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ORIGINAL RESEARCH

Analysis of the Clinical Efficacy of Conservative Treatment for an Unruptured Cornual Pregnancy

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ABSTRACT

Context • Early diagnosis and early treatment of cornual pregnancy are very important. Conservative treatment before rupture can greatly reduce the patient's trauma. It's very important to choose a treatment method for cornual pregnancy with a high level of effectiveness, few adverse reactions, and no effects on fertility.

Objective • The study intended to compare the clinical efficacy of different treatments for unruptured cornual pregnancy to find a safe, effective, minimally invasive treatment for unruptured cornual pregnancy that has few side effects and doesn't affect fertility.

Design • The research team retrospectively collected the clinical data of patients to analyze the benefits of treatments for cornual pregnancy.

Setting • The study took place in the Department of Obstetrics and Gynecology at the Wuhan Third Hospital in Wuhan, Hubei Province, China.

Participants • Participants were 61 patients with an unruptured cornual pregnancy who had been admitted to the hospital between September 2002 and May 2012.

Intervention • Participants were divided into four groups according to the treatment they received: (1) 20 patients who had been orally administered mifepristone combined with misoprostol and received uterine curettage were included in the drug abortion + curettage group (D group); (2) 16 patients who had received ultrasound-guided uterine aspiration were included in the uterine aspiration group (U group); (3) 15 patients who had received methotrexate (MTX) chemotherapy were included in the chemotherapy group (C group); and (4) 10 patients who had received ultrasound-guided hysteroscope operation were included in the hysteroscope operation group (H group).

Outcome Measures • Adverse reactions and the decrease in participants' blood β-HCG were recorded in detail. The participants were followed up for two months.

Results • Of the 61 participants, 12 underwent surgery after failed conservative treatment, one in the D group, four in the U group, three in the C group, and four in the H group. No significant difference existed in the baseline data among the four groups. The decline rates of β-HCG at seven days after treatment and the treatment success rates of participants in the D group were significantly higher than those in the U group, the C group, and the H group (all $P < .05$). The time at which the β-HCG turned negative and the average hospital stays weren't significantly different among the four groups.

Conclusions • The current study found that oral administration of mifepristone, combined with misoprostol, plus uterine curettage was superior to the other three methods in treatment of unruptured cornual pregnancy. The drug abortion + curettage treatment was found to be a safe, effective, minimally invasive treatment for unruptured cornual pregnancy, which has few side effects and doesn't affect fertility. (*Altern Ther Health Med.* 2022;28(6):118-123)

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Cornual pregnancy refers to a pregnancy in which a fertilized egg implants in the uterine horn, which is rare clinically. The fertilized egg is attached to the opening of the fallopian tube near the uterine cavity and develops towards the uterine cavity rather than in the interstitial part of the fallopian tube.

In cornual pregnancies, Marian et al found that no pregnancy sac could be seen in participants' uterine cavities during transvaginal ultrasound examinations and that the sac was found to be located more than one cm from the side

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of the uterine cavity.[2] Those researchers also found that the surrounding muscle layer was very thin, with a thickness of <5 mm and that patients with these characteristics can basically be diagnosed as having a cornual pregnancy.

Early diagnosis and early treatment of cornual pregnancy are very important. Conservative treatment before rupture can greatly reduce the patient's trauma. Chopra et al found that a rudimentary horn of the uterus, a salpingectomy, and proximal fallopian-tube adhesion can be predisposing factors for cornual pregnancy.[1]

Lu et al found that conservative treatment can be suitable for patients with a thick muscle layer of the uterine horn and with a pregnancy sac that is close to the uterine cavity line.[9] Those researchers indicated that conservative treatment can't be recommended if the uterus protrudes significantly and the pregnancy sac is large, possibly showing formed fetal and placental tissues, and that surgical treatment is recommended to occur in that situation as soon as possible.

With the popularization of assisted reproductive technology, the incidence of cornual pregnancy has tended to increase. The diagnostic criteria of cornual pregnancy proposed by JaDseD includes[6]: (1) abdominal pain and vaginal bleeding, with an asymmetric enlargement of the uterus; (2) enlargement of one uterine horn, with lateral displacement of the round ligament as observed under direct vision; and (3) the placenta's continued placement at the uterine horn. However, among the above diagnostic criteria, only the first criteria might be diagnosed before surgery; the second and third criteria can only be diagnosed during or after surgery and can't play a guiding role in clinical diagnosis before surgery.

The literature has reported that the misdiagnosis rate for cornual pregnancy is approximately 45% to 75%.[7,8] With the improvements in ultrasonic diagnosis and the popularization of hysteroscopy technology, clinicians are now highly alert to the cornual pregnancy, and the diagnosis of unruptured cornual pregnancy in an early stage is also increasing. With improvements in ultrasonic diagnosis technology, most uterine-horn pregnancies are found and confirmed before rupture.

For participants whose menstruation had stopped for more than eight weeks, Jin found that a laparotomy can usually be performed to remove the embryo from the uterine horn, or a wedge-shaped resection of the uterine horn can occur.[3] However, laparoscopy and laparotomy are both invasive treatments, can cause great damage to patients, and may affect postoperative fertility function.

The traditional treatments for cornual pregnancy have been ultrasound-guided uterine aspiration and curettage or a hysteroscope operation at six to seven weeks after the start of amenorrhoea. For ultrasound-guided uterine aspiration, the success rate isn't high. Due to the relatively thin muscle layer of the uterine horn and the rich blood supply, the contractility of the uterine horn can be poor during the process of sucking in uterine aspiration, which can easily lead to high blood loss and a large chance of rupture.[12] Therefore, a high chance of fetal residue exists.

At present, the conservative treatment methods for unruptured cornual pregnancy include: (1) drug abortion + curettage, (2) ultrasound-guided uterine aspiration, (3) MTX chemotherapy, and (4) hysteroscopy-guided uterine aspiration.[10]

To reduce the trauma to patients and preserve their reproductive functions, more and more conservative treatments have been applied in clinical practice. Currently, the conservative treatment methods mainly include: (1) ultrasound-guided uterine curettage after oral administration of mifepristone and misoprostol, (2) direct uterine curettage under the guidance of ultrasound, and (3) uterine curettage after administration of local or systemic chemotherapy with methotrexate (MTX).

The risk of vaginal bleeding and uterine horn rupture could be greatly reduced for ultrasound-guided uterine curettage if the pregnancy tissue can be discharged after a medical abortion and a reexamination of the vaginal ultrasound shows that the uterine mass has decreased in size, the blood flow signal has decreased, and the beta human chorionic gonadotropin (β-HCG) in the blood has been reduced to normal or close to normal.[11] Blood β-HCG and ultrasound should be completed after the aspiration, and if necessary, curettage, MTX chemotherapy, or hysteroscopic supplementary treatment should be performed again.

Because hysteroscopy-guided uterine aspiration requires uterine distention, the uterine horn muscle layer is thin, the blood supply is abundant, and the pressure in the uterine cavity can increase after uterine distention, the risk of pregnancy rupture increases. The local injection of MTX under direct ultrasound-guided treatment has a high risk of uterine rupture during the puncture process and is rarely used at present. Because the blood supply is rich, the effects of systemic chemotherapy can be relatively poor, the patient must have a long hospital stay, and the side effects are large.

It's very important to choose a treatment method for cornual pregnancy with a high level of effectiveness, few adverse reactions, and no effects on fertility. The current study intended to compare the clinical efficacy of different treatments for unruptured cornual pregnancy to find a safe, effective, minimally invasive treatment for unruptured cornual pregnancy that has few side effects and doesn't affect fertility.

METHODS

Participants

The research team retrospectively collected the clinical data of patients admitted to the Department of Obstetrics and Gynecology at the Wuhan Third Hospital of Cardiology in Wuhan, Hubei, China between September 2002 and May 2012 with cornual pregnancy, as indicated by an ultrasonic examination. All patients had a history of amenorrhoea before admission.

The research team created four groups: (1) the drug abortion + curettage group (D group), which was to include patients who had received orally administered mifepristone

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combined with misoprostol and had undergone uterine curettage[4,5]; (2) the uterine aspiration group (U group), which was to include patients who had received an ultrasound-guided uterine aspiration; (3) the chemotherapy group (C group), was to include patients who had received methotrexate (MTX) chemotherapy[4,5]; and (4) the hysteroscope operation group (H group), which was to include patients who had undergone an ultrasound-guided hysteroscope operation.

Potential participants were included in the D group if: (1) their gestational sac was connected to the uterine cavity; (2) their amenorrhoea duration was less than 8 weeks; (3) the thickness of the muscle layer of their cornual area was uniform, with a thickness greater than 3 mm; and (4) their blood β-HCG was lower than 100 000.

Potential participants were included in the U group if: (1) their gestational sac was connected to the uterine cavity; (2) their amenorrhoea duration was less than 7 weeks; (3) the thickness of the muscle layer of their cornual area was uniform, with a thickness greater than 3 mm; and (4) their blood β-HCG was lower than 100 000.

Potential participants were included in the C group if: (1) their gestational sac was connected to the uterine cavity; (2) their amenorrhoea duration was less than 8 weeks; (3) the thickness of the muscle layer of their cornual area was uniform, with a thickness greater than 2 mm; and (4) their blood β-HCG was lower than 200 000.

Potential participants were included in the H group if: (1) their gestational sac was connected to the uterine cavity; (2) their amenorrhoea duration was less than 7 weeks; (3) the thickness of the muscle layer of their cornual area was uniform, with a thickness greater than 2 mm; and (4) their blood β-HCG was lower than 100 000.

Intervention

D group. Combined with misoprostol, participants took one 25 mg mifepristone tablet orally 3 times per day for 2 days. On the third day, participants took one 400-ug misoprostol tablet orally, and 200-ug misoprostol tablets were placed in their posterior vaginal fornix. If no pregnancy tissue was found to be discharged, 75-mg misoprostol tablets were administered again on the fourth day, with the same method as was used on the third day.

The participants were observed for 72 hours after withdrawal of the drug. If no pregnancy tissue was found to be discharged, the patient underwent ultrasound-guided hysteroscopy.

U group. Participants underwent ultrasound-guided uterine aspiration. When the microtubule suction head under ultrasound guidance reached the participant's uterine horn on the side of the pregnancy, 400-mmHg, negative-pressure suction was performed. If the negative-pressure suction failed, chemotherapy or surgical treatment was performed.

C group. Some participants underwent ultrasound-guided local injection of MTX chemotherapy; 50 mg of MTX was injected into the pregnancy sac under ultrasonic guidance.

Other participants received systemic MTX chemotherapy, with a course of 8 days. Intramuscular injection of the 50 mg of MTX was performed on days 1, 3, 5, and 7, and intramuscular injection of 5 mg of calcium folinate was performed on days 2, 4, 6, and 8 for detoxification treatment. If a participant's blood β-HCG had decreased by less than 30% to 50% within one week after the end of chemotherapy and if the participant had no signs of cornual pregnancy rupture, a second course of chemotherapy was given.

H group. Participants were treated with direct hysteroscopic surgery. Microtubule negative-pressure suction was performed after the pregnancy sac's attachment position was confirmed by hysteroscopy.

Outcome Measures

After treatment, clinical manifestations of participants such as abdominal pain and vaginal bleeding were observed, vital signs were monitored, and the blood β-HCG and blood routine were examined every two to three days. The size of the uterine horn mass and the occurrence of abdominal bleeding, abdominal pain, or anal distention were examined by ultrasound re-examination.

Adverse reactions and the decrease in participants' blood β-HCG were recorded in detail. The participants were followed up for two months. If the medical practitioners saw an signs of rupture at any time, participants received surgical treatment.

Statistical Analyses

All the data were analyzed using SPSS 20.0 software (IBM, LA, CA, USA). Normally distributed data were expressed as means ± standard deviations (SD)s, while non-normally distributed data were expressed as medians (interquartile range). The measurement data were compared by one-way analysis of variance (ANOVA), and the comparison between two groups was performed using the least significant difference (LSD) method. The categorical data were expressed as n (%), and the differences among the four groups were examined by chi-square test or Fisher's exact test. $P < .05$ was considered to be statistically significant.

RESULTS

Participants

Of the 61 participants, 20 were included in D group, 16 in the U group, 15 in the C group, and 10 in the H group.

Ten participants had been misdiagnosed as having a normal pregnancy and underwent uterine aspiration, but no typical villi were found. Re-examination of their vaginal ultrasonography showed a pregnancy sac in the uterine horn. For three participants, ultrasonography suggested a cornual pregnancy, and embryo development was stopped. For some participants, ultrasound showed that the uterine horn had an outward protrusion, and the embryo and the original heart-tube beat were seen. For two participants, the preliminary fetus and placental tissue were seen. The participants ranged in age

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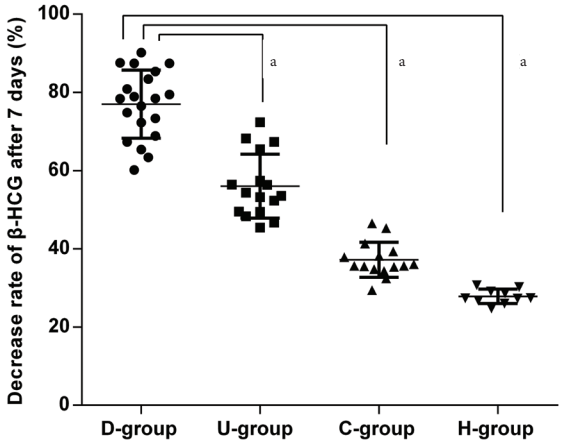
Table 1. Comparison of Baseline Data of the Groups

Indicator	D Group n = 20	U Group n = 16	C Group n = 15	H Group n = 10
Age, y	26.9 ± 1.3	30.2 ± 2.0	30.8 ± 2.4	28.7 ± 3.1
Number of pregnancies	2.1 ± 1.1	2.5 ± 2.5	2.4 ± 1.6	2.6 ± 1.2
Duration of amenorrhoea, wks	8.2 ± 3.8	8.3 ± 2.9	8.1 ± 1.8	8.0 ± 2.3
Diameter of the pregnancy sac, cm	3.8 ± 0.4	3.8 ± 0.2	4.0 ± 0.3	3.5 ± 0.5
Blood β-HCG level before treatment	3668 ± 232.5	3889 ± 334.8	3778 ± 345.6	3996 ± 256.5

Abbreviations: β-HCG, beta human chorionic gonadotropin; D Group, drug abortion + curettage group; U Group, uterine aspiration group; C Group, chemotherapy group; H Group, hysteroscope operation group.

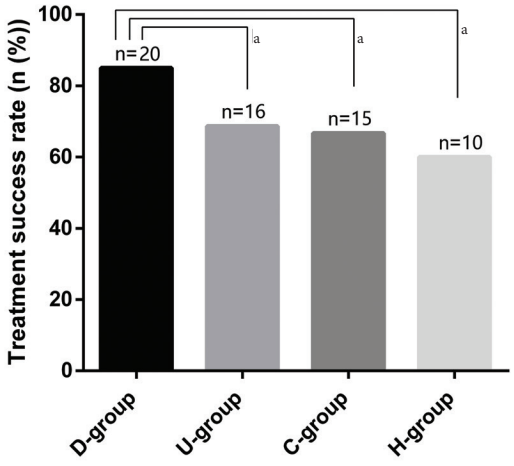
Figure 1. Decrease in β-HCG at Seven Days After Treatment by Group (N = 61)



[a]$P < .001$, showing a statistically larger decrease in the β-HCG for the D group than that in each of the other groups.

Abbreviations: β-HCG, beta human chorionic gonadotropin; D group, drug abortion + curettage group (n = 20); U group, uterine aspiration group (n = 16); C group, chemotherapy group (n = 15); H group, hysteroscope operation group (n = 10).

Figure 2. Participants' Treatment Success Rate by Group (N = 61)



[a]$P < .05$, showing a statistically greater success rate for the D group as compared to that of each of the other groups.

Abbreviations: D group, drug abortion + curettage group (n = 20); U group, uterine aspiration group (n = 16); C group, chemotherapy group (n = 15); H group, hysteroscope operation group (n = 10).

from 18 to 38 years, with an average age of 30.5 years (data not shown). The amenorrhoea duration was 40-75 days, with an average of 56.8 days (data not shown). Participants' number of pregnancies ranged from one to six; 25 were a first pregnancy, 29 participants were childless; and 19 participants had used assisted-reproductive technology. No statistically significant differences existed at baseline in age, number of pregnancies, duration of amenorrhoea, diameter of the pregnancy sac, or blood β-HCG level before treatment among the four groups (all $P > .05$), as shown in Table 1.

Efficacy

Twelve participants underwent surgical treatment after failed conservative treatment: one participant in the D group, 4 participants in the U group, 3 participants in the C group, and 4 participants in the H group.

The decrease in the β-HCG at seven days after treatment was significantly higher in the D group than that in the U group, C group, and H group, with all comparisons being statistically significant at $P < .001$ (Figure1). The treatment success rate for the D group was significantly higher than that of U group, C group and H group, with all comparisons being statistically significant at $P < .05$ (Figure 2).

No significant differences existed among the four groups in the time at which the β-HCG turned negative or in the average hospital stays, with $P > .05$ (Figures 3 and 4).

Adverse Reactions

D group. Three participants experienced adverse reactions. All had diarrhea and a low-grade fever while taking the misoprostol tablets, but the symptoms were relieved spontaneously after stopping the drug (Table 2).

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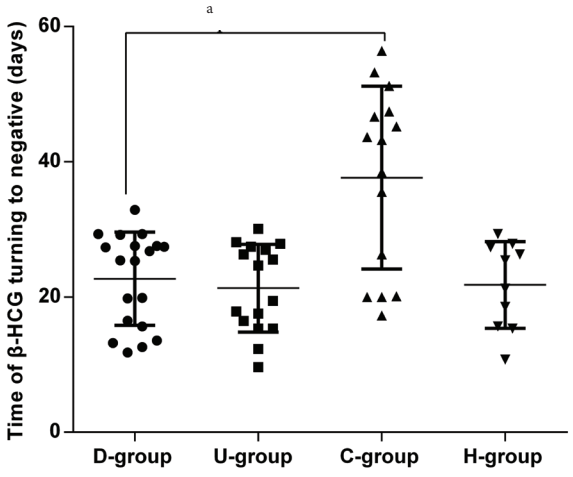
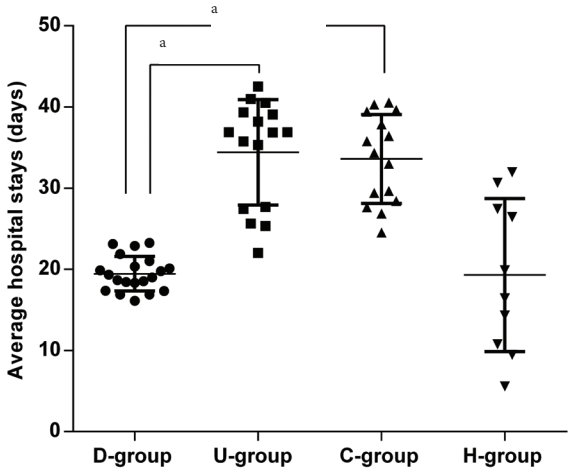
Figure 3. Time at Which Participants' β-HCG Turned Negative by Group (N = 61)



[a]$P < .001$, showing a statistically greater time for the β-HCG to turn negative for the C group than for the D group.

Abbreviations: β-HCG, beta human chorionic gonadotropin; D group, drug abortion + curettage group (n = 20); U group, uterine aspiration group (n = 16); C group, chemotherapy group (n = 15); H group, hysteroscope operation group (n = 10).

Figure 4. Average Hospital Stay by Group (N = 61)



[a]$P < .001$, showing statistically longer stays for the U group and the C group than for the D group.

Abbreviations: D group, drug abortion + curettage group (n = 20); U group, uterine aspiration group (n = 16); C group, chemotherapy group (n = 15); H group, hysteroscope operation group (n = 10).

Table 2. Adverse Reactions of Participants (N = 61)

Groups	Adverse Reactions (n)	Note
D group (n = 20)	3	Three participants experienced diarrhea and a low-grade fever while taking the misoprostol tablets, but the symptoms were relieved spontaneously after stopping the drug.
U group (n = 16)	4	Four participants were unable to complete the surgery due to excessive vaginal bleeding during uterine aspiration.
C group (n = 15)	1	One participant developed an oral ulcer; six had gastrointestinal reactions such as nausea, vomiting and diarrhea; two had mild bone-marrow suppression; and two had elevated transaminase.
H group (n = 10)	2	Two participants received surgical treatment due to massive vaginal bleeding during the hysteroscopic aspiration, and two underwent other treatments

Abbreviations: D Group, drug abortion + curettage group; U Group, uterine aspiration group; C Group, chemotherapy group; H Group, hysteroscope operation group.

U group. Four participants experienced adverse reactions. All were unable to complete the operation due to excessive vaginal bleeding during uterine aspiration.

C group. Eleven participants experienced adverse reactions: (1) one developed an oral ulcer; (2) six had gastrointestinal reactions such as nausea, vomiting and diarrhea; (3) two had mild bone-marrow suppression; and (4) two had elevated transaminase.

H group. Four participants experienced adverse reactions: (1) two underwent other treatments because the increased pressure that occurred during uterine distention caused a high risk of uterine corner rupture, and (2) two underwent surgical treatment due to massive vaginal bleeding during the hysteroscopy aspiration.

DISCUSSION

In the current study, by retrospectively analyzing the clinical data of 61 patients with cornual pregnancy, the research team found that the drug abortion + curettage treatment had obvious advantages. In the D group, the decline rate in the β-HCG at seven days after treatment and participants' treatment success rate were significantly higher than those in the other groups.

If conservative treatment has failed, active remedial measures should be taken to minimize the damage to participants. Contraception education should be strengthened to enhance participants' awareness of seeking medical treatment. After pregnancy is determined, the possibility of cornual pregnancy should be considered, and an ultrasound

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examination should be performed to exclude cornual pregnancy. Practitioners shouldn't blindly take measures to terminate the pregnancy, which can lead to uterine horn rupture, resulting in physical trauma for the patient.

Some limitations existed in the current study. First, because the study was a single-center retrospective study, the sample size was limited. A prospective study with a larger sample size needs to be conducted to investigate the efficacy of conservative treatment for cornual pregnancy. Second, further studies with a longer follow-up should be performed to explore the effects of conservative treatment of drug abortion on the long-term fertility of participants as compared with other treatments.

CONCLUSIONS

The current study found that oral administration of mifepristone, combined with misoprostol, plus uterine curettage was superior to the other three methods of treatment for unruptured cornual pregnancy. The drug abortion + curettage treatment was found to be a safe, effective, minimally invasive treatment for unruptured cornual pregnancy, which has few side effects and doesn't affect fertility.

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