

Maternal outcome of selective feticide due to fetal anomaly in late trimester: a retrospective 10 years' experience in Taiwan

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Abstract

Background

With advanced diagnostic techniques, early identification of fetal anomaly becomes more accurate. However, certain diseases could only be diagnosed in late gestation. Feticide was suggested to avoid delivering children with abnormalities. Recently, twin pregnancies have increased gradually, and so have their complications. Selective feticide was considered to achieve good outcome of pregnancy. This study aimed to evaluate the performance of feticide in twin pregnancy with fetal anomaly.

Methods

This was a retrospective study enrolled from 2009 to 2018. A total of 68 pregnancies complicated with fetal anomalies received feticide were recorded. Potassium Chloride (KCl) was injected into left ventricle to induce fetal asystole. Monochorionic twin pregnancies were excluded, maternal and fetal characteristics of 16 dichorionic twins were documented to compare the effectiveness of feticide performed before and after 24th gestational week.

Results

All the pregnant women received feticide smoothly without any maternal complication. The reasons for choosing feticide were divided into four groups, including morphologic defect (61.8%), genetic-chromosomal abnormality (30.9%), obstetrical complication (5.9%) and maternal request (1.5%). Mean gestational age at delivery was significantly higher in dichorionic twins underwent selective feticide before and after 24th gestational week (36.7 vs 33.4, [p < .05]). No fetal loss in twin pregnancy demonstrated a high successful rate of selective feticide.

Conclusion

Intra-cardiac injection of KCl was effective for feticide and safe for mothers and fetuses. Selective feticide was beneficial to late gestation of dichorionic twin pregnancy. With sufficient discussion with patients, selective feticide served as an alternative approach for twin pregnancy with fetal anomaly.

Background

Gradual evolution of high-resolution ultrasound sonography (US) and prenatal diagnostic technique have assisted in early diagnosis of fetal abnormality. However, certain diseases are lately identified in second or third trimester. Induced feticide is necessary for avoiding termination of pregnancy with viable fetus.¹ Feticide refers to causing death of fetus, that is generally conducted prior to mid- to late-second trimester

of pregnancy. Parents could opt for feticide before termination of pregnancy in order to relieve themselves of unwarranted legal, financial or emotional burden.

In recent years, number of twin pregnancy has increased gradually, and more complications have been observed in mothers and fetuses.² Twin pregnancy achieved higher rate of chromosomal or structural abnormality than singleton pregnancy.³ Therefore, selective feticide is considered a way to avoid giving birth to a viable fetus with severe disease.⁴ In this article, we assessed several cases of late termination of pregnancy in a tertiary medical center in Taiwan. Maternal and fetal outcomes of surgery were documented to evaluate the performance of feticide in dichorionic twin with fetal anomaly.

Methods

This retrospective study collected data from patients who underwent feticide in Linkou and Taipei Chang Gung Memorial Hospital in Taiwan between January, 2009 and December, 2018. All cases admitted for feticide were previously reviewed by primary healthcare facilities and transferred to Linkou or Taipei Chang Gung Memorial Hospital which patients diagnosed with congenital abnormality were frequently referred. Written informed consents were obtained from all pregnant women for participation. The study was approved by Chang Gung Medical Foundation Institutional Review Board (CGMF Ref. No. 201801716B0C601).

Participants

A total of 115 women were admitted for feticide between January, 2009 and December, 2018. With exclusion of multiple gestation and heterotopic pregnancy reduction, 68 cases with fetal anomalies remained in the study. All cases were divided into four groups according to their reasons for choosing feticide, including morphologic defect, genetic-chromosomal abnormality, obstetrical complication and maternal request. In the beginning, the patient was taken over by a consultation team. The professional consultant would obtain prenatal information, confirm diagnosis and inform potential neonatal outcomes. Then, feticide was suggested in discussion about termination of pregnancy diagnosed with fetal anomaly in second or third trimester. If the agreement of feticide was reached, the patient should sign a written consent form. A committee would examine the feasibility of procedure based on national legal requirement whose limited gestational age of termination is 24th gestational week.

Procedures

The procedure is performed by an experienced and skillful obstetrician. After eligible patients are admitted, serum hemogram and prothrombin time should be tested. Patients receive surgical draping in order to establish aseptic areas. Under US guidance, the obstetrician utilizes a 22G X 150mm needle (TOP Corporation, Japan) to puncture left ventricle of fetus and administer Potassium Chloride to (KCl) induce asystole. First dose of KCl is 2-3mL, and additional dose (1-2mL) could be given if bradycardia is not observed. Fetal asystole is identified with US 30 minutes after the procedure. Total amount of KCl is recorded until fetal death is confirmed. A total of 49 singleton pregnancies with fetal anomalies were

terminated after feticide. Termination of pregnancy is conducted with misoprostol in oral, sublingual or vaginal route. The viability of 19 survivors of twin pregnancies should be checked one day after selective feticide. Patients are recommended weekly follow-up at outpatient clinic until delivery. With exclusion of two monochorionic twins and one dichorionic twin with previous laser ablation for twin-twin transfusion syndrome, the detail of delivery time, maternal outcome and complication of procedure from 16 dichorionic twins are all recorded.

Statistical analysis

Maternal and fetal outcomes between gestational age of receiving feticide before and after 24th gestational week were analyzed by two sample t test. Considering statistical software, Prism version 8.0.1 (GraphPad Software Inc., San Diego, CA, USA) was used for data analysis.

Results

Characteristics of pregnancy with fetal anomaly and maternal outcome

Maternal characteristics of pregnancy with fetal anomaly were listed in Table 1. Mean maternal age of patients was 32.3 (maximum: 42; minimum: 18) years. Mean gestational age of fetus receiving feticide was 21.1 (maximum: 35; minimum: 15) weeks. Primigravida and multigravida account for 45.6% and 54.4%. Nulliparous and multiparous account for 66.2% and 33.8%. All reasons for choosing feticide were listed in Table 2, that included morphologic defect (61.8%), genetic-chromosomal abnormality (30.9%), obstetrical complication (5.9%) and maternal request (1.5%). In morphologic defect group, brain anomaly is the most common (45.2%), followed by limbs (16.7%) and multiple anomalies (16.7%). In genetic-chromosomal abnormality group, trisomy 21 is the most common (33.3%), followed by other causes (28.6%) and trisomy 18 (19.0%). In obstetric disorder groups, three patients received feticide for severe oligohydramnios and one for twin-twin transfusion syndrome. In maternal request group, one patient with thyroid malignancy received feticide. All the pregnant women received feticide smoothly without any maternal complication. The procedures including singleton or twins were completed within 20 minutes.

Table 1
Maternal characteristics of pregnancies with fetal anomalies.

| | All pregnancies (n = 68) |
|---------------------|---------------------------------|
| Maternal age, y | 32.29 ± 5.15 |
| Gestational age, w | 21.11 ± 7.99 |
| Gravidity | |
| Primigravida, % (n) | 45.6% (31) |
| Multigravida, % (n) | 54.4% (37) |
| Parity | |
| Nulliparous, % (n) | 66.1% (45) |
| Multiparous, % (n) | 33.8% (23) |

Table 2
Categorization of fetal anomalies.

| | All pregnancies (n = 68) |
|-------------------------------------|---------------------------------|
| Morphologic defect, % (n) | 61.8% (42) |
| Brain, % (n) | 27.9% (19) |
| Limbs, % (n) | 10.3% (7) |
| Heart, % (n) | 7.4% (5) |
| Face, % (n) | 5.9% (4) |
| Multiple organs, % (n) | 10.3% (7) |
| Genetic-chromosomal disorder, % (n) | 30.9% (21) |
| Trisomy 21, % (n) | 10.3% (7) |
| Trisomy 18, % (n) | 5.9% (4) |
| 22q 11.2 deletion, % (n) | 2.9% (2) |
| Microdeletion, % (n) | 2.9% (2) |
| Other, % (n) | 8.8% (6) |
| Obstetrical complication, % (n) | 5.9% (4) |
| Maternal request, % (n) | 1.5% (1) |

Selective Feticide In Twin Pregnancy

All singleton pregnancies underwent feticide with KCl and were terminated with misoprostol. Mean time of feticide was 19.3 (maximum: 36; minimum: 1) minutes. Mean volume of injected KCl was 3.6 (maximum: 10; minimum: 2) mL. No immediate maternal complications were noted after termination of pregnancy. Other twin pregnancies received selective feticide. Maternal and fetal characteristics of selective feticide in dichorionic pregnancies were described in Table 3. All patients were divided into two groups according to gestational age of receiving feticide before or after 24th gestational week (group 1 and 2). No immediate maternal complications were noted after selective feticide. Mean gestational age at delivery was significantly higher in group 1 than group 2 (36.7 vs 33.4, [p < .05]) weeks. (Fig. 1) Mean maternal age was lower in group 1 than group 2 (33.3 vs 34.6) years with no significant difference. Ratio of conception by assisted reproductive technology was lower in group 1 than group 2 (36.3% vs 60.0%) with no significant difference. Mean gestational age of procedure was lower in group 1 than group 2 (20.1 vs 27.6) weeks with no significant difference. Mean procedure time was higher in group 1 than group 2 (16.8 vs 13.0) minutes with no significant difference. Average hospitalization time was lower in group 1 than group 2 (2.7 vs 8.4) days with no significant difference.

Table 3

Maternal and fetal characteristics of feticide in dichorionic twin pregnancy. ART: Assisted reproductive technology; CS: Cesarean section; GA: Gestational age at procedure; IUI: Intrauterine insemination; IVF: In vitro fertilization; NICU: Neonatal intensive care unit; SD: Spontaneous delivery; SF: Selective feticide.

| | GA < 24 week (n = 11) | GA > 24 week (n = 5) | P value |
|---------------------------|---------------------------|---------------------------|---------|
| Age, y | 33.3 | 34.6 | 0.743 |
| Parity | | | |
| Nulliparity, n | 7 | 4 | |
| Multiparity, n | 4 | 1 | |
| Causes of fetal anomaly | | | |
| Morphological, n | 5 | 2 | |
| Chromosomal, n | 6 | 3 | |
| Conception by ART, n (%) | IUI: 0; IVF: 4 (36.3%) | IUI: 2; IVF: 1 (60.0%) | 0.630 |
| GA at procedure, w | 20.2 | 27.6 | < 0.001 |
| Procedure time, min | 16.8 | 13.0 | 0.913 |
| Hospitalization period, d | 2.7 | 8.4 | 0.900 |
| Mode at delivery, n (%) | SD: 6; CS: 5 (45.5%) | SD: 4; CS: 1 (20.0%) | 0.580 |
| GA at delivery, w | 35.4 | 33.4 | 0.410 |
| Preterm labor, n (%) | 6 (54.4%) | 4 (80%) | > 0.99 |
| Birth weight, g | 2257 | 2020 | 0.503 |
| NICU admission, n (%) | 2 (22.2%) | 3 (75%) | 0.25 |

Discussion

In spite of technological and technical advancements, some abnormalities occurred after 24th gestational week. According to the report from World Health Organization (WHO), administration of misoprostol alone or with Mifepristone is not directly fetocidal.¹ With increasing gestational age of termination, transient fetal survival rate also elevates. Therefore, before termination with medical methods in third trimester, inducing pre-procedural fetal demise should be considered. WHO recommends two regimens, including KCl and Digoxin. KCl was injected into umbilical cord or cardiac chamber. This procedure is highly effective because fetal asystole could be identified with US immediately.⁵ However,

the advanced technique requires more expertise. Injection of Digoxin into amniotic fluid is technically easier, although whole procedure takes almost one day for fetus to absorb.^{6,7} Intracardiac injection of KCl is our first choice to perform feticide. This technique consists of good quality of US and skillful obstetricians. Pasquini et al. conducted a retrospective study of 239 women who undertook feticide with the same method.⁵ Successful fetal asystole was confirmed in all cases and no patients needed second injection. Our result was consistent with the above study. Intracardiac KCl serves as a safe and effective method for feticide.

Dichorionic twin pregnancies with one abnormal fetus could choose selective feticide and continue pregnancy. A previous study showed that selective feticide increased gestational age at delivery and birth weight.⁸ Hence, selective feticide is regarded as a choice for twin pregnancy with fetal anomaly. It is important to identify chorionicity in twin pregnancy.⁹ The placenta in dichorionic twin is separated that made it impossible to perform intracardiac injection of KCl for inducing asystole. However, anastomosis is rich in the placenta if monochorionic pregnancy. To avoid the effect of cardiotoxic agents toward healthy fetus, selective feticide in monochorionic twin is suggested to be completed with radiofrequency ablation (RFA) in umbilical cord.

The timing to perform selective feticide in twin pregnancy is also under debate. A retrospective study concluded that selective feticide performing in third trimester seemed to be a safe approach to reduce total fetal loss and early preterm birth rate.¹⁰ In our study, patients were categorized according to gestational age of receiving feticide. Higher gestational week at delivery was observed in selective feticide before than after 24th gestational week. That is, selective feticide in later gestation might cause preterm delivery. However, no fetal loss occurred in twin pregnancy demonstrated a high successful rate of selective feticide.

Our study demonstrated similar proportion of reasons for choosing feticide with previous literatures.^{5,11} Brain abnormality and aneuploidy accounted for major causes of feticide. Reasons for late diagnosis might be derive from misdiagnosis in early gestation and variation of disease. When an abnormality is discovered, an obstetrician would initiate a series of surveys to determine a definite diagnosis. Amniocentesis and level II ultrasound scan are offered to patients older than 34 years for free because these procedures are covered by National Health Insurance in Taiwan. Referral to tertiary medical center is often required, that usually takes several weeks.

Legal regulation in Taiwan is illustrated in Genetic Health code. According to Enforcement Rules of Genetic Health Act, medical abortion is indicated when pregnancy or childbirth might affect physical or mental health or when potential abnormalities are identified during the development of fetus. Law in Taiwan puts an emphasis on induced abortion before 24th gestational weeks. Certain conditions, including identification of anomaly and exposure to teratogenic agent or radiation, are beyond the above regulation. All termination after 24th gestational weeks would be examined and reviewed by a joint committee and agreed by two obstetricians. In the UK, RCOG stated that feticide should only be recommended after 22th gestational week because live birth rate increased significantly then.¹² Patients

might deliver fetus with abnormality or short lifespan without feticide in an adequate period. Between 2002 and 2008, 120–130 out of 1900 terminations occurred after 20th gestational week every year in the UK. If patients decide to receive feticide due to diagnosis with abnormality in the second or third trimester, the procedure could be performed before medical termination. The comfort and dignity of fetus counts throughout the period of terminal care.

Conclusion

Intra-cardiac injection of KCl was effective for feticide and safe for mothers and surviving fetuses. Selective feticide showed therapeutic potential in late gestation of dichorionic twin pregnancy. With sufficient discussion about all related benefits and risks with the patient and family, selective feticide could be suggested for twin pregnancy with fetal anomaly.

Abbreviations

KCl: Potassium Chloride; US: Ultrasound sonography.

Declarations

Ethics approval and consent to participate

This study was approved by Chang Gung Medical Foundation Institutional Review Board (CGMF Ref. No. 201801716B0C601). Written informed consent were obtained from all pregnant women for participation.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

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Authors' contributions

CAS and SWS designed the study. CAS, THH and SWS collected the data. CAS and HNL analyzed the data. CAS, HNL and TYL drafted the manuscript. KSC and SWS revised the manuscript. SWS conducted critical review. All authors were involved in the amendment and approval of final manuscript.

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Figures

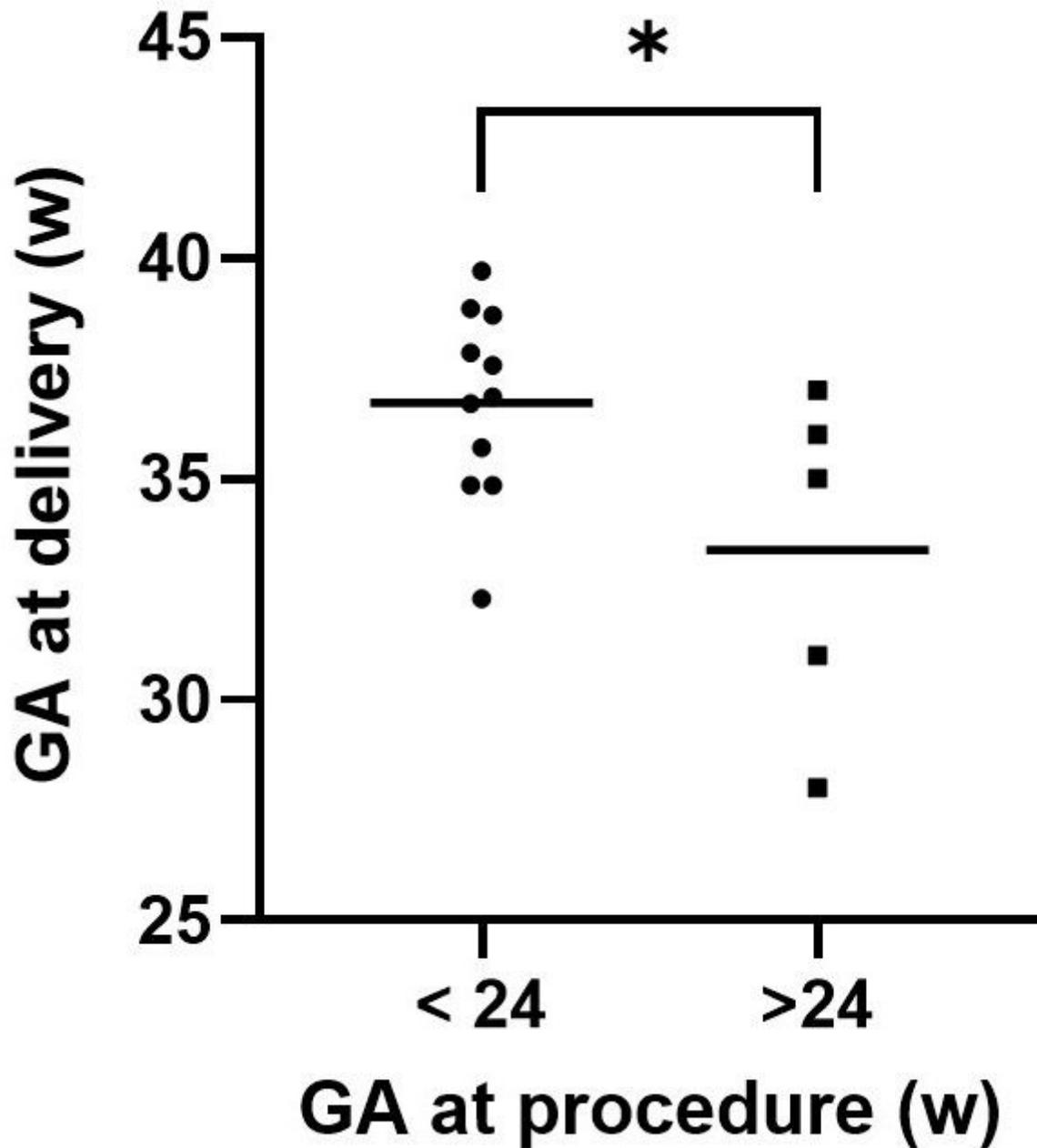


Figure 1

Comparison of gestational age (GA) at delivery between pregnancies receiving feticide before and after 24th gestational week