of 24 h	Every 2 weeks	32 weeks; C-section			
5	< 10	Achieve at least 1 criteria of severity: pathologic BPP Oligohydramnios reverse diastolic flow in umbilical artery Abnormal CTG venous duct PI > 95%	Every 12-24 h	> 28 weeks; C-section			

BPP: biophysical profile, CPR: cerebroplacental ratio, CTG: cardiotocography, EFW: estimated fetal weight, MCA: middle cerebral artery, PI: pulsatility index, UA: umbilical artery, UtA: uterine artery

first trimester ultrasound, fetuses with chromosomal abnormality markers in the ultrasound, multiple pregnancies, or patients where Doppler flowmetry was impossible to assess.

SPSS IBM statistics v.17 was used to analyze all the data collected from the participants. The median was used for the descriptive analysis of discrete variables, and in the continuous ones, the mean was used. The demographic variables were analyzed with contingency tables using the Chi-square and Fisher's exact tests, comparing means with Chi-square were used in the quantitative variables. Kolmogorov–Smirnov was used to verify the normality of the sample, Student's t-test was applied in parametric data and Mann–Whitney U-test was used in non-parametric data. $p < 0.05$ was taken as statistically significant, with a 95% confidence interval.

Results

Forty patients were included and compared to 40 previously treated patients, obtaining data from clinical records. No patients were lost in the follow-up. Demographic characteristics did not show any differences between groups (Table 2).

The mean gestational age at the first medical appointment in our institution was approximately of 31.6 WOG (SD 6.63), in Group A, the mean was 32 WOG, and in Group B, it was 31.4 WOG ($p = 0.881$). Mean gestational age at time of diagnosis was 36.4 WOG, being similar between groups (36.5 vs. 36.2 WOG, $p = 0.602$). Mean gestational age at time of birth for Groups A and B was 38.0 WOG (SD 1.23) and 39.2 WOG (1.19) ($p \leq 0.001$), respectively.

Table 2. Demographic characteristics and gestational age

Variable	General	Group A	Group B	p
N	80	40	40	
Age median (range)	23 (16-43)	23 (16-40)	23 (16-43)	0.970
Gestation median (range)	2 (1-5)	2 (1-4)	2 (1-5)	0.111
Gestational Age at the first consult Mean (SD)	31.6 (6.63)	32.0 (6.71)	31.4 (6.64)	0.881
Gestational age at diagnosis Mean (SD)	36.4 (2.37)	36.5 (2.63)	36.2 (2.11)	0.602
Gestational age at birth Mean (SD)	38.6 (1.31)	38 (1.23)	39.2 (1.19)	< 0.001

In relation to delivery type, vaginal delivery was seen in 52 patients (65%) and cesarean delivery in 28 (35%). Comparing the groups, in Group A, 23 (57.5%) patients had vaginal deliveries and 17 (42.5%) had cesarean sections; whereas in Group B, 29 (72.5%) patients had vaginal deliveries and 11 (27.5%) had cesarean sections. A significant difference was found in the prevalence of induction of labor between groups, 29 (72.5%) from Group A and 17 (42.5%) from Group B ($p = 0.007$) (Table 3).

EFW evolution was measured in all fetuses. Overall, 58 fetuses (72.5%) maintained the same weight classification, 15 (18.8%) fetuses progressed into type 1 IUGR, and 1 fetus (1.2%) to type 2 IUGR; six fetuses returned to normal weight. Between groups, 30 (75%) of the products in Group A remained at the same classification and 28 (70%) from Group B; 8 (20%) from Group A and 7 (17.5%) from Group B evolved to IUGR Type 1; and one from Group A to IUGR Type 2; five products returned to normal weight in Group B, in contrast to a single fetus in Group A (Table 4).

Newborn characteristics

When assessing birth weight among all newborns, the average weight was 2699 g, showing a significant difference between Groups A and B, with 2614 g and 2783 g, respectively ($p = 0.0017$). The average height was 48 cm (SD 1.84), without differences between the groups.

The median APGAR score in all products at the 1st min was 8 (6-8) and 9 (8-10) at 5 min, with no difference between groups. Fenton growth charts were used to analyze and classify the products, among all the cases, 28 (35%) newborns had an adequate weight for their gestational age, 35 (43.8%) were situated between > 3% and < 10% percentiles and 17 (21.2%) were below the < 3% percentile.

Table 3. Delivery route and induction of labor

	General n (%)	A n (%)	B n (%)	p
Delivery route				0.160
Vaginal	52 (65)	23 (57.5)	29 (72.5)	
Cesarean section	28 (35)	17 (42.5)	11 (27.5)	
Induction of labor				0.007
Yes	46 (57.5)	29 (72.5)	17 (42.5)	
No	34 (42.5)	11 (27.5)	23 (57.5)	

Discussion

IUGR continues to be an important entity, as it increases morbidity and mortality in newborns²⁰. It is estimated that IUGR affects up to 15% of all pregnancies, with large differences between developed and developing countries²¹.

Due to its medical, social, and economic implications, IUGR diagnosis and treatment have been of great interest. Several studies have attempted to classify the different types of the disease, with complications and recommended treatments for each of them^{16,22,23}.

A multicentric randomized trial that included 650 patients with IUGR products was divided into two groups to receive either induction of labor or expecting management. There were no differences in cesarean section rates between the groups, although those patients with conservative treatment had a higher risk of gestational hypertension. Newborns that were in the induction of labor group had lower weight, and a higher percentage was admitted to the intermediate care unit. Even with the results obtained, they do not rule out the possibility of choosing between the induction of labor in those patients with a pregnancy near term and products with low weight or IUGR^{17,24}.

Table 4. Newborns characteristics

Variable	General	Group A	Group B	p
Weight (g) mean (SD)	2699 (318.31)	2614 (305.00)	2783 (312.40)	0.017
Height (cm) mean (SD)	48 (1.84)	47.9 (1.81)	48.5 (1.86)	0.174
APGAR score	Median (range)	Median (range)	Median (range)	0.407
– 1 min	8 (6-8)	8 (6-8)	8 (6-8)	0.983
– 5 min	9 (8-10)	9 (8-10)	9 (8-10)	
Weight percentile	n (%)	n (%)	n (%)	0.011
– < 3	17 (21.2)	3 (7.5)	14 (35)	
– < 10	35 (43.8)	21 (52.5)	14 (35)	
– Adequate	28 (35)	16 (40)	12 (30)	
Progression	n (%)	n (%)	n (%)	0.284
– Without changes	58 (72.5)	30 (75)	28 (70)	
– Progression in IUGR Type 1	15 (18.8)	8 (20)	7 (17.5)	
– Normal	6 (7.5)	1 (2.5)	5 (12.5)	
Fetal distress	n (%)	n (%)	n (%)	1.00
	2 (2.5)	1 (2.5)	1 (2.5)	

In our study, abdominal delivery rate was higher in the group of patients that were interrupted at 37 WOG in comparison to those who were in the expectant management group, without finding a significant difference. On the other hand, a greater number of inductions of labor were obtained in the interruption group, and differences in the weight of the products in both groups were similar to the Disproportionate Intrauterine Growth Intervention Trial at Term (DIGITAT) study. It should be considered that in the DIGITAT report¹⁷, the classification is not based on the proposal by various authors, since it took into consideration abdominal circumference < 10th percentile, EFW < 10% percentile, flattening of the growth curve, or the presence of all of the above, without taking into account Doppler flowmetry and not making a distinction between products with a percentile < 10 or < 3²⁵.

Hershkovitz et al. evaluated more than 4000 cases of newborns with SGA, described as those below the 10th percentile, comparing maternal and neonatal outcomes based on groups. Reviewing the group of patients with term pregnancy, a higher percentage of births by cesarean section was obtained in the interventionist group compared to the control group, 20.7% and 10.7%, respectively ($p < 0.0001$). In newborns of mothers undergoing labor induction, APGAR score < 7 at 5 min was more frequent compared to those in the spontaneous evolution group (1.6% vs. 0.8%, $p = 0.02$)²⁶. These results support the main hypothesis in our study, and the results obtained.

In 2011, a retrospective analysis included newborns with a percentile < 10, children of nulliparous mothers

of a single product pregnancy of 36 WOG or older, with or without hypertension. In their results, an increase of cesarean section rates is observed in those patients undergoing labor induction (mainly in those who used prostaglandins), as well as the need for instrumental delivery when compared to spontaneous labor patients. There was no difference in neonatal outcomes between groups. Another finding was that induction of labor increased the risk of a lower APGAR score compared to the spontaneous labor group²⁷.

The results obtained in the current study are consistent with those reported by Boers et al.²⁷. Although the APGAR score was not affected in either of the two groups, it should be taken into account that the results published by Boers et al. are based on products that at birth were below the 10th percentile and being careful not to extrapolate these results with those cases of low weight or even with IUGR diagnosed prenatally.

Further research in IUGR is needed for better disease classification and management guidelines, to reduce both fetal and maternal morbidity and mortality. The present study has shown that weekly surveillance to reach 40 WOG or spontaneous labor is safe. A limitation of this study is the limited number of patients in each group.

Conclusion

As a general conclusion, it can be inferred that the decision to continue the pregnancy after 37 WOG and reaching 40 WOG with weekly surveillance of maternal-fetal

well-being in patients diagnosed with IUGR Type 0 decreases the number of patients that undergo labor induction and cesarean delivery rate, and allows a greater weight gain in fetuses without increasing the risk of disease progression.

Conflicts of interest

The authors declare not to have any conflicts of interest. The costs generated by the present study were financed by the Department of Obstetrics and Gynecology at "Dr. José Eleuterio González" University Hospital of the Autonomous University of Nuevo Leon in Monterrey, México.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

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