Lactate acidosis and hypoglycaemia in twin anaemia polycythemia sequence donors

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Letters

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Twin anaemia polycythemia sequence (TAPS) is a monochorionic twin condition that occurs due to imbalanced chronic feto-fetal transfusion through minuscule vascular placental anastomoses, leading to anaemia in the donor twin and polycythemia in the recipient twin. Donors are significantly more at risk of developing severe long-term neurodevelopmental impairment (NDI) (18%) than recipients (3%).[1] The cause for this difference in outcome is not well understood. Previous studies showed that neonatal lactate acidosis and hypoglycaemia are associated with long-term impairment.[2 3] To date, the prevalence of these metabolic conditions has not been studied in TAPS. This study was set up to investigate the prevalence of lactate acidosis and hypoglycaemia in TAPS donors and recipients, to explore potential hypotheses for the difference in NDI.

Monochorionic twins diagnosed with TAPS postnatally between 2002 and 2021 at our hospital were included. TAPS was defined as a postnatal haemoglobin difference >8 g/dL, together with a reticulocyte count ratio >1.7 or the presence of minuscule placental anastomoses (diameter <1 mm) identified through color-dye injection. Maternal, fetal and neonatal outcome were retrieved from medical records. The pH and BE value, and highest lactate value measured in the umbilical cord and in neonates within 2 hours after birth were collected. To evaluate hypoglycaemia, glucose levels measured within 24 hours after birth and the need of medical intervention (glucose bolus or extra glucose intravenous infusion) were collected. Primary outcomes were lactate acidosis (lactate level ≥5 mmol/L) and hypoglycaemia (glucose level <2.6 mmol/L). Statistical analysis was performed using SPSS V.25. Data were analysed using generalised estimating equations module and were corrected for the presence of fetal growth restriction (birth weight <p3).

In total, 103 TAPS twins were included. Lactate acidosis occurred more often in donors (49%, 23/47) compared with recipients (49% (23/47) vs 20%

Table 1 Data on neonatal acidosis directly after birth and hypoglycaemia within 24 hours after birth in TAPS pregnancies

	Total (N=206)	TAPS donors (N=103)	TAPS recipients (N=103)	P value
Gestational age at birth (weeks)	33.0 (29.7–35.0)			
Birth weight	1703 (1213–2029)	1623 (1107–1958)	1793 (1323–2246)	**<0.001**
Birth weight <p10*	88/204 (43)	64/102 (63)	24/102 (24)	**<0.001**
Birth weight <p3*	51/204 (25)	41/102 (40)	10/102 (10)	**<0.001**
Lactate acidosis†	32/93 (34)	23/47 (49)	9/46 (20)	**0.017**
Lactate U.C.+N.N.†	(n=93) 4.0 (2.5–5.5)	(n=47) 4.8 (3.6–6.6)	(n=46) 2.9 (1.5–4.6)	**<0.001**
Lactate U.C.†	(n=27) 4.6 (3.6–6.0)	(n=12) 4.9 (3.7–5.4)	(n=15) 4.3 (3.5–6.2)	**0.004**
Lactate N.N.§	(n=84) 3.0 (1.8–5.1)	(n=43) 4.6 (3.2–6.2)	(n=41) 1.9 (1.2–3.0)	**<0.001**
pH U.C.¶	(n=137) 7.25 (7.18–7.31)	(n=68) 7.23 (7.17–7.28)	(n=69) 7.27 (7.20–7.34)	**<0.001**
BE U.C.††	(n=129) −5.7 (−7.9 to −3.6)	(n=64) −6.1 (−8.0 to −4.0)	(n=65) −4.3 (−7.5 to −3.1)	**0.003**
pH N.N.**	(n=68) 7.22 (7.14–7.29)	(n=34) 7.24 (7.14–7.30)	(n=34) 7.22 (7.14–7.28)	0.784
BE N.N.‡‡	(n=77) −6.0 (−8.0 to −4.3)	(n=39) −7.0 (−8.8 to −5.0)	(n=38) −5.9 (−7.4 to −3.6)	0.084
Hypoglycaemia¶¶	79/176 (45)	46/87 (53)	33/89 (37)	**0.046**
Medical intervention¶¶	41/176 (23)	27/87 (31)	14/89 (16)	**0.034**
No of medical interventions	1 (1–1)	1 (1–2)	1 (1–1)	0.318
No of low glucose levels	1 (1–2)	2 (1–3)	1 (1–1)	**<0.001**

Data are presented as median (IQR) or n/N (%).
Lactate acidosis defined as a lactate level ≥ 5.0 mmol/L within 2 hours after birth.
Lactate U.C. + N.N. defined as the highest level of lactate measured within 2 hours after birth.
Lactate U.C. defined as the highest level of lactate measured in the umbilical cord.
Lactate N.N. defined as the highest level of lactate measured in the neonate within 2 hours after birth.
pH/BE U.C. defined as the lowest level of pH/BE measured in the umbilical cord. pH/BE N.N. defined as the lowest level of pH/BE measured in the neonate within 2 hours after birth.
Glucose levels were collected until 24 hours after birth.
Hypoglycaemia defined as at least one serum glucose level <2.6 mmol/L within 24 hours after birth.
Intervention defined as glucose bolus or extra glucose intravenous infusion.
Low glucose level defined as serum glucose level <2.6 mmol/L.
*2 missing values: 1 TAPS donor and 1 TAPS recipient with missing birth weight values.
†113 missing values: 56 TAPS donors and 57 TAPS recipients with lacking data about lactate acidosis.
‡179 missing values: 91 TAPS donors and 88 TAPS recipients with lacking lactate levels measured in the umbilical cord.
§122 missing values: 60 TAPS donors and 62 TAPS recipients with lacking lactate levels measured in the neonate within 2 hours after birth.
¶77 missing values: 39 TAPS donors and 38 TAPS recipients with lacking pH levels measured in the umbilical cord.
**138 missing values: 69 TAPS donors and 69 TAPS recipients with lacking pH levels measured in the neonate within 2 hours after birth.
††77 missing values: 39 TAPS donors and 38 TAPS recipients with lacking BE levels measured in the umbilical cord.
‡‡129 missing values: 64 TAPS donors and 65 TAPS recipients with lacking BE levels measured in the neonate within 2 hours after birth.
§§5 missing values: 1 TAPS donor and 4 TAPS recipients with lacking data about asphyxia.
¶¶30 missing values, 16 TAPS donors and 14 TAPS recipients with missing glucose levels.
TAPS, twin anaemia polycythemia sequence.

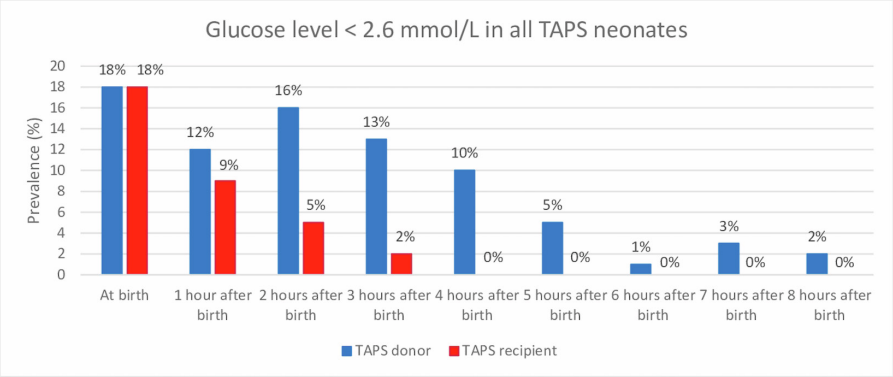

Figure 1 Prevalence of hypoglycaemia (glucose <2.6 mmol/L) in donors and recipients up to 8 hours after birth.

(9/46), respectively (p=0.017) (table 1). Donors also showed lower pH and BE values than recipients: pH 7.23 (IQR 7.17–7.28) versus pH 7.27 (IQR 7.20–7.34), p<0.001; and BE −6.1 (IQR −8.0 to −4.0) versus BE −4.3 (IQR −7.5 to −3.1), p=0.003. Donors more often had hypoglycaemia than recipients, 53% (46/87) versus 37% (33/89), respectively (p=0.046), and more often needed medical intervention (31% (27/87) versus 16% (14/89), respectively) (p=0.034). Moreover, hypoglycaemia persisted more often in donors than in recipients during the first 8 hours after birth (figure 1).

In conclusion, this study showed that TAPS donors are more prone for lactate acidosis and hypoglycaemia at birth than recipients. Lactate acidosis in donors might be a direct result of the chronic hypoxic intrauterine environment caused by chronic fetal anaemia.[4] Hypoglycaemia, on the other hand, could be caused by a chronic glucose loss into the recipients' circulation.

Given the potential long-term adverse effects of prolonged and severe neonatal hypoglycaemia, we advocate for active screening to ascertain normoglycaemia in the first 24 hours after birth in TAPS twins. Future studies should explore whether lactate acidosis and hypoglycaemia in TAPS is associated with long-term impairment.

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Contributors MJAvdS and LSAT were responsible for conceptualisation, (monitoring and interpreting) data collection, wrote the statistical analysis plan, analysed the data and drafted and revised the final paper. FS and EL were responsible for the conceptualisation, supervised in the data interpretation and reviewed and edited the final paper. CdB was responsible for monitoring and interpreting data collection and reviewed the final paper. EJTV reviewed the final paper.

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