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RESEARCH ARTICLE

Archives of Obstetrics and Gynecology

Neonatal differences in hematologic parameters of monochorionic twins pregnancies affected by intrauterine growth restriction.

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Abstract

Objective: *The aim of our study was to investigate whether in monochorionic diamniotic twin pregnancies complicated by selective intrauterine growth restriction (sIUGR) a birth-order dependent difference in hemoglobin concentration exists between the neonates delivered by caesarean section (CS) .*

Study design: *sIUGR twin pregancnies presenting to our facility between 2005 and 2017 and delivered by CS were retrospectively analyzed. Hemoglobin concentration (Hb) at delivery was compared between both twins.*

Result: *We included 70 neonates from 35 sIUGR twin pregnancies. A significant difference in hemoglobin concentration between twins was observed if the IUGR twin was delivered first. This difference was no longer significant when the smaller twin was delivered second.*

Conclusions: *Birth order significantly influences the difference in hematologic parameters between neonates in sIUGR twin deliveries, even when the mode of delivery is CS.*

Keywords: *Monochorionic diamniotic twins, selective intrauterine growth restriction, hematologic characteristics, newborns*

Introduction

The first seconds after birth are recognized as a potential time of significant blood volume transfer from placenta to the newborn. In keeping with this concept, studies of singleton pregnancies deliverd vaginally and by caesarean section have demonstrated a sustained increase in neonatal hemoglobin values when umbilical cord clamping is delayed, allowing postnatal blood transfer from placenta to newborn and resulting in sustained benefit for the term and preterm neonate [1]. As a result, numerous professional organizations now recommend that cord clamping be delayed for at least 30-60 seconds after delivery [1].

The dynamics of blood volume transfer at the time of birth are particularly interesting in the case of monochorionic, diamniotic twin pregnancies (MCDA), in which a single placenta is shared between two fetuses and both systems are interconnected with various types of placental anastomoses [2]. Indeed, studies of uncomplicated MCDA deliveries demonstrate consistently higher Hb values in the twin delivered second. The mechanism of this Hb difference is hypothesized to involve acute transfer of blood at the time of birth through A-A and V-V vascular anastomoses on the placental surface from one twin to the other at the time of birth. Other suggested theories include a role for uterine contractions and fetal positioning, prolonged delivery time interval between the twins and differences in the timing of cord clamping between twin 1 and 2. [3-7].

MC pregnancies are prone to unique complications during pregnancy due to either unequal placental mass distribution between both fetuses and/or quantitative as well as qualitative differences of the feto-fetal anastomoses. One of these complications is sIUGR in which one of the fetuses exhibits growth restriction due to a smaller supplying placenta. While birth-order dependent hemoglobin differences in uncomplicated MCDA twin pregnancies with similar placental masses have been reported, the hemoglobin concentrations of sIUGR infants in relation to birth order have to our knowledge not been studied. We set out to determine whether in the case of MCDA complicated by sIUGR delivered by caesarean section, birth order significantly impacts the difference in Hb values between twins at birth.

Materials and methods

All cases of MCDA pregnancies with selective-IUGR delivered through Caesarean section in at the department of obstetrics and gynecology of the university of Bern between January 2005 and December 2017 were retrospectively analyzed.

During the study period, MCDA pregnancies with selective-IUGR were defined as those in which the estimated fetal weight of the smaller fetus was below the 10th percentile for gestational age with at least a 20% weight discrepancy between both twins [8]. Exclusion criteria were immune or alloimmune thrombocytopenia, evidence of maternal chorioamnionitis, development of neonatal sepsis and MCDA twins affected by twin-to-twin transfusion

syndrome (TTTS), twin anemia-polycythemia sequence (TAPS), twin reversed arterial perfusion (TRAP), anomalies as well as pregnancies with single fetal demise. Similarly, if the first twin was delivered vaginally and the co-twin through emergency CS, the twin pair was excluded. All sIUGR pregnancies were followed in our hospital and all medical information were recorded in an electronic records system.

Gestational age was determined by a reliable recollection of the last menstrual period and either confirmed by ultrasound examination within the first 14 weeks of gestation or calculated from the day of oocyte retrieval in pregnancies conceived through assisted reproduction technologies (oocyte retrieval day minus 14). Our surveillance protocol consisted of weekly or biweekly sonographic assessment starting at 16 weeks of gestation in cases with normal first trimester findings. Fetal anthropometric parameters including biparietal diameter, abdominal circumference and femur length were measured in all the fetuses. Umbilical artery, middle cerebral artery, and ductus venosus Doppler assessment was conducted in all cases and the pulsatility index was calculated.

After diagnosis of sIUGR, women underwent intensive outpatient or inpatient follow-up based on gestational age at diagnosis and/or fetal hemodynamic assessment. Our policy at the time of the current study was to deliver MCDA pregnancies with sIUGR by CS at 32 to 34 weeks of gestation depending on the type of sIUGR [2]. Prophylactic antenatal corticosteroids (2 intramuscular doses of 12 mg betamethasone, 24 hours apart) were administered.

Newborn blood samples obtained at delivery were collected and examined for hemoglobin (Hb) and hematocrit (Hct).

Ethical approval for the current study was obtained by the local institutional review board (Ethics Committee of the Canton of Bern, Switzerland, approved on 18.04.2016).

Statistical analysis

Values are expressed as mean ± standard deviation (SD). Continuous variables within twin pairs were analyzed using the paired t test. Paired nominal data were analyzed using the NcNemar test. A p value <0.05 was considered to be statistically significant. Data analysis were performed with GraphPad version 5.0 for Mac (GraphPad Software, San Diego CA).

	MCDA (N° 35) pregnancies		
	sIUGR	Co-Twin	p-value
Gestational age at delivery (mean±SD - week)	31.95±2		
Caesarean section—N° (%)	35 (100%)		
Female—N° (%)	19(54.28)		
Birth weight (mean±SD - g)	1143 ±338	1702 ±380	<0.0001
Median Apgar score at 5 min (mean±SD)	7.8±1.5	7.9±1.5	NS
Neonatal death—N° (%)	1(2.8)	0(0)	NS
CPAP—N° (%)	19(54.2)	26(74.2)	NS
NEC—N° (%)	3(8.5)	3(8.5)	NS

Abbreviations: N°= number, CPAP= Continuous Positive Airway Pressure, NEC= Necrotizing Enterocolitis, MCDA= Monochorionic diamniotic twins, sIUGR= selective intrauterine growth restriction, IUGR= Intrauterine growth restriction.

Table 1. *Study population characteristics.*

	MCDA pregnancies (N° 14/35)		
	sIUGR	Co-Twin	p-value
Hb at delivery (g/L, mean±SD)	161.8±24	184.7±20	0.03
HCT at birth (L/L, mean±SD)	0.48±0.07	0.53±0.04	0.03

Abbreviations: N°= number, Hb= hemoglobin, Hct= hematocrit, MCDA= Monochorionic diamniotic twins, sIUGR= selective intrauterine growth restriction,

Table 2. *Hematologic parameters in monochorionic diamniotic twins in whom the selective intrauterine growth restriction newborn is delivered as first.*

	MCDA pregnancies (N° 21/35)		
	sIUGR	Co-Twin	p-value
Hb at delivery (g/L, mean±SD)	175.5±20	179.5±17	NS
HCT at birth (L/L, mean±SD)	0.5±0.06	0.5±0.05	NS

Values are shown as mean±SD. Abbreviations: N°= number, Hb= hemoglobin, Hct=hematocrit, MCDA= Monochorionic diamniotic twins, sIUGR= selective intrauterine growth restriction, IUGR= Intrauterine growth restriction.

Table 2. *Hematologic parameters in monochorionic diamniotic twins in whom the selective intrauterine growth restriction newborn is delivered as second.*

Results

During the study interval 70 neonates of 35 MCDA pregnancies with sIUGR met the inclusion criteria. The clinical characteristics of the study population are summarized in table 1. Median maternal age at delivery was 32 years (range 23-41). Mean gestational age at delivery was 31.95 weeks. Median Apgar score, need for CPAP, prevalence of necrotizing enterocolitis (NEC), and the neonatal death rate were similar between the smaller and larger twins. As expected, a significant difference in birth weight was found between the two twins. All twin pregnancies (100%) were delivered by caesarean section.

Hematologic parameters were compared between twins as reported in tables 2 and 3. When the smaller twin was delivered first, its Hb and Hct values were consistently lower compared to the larger twin while no hematological differences were found when the smallerfetus was delivered second.

Discussion

Our study shows that in MCDA twins affected by sIUGR and delivered by CS, whether or not there is a significant difference in Hb and Hct values between twins depends on the birth order. We show that if the smaller twin is delivered first, its Hb and Hct are significantly lower in comparison with the larger twin. In contrast, if the larger twin is delivered first, no significant difference in Hb and Hct between the twins at birth is detected. .

Mode of delivery and Hb differences in MCDA pregnancies.

Recent work has demonstrated inter-twin Hb differences in MCDA twins after vaginal delivery, but not caesarean section [3]. Accordingly we were surprised to see that in our cohort of MCDA pregnancies complicated by sIUGR birth order determines whether

the smaller twin has an equal or significantly lower Hb and Hct in comparison with the larger twin. It is possible that differences in the delay between delivery of the twins or delay before cord clamping between studies can explain this difference. Indeed, in singleton deliveries, delayed cord clamping results in increased Hb levels in both caesarean and vaginal birth. Alternatively, it may be that differences in placental vascular architecture in sIUGR MCDA twins versus uncomplicated MCDA twins leads to a different hemodynamic scenario at the time of birth in sIUGR twins, allowing significant acute transfer of blood during caesarean section.

Origin of hematologic disparity between IUGR and non-IUGR co-twins

Given that birth order affected Hb values in our study neonates, we lack direct knowledge of fetal Hb values prior to the time of birth. One possibility is that twins have equal Hb concentration before birth and that acute transfusion only occurs in the direction of the unborn twin when the smaller twin is delivered first. Another more likely scenario is that the smaller twin has a lower Hb concentration leading up to the time of birth, that transfusion towards the unborn twin lowers this concentration farther when the smaller twin is delivered first and increases it up to the level of the larger when the smaller twin is deliverd second. Indeed, given published data that singleton neonates with a history of severe placental insufficiency are more likely to be anemic at birth and during the first week of life, we hypothesize that prior to delivery, fetuses affected by IUGR have lower average Hb and Hct values than their healthy co-twins. This notion is supported by the work of Yao-Lung et al, who reported an increased concentration of fetal plasma erythropoietin in MCDA twin pregnancies complicated by selective-IUGR and abnormal umbilical artery Doppler, a possible sign of uncompensated hypoxia [9]. In general, sIUGR is explained by unequal placental sharing rather than significant unidirectional blood flow through A-V placental anastomoses. However, so-called “rescue transfusions” through A-A or V-V anastomoses from the normally grown twin to the IUGR twin during gestation have been observed. Flow through these anastomoses could theoretically occur in both directions at the time of delivery in a birth order-dependent manner depending on blood pressure changes. How these A-A and V-V anastomoses actually behave during delivery in sIUGR pregnancies is unknown. Finally, the hematologic pattern observed could be explained simply by movement of blood between corresponding fetal and placental shares without the involvement of anastomoses. Future studies will be needed to clarify the underlying mechanisms leading to the findings reported.

In summary, we report birth-order dependent significant differences in neonatal hemoglobin in MCDA pregnancies complicated by selective IUGR after caesaream section. Further studies are needed to confirm our findings.

Financial support

This research received no specific grant from any funding agency, commercial or not-for-profit sectors.

Conflicts of interest

None

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Rec: Feb 12, 2020; Acc: Feb 25, 2020; Pub: Feb 28, 2020

Archives Obs Gynec. 2020;1(1):05
DOI: gsl.aog.2020.0005