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Placental plasticity in monochorionic twins: Impact on birth weight and placental weight

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ABSTRACT

Introduction: The knowledge about adaptive mechanisms of monochorionic placentas to fulfill the demands of two instead of one fetus is largely speculative. The aim of our study was to investigate the impact of chorionicity on birth weight and placental weight in twin pregnancies.
Methods: Forty Monochorionic (MC) and 43 dichorionic (DC) twin pregnancies were included in this retrospective study. Individual and total (sum of both twins) birth weights, placental weights ratios between placental and birth weights and observed-to-expected (O/E)-ratios were calculated and analyzed. Additionally, we investigated whether in twin pregnancies placental and birth weights follow the law of allometric metabolic scaling.
Results: MC pregnancies showed higher placental O/E-ratios than DC ones (2.25 ± 0.85 versus 1.66 ± 0.61; $p < 0.05$), whereas the total neonatal birth weight O/E-ratios were not different. In DC twins total placental weights correlated significantly with gestational age ($r = 0.74$, $p < 0.001$), but not in MC twins. Analysis of deliveries ≤32 weeks revealed that the placenta to birth weight ratio in MC twins was higher than in matched DC twins (0.49 ± 0.3 versus 0.24 ± 0.03; $p = 0.03$). Allometric metabolic scaling revealed that dichorionic twin placentas scale with birth weight, while the monochorionic ones do not.
Discussion: The weight of MC placentas compared to that of DC is not gestational age dependent in the third trimester. Therefore an early accelerated placental growth pattern has to be postulated which leads to an excess placental mass particularly below 32 weeks of gestation. The monochorionic twins do not follow allometric metabolic scaling principle making them more vulnerable to placental compromise.

1. Introduction

The most important factors determining fetal growth and wellbeing are placental size and function. Placental weight has been shown to be closely associated with fetal size [1]. In multiple pregnancies, a reciprocal behavior of the mean birth weights with increasing number of fetuses has been reported [2,3]. Mean birth weight of each neonate from multiple pregnancies was shown to be significantly lower than the expected mean of singletons. Papageorghiou et al. showed by multiple regression analyses that the most important factors influencing birth weight of multiple pregnancies are the number of fetuses followed by the presence of a monochorionic placenta and gestational age [3]. It seems plausible that the individual birth weight of monochorionic twins is lower compared to dichorionic dizytgotic or even dichorionic monozygotic twins [3–5]. However, the total twin birth weight (sum of birth weights of both twins) usually exceeds the 90th birth weight percentile for singletons; a phenomenon, which becomes apparent as early as 25 weeks of gestation [3–5]. Only few investigators have presented their data stratified by chorionicity [3,5]. Furthermore,

Abbreviations: MC, monochorionic placenta; DC, dichorionic; O/E, observed-to-expected; O, observed; E, expected; y, mean placental weight; x, given gestational age; x', mean birth weight; y', gestational age; NICU, neonatal intensive care unit; β-hCG, free β-hCG; PAPP-A, pregnancy-associated plasma protein-A.

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placental growth and its weight in relation to chorionicity and individual as well as total birth weights has rarely been analyzed. This subject needs further attention since monochorionic placentas, intrinsically programmed to supply the demands of only one fetus, are confronted with the need to support two fetuses. Chorionicity is established at or around the time of implantation and placental division is unlikely to occur after this period. In twin pregnancies, early and complex placental adaptation seems to be crucial for optimal fetal growth and wellbeing. However, it remains largely speculative how these adaptive processes are regulated.

In 1932, Kleiber, a Swiss agricultural chemist, demonstrated that the body weight raised to the power of ¾ is the most reliable way of predicting basal metabolic rate in mammals and birds [6]. Inspired by this allometric metabolic scaling model Aherne formulated a pregnancy-equivalent: total placental weight = α(total birth weight)$^{\beta}$, where α is a normalization constant [7]. Slafia et al. have shown that in singleton pregnancies the behavior of placental and birth weights is congruent with the Aherne's law and determined the exponent β to be 0.78, which is close to the value of ¾ in Kleiber's law [8]. Whether twin pregnancies follow this general law of metabolic scaling has not been elucidated yet.

The objectives of our study were to investigate the impact of chorionicity on birth weight and placental weight, and to determine whether the principle of allometric metabolic scaling applies to twin pregnancies.

2. Methods

Consecutive twin pregnancies delivered at our tertiary referral institution between 2003 and 2006 were analyzed in this retrospective study. Inclusion criteria were known gestational age (determined by a reliable recollection of the last menstrual period and confirmed by an ultrasonographic examination between 11 and 14 weeks of gestation) and availability of follow-up data and pregnancy outcomes. Exclusion criteria were twin-to-twin transfusion syndrome, monoamniotic twins, intrauterine demise of one or both twins and fetal structural or chromosomal abnormalities. All other cases, such as selective intrauterine growth restriction (IUGR) were not excluded since the focus of the study was not on the birth weight of the single fetus, but on the combined weights of the twins. The fetuses with estimated fetal weight below the 10th percentile and abnormal umbilical artery Doppler were diagnosed as being IUGR and all neonates with a birth weight below the 10th centile were considered to be small for gestational age (SGA). The chorionicity was determined according to standard ultrasound criteria between 11 and 14 weeks of gestation. Briefly, a monochorionic placenta (MC) was sonographically defined as single placental mass with typical T-sign. On the other hand, a single placental mass with a λ-sign or two separate placentas were considered dichorionic (DC). In addition, to ensure dizygosity, only sex discordant twins were included.

Placental weight was assessed on the delivery ward following removal of fetal membranes, the umbilical cord, and blood clots. The placentas were weighed by midwifes using an accurate electronic bench scale (PBA655-A6, Mettler Toledo, Switzerland). For dichorionic placentas total placental weight represents the sum of the two individual placentas. The total placental weights were compared with reference values for singletons [9]. In order to correct for gestational age and to compare total placental weights of MC with those of DC twins, ratios between the observed (O) and the expected (E) birth weight for the given gestational age in singletons were calculated. Pinar et al. [9] have published placental weight reference values in singleton pregnancies allowing to calculate the expected (E) placental weight for a given gestational age: the polynomial regression equations that best fitted the mean placental weight (y) for singletons at a given gestational age (x) was derived from Pinar et al. [6] and yielded $y = -531.3 + 33.22x - 0.1623x^2$. Analogous calculations were performed regarding the total birth weight. The expected mean birth weight (x') for a determined gestational age (y') was derived from a third order polynomial regression ($y' = 27{,}789 - 2790x' + 91.49x'^2 - 0.9235x'^3$) based on published reference values for singletons by Yudkin et al. [10] A similar procedure was used to investigate the association between the placental weight and birth weight.

To analyze the relationship between total placental and total birth weights in twin pregnancies the metabolic scaling equation was applied and fitted as described by Salafia et al. [8] Briefly, Aherne's power function relationship, i.e. total placental weight = α(total birth weight)$^{\beta}$ was recast into its logarithmic form. The data were then fitted by ordinary linear least-square regression using the curve fitting tool of MATLAB (The MathWorks, Natick, MA). Other functions ranging from linear to second/third order polynomial equations were tested to identify the best fitting curve.

Statistical analysis was performed with GraphPad Prism version 5.0 for Windows, (GraphPad Software, San Diego CA, USA). Independent sample student's t-test was used to compare continuous variables. Proportions were analyzed by using Fisher's exact test. Spearman rank correlation and linear logistic regression was used to assess the relationship between gestational age, birth weights, and total placental weights. A p-value of <0.05 was considered significant. This study was approved by the local ethical committee (Kantonale Ethikkommission Bern, date of approval: 11/18/2013).

3. Results

During the study period a total of 146 twin pregnancies were delivered at our institution. Of those, 83 cases (40 MC and 43 DC) fulfilled the inclusion criteria. The clinical characteristics of the study population are presented in Table 1. The two groups showed significant differences comparing maternal age, parity, and incidence of hypertensive complications of pregnancy. However, the proportion of IUGR was not different between groups. Over 80% of all pregnancies were delivered by caesarean section, and a relevant proportion of the neonates had to be transferred to the neonatal intensive care unit (NICU), mainly due to prematurity. In three cases with vaginal delivery of the first twin a caesarean section was performed for the second twin because of non-reassuring fetal heart rate trace.

The individual birth weights interposed on the reference ranges for singletons are depicted in Fig. 1a. Mean birth weights were not different between the two groups (Table 1). Similarly, although the incidence of individual birth weights below the 5th gestational age-specific percentile of singleton pregnancies was higher in the MC than in the DC group, this difference was not significant (MC: 23/80 [28.8%] vs. DC: 14/86 [16.3%]; $p = 0.06$). There were no differences in birth weight discordancy (DC versus MC: 315 $\pm$ 219 g [15.7 $\pm$ 10.9%] versus 358 $\pm$ 243 g [14.4 $\pm$ 9.1%]; $p = 0.52$ [$p = 0.71$]), nor in the prevalence of birth weight discordancy >20% (DC versus MC: 30.2% (13/43) versus 37.5% (15/40; $p = 0.49$) between the two groups. The O/E-ratio for the estimated birth weight was also not different (MC: 0.82 $\pm$ 0.15 vs. DC: 0.84 $\pm$ 0.12; $p = 0.39$). Total birth weights are shown in Fig. 1b. Almost all cases (except one MC twin) were above the 95th percentile for gestational age for singletons. Between MC and DC no significant differences were found regarding the total birth weights (MC: 4085 $\pm$ 1272 gr vs. DC: 4458 $\pm$ 661 gr; $p = 0.13$) and the total birth weight O/E-ratios (MC: 1.64 $\pm$ 0.24 vs. DC: 1.69 $\pm$ 0.18; $p = 0.28$).

Forty-three placentas of the 83 twin pregnancies were weighed in the delivery ward and available for analysis, whereas the others were sent directly to histopathologic examinations and