Original Article

Comparison between vacuum aspiration and forceps plus blunt curettage for the evacuation of complete hydatidiform moles

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ABSTRACT

Objective: Suction curettage is recommended for molar evacuation rather than sharp curettage because of its safety. However, the superiority of suction curettage with respect to the incidence of gestational trophoblastic neoplasia (GTN) has not been reported. This study aimed to compare the efficacy and safety of two evacuation procedures, vacuum aspiration and forceps/blunt curettage, for complete hydatidiform moles (CHMs) to determine the differences between them.
Materials and methods: Patients with androgenetic CHM determined by multiplex short tandem repeat polymorphism analysis were included in this observational cohort study. Patients underwent evacuation with forceps and blunt curettage (forceps group) before March 2013 and with vacuum aspiration (vacuum group) thereafter. GTN was diagnosed based on the International Federation of Gynecology and Obstetrics 2000 criteria. The incidence of GTN and other clinical parameters were compared.
Results: Ninety-two patients were diagnosed with androgenetic CHM. The number of patients in the forceps and vacuum groups was 41 and 51, respectively. The incidence of GTN was 12.2% (5/41) and 13.7% (7/51) in the forceps and vacuum groups, respectively, which was not significantly different (P = 1, Fisher's exact test). No major adverse events, such as uterine perforation and blood transfusion, were noted in either group. The median surgery time was shorter in the vacuum group (16 min) than in the forceps group (25 min) (P = 0.05, Mann–Whitney U test).
Conclusion: There were no differences in the incidence of GTN between the forceps and vacuum groups for androgenetic CHM. However, vacuum aspiration could have the advantage of a shorter surgery period. The use of vacuum aspiration for molar pregnancy seems to be safer. Therefore, we recommend suction curettage for the first evacuation of hydatidiform moles.

Introduction

Hydatidiform moles are abnormal growths that form at the beginning of pregnancies and are characterized by trophoblastic hyperplasia that has the potential to develop into gestational trophoblastic neoplasia (GTN) [1]. Patients with GTN require chemotherapy for remission, although almost all patients can be cured. The primary treatment for molar pregnancy is evacuation of the intrauterine contents. The recommended procedure for molar evacuation is suction curettage rather than sharp curettage because of its safety [1–3].

Hydatidiform moles are divided into two classes: complete hydatidiform moles (CHMs) and partial hydatidiform moles

(PHMs). CHM is an androgenetic diploid, whereas PHM is a diandric monogynic triploid [1,4]. The incidence of GTN from CHMs is much higher than that from PHMs (15–20% *vs.* 1–2%) [1,5,6]. Distinguishing between CHMs and PHMs by pathological diagnosis can occasionally be difficult [7]. To overcome this, we performed molecular cytogenetic diagnosis using multiplex short tandem repeat (STR) polymorphism analysis [5]. The incidence of GTN was higher in CHMs than in PHMs. Thus, the occurrence of GTN would differ according to the distribution of patients with CHMs and PHMs. The genetically defined CHM cohort (consecutive androgenetic CHMs) enabled accurate evaluation of outcomes for the evacuation of hydatidiform moles [5].

Few reports have shown the superiority of procedures for the evacuation of hydatidiform moles. To the best of our knowledge, there is no report based on the population with defined androgenetic CHMs. Therefore, the present study aimed to evaluate the

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outcomes of the evacuation of androgenetic CHMs using vacuum aspiration or forceps/blunt curettage. We compared clinical parameters, including the incidence of GTN and adverse events, in patients from a single institute.

Materials and methods

Approval and consent

This observational cohort study was conducted at Chiba University Hospital. The study protocol was approved by the Institutional Ethical Committee at the Graduate School of Medicine, Chiba University (numbers 673 and 2406), and each participant provided written informed consent.

Patient selection

Most patients were referred to our hospital because they were suspected of having molar pregnancies on the basis of ultrasonography findings. The first evacuations were performed at our hospital between April 2010 and February 2016. The patients were enrolled into this molecular diagnostic study as previously described [5]. The villous tissues of the patients were diagnosed as androgenetic CHM, diandric monogynic triploid PHM, and biparental abortion [5].

Patients who were diagnosed with androgenetic CHMs using STR polymorphism analysis were eligible. Those with CHM with a co-existing live fetus and those who underwent primary hysterectomy were excluded.

Clinical management and evacuation procedures

Upon the diagnosis of suspected molar pregnancy, patients underwent clinical and preoperative evaluations, including blood tests (blood type, complete blood count, and liver and kidney function), and chest radiography; their serum human chorionic gonadotropin (hCG) levels were measured. Except for six patients, the surgeries were performed or supervised by H.U. The surgeons were classified into two categories: specialists and residents. Before March 2013, we performed placental forceps and blunt curettage (forceps group). We changed the first evacuation procedure in April 2013, after which we used a vacuum aspiration instrument (vacuum group; Fig. 1).

Patients were admitted on the day before surgery. In the evening, two or more laminaria tents were routinely inserted depending on the cervical condition. Prophylactic intravenous antibiotics were administered just before surgery. The entire surgery was performed under intravenous anesthesia (diazepam 5–10 mg and ketamine hydrochloride 30–100 mg). In three patients with huge moles, general anesthesia and intubation were performed by a certified anesthesiologist. The procedure was performed under transabdominal ultrasound guidance to ensure complete evacuation. We routinely checked for intrauterine residual tissue by transvaginal sonography before surgery completion. After the completion of evacuation, methylergometrine maleate (0.2 mg) was mixed with 500 mL of crystalloids and intravenously administered to patients who did not have an elevated blood pressure (<130/85 mmHg). Patients were discharged on the day of surgery when they did not show continuous bleeding.

Pathological evaluation

All intrauterine contents were submitted for pathological examination. Certified pathologists analyzed them using hematoxylin-eosin staining and p57KIP2 immunohistochemical analysis [8].

Management after evacuation and GTN diagnosis

The residual tissue in the uterine cavity was monitored by transvaginal sonography in all patients one week after evacuation. Serum hCG levels were monitored weekly. Patients were monitored bi-weekly or monthly when hCG levels fell below 50 mIU/mL or 10 mIU/mL, respectively. Unfavorable rates of reduction in serum hCG levels were roughly defined as serum hCG levels that did not decrease by 20% or more compared to the previous measurement value. When the reduction rate of serum hCG level was unfavorable, we re-monitored the uterine cavity by transvaginal ultrasonography. A second curettage was performed when residual tissue was detected on ultrasonography. Following this, we diagnosed patients with GTN according to the International Federation of Gynecology and Obstetrics (FIGO) 2000 criteria [9]. We also performed imaging studies when we diagnosed patients with GTN, including transvaginal ultrasonography with color flow mapping, chest radiography, and computed tomography of the region between the chest and pelvis. We assessed the FIGO risk score using clinical information and imaging studies. Resolution and spontaneous remission were defined as when the serum hCG level (total hCG) was within the normal range (<1.0 mIU/mL) and maintained for three months, respectively.

Clinical data collection and statistical analyses

Clinical information and data were retrieved from medical charts. Data are presented as median (interquartile range), mean ± standard deviation, or number (percentage). Statistical analyses were performed using R software v.3.4. (http://www.r-project.org/). Fisher's exact test (two-sided test) was used for categorical variables. Student's *t*-test or the Mann–Whitney *U* test was used for continuous variables, depending on the variance. Relative risk and confidence interval (CI) were calculated with Wald's method. $P < 0.05$ was considered statistically significant.

Results

Patient characteristics

We performed uterine evacuation in 155 patients with suspected molar pregnancies between April 2010 and February 2016. Among them, 97 were diagnosed as having androgenetic CHMs, according to the multiplex STR polymorphism analysis. One patient who underwent primary hysterectomy and four patients with CHM with a co-existing fetus were excluded from this study. Finally, 92 patients were enrolled in this observational cohort study. The number of patients in the forceps and vacuum groups was 41 and 51, respectively (Fig. 1). Six patients in the vacuum group were partly assisted by forceps for completing the surgery.

Patients' characteristics were not significantly different between the forceps and vacuum groups in terms of age, gravidity, gestational age at diagnosis, and pre-evacuation hCG levels (Table 1).

Histological diagnosis

The pathologists initially diagnosed four patients (two each in the forceps and vacuum groups) as having PHM by hematoxylin-eosin staining. All villous tissues should have been androgenetic CHM because STR analysis determined the androgenetic origin. During the study period, p57KIP2 immunohistochemistry was
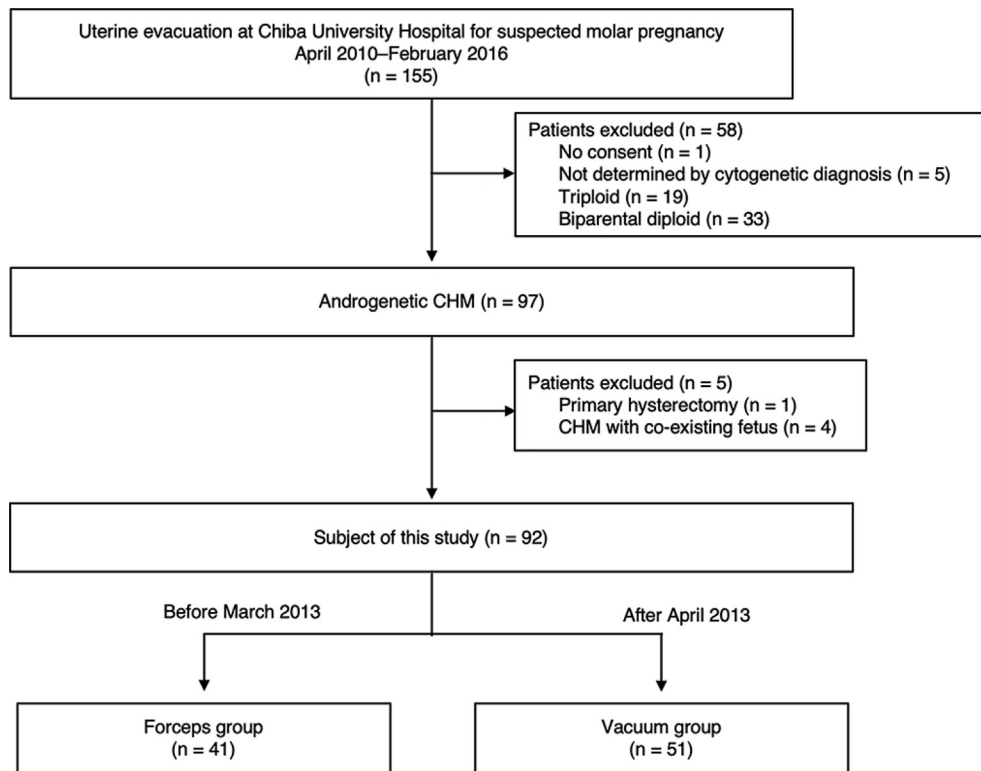
Fig. 1. Flow diagram summarizing patient recruitment and derivation of the study groups. CHM; complete hydatidiform mole.

Table 1
Demographic characteristics of patients with androgenetic complete hydatidiform moles according to uterine evacuation.

Characteristic	Forceps group (n = 41) (April 2010 to March 2013)	Vacuum group (n = 51) (April 2013 to February 2016)	P value*
Age (y)	31.0 ± 7.7	32.7 ± 0.9	0.29[a]
Gravidity	2 [1–3]	2 [1–4]	0.82[b]
Parity	1 [0–1]	1 [0–1]	0.45[b]
Gestational age at termination (wk)	9.6 ± 1.4	9.6 ± 1.6	0.97[a]
hCG pre-evacuation level (international units/L)	142,491 [83,849–212,334]	148,321 [79,701–257,874]	0.72[b]
Initial histology of molar pregnancy			
Complete hydatidiform mole	39 (95%)	49 (96%)	
Partial hydatidiform mole	2 (5%)	2 (4%)	
Immunohistochemistry of p57KIP2			
Not performed	22 (54%)	5 (10%)	
Performed	19 (46%)	46 (90%)	
Surgeon			
Specialist	37 (90%)	32 (63%)	
Resident	4 (10%)	19 (37%)	

Values represent median [interquartile range], mean ± SD, or number (percentage).
hCG, human chorionic gonadotropin.
*$P < 0.05$ was considered statistically significant.
[a] Student's t-test.
[b] Mann–Whitney U test.

performed in 46% and 90% of patients in the forceps and vacuum groups, respectively (Table 1).

Incidence of gestational trophoblastic neoplasia

All 12 patients with GTN were classified as low risk according to the FIGO 2000 scoring system [9]. The incidence of GTN was 12.2% (5/41) in the forceps group and 13.7% (7/51) in the vacuum group, which was not significantly different ($P = 1$, Fisher's exact test). The mean duration between the first evacuation and the diagnosis of GTN was 32.4 ± 12.7 and 60.7 ± 35.9 days in the forceps and vacuum groups, respectively ($P = 0.13$, Student's t-test; Table 2).

Comparison of metastatic sites between the two groups

We compared the metastatic sites after the diagnosis of GTN, as listed in Table 2. One patient was diagnosed with GTN without any focus. Intramural metastasis was found in four and zero patients in the forceps and vacuum groups, respectively.

Incomplete uterine evacuation and second curettage

Nineteen patients (46.3%) from the forceps group underwent a second curettage; among them, five developed GTN. On the other hand, 17 patients (33.3%) underwent a second removal in the

Table 2
Clinical outcomes for patients with androgenetic CHM according to the procedure of uterine evacuation.

Variable		Forceps group (n = 41)	Vacuum group (n = 51)	P value*
Occurrence of post-molar GTN		5 (12.2%)	7 (13.7%)	1[a]
Low-risk GTN		5	7	
High-risk GTN		0	0	
Focus	(+)	5	6	
	(−)	0	1	
Lung (detected with CT)		3	5	
Uterus		5	1	
Myometrium		4	0	
Endometrium		1	1	
Time between the first evacuation to the diagnosis of GTN (day)		32.4 ± 12.7	60.7 ± 35.9	0.13[b]
Second curettage	All	19 (46.3%)	17 (33.3%)	0.28[a]
	SR	14	12	
	GTN	5	5	
Interval between the first and second evacuations (day)	All	8 [5.0–23.0]	13 [8.0–24.0]	0.23[c]
	SR	10 [4.3–24.0]	18.5 [11.0–24.3]	0.16[c]
	GTN	8 [8.0–17.0]	8 [7.0–8.0]	0.27[c]
Time to resolution[d] (day)	All	91.0 ± 28.4	104.8 ± 29.1	0.03[b]
	SR	88.4 ± 28.8	98.8 ± 26.4	0.11[b]
	GTN	108.8 ± 18.6	142.4 ± 11	0.003[b]
Time to remission for GTN (day)[e]		76.4 ± 15.6	81.7 ± 36.7	0.77[b]

Values represent median [interquartile range], mean ± SD, or number (percentage).
GTN, gestational trophoblastic neoplasia; CT, computed tomography; SR, spontaneous resolution.
*$P < 0.05$ was considered statistically significant.
[a] Fisher's exact test (two-sided test).
[b] Student's t-test.
[c] Mann-Whitney U test.
[d] Interval between first evacuation and hCG cut-off.
[e] Period from starting chemotherapy to remission.

vacuum group (relative risk = 0.72, 95% CI [0.43–1.20], $P = 0.28$). Among them, five developed GTN. Two patients who did not require a second curettage were diagnosed with GTN with lung metastases (Table 2). The median intervals between the first evacuation and second curettage were 8 and 13 days in the forceps and vacuum groups, respectively ($P = 0.23$, Mann–Whitney U test).

Time to resolution

In patients with spontaneous remission, the mean duration from the first evacuation to the day when the hCG cut-off level was reached was 88.4 ± 28.8 (forceps group) and 98.8 ± 26.4 (vacuum group) days ($P = 0.11$, Student's t-test). In patients with GTN, the mean duration from the first evacuation to the day that the hCG cut-off level was reached was 108.8 ± 18.6 (forceps group) and 142.4 ± 11.0 (vacuum group) days ($P = 0.003$, Student's t-test). The duration from starting chemotherapy to resolution for patients with GTN was 76.4 ± 15.6 (forceps group) and 81.7 ± 36.7 (vacuum group) days ($P = 0.77$, Student's t-test; Table 2).

Surgery time and surgical complications

Surgery times were shorter in the vacuum group (16 min) than in the forceps group (25 min; $P = 0.05$, Mann–Whitney U test; Table 3). During both study periods, we experienced no major complications, including uterine perforation, profuse bleeding requiring blood transfusion, or hysterectomy. We could not effectively compare the amount of bleeding because of missing data in the medical records in earlier cases. In the vacuum group, the amount of bleeding was co-related with the pre-evacuation hCG level ($r^2 = 0.60$; linear model) but not with surgery time ($r^2 = 0.17$; linear model; Fig. 2).

Surgeon attribution

Surgeons were classified as specialists and residents. The number of evacuations performed by residents was 4 (9.8%) and 19 (37.3%) in the forceps and vacuum groups, respectively (Table 1). In the vacuum group, bleeding and surgery times were not different between residents and specialists ($P = 0.72$ and $P = 0.77$, Mann–Whitney U test; Table 4).

Fertility outcomes

In total, 19 and 29 patients in the forceps and vacuum groups, respectively, conceived and delivered healthy babies. Fertility outcomes are summarized in Table 5. Among 23 nulliparous women in the vacuum group, 17 (74%) delivered healthy babies. Women desiring pregnancy in the vacuum group had favorable results compared to those in the forceps group, as 84% patients gave birth, although this was not statistically significant.

Discussion

The incidence of GTN was not different between the two procedures. The surgery time was shorter in the vacuum group than in the forceps group. To the best of our knowledge, this is the first report that compared the two procedures based on the cytogenetically diagnosed population of androgenetic CHMs. Vacuum evacuation is recommended for the termination of early pregnancy (up to 12 weeks) [10,11]. The recommended procedure for molar uterine evacuation is suction curettage rather than sharp curettage, as it is safer [1,3,12]. The safety of suction curettage compared with that of dilation and sharp curettage has been reported in early abortion treatments [11]; however, there is no conclusive evidence regarding the safety of molar evacuation. One study described the minor superiority of sharp curettages over suction curettage with
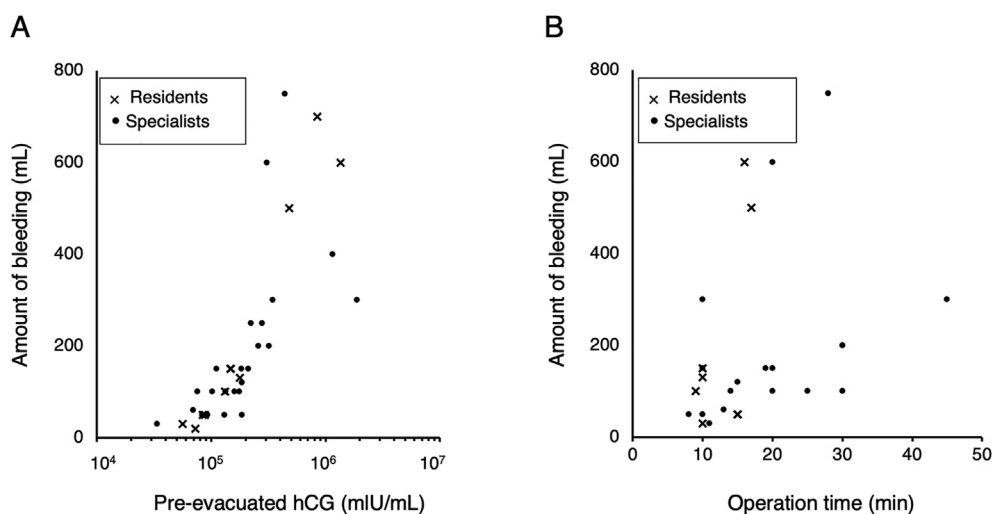
Table 3
Surgery time and adverse events based on the procedure of uterine evacuation.

Variable		Forceps group (n = 41)	Vacuum group (n = 51)	P value*
Adverse events	Uterine perforation	0	0	
	Blood transfusion	0	0	
Surgery time (min)	All	25 [16–30] (n = 25)	16 [10–25] (n = 35)	0.05[a]
	SR	25 [17–30]	15 [10–25]	0.04[a]
	GTN	25 [18–25]	16.5 [11.5–25.3]	1[a]
Volume of blood[b] (mL)	All	300 [150–340] (n = 5)	130 [55–250] (n = 35)	
	SR	300 [150–340]	110 [53–188]	
	GTN		300 [300–600]	

Values represent median [interquartile range].
GTN, gestational trophoblastic neoplasia; SR, spontaneous resolution.
*P < 0.05 was considered statistically significant.
[a] Mann-Whitney U test.
[b] Volume of blood including tissue content.

Fig. 2. Factor associated with the amount of bleeding. (A) Relationship between the amount of bleeding and pre-evacuation serum hCG levels. (B) Relationship between the amount of bleeding and operation time. Filled circles (●) and (×) indicate operations undertaken by the specialists and residents, respectively. hCG, human chorionic gonadotropin.

Table 4
Comparison of the amount of bleeding and surgery time among surgeon categories in the vacuum group.

Variable	Residents (n = 19)	Specialists (n = 32)	P value*
Amount of bleeding[a] (mL)	n = 11	n = 32	
	130 [50–325]	135 [90–250]	0.72[b]
Surgery time (min)	n = 13	n = 22	
	16 [10.0–18.0]	17 [10.3–25.0]	0.77[b]

Values are given as median [interquartile range].
*P < 0.05 was considered statistically significant.
[a] Amount of bleeding including the tissue content.
[b] Mann-Whitney U test.

respect to the incidence of GTN after hydatidiform mole evacuation; however, this effect was not emphasized [2]. In Japan, the combination of forceps evacuation and blunt curettage has been applied in cases of molar evacuation, similar to the process in cases of abortion.

Evaluation of the incidence of GTN is generally difficult as patients have various disease severities. CHM is associated with a much higher risk of GTN occurrence than PHM [5,6]. We experienced difficulty in diagnosing CHM using only hematoxylin-eosin staining [7]. However, almost all recent specimens were evaluated by p57KIP2 immunohistochemical analysis. The proportion of CHM and PHM would directly influence the incidence of GTN, rate of second curettage, and adverse effects. We were able to overcome

Table 5
Fertility outcomes for patients with androgenetic complete hydatidiform moles according to the procedure.

Status		Forceps group	Vacuum group	P value*
Total	Number of cases	41	51	0.40[a]
	Live birth	19 (46%)	29 (57%)	
Nulliparous	Number of cases	15	23	0.17[a]
	Live birth	7 (47%)	17 (74%)	
Women who desire to bear children	Number of cases	31	32	0.09[a]
	Live birth	20 (66%)	27 (84%)	

*P < 0.05 was considered statistically significant.
[a] Fisher's exact test (two-sided test).

this problem by restricting our cohort of patients to those who were cytogenetically diagnosed with androgenetic CHMs. In addition, patient characteristics were not different between the two cohorts. Taken together, these data confirmed that there was no difference in the incidence of GTN in terms of surgical procedures.

No major adverse events, such as uterine perforation and blood transfusion, were observed in both groups, including when the second curettage was performed. Surgery times were shorter in the vacuum group than the forceps group in this study. In a recent representative large study by Padron et al., the proportion of patients requiring blood transfusion was 6.3% and 8.6% in the electric vacuum aspiration and manual vacuum aspiration groups, respectively [13]. The median surgical durations were 25 and 34 min in the electric and manual vacuum aspiration groups, respectively. However, no blood transfusions were necessary in the present study. Additionally, the median surgery times were 16 min in the vacuum group. The reason for the safety achieved may be the routine cervical ripening by laminaria tents and routine use of abdominal ultrasonography.

The time from evacuation to hCG disappearance in patients with GTN was longer in the vacuum group than in the forceps group. Chemotherapy periods in both groups were similar. There was an increase in the time between the first evacuation to initial chemotherapy in the vacuum group compared with that in the forceps group, although this was not statistically significant; therefore, the main reason for the extension of resolution would be a policy change regarding chemotherapy initiation. The common practice in our institution was to postpone chemotherapy when the hCG levels showed a decreasing trend, in accordance with that seen in recent reports [14–16]. Thus, the difference in the time from evacuation to hCG disappearance in patients with GTN would not be dependent on the procedures but on the policy for the initiation of chemotherapy.

The limitation of this study is the small number of research participants. We could not detect the difference in the incidence of GTN between the groups, and major adverse events were not seen. Thus, we require a larger cohort to confirm the frequency of adverse events with respect to these procedures.

In conclusion, our study revealed that the incidence of GTN after the evacuation of androgenetic CHM was not different between vacuum aspiration and forceps/blunt curettage in our institution. Surgery time was shorter using vacuum aspiration than using forceps/blunt curettage. This study offers evidence for the use of vacuum aspiration for molar pregnancy because it is important to promote safer surgical techniques. We recommend suction curettage for the first evacuation of hydatidiform moles in view of its technical safety.

Conflicts of interest statement

There are no conflicts of interest to declare.

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