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Comparison of Intracardiac and Intrathecal KCL Application as an Alternative Method in the Reduction of Multiple Pregnancies in the First Trimester: Results of a Tertiary Centre

ABSTRACT

Objectives: This retrospective study compares the outcomes of intracranial (IC) and intrathoracic (IT) potassium chloride (KCl) applications for fetal reduction in multiple pregnancies.

Methods: Nineteen patients undergoing termination between December 2022 and November 2023 were analyzed. Transabdominal IC (n=8) and IT (n=11) KCl groups were compared for maternal age, gestational age, indication for reduction, and procedural details. P-values <0.05 were interpreted as statistically significant.

Results: While both groups exhibited similar maternal characteristics, the number of fetuses before reduction differed significantly (p=0.016). No significant distinctions were observed in operative time, reduction outcomes, or obstetric complications between the IC and IT groups (p>0.05). Premature rupture of membranes occurred in 13.3% (IT) and 23.1% (IC), with no significant intergroup differences.

Conclusion: The study suggests that IC KCl application may be a viable alternative, potentially simplifying the procedure without compromising safety or efficacy. The findings advocate for a nuanced approach to selecting the reduction method based on fetal position and number, highlighting the need for further research with larger sample sizes.

Keywords: Fetal reduction, intracardiac fetosid, intrathecal fetosid, multiple pregnancy

It is known that the frequency of multiple pregnancies is increasing today. The widespread use of assisted reproductive techniques and ovulation induction drugs are the main reasons for this (1). Above all, the difficulty of achieving pregnancy forces clinicians to transfer two or more embryos (2). However, increased perinatal morbidity and mortality are directly related to the number of fetuses. The risk of premature birth between 28-32 weeks increases fivefold for twin pregnancies and twentyfold for triple pregnancies (3).

Additionally, the presence of congenital anomalies in multiple pregnancies is another important factor that increases the risk of premature birth. The loss of the baby with the anomaly in the womb also leads to impaired neurological development and potentially to the fetal death of the other twin (4).

Reduction of multiple pregnancies (RMP) is a procedure preferred in the first trimester or early second trimester to reduce the number of fetuses. The aim is to decrease the number of fetuses to one or two and improve the poor outcome for the mother and newborn by selecting the fetus with the anomaly, if present, when performing the procedure (3). Reducing pregnancy to a singleton or twins by means of reduction has been shown in many studies to significantly improve outcomes compared to doing nothing (5).

RMP can be performed transvaginally or transabdominally under ultrasound guidance (6). Various methods are available, including the route of access, the timing of the procedure, and the fetotoxic agents used. KCl is generally used as a fetotoxic agent, but other agents such as digoxin have also been tested in some studies (7). Amniotic fluid, the fetal umbilical cord, intracardiac, intrathoracic (IT), and intracranial (IC) methods may be preferred for the application of the fetotoxic agent (8).

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Our study aimed to compare two procedures preferred in our clinic for fetal reduction: intracranial KCl administration and intracardiac KCl application. All these methods are applied transabdominally. The objective of our study was to assess and evaluate the procedural duration, maternal complication rate, and neonatal outcomes. As the number of fetuses increases, the process becomes progressively more challenging due to the increase in the number of placentas, amniotic membranes, and the varying positions of the fetuses. Hence, we aimed to demonstrate that the intracranial technique, as an alternative approach, can be employed with equivalent safety and duration.

METHODS

This research retrospectively analyzed a total of 19 patients who had pregnancy terminations at the Etlik City Hospital Perinatology Clinic, between December 2022 and November 2023. The study was conducted under the principles of the Declaration of Helsinki. The local ethics committee granted ethical permission (approval number: AEŞH-EK1-2023-745). Medical records and the hospital information management system were used to retrieve patient data.

Maternal age, parity, gestational weeks, type of pregnancy (spontaneous or assisted reproduction), number of pregnancies (triplets or higher order fetuses), indication for fetal reduction (fetal anomaly or multiple pregnancy), number of fetuses before fetal reduction, reduced number of fetuses, and finishing number of fetuses were recorded from the hospital database.

Indications for fetal reduction include multiple pregnancies, fetal malformation, cervical factors (post-cervical conization, cervical insufficiency), uterine malformation, and uterine fibroids. Indications for fetal termination include fetal structural anomalies, chromosomal anomalies, amniotic fluid abnormalities, fetal hydrops, infections, maternal drug or teratogen use, radiation exposure, and maternal reasons.

According to the specific puncture site, the patients were divided into a transabdominal intracranial KCl fetal reduction injection group (Transcranial KCl group) and a transabdominal KCl fetal reduction injection group (Transabdominal KCl group). An ultrasound examination is performed before the operation. The fetal position and placenta position are determined. A 22-gauge needle was used to puncture the fetal heart or cranium through the abdomen under ultrasound guidance. KCl was injected for fetal termination. A 22-gauge needle is placed into the thorax or cranium of the targeted fetus, 2 to 3 mL of potassium chloride is injected, and asystole is observed for at least 3 minutes. The procedure is then repeated for additional fetuses as required, with a different needle or occasionally with the same needle puncture.

Statistical Analysis

All statistical analyses were performed using the RStudio integrated development environment for statistical computing (Affero General Public License v3; published 2011. RStudio for Linux, version v2021.09.4+403.pro3 Ghost Orchid; September 19, 2022; developed by Posit, PBC) to analyze the data. The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogorov-Smirnov/Shapiro-Wilk test) to determine whether or not they are normally distributed. The Levene test was used to assess the homogeneity of variances. Descriptive analyses were presented using means and standard deviations for normally distributed variables. An independent samples t-test was used to compare these parameters among the groups. For the non-normally distributed numerical data, descriptive analyses were presented using medians and interquartile ranges (Q1-Q3). The Mann-Whitney U test was conducted to compare these parameters among the groups. For categorical variables, descriptive analyses were presented using frequency and percentage. Relationships between categorical variables were analyzed with the Chi-square test or Fisher's exact test (when Chi-square test assumptions do not hold due to low expected cell counts). A p-value of less than 0.05 was considered to show a statistically significant result.

RESULTS

Table 1 shows the comparison between the two different treatment groups of pregnant women who underwent the feticide procedure.

Table 1. Maternal and gestational characteristics

	Transabdominal KCL n (11)	Transcranial KCL n (8)	p
Age	31.8±6.0	30.0±4.2	0.474
Parity (Median (min-max))	1 (0-3)	1 (1-2)	0.490
Mode of conception			
Assisted reproduction	6 (54.5%)	6 (75%)	0.633
Spontaneous	5 (45.5%)	2 (25%)	
Indications for fetal reduction			
Fetal anomaly	4 (36.4%)	1 (12.5%)	0.243
Triplet or higher order of fetuses	7 (63.6%)	7 (87.5%)	
Gestational age at reduction	13.6±1.9	12.3±1.0	0.081
Number of fetuses prior to fetal reduction			
2	5 (45.5%)	1 (12.5%)	0.016
3	3 (27.3%)	7 (87.5%)	
4	3 (27.3%)	0	

The study was conducted with a total of 19 pregnant women who underwent transabdominal KCl (n=11) and transcranial KCl (n=8) procedures. The mean ages of transabdominal KCl and transcranial KCl patients were 31.8±6.0 and 30.0±4.2 years, respectively (p=0.474). There was no significant difference between the two groups in terms of parity, mode of conception (assisted reproduction, spontaneous), indications for fetal reduction (fetal anomaly, triplet or higher order of fetuses), or gestational age at reduction (p>0.05 for all). There was a significant difference between the two groups in terms of the number of fetuses before fetal reduction (p=0.016). The number of patients with two fetuses before fetal reduction was five in the transabdominal KCl group and one in the transcranial KCl group. The number of patients with three fetuses before fetal reduction was three in the transabdominal KCl group and seven in the transcranial KCl group. The number of patients with four fetuses before fetal reduction was three in the transabdominal KCl group and none in the transcranial KCl group.

Table 2 shows the comparison between the two different treatment groups of pregnant women who underwent the feticide procedure. There was no significant difference between the two groups in terms of operative time per fetus, reduced number of fetuses, or finishing number of fetuses (p>0.05 for all). The operative time per fetus for transabdominal KCl and transcranial KCl patients was 31±4.0 and 30.2±3.2 minutes, respectively (p=0.831). The number of patients who underwent fetal reduction for a single fetus was seven in the transabdominal KCl group and six in the transcranial KCl group. The number of patients who underwent fetal reduction for two fetuses was two in both the transabdominal KCl and transcranial KCl groups. The number of patients who underwent fetal reduction for three fetuses was one in the transabdominal KCl group and none in the transcranial KCl group. The number of patients with one fetus after fetal reduction was seven in the transabdominal KCl group and three in the transcranial KCl group. The number of patients with two fetuses after fetal reduction was four in the transabdominal KCl group and five in the transcranial KCl group.

Table 3 shows the comparison of obstetric outcomes of the remaining fetuses after the feticide procedure between the two different treatment groups. There was no significant difference between the two groups in terms of preterm premature rupture of membranes, preterm labor, fetal growth restriction, gestational hypertension,

Table 2. Comparison of procedural features and complications

	Transabdominal KCL n (11)	Transcranial KCL n (8)	p
Operative time per fetus	31±4.0	30.2±3.2	0.831
Reduced number of fetuses			
1	7 (63.6%)	6 (75%)	0.662
2	2 (27.3%)	2 (25%)	
3	1 (9.1%)	0	
Finishing number of fetuses			
1	7 (63.6%)	3 (37.5%)	0.370
2	4 (36.4%)	5 (62.5%)	

Table 3. The obstetric outcomes of procedures

Neonatal outcomes	Remaining fetuses after transabdominal KCL n= 15	Remaining fetuses after transcranial KCL n= 13	p
PPROM	2 (13.3)	3 (23.1)	0.639
Preterm labor	5 (33.3)	7 (53.8)	0.477
Fetal growth restriction	3 (20)	2 (15.4)	1.000
Gestational hypertension	1 (6.7)	1 (7.7)	1.000
Mean GA at delivery (weeks)	37±4.7	38±1.7	0.526
GA at birth 24–31 6/7	1 (6.7)	0 (0)	0.824
32–36 6/7 weeks	4 (26.7)	5 (41.7)	
> 37 weeks	10 (66.7)	7 (58.3)	
Take-home-baby rate	14 (93.3)	12 (92.3)	0.722
Co-twin death ≤1 week	0	1	0.942
Co-twin death > 1 week	0	0	
Perinatal mortality	1	0	1.000

KCL: potassium chloride, PPROM: preterm premature rupture of membranes, GA: gestational age. Data are expressed as mean±SD or number (percentage) where appropriate. p<0.05 indicates significant difference.

mean gestational age at delivery, take-home baby rate, or perinatal mortality (p>0.05 for all).

DISCUSSION

Termination of pregnancy in the first trimester is a procedure that may be necessary due to various medical indications or serious risks to the mother's health. In this procedure, various methods are used to terminate fetal life. Intrathoracic (IT) and intracranial (IC) potassium injections are among the frequently used methods for fetal termination. These are invasive procedures in which a potassium solution is injected into the heart or brain of the fetus (9).

In IT potassium injection, a potassium solution is injected directly into the fetus's heart. This method acts quickly on the fetus and ensures the termination of fetal life. IC potassium injection, on the other hand, is carried out by injecting a potassium solution into the fetal brain. This method aims to quickly shut down the brain functions of the fetus (10).

In this study, we wanted to compare the results of IT and IC potassium injections for the termination of the fetus in the first trimester. We examined the impact of both the degree of invasiveness and effectiveness on maternal health, the risk of complications, and neonatal outcomes.

Our study included 19 patients who underwent fetocide in the first trimester at our clinic between October 2022 and July 2023. We performed fetocide by administering IT potassium to 11 of these patients and IC potassium to 8 of them. Five of these patients had fetal anomalies, and the indication for termination was a fetal anomaly. This procedure was performed on 14 patients for fetal reduction, to reduce pregnancies with triplets or more fetuses to twins or singleton pregnancies. In addition, 12 of our 19 patients became pregnant through assisted reproductive techniques. It is well known that the need for fetal reduction procedures has increased significantly due to the rise in multiple pregnancies caused by the increasing use of assisted reproductive techniques and the negative impact of the increasing number of fetuses on perinatal and neonatal outcomes (11). One of the most common indications among the patients in our study was the reduction of multiple pregnancies. Only seven of our patients became pregnant spontaneously. The indication for termination of pregnancy in five of these patients was a fetal anomaly. In one study in the literature, the average week of pregnancy in which the reduction was carried out was given as 12+6 weeks (1). In our study, the average gestational age at which we performed the IT fetocide was 13.6 weeks, and for the IC fetocide, it was 12.3 weeks (p=0.081). For this reason, the most ideal time, as in our study, is the end of the first trimester or the beginning of the second trimester (8).

In the reduction procedures that we perform for multiple pregnancies, six patients had twin pregnancies, ten had triplets, and three had quadruplets. In the fetal reduction we performed, we selected the fetuses with an increase in NT, according to the literature, or the fetuses on which we could more easily perform the procedure, after detailed information and consent from the patients and their relatives regarding the selection of patients, the number of fetuses to be reduced, and the selection of fetuses. When planning this procedure, we preferred another alternative method, intracranial potassium administration, in fetuses where we thought that intracardiac potassium administration might be difficult, especially due to the fetal position. In one twin pregnancy, we had to administer IC potassium to a patient, but in 87.5% of the triplet pregnancies, we performed fetocide using the IC method (p=0.016). This suggests that, as in previous studies, the administration of IC potassium is an option to further reduce the complication rate and technical difficulties during the procedure, taking into account the risks associated with fetal position and the number of fetuses (9).

There was no significant difference in the application times between the two methods we used (p=0.474). Our average procedure time was 31 seconds for patients for whom we performed fetocide using the IT method and 30.2 seconds for patients for whom we performed fetocide using the IC method. In a study presented in a series of 3 patients, KCl was injected for 15 seconds in one patient, in the second patient it was observed that the fetal heartbeat stopped after a 45-second injection, and in the third patient the result was obtained after a 30-second procedure (9). Although our transaction times are similar, we have had no unsuccessful transactions. In addition, the procedure times were similar in the cases in which IT fetocide was performed. Although we do not prolong the duration of the procedure and there is no difference in terms of complications, we believe that fetal reduction using the IC method is advantageous in appropriate cases in terms of the comfort and safety of the procedure.

In multiple pregnancies in which we performed a reduction, the number of patients we reduced to 1 fetus was 7 patients (63.6%) with the IT method and 3 patients (37.5%) with the IC method. With regard to the number of pregnant women who had twin pregnancies, there were 4 patients (36.4%) with the IT method and 5 patients (62.5%) with the IC method. We found no significant difference between the choice of procedure and the final number of fetuses between the two groups. There are many factors related to the selection of procedures. Each patient must be assessed individually, and the decision depends on the patient, the number of fetuses, the presence of a fetal abnormality, the patient's wishes, and the technical suitability of the procedure to be performed. In one study in the literature, they reduced all quintuplet and quadruplet pregnancies in the included patients to twin pregnancies, and in triplet pregnancies, they reduced 50 out of 63 patients to twin pregnancies and 13 to singleton pregnancies (1). In this study, however, the same method, IT potassium injection, was used for each pregnancy. In our study, premature rupture of membranes occurred in 2 of the 15 babies (13.3%) in whom we performed IT procedures and in 3 of the 13 babies (23.1%) in whom we performed IC procedures (PPROM). The number of babies who went into premature labor was 5 (33.3%) in the IT group and 7 (53.8%) in the IC group. The difference between these groups was not statistically significant (Table 3). This included 1 baby (6.7%) that was born between 24-32 weeks and belonged to the IT procedure group. The rate of babies born between 32 and 36+6 weeks was 26.7% in the IT procedure group and 5% in the IC procedure group. No statistical difference was found between the groups (Table 3). In a comprehensive literature review on this topic, the rate of births under 28 weeks was given as 2.9%, and the rate of births under 32 weeks as 8.9% (11). In this study, a comparison was made with patients who were not treated and were observed spontaneously, and it was shown that extreme premature births, i.e., births under 28 weeks, were significantly reduced in the groups in which a reduction was carried out. This underlines the importance of reducing the number of fetuses by reducing the rate of babies born under 28 weeks gestation who have the worst neonatal outcomes. In another study, the PPROM rate

in the reduction group was 11.1%, and the preterm birth rate was 10%, and these results are comparable to the rates in our study (12).

In our study, the number of fetuses with fetal growth retardation in ongoing pregnancies was 3 (20%) in the IT group and 3 babies (15.4%) in the IC group. In both groups, one patient developed gestational hypertension. The difference between the groups was insignificant, suggesting that the method of intervention does not influence maternal and neonatal outcomes. However, the processing technique was the same in these studies; KCl was administered using a transabdominal method, and the groups that underwent reduction were compared with those that did not (12).

There was only one patient in the IC group whose other twin died within one week of the procedure. In the IT group, we had no patients with complications within one week. The difference between these two groups was not statistically significant (p=0.942). Perinatal mortality was observed in 1 patient, who belonged to the IC intervention group. These results indicate that the complication rate is very low, akin to the literature (13). The number of babies taken home was 14 (93.3%) in the group with IT procedures and 12 (92.3%) in the IC group. No significant difference was found between the two groups (Table 3). In a study comparing reduction results in 148 triplet, quadruplet, and quintuplet pregnancies, the groups in which IT KCl was used were compared with an intravaginal method in which a needle was inserted into the fetal thorax and the amniotic fluid was aspirated. This study aimed to reduce the complication rate with an alternative and earlier method, finding that the rate of babies taken home was 69.7% in the KCl group and 86.1% in the non-KCl group (p=0.045) (7). Although these rates do not compare with our study, they are still lower than our results.

The number of patients with multiple pregnancies is increasing due to the growing use of assisted reproductive techniques for infertility, one of the most significant problems of our time. It is known that 30-50% of multiple pregnancies in developing countries result from infertility treatments (13). As is well known, in multiple pregnancies, maternal and neonatal outcomes deteriorate as the number of fetuses increases (14). For this reason, fetal reduction will likely be employed more frequently, especially in triplet pregnancies and beyond. It is known that the number of fetuses, the position of the fetus, and the chorionic status increase the technical difficulty of the fetus reduction procedure. Moreover, our results show no difference in terms of procedure duration and maternal complications, which favors using this method.

CONCLUSION

Very few studies similar to ours exist in the literature. We believe that the intracranial KCl application is technically simpler and more convenient than the IT application. This method may be preferred due to its technical ease, particularly in clinics where there is a need to improve the learning curve for selecting suitable patients. However, as a limitation of our study, we acknowledge that neonatal outcomes and complication rates should be evaluated with a larger number of patients.

Ethics Committee Approval: This study was conducted with the permission of the Ankara Etlik City Hospital Local Ethics Committee (decision no: AEŞH-EK1-2023-745 date: 06.12.2023).

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

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