

Zoltan Kozinszky*, Norbert Pásztor, Virág Márton, János Sikovanyecz^a, Attila Keresztúri^a and Gábor Németh^a

Transabdominal amnioinfusion in the correction of oligohydramnios following twin-to-singleton reduction – A report of two cases

DOI 10.1515/crpm-2016-0021

Received February 2, 2016. Accepted October 14, 2016. Previously published online November 29, 2016.

Abstract

Background: On rare occasions, elective iatrogenic reduction of a dichorionic twin is performed due to maternal request and in order to improve the perinatal outcome.

Materials and methods: Nine twin-to-singleton reductions were identified retrospectively at the Feto-maternal Unit, University of Szeged, Hungary, between December 1997 and June 2015. A post-procedure, routine weekly sonographic scan revealed severe oligohydramnios in two out of the nine cases (22.2%) and amnioinfusion was performed in the mid-trimester to prolong gestation. The fetus survived in one case (11.1%) and the pregnancy continued until preterm birth.

Conclusion: A repeated sonographic follow-up for an early diagnosis of oligohydramnios is feasible to avoid miscarriage after artificial embryo reduction.

Keywords: Amnioinfusion; embryo reduction; oligohydramnios; serial sonographic follow-up.

Introduction

An escalating prevalence of infertility results in more infants being conceived with assisted reproductive technologies, leading to a dramatic increase in multifetal gestations [1]. Multiple births frequently have adverse perinatal sequelae, but the iatrogenic termination of

one or more presumably healthy fetuses is advocated for avoiding an array of adverse maternal and fetal outcomes [2].

Some evidence suggests that reduced dichorionic twins are at lower risk compared to that of their unreduced counterparts [3, 4]. Hence, electively performed iatrogenic twin-to-singleton reduction is employed as a treatment option to prolong gestation, particularly for those mothers who do not want more than one infant or have serious medical/psychiatric illness [3]. The pregnancy loss rate of this intervention is well documented, but there is a paucity of information on post-procedure oligohydramnios following early/late fetal reduction from twins to singletons [3–5]. The purpose of this study was to assess the clinical value of detecting oligohydramnios following artificial embryo reduction of twin pregnancies and the treatment of transabdominal fluid replacement (amnioinfusion).

Materials and methods

In our retrospective case series, we have reviewed nine elective twin-to-singleton reductions performed in the first trimester at the Feto-maternal Unit of the Department of Obstetrics and Gynecology, University of Szeged, Hungary, between December 1997 and June 2015. Hungarian regulations allow twin reduction for mothers who do not want more than one infant. Our work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans, and our study has been approved by the institutional research Ethics Committee. Informed consent was obtained from all participants.

The study group included dizygotic twin pregnancies who underwent elective reductions, in an attempt to improve the expected poor outcome of their multiple pregnancies. The fetus chosen for *in utero* intervention would be the one with suspicious ultrasonographic (US) findings, such as enlarged (≥ 3 mm) nuchal translucency or delayed growth in comparison with its co-twin. In the absence of any pathognomic signs of abnormalities (Kretz Sonace 8000, Voluson 730 Pro, Zipf, Austria), the more readily accessible fetus was chosen usually the one in a ventral and fundal location. Amniotic fluid volume (AFV) was appropriate for both fetuses and there was no sign of hydrops. No symptoms indicative of incomplete miscarriage were present and no clear signs of maternal or fetal infection (maternal tachycardia $>100/\text{min}$, maternal temperature $>38^\circ\text{C}$,

*János Sikovanyecz, Attila Keresztúri and Gábor Németh: These authors contributed equally to this work.

*Corresponding author: Zoltan Kozinszky, MD, PhD, Kvinnokliniken, Landstinget Blekinge, Lasarettvägen, 371 81 Karlskrona, Sweden; and Department of Obstetrics and Gynecology, Blekinge Hospital, Karlskrona, Sweden, Tel.: +46730720835, E-mail: kozinszky@gmail.com

Norbert Pásztor, Virág Márton, János Sikovanyecz, Attila Keresztúri and Gábor Németh: Department of Obstetrics and Gynecology, Faculty of General Medicine, University of Szeged, Szeged, Hungary

maternal white blood cell count >15,000/mL, maternal C-reactive protein >20 mg/L, uterine tenderness, foul-smelling vaginal discharge, fetal tachycardia >160 bpm) were noted.

Terminating one of the fetuses was achieved by intrathoracic injection of KCl 10% (0.6–3.1 mL) via a Chiba 20[®] 150-mm needle (Neomed Corporations, Debrecen, Hungary), which took place under continuous US control between weeks 11 and 12 of gestation via a transabdominal approach, after measuring nuchal translucency. Thereafter, the patients received a weekly US scan until the viability of the remaining fetus (22nd week of gestation), and then every second week until the 36th week. US was performed in order to assess the growth and well-being of the fetus, as well as to identify oligohydramnios during mid-to-late gestation that could require further intervention. The diagnosis of severe pathologic deficiency of the amniotic fluid (AF) was based on the AF index (AFI). AFI values lower than 5 cm necessitated performing transabdominal amnioinfusion (TAAI) [6]. Persistent severe oligohydramnios prior to 22–24 weeks may impede fetal lung development, predispose to limb contractures and prognosticate extreme prematurity [7]. A certain volume of 37°C saline solution (0.9% NaCl) was infused transabdominally into the amniotic cavity under continuous US control in order to restore the AFI to >8 cm, with the aim of prolonging gestation in all cases of oligohydramnios. Eligibility criteria for TAAI were the same as for those for fetal reduction, with the addition of no clinical sign of occult/apparent preterm premature rupture of membranes and no suspicion of placental abruption (uterine tenderness/contractions and bleeding episodes) [6]. The intervention procedure was described in our previous article [7]. In brief, under sterile circumstances, a needle was introduced transabdominally into the amniotic cavity and a variable volume of 37°C saline solution was infused into the uterus under continuous US control.

Results

Out of the nine elective reductions performed, two pregnancies (22.2%) were complicated, with mid-trimester oligohydramnios for the remaining healthy fetuses. The overall pregnancy loss rate was 11.1%. A healthy 35-year-old nulliparous woman with a dichorionic diamniotic pregnancy requested fetal reduction at the 12th week of gestation, which was carried out without any complications. Following the initial intervention, the patient received repeated US scans that showed severe oligohydramnios at 18 + 5 weeks of gestation. Normalization of the AF level was performed by instilling 180 mL saline solution via TAAI under real-time guidance, and it resulted in retroamniotic filling. The pregnancy finished with miscarriage in the second trimester as a consequence of rupture of membranes within one day and clinical signs of chorioamnionitis that required a surgical uterine evacuation. The patient was administered intravenous antibiotics managed at ward level and the combined treatment was without complications. A placenta swab later indicated intrauterine mycoplasma infection. Fetopsy and placental

histological examination did not reveal any pathological malformation of the remaining fetus.

A 32-year-old non-obese woman with no pre-existing medical condition was referred to our unit at 11 + 3 weeks of gestation with a clinically unremarkable dichorionic, diamniotic twin pregnancy for a detailed anatomy scan and reduction to a singleton. The patient had had a previous full-term cesarean section. Both the current and previous pregnancies were achieved by *in vitro* fertilization. Multifetal pregnancy reduction had been done according to the standard guidelines without any complications. In the index pregnancy, the 18th week anomaly scan was reported as normal, the glucose tolerance test was negative and the mother had been at low risk on combined first trimester screening for Down's syndrome. The pregnancy was uncomplicated until 24 + 5 weeks of gestation when severe oligohydramnios was detected at the serial sonographic follow-up accompanied by no other contributing maternal condition (i.e. symptoms of intrauterine infection, hypertension or other complications) or fetal malformation (i.e. malformations or growth retardation). Prior to the procedure, AFI was 2 cm, and 500 mL saline solution was infused until a normal amount of fluid was restored, exceeding the upper limit of moderate oligohydramnios (AFI > 8 cm). No transplacental puncture was needed as the posterior placenta was described and the patient denied any drug abuse. Serology for cytomegalovirus, toxoplasmosis, syphilis, rubella and parvovirus B19, thyroid function tests, thrombophilia and autoantibody screens during pregnancy were also negative. Repeated measurements of the AF demonstrated that oligohydramnios did not recur. Doppler velocimetric indices of the uterine, umbilical, renal and middle cerebral arteries were within normal ranges in the second trimester (<https://fetalmedicine.org/var/uploads/Doppler-in-Obstetrics.pdf>). The patient was admitted to the maternity ward due to a subsequent rupture of membranes 72 h after TAAI. As per the policy of expectant management, to try to gain additional time for the fetus *in utero*, the patient obtained prophylactic antibiotic treatment. Chorioamnionitis had not emerged in the clinical course and TAAI had not been repeated as US scans confirmed only moderate oligohydramnios (AFI = 5–8 cm). The pregnancy continued until premature delivery at 29 + 0 weeks of gestation when the patient had lower abdominal pain and several antecedent episodes of small vaginal bleeding. The patient exhibited painful uterine tenderness during physical examination and abdominal US demonstrated a 2.4 cm × 2.8 cm hematoma behind the posteriorly attached placenta. Minimal bleeding through the cervical os was recorded during pelvic examination. The mother delivered a healthy male

neonate with a birthweight of 1380 grams via an immediately performed cesarean section. The infant had no "oligohydramnios sequence" or pathologies caused by prolonged exposure to oligohydramnios and is currently a healthy 8-year-old. The postpartum period was uneventful. The mother did not smoke and had no history of abruption or thromboembolism. Microbiological examination of high vaginal, placental and mid-stream urinalysis revealed no infection. Gross examination of the placenta revealed blood clots tenuously adhered to the placental floor and old fibrin and necrotic tissue on the decidual plate with infarcted areas as in acute abruption. Microscopic analysis demonstrated hemorrhage and edema in the decidua and villous stroma and intervillous thrombi [8].

Discussion

To our knowledge, this is the first report of oligohydramnios as a sporadic post-procedural clinical finding after an artificial fetal reduction in a twin pregnancy. The rate of oligohydramnios was 22% in our dataset; however, a relatively low number of participants were included in our study. One of our cases was a consequence of intrauterine infection. However, the exact pathomechanism of the AFV anomaly remained uncertain, and it can be considered unexplained or intervention-related in the other case. Another possible explanation for decreased fluid provision for the remaining fetus could be the altered uteroplacental circulation, but we could not notice any pathology in the 2-D Doppler-indices (<https://fetalmedicine.org/var/uploads/Doppler-in-Obstetrics.pdf>).

The etiology of placental abruption also remains speculative in our case; however, a history of a cesarean delivery and the two previous invasive procedures represent a clear predisposition [9]. In addition, oligohydramnios is a predisposing factor for placental abruption, and vice versa, small placental hematomas pose a risk of oligohydramnios [8]. It is pivotal to detect the oligohydramnios in time because this obstetric condition could be corrected via amnioinfusion in order to prevent uterine contractions and a subsequent pregnancy loss [7].

Some evidence suggests that reduced dichorionic twins are at lower risk compared to their unreduced counterparts [3, 4]. The risk of loss of the remaining fetus associated with the iatrogenic twin-to-singleton reduction due to the post-procedural amniotic leakage and chorioamnionitis is a major concern [2]. Early elective reduction of twins is associated with a less-than-10% pregnancy loss, and procedure-to-loss interval is often 4–8 weeks [5], whereas

others reported a miscarriage rate of 2.5%–11.9% following fetal reduction [3, 4].

Although severe oligohydramnios of the surviving fetus after elective reduction is not investigated [3–5], mid-trimester oligohydramnios poses a risk of perinatal mortality as high as 80% [7]. It is noteworthy that amnioinfusion can significantly prolong the pregnancy and artificially increased AFV could prevent 49.1% of the fetal deaths [7].

Our data highlight that a series of weekly repeated sonographic follow-ups are beneficial in order to detect non-infectious oligohydramnios that could be related to mid-trimester post-procedure miscarriage. Further research is needed to determine the post-procedural incidence of this preventable, unfavorable antenatal condition and to establish the benefit of amnioinfusion in the improvement of neonatal survival.

Author's statement

Conflict of interest: Authors state no conflict of interest.

Material and methods

Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: The research related to human use has been done in compliance with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

References

- [1] Sunderam S, Kissin DM, Crawford SB, Folger SG, Jamieson DJ, Barfield WD, et al. Assisted reproductive technology surveillance – United States, 2011. *MMWR Surveill Summ* 2014;63:1–28.
- [2] Evans MI, Berkowitz R, Wapner R, Carpenter RJ, Goldberg JD, Ayoub MA, et al. Multifetal pregnancy reduction (MFPR): Improved outcomes with increased experience. *Am J Obstet Gynecol* 2001;184:97–103.
- [3] van de Mheen L, Everwijn SM, Knapen MF, Haak MC, Engels MA, Manten GT, et al. Pregnancy outcome after fetal reduction in women with a dichorionic twin pregnancy. *Hum Reprod* 2015;30:1807–12.
- [4] Evans MI, Kaufman M, Urban AJ, Britt DW, Fletcher JC. Fetal reduction from twins to a singleton: a reasonable consideration. *Obstet Gynecol* 2004;104:102–9.
- [5] Yaron Y, Johnson KD, Bryant-Greenwood PK, Kramer RL, Johnson MP, Evans MI. Selective termination and elective reduction in twin pregnancies: 10 years experience at a single centre. *Hum Reprod* 1998;13:2301–4.
- [6] Kozinszky Z, Pásztor N, Vanya M, Sikovanyecz J, Pál A. Management of severe idiopathic oligohydramnios: is antepartum transabdominal amnioinfusion really a treatment option? *J Matern Fetal Neonatal Med* 2013;26:383–7.

[7] Kozinszky Z, Sikovanyecz J, Pásztor N. Severe midtrimester oligohydramnios: treatment strategies. *Curr Opin Obstet Gynecol* 2014;26:67–76.

[8] Elsasser DA, Ananth CV, Prasad V, Vintzileos AM. New Jersey-Placental Abruption Study Investigators. Diagnosis of placental

abruption: relationship between clinical and hystopathological findings. *Eur J Obstet Gynecol Reprod Biol* 2010;148:125–30.

[9] Minna T, Mika G, Tiina L, Marjo M, Sture A, Olavi Y, et al. Risk for placental abruption following amniocentesis and chorionic villus sampling. *Prenat Diagn* 2011;31:410–2.

transabdominal amnioinfusion (TAI) is a noninvasive procedure that can significantly prolong the pregnancy and increase the fetal weight. The data highlight that a series of weekly repeated amniocentesis followed by TAI is beneficial in order to obtain non-invasive oligohydramnios that could be related to mid-trimester post-procedure miscarriage. Further research is needed to determine the post-procedure risk factor of this procedure, unfavorable obstetrical course and to establish the benefit of amnioinfusion in the improvement of neonatal survival.

Author's statement
 Conflict of Interest: Author state no conflict of interest.
Statistical and methods
 Retrospective cohort, informed consent has been obtained from all individuals included in this study.
Ethical approval The research related to human use has been done in compliance with all the relevant national regulations, institutional policies and in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

References

1. Shidlow K, Mann DA, Cavener SK, Fieger SM, Janssen BJ, et al. A study of severe oligohydramnios. *Am J Obstet Gynecol* 1977;107:1043–50.

2. Chang H, Berek JS, Wang R, Casper R, Odibo A, et al. Maternal pregnancy reduction (MWR) improved outcomes with increased satisfaction. *Am J Obstet Gynecol* 2013;209:107–12.

3. van de Ven L, Evers W, van der Wal AC, van der Wal AC, et al. Pregnancy outcomes after fetal reduction. *Am J Obstet Gynecol* 2004;191:103–6.

4. Kim Y, Johnson KD, Wilson-Genderson FS, Johnson KD, et al. Maternal satisfaction with pregnancy reduction. *Am J Obstet Gynecol* 2004;191:103–6.

5. Kim Y, Johnson KD, Wilson-Genderson FS, Johnson KD, et al. Maternal satisfaction with pregnancy reduction. *Am J Obstet Gynecol* 2004;191:103–6.

6. Kim Y, Johnson KD, Wilson-Genderson FS, Johnson KD, et al. Maternal satisfaction with pregnancy reduction. *Am J Obstet Gynecol* 2004;191:103–6.

7. Kim Y, Johnson KD, Wilson-Genderson FS, Johnson KD, et al. Maternal satisfaction with pregnancy reduction. *Am J Obstet Gynecol* 2004;191:103–6.

8. Kim Y, Johnson KD, Wilson-Genderson FS, Johnson KD, et al. Maternal satisfaction with pregnancy reduction. *Am J Obstet Gynecol* 2004;191:103–6.

9. Kim Y, Johnson KD, Wilson-Genderson FS, Johnson KD, et al. Maternal satisfaction with pregnancy reduction. *Am J Obstet Gynecol* 2004;191:103–6.

reduced fetal weight. The postpartum period was increased. The mother did not smoke and had no history of abruption. Microbiological examination of placental, fetal and mid-stream analysis revealed no infection. Gross examination of the placenta revealed blood clots remaining adhered to the placental base and the fetal and maternal bases on the decidua. Histologic analysis of placental and fetal membranes and decidua to the decidua and chorionic plate revealed placental abruption (Fig. 1).

Discussion

To our knowledge, this is the first report of oligohydramnios as a sporadic post-procedure clinical finding after an artificial fetal reduction in a twin pregnancy. The rate of oligohydramnios was 2.5% in our dataset; however, a relatively low number of participants were included in our study. One of our cases was a consequence of intrauterine infection. However, the exact pathogenesis of the AI is not known. Therefore, we can be considered as a secondary or tertiary amnioinfusion. In the other case, another possible explanation for the need for amnioinfusion for the remaining fetus could be the fetal demise. In our study, we could not notice any difference in the 2-3 population compared to the control population. The study of placental abruption also remains speculative in our case; however, a history of a previous delivery and the two previous invasive procedures were not a clear predisposition. In addition, oligohydramnios is a predisposing factor for placental abruption, and a very small placental volume may pose a risk of placental abruption. It is pivotal to detect the oligohydramnios because this obstetric condition could be corrected by amnioinfusion in order to prevent uterine contractions and subsequent pregnancy loss [7].

Some evidence suggests that reduced fetal weight is at a lower risk compared to their unselected counterparts. At the risk of loss of the remaining fetus was associated with the fetoprotein twin-to-singleton reduction due to the post-procedure amniotic leakage and chorionic amnion. A major concern [2] that elective reduction of twins is associated with a less than 10% pregnancy loss, and a lifetime-to-for-twin is only 4–5 weeks [2] whereas