Original Research

Cabergoline for Lactation Inhibition After Second-Trimester Abortion or Pregnancy Loss

A Randomized Controlled Trial

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OBJECTIVE: To assess cabergoline's efficacy at decreasing breast symptoms after second-trimester abortion or pregnancy loss.

METHODS: This was a double-blinded, block-randomized superiority trial comparing cabergoline 1 mg once to placebo for preventing bothersome breast engorgement after second-trimester uterine evacuation. We enrolled pregnant people at 18–28 weeks of gestation who were English- or Spanish-speaking and without contraindication to the study drug. Participants completed a validated, piloted, electronic survey at baseline and at multiple timepoints through 2 weeks postprocedure to assess breast symptoms, side effects, and bother. Our primary outcome was any breast symptoms (a composite of engorgement, milk leakage, tenderness, and need for pain relief) on day 4; we planned to enroll 80 patients to show a 30% difference in breast symptoms (80% power, $\alpha=0.049$). A subgroup of participants returned for serum prolactin levels.

RESULTS: After screening 150 patients from April 2021 to June 2022, we enrolled 73 participants. Baseline demographics were balanced between groups: median gestational age was 21 weeks (range 18–26 weeks), 56.2% of participants were nulliparous, 34.2% self-identified as Hispanic, and 37.0% had public insurance. At baseline, reported breast symptoms were similar between groups. Among 69 participants who returned surveys on day 4, significantly fewer participants receiving cabergoline reported any breast symptoms compared with placebo (27.8% vs 97.0%, $P<.001$) (primary outcome) and fewer reported significant bother (2.8% vs 33.3%, $P=.001$) (secondary outcome). These differences persisted through day 14. Reported incidence and severity of bother from side effects were similar between groups: most common were constipation, fatigue, and headache. Serum prolactin levels were similar at baseline. On day 4, mean serum prolactin level was 6.5 ng/mL (SD 2.2) for those who received cabergoline and 18.0 ng/mL (SD 5.9) for placebo ($P=.049$).

CONCLUSION: Cabergoline is an effective and well-tolerated strategy to prevent breast symptoms after second-trimester abortion or pregnancy loss.

CLINICAL TRIAL REGISTRATION: ClinicalTrials.gov, NCT04701333.

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Breast symptoms after second-trimester abortion are common. Most people do not expect to lactate after a mid-trimester pregnancy loss,[1] but, after a 14–20-week pregnancy loss or abortion, 50% of people report breast tenderness, 45% of people report breast

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engorgement, and 20% of people report milk leakage.[2] Prior qualitative work surrounding second-trimester perinatal loss suggests that breast engorgement and milk leakage cause physical pain and exacerbate emotional distress.[3]

Lactogenesis is a two-stage physiologic process of developing the ability to secrete milk that starts from the 16th week of pregnancy and continues after delivery, regardless of the birth outcome.[4] Lactogenesis I starts in the early second trimester as high level of estrogen, progesterone, and prolactin stimulate anatomic growth of breasts. Lactogenesis II starts after the removal of the placenta and the associated rapid drop in progesterone. The fall in progesterone removes its antagonizing effect on prolactin and starts milk production, resulting in swelling of the breasts, peaking at postpartum day 4. Breast engorgement occurs when milk supply exceeds what is expressed from breasts. In absence of milk expression, lactation eventually stops.[5]

Management of painful breast engorgement in those who choose not to breastfeed or those who experience a fetal loss has been described by physicians and midwives for centuries. However, a Cochrane Review of nonpharmacologic interventions for breast engorgement found that there was no evidence that these modalities result in a more rapid resolution of symptoms.[6] There is both biological plausibility and existing evidence that a dopamine agonist can antagonize prolactin release, which then prevents lactogenesis. Prolactin is a peptide synthesized in the anterior pituitary and is both positively and negatively regulated.[7] Dopamine released by the hypothalamus binds to D2 receptors in the anterior pituitary to inhibit prolactin release.

Previous research showed a 2-week course of twice-daily bromocriptine, a dopamine agonist, caused a significant reduction in breast tenderness, milk secretion, and serum prolactin levels on day 4, compared with placebo after second-trimester abortion.[8] However, the U.S. Food and Drug Administration (FDA) asked the manufacturer to voluntarily stop selling bromocriptine as a lactation suppressant after reports in the early 1980s of postpartum hypertension, seizures, and strokes associated with the use of bromocriptine for lactation suppression.[9]

Cabergoline is a dopamine agonist FDA-approved for the treatment of hyperprolactinemic disorders, either idiopathic or due to pituitary adenomas (DOSTINEX FDA package insert). In a recent, large systematic review that investigated cabergoline for postpartum lactation inhibition after a term delivery, adverse events were rare, generally mild, transient, and self-resolving.[10] Cabergoline has an approved indication for the prevention of physiologic postpartum lactation after full term birth in multiple countries. The 2020 U.S. Department of Health & Human Services Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission recommends the use of cabergoline after live birth to suppress breast-milk production.[11]

Given the lack of evidence for existing nonpharmacologic or pharmacologic modalities and the absence of society guidelines for management of breast engorgement after second-trimester abortion or pregnancy loss, we seek to improve patient experience and contribute evidence to establishing a standard of care for lactation inhibition in the second trimester. This study aimed to answer whether cabergoline is superior to placebo at preventing breast symptoms after second-trimester abortion or pregnancy loss.

METHODS

We conducted a double-blinded, placebo-controlled, block-randomized superiority trial at Stanford University in Palo Alto, California, from April 2021 to June 2022 to evaluate off-label use of cabergoline in preventing breast engorgement after second-trimester abortion or fetal death. The study was approved by the Institutional Review Board at Stanford University and prospectively registered on ClinicalTrials.gov. This study was designed and reported using CONSORT (Consolidated Standards of Reporting Trials) guidelines.[12]

We recruited English- or Spanish-speaking pregnant people aged 18 years or older who were between 18 0/7 and 28 0/7 weeks of gestation and who were consented for abortion or management of fetal death. We exclude those with prior mastectomy, those currently breastfeeding, those currently receiving a dopamine agonist or antagonist for other induction, or those with a contraindication to cabergoline per the package insert. Participants were compensated for their time.

Standard counseling regarding medical or surgical management was provided, as applicable. A complete history and physical was performed. If an ultrasound report was not available to confirm gestational age dating, an informal bedside abdominal ultrasonogram was performed to determine gestational age. All patients received mifepristone 200 mg orally. Those choosing dilation and evacuation also had osmotic dilators placed. Participants at more than 22 weeks of gestation with a viable intrauterine

pregnancy received feticidal injection with digoxin. Standard-of-care antibiotics for prophylaxis was provided.

A research coordinator obtained informed consent and randomized the patient to cabergoline or placebo during this initial consultation visit. Alternating blocks of eight and four were used to ensure equal sample sizes at planned interim analysis. Participants, clinicians, and clinical researchers remained blinded to allocation until data analysis occurred. Basic demographic information was collected and entered into REDCap by a research coordinator.[13] Standard demographics including self-identified gender identity and race and ethnicity, prior breastfeeding or chestfeeding experience, and prior breast surgery was asked of participants. Race and ethnicity were collected to determine whether there were differences between the two study groups and to provide clinicians information regarding the generalizability of results to patient populations outside of our institution. Participants completed a baseline survey to establish existing breast symptoms and bother.

Dilation and evacuation was completed in the outpatient gynecology clinic or ambulatory surgical center, depending on patient preference and medical considerations. All participants received misoprostol 400 micrograms buccally 120 minutes before the procedure. Those seeking medical abortion and those with fetal death at more than 24 weeks of gestation were admitted to the labor and delivery unit, where they received repeat doses of misoprostol until fetal expulsion occurred. Rhogam was provided, as applicable.

Participants were randomized to take either cabergoline 1 mg orally or placebo (identical sugar tablets) within 4 hours of the procedure or fetal expulsion. All participants received written instructions with the existing standard of care for symptomatic breast engorgement: breast support and ice packs to the breasts as needed.

Electronic, online surveys were collected at baseline, and on days 2, 3, 4, 7, and 14. Additionally, participants were asked on day 14 to rate overall acceptability of the protocol, and likelihood to recommend to a friend. Surveys were sent by email through REDCap at 8:00 am. A phone call was made to participants between 5:00 pm and 8:00 pm if the survey was not completed that day.

Our primary outcome was presence of any breast symptoms on day 4 postprocedure. The Bristol Breast Symptoms Inventory assesses the four domains of breast symptoms: engorgement, milk leakage, tenderness, and need for pain relief modalities (scale range: 1, absence of symptoms; 2–4, symptomatic)[14] (Appendix 1, available online at http://links.lww.com/AOG/D152). To be classified as having an absence of breast symptoms, participants must respond with a "1" in all four domains; otherwise, they are considered symptomatic. The survey is a validated measure in the postpartum setting but not specifically in this second-trimester abortion population. The survey was first piloted on three patients with a prior second-trimester abortion and questions did not require modification. We assessed bother from breast symptoms using a facial pain score (scale range 0–6, significant bother 4 or higher), side effects per the FDA drug package insert, bother from side effects (scale range 0–6, significant bother 4 or higher), and bleeding patterns.[15]

A substudy of participants were recruited for serum prolactin levels on days 0, 4, 7, and 14. The Stanford University laboratory runs serum prolactin tests on an electrochemiluminescence immunoassay with a working range of 0.5–150 ng/mL and an interassay coefficient of variation is 4.68%. The reference range in this laboratory for nonpregnant, nonlactating female-assigned at birth individuals is 4.8–23.3 ng/mL.

Incidence of symptomatic breast engorgement after second-trimester abortion has been reported to occur between 50% and 91% of individuals.[2,8] In prior studies of term lactation inhibition using cabergoline 1 mg, complete absence of lactation was noted in 78–100% of study participants.[16–18] Assuming 90% would be symptomatic without intervention, we estimated that 33 participants in each group would be required to show a 30% decrease in those reporting breast symptoms compared with the control group, with a power of 0.8 and an alpha of 0.049 (using the O'Brien-Fleming rule for a planned interim analysis at 50% recruitment).[19] We planned to recruit 80 participants, anticipating 20% missing data and loss to follow-up.

For the substudy, we determined the number of participants needed based on a prior trial comparing bromocriptine to placebo after second-trimester abortion in which the mean serum prolactin level in the placebo group was 44 ± 8 ng/mL on day 4 and 12.2 ± 2 ng/mL in the bromocriptine group.[8] We needed six patients to have an 80% chance of detecting, at the 5% significance level (no interim look), a decrease in serum prolactin level from 44 ng/mL in the control group to 23 ng/mL in the experimental cabergoline group. We planned to recruit eight patients, anticipating 25% loss to follow-up and missing data.

Data collected through REDCap surveys were exported to SAS OnDemand for Academics for

analysis. Loss to follow-up was low; 94.5% of participants provided survey data for our primary outcome. Participants with missing outcomes are excluded from analysis; this modified intent-to-treat analysis approximates intention to treat as such low loss to follow-up that it is unlikely to bias statistical analysis[20]

Baseline characteristics between the two groups were compared using χ^2 and t tests. For our primary outcome (proportion with any breast symptoms), we used χ^2 or Fisher exact testing, as appropriate. Using similar statistical testing, we also compared the two groups on the four domains of breast pain. Secondary outcome measures of bother and satisfaction are ordinal in nature and their distribution was nonparametric; thus, we compared the medians between groups with Wilcoxon rank sum test. Serum prolactin levels were assumed nonparametric and compared with Wilcoxon rank sum test.

RESULTS

From April 2021 to June 2022, we screened 150 patients for participation and enrolled 73 people (Fig. 1). The most common reason for individuals not meeting inclusion criteria was speaking a language other than English or Spanish. We closed enrollment when we were powered for our primary outcome, given better than anticipated follow-up response rates.

Baseline demographics were similarly balanced between groups: the median age was 33 years (range 20–43 years), median gestational age was 21 weeks (range 18–26 weeks), 56.2% were nulliparous, 34.2% self-identified as Hispanic, and 37.0% had public insurance (Table 1). Most people (56.2%) did not anticipate breast engorgement would occur after their procedure.

At baseline, report of breast symptoms was similar between people randomized to receive

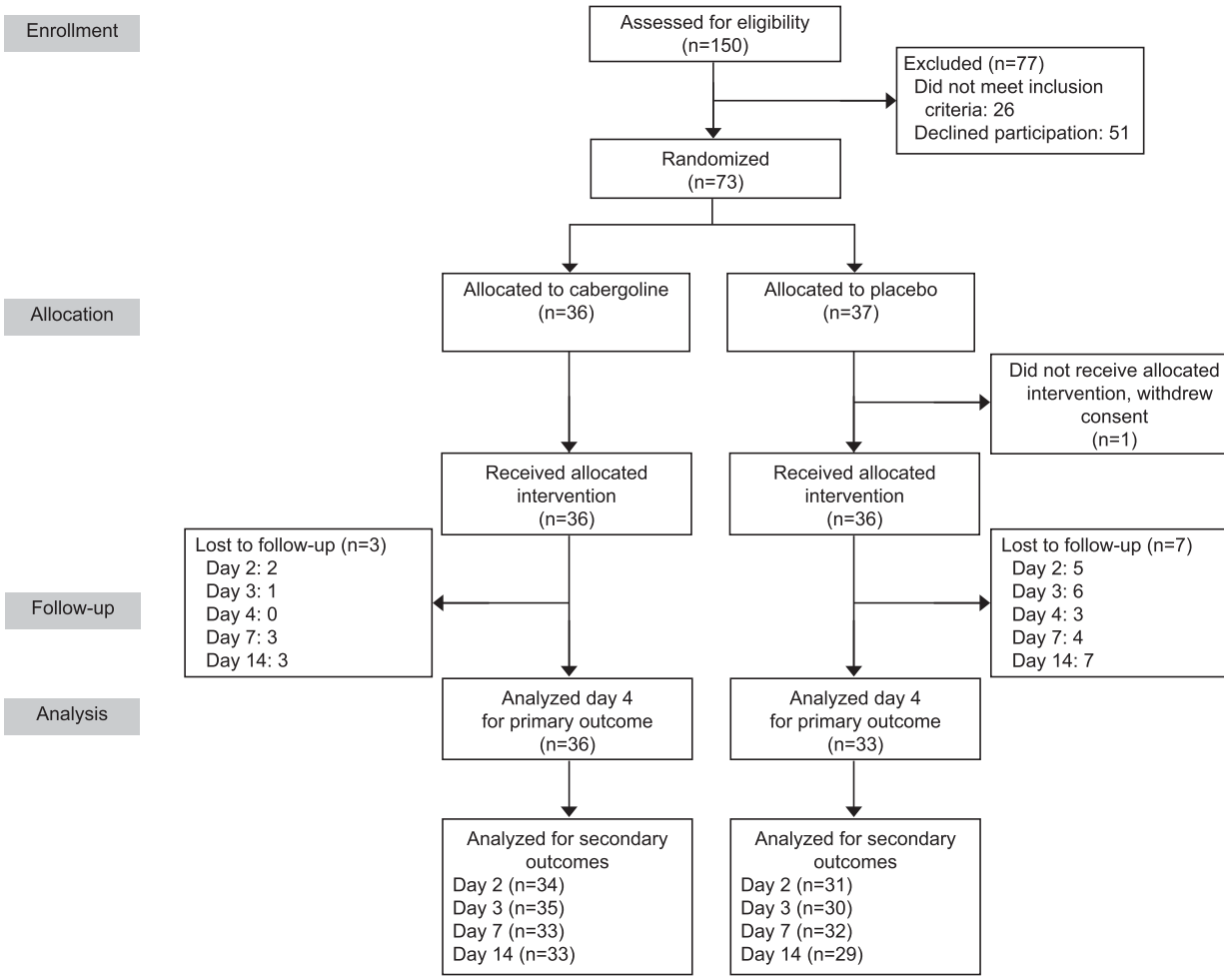

Fig. 1. CONSORT (Consolidated Standards of Reporting Trials) flow chart.
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Table 1. Demographic and Clinical Characteristics of Participants Randomized to Cabergoline or Placebo to Prevent Breast Pain After Second-Trimester Abortion or Pregnancy Loss

Characteristic	Cabergoline (n=36)	Placebo (n=37)
Age (y)	30.5±5.4	31.6±5.7
Parity	1 (0–4)	0 (0–4)
Nulliparous	16 (44.4)	25 (67.6)
Gestational age (d)	148.9±13.4	147.7±12.8
Gestational age (wk)		
18 0/7–19 6/7	10 (27.8)	9 (24.3)
20 0/7–21 6/7	11 (30.6)	12 (32.4)
22 0/7–23 6/7	15 (41.7)	15 (40.5)
24 0/7–28 0/7	0 (0)	1 (2.7)
Indication		
Undesired pregnancy	14 (38.9)	8 (21.6)
Fetal anomaly	20 (55.6)	27 (73.0)
Maternal comorbidity	0 (0)	1 (2.7)
Fetal death	2 (5.6)	1 (2.7)
Abortion method		
Procedural	31 (86.1)	32 (86.5)
Medication	5 (13.9)	5 (13.5)
Insurance		
Private	22 (61.1)	24 (64.9)
Medicaid	14 (38.9)	13 (35.1)
Gender*		
Female	35 (97.2)	37 (100)
Nonbinary	1 (2.8)	0 (0)
Race*		
American Indian	0 (0)	1 (2.7)
Asian or Pacific Islander	14 (38.9)	15 (40.5)
Black	1 (2.8)	1 (2.7)
White	11 (30.6)	15 (40.5)
None of the above	3 (8.3)	0 (0)
No response	7 (19.4)	5 (13.5)
Ethnicity*		
Non-Hispanic	24 (66.7)	24 (64.9)
Hispanic	12 (33.3)	13 (35.1)
Prior breast surgery	2 (5.8)	2 (5.4)
Prior breastfeeding	17 (47.2)	13 (35.1)
Length of breastfeeding (mo)		
Less than 6	8 (47.1)	5 (38.5)
More than 6	9 (52.9)	8 (61.5)

Data are mean±SD, median (range), or n (%).
* Self-identified.

cabergoline and those randomized to placebo (Fig. 2). The proportion of those reporting any breast symptoms differed at all subsequent timepoints. On day 4, significantly fewer participants reported any breast symptoms (our primary outcome) in the cabergoline group compared with placebo (27.8% vs 97.0%, relative risk [RR] 0.05, 95% CI 0.01–0.33). This difference was significant in all four domains of breast symptoms: engorgement (RR 0.17, 95% CI 0.07–0.45), breast tenderness (RR 0.18, 95% CI 0.08–0.42), leaking milk (RR 0.36, 95% CI 0.24–0.53), and requiring pharmacologic pain relief (RR 0.39, 95% CI 0.26–0.59) (Appendix 2, available online at http://links.lww.com/AOG/D152).

For both those randomized to cabergoline or placebo, the baseline median bother from breast symptoms was 0 (*P*=.464) (Table 2). The median bother differed significantly at all future timepoints. On day 4, 2.8% of those randomized to cabergoline reported significant bother from breast symptoms, compared with 33.3% randomized to placebo (*P*=.001).

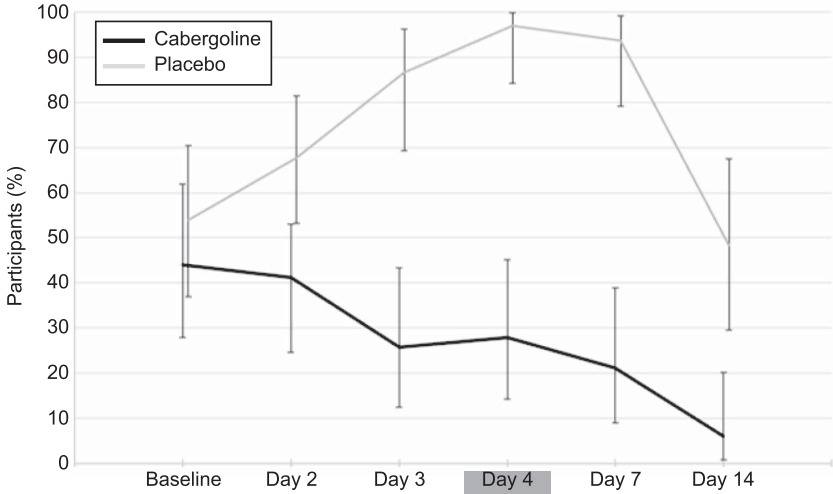
In an exploratory analysis of those at less than 20 weeks of gestation (cabergoline n=10, placebo n=9), 30.0% of those who received cabergoline reported breast symptoms on day 4, compared with 100% of those who received placebo (*P*=.004) (Appendix 3, available online at http://links.lww.com/AOG/D152). The median bother also differed significantly on day 4.

In the substudy, serum prolactin levels were similar at baseline in those who received cabergoline compared with placebo (Fig. 3). On day 4, serum prolactin level was 6.5±2.2 ng/mL for those who received cabergoline compared with 18.0+5.9 ng/mL receiving placebo (*P*=.049).

The most common side effects were constipation, headache, fatigue, and insomnia and did not differ between groups (Table 3). Of those who received cabergoline, 5.6% reported hot flushes in the 2 weeks postprocedure, whereas 24.3% of those who received placebo reported hot flushes (*P*=.025). The median bother from side effects at all timepoints was 0; however, on day 4, the distribution bother scores differed, with those who received placebo reporting more bother (*P*=.019) (Table 4). Most (60.6%) of those who received cabergoline were extremely satisfied with their allocation compared with 32.1% receiving placebo (*P*=.027). Ongoing vaginal spotting or bleeding at day 14 was similar between allocation groups: cabergoline 83.3% compared with placebo 85.2% (*P*=.850).

DISCUSSION

This randomized trial demonstrated that a one-time dose of cabergoline is superior to placebo in preventing breast symptoms after second-trimester abortion or pregnancy loss. Fewer people receiving cabergoline were significantly bothered by breast symptoms.



	Baseline	Day 2	Day 3	Day 4	Day 7	Day 14
Cabergoline	16/36	14/34	9/35	10/36	7/33	2/33
Placebo	20/37	21/31	26/30	32/33	30/32	14/29
P value	.41	.032	<.001	<.001	<.001	<.001

Fig. 2. Presence of breast symptoms experienced by participants randomized to cabergoline or placebo after second-trimester abortion or pregnancy loss. Data are percentage of total with 95% CIs. Day 4 *shaded* to denote the sole primary outcome.

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This prospective trial comparing cabergoline to placebo in the second trimester showed similar efficacy to prior non–placebo-controlled prospective studies. In a large, multicenter randomized control trial comparing bromocriptine (0.2 5 mg twice daily for 14 days) to cabergoline (1 mg once, day of birth) after term delivery, a complete absence of breast symptoms was reported in 90.4% of individuals in the cabergoline group and 83.8% in the bromocriptine group.[17] In the only prospective study to look at cabergoline use in the second trimester, cabergoline (1 mg on day of abortion) was compared with terguride (0.5 mg three times daily for a 10-day period). No significant difference was found between groups in the need to repeat administration of the drug.[21]

In an exploratory analysis of patients at less than 20 weeks of gestation, we still found that significantly fewer people who received cabergoline had breast symptoms than those who received the placebo. Although this study was underpowered to detect the full extent of this difference, clinicians who offer cabergoline for lactation suppression in the second trimester should consider including patients at 18 weeks of gestation or more based on this limited but promising efficacy. Future studies may consider investigating use of cabergoline starting at 15–16 weeks of gestation based on the physiology of lactogenesis.

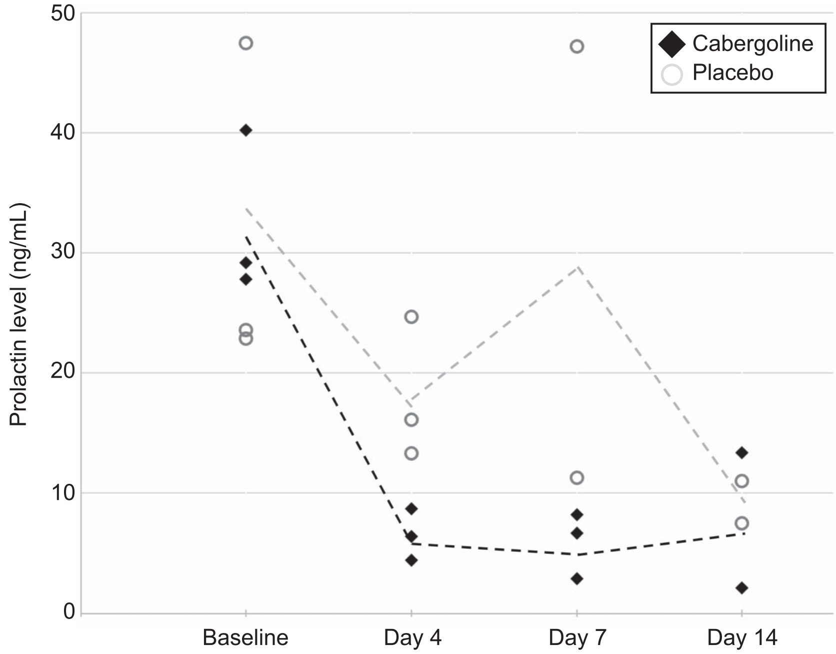
In the substudy, serum prolactin levels were significantly lower on day 4 for those allocated to cabergoline compared with those who received placebo. Our findings were consistent with the prior study, on which ours was powered, where the mean serum prolactin level in the placebo group was 44+8 ng/mL on day 4 and 12.2+2 ng/mL in the bromocriptine group.[8] The difference in serum prolactin levels adds biological plausibility to the difference in reported breast symptoms based on the

Table 2. Bother* Associated With Breast Symptoms of Participants Randomized to Cabergoline or Placebo After Second-Trimester Abortion or Pregnancy Loss

	Cabergoline	Placebo	*P*
Baseline	n=36	n=37	
Bother rating	0 (0–4)	0 (0–4)	.464
Significant bother	1 (2.8)	1 (2.7)	>.99
Day 2	n=34	n=31	
Bother rating	0 (0–3)	1 (0–4)	.040
Significant bother	0 (0)	1 (3.2)	>.99
Day 3	n=35	n=30	
Bother rating	0 (0–4)	2 (0–6)	<.001
Significant bother	1 (2.8)	1 (3.3)	>.99
Day 4	n=36	n=33	
Bother rating	0 (0–4)	3 (0–6)	<.001
Significant bother	1 (2.8)	11 (33.3)	.001
Day 7	n=33	n=32	
Bother rating	0 (0–3)	1.5 (0–5)	<.001
Significant bother	0 (0)	4 (12.5)	.11
Day 14	n=33	n=29	
Bother rating	0 (0–3)	0 (0–3)	.001
Significant bother	0 (0)	0 (0)	>.99

Data are median (range) or n (%) unless otherwise specified.

* Bother on facial pain score (0=none, 6=extremely); significant bother 4 or higher.



	Baseline	Day 4	Day 7	Day 14
Cabergoline	n=3 32.4+6.8	n=3 6.5+2.2	n=3 5.9+2.7	n=2 7.7+8.0
Placebo	n=3 31.3+14.0	n=3 18.0+5.9	n=2 29.3+25.4	n=2 9.3+2.5
P value	.513	.049	.083	.999

Fig. 3. Serum prolactin levels of substudy participants randomized to cabergoline or placebo after second-trimester abortion or pregnancy loss. Data are mean±SD. *Dashed lines* indicate mean.

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mechanism of action that dopamine agonism inhibits prolactin.

In our study, side effects were common after both cabergoline and placebo administration, likely reflecting the high rate of systemic symptoms after second-trimester abortion or pregnancy loss. Our study was not powered to detect differences in side effects, owing to the relatively low counts for each side effect. A large systematic review similarly reported that the most common side effects after cabergoline use for lactation suppression at term were dizziness, headache, and nausea or vomiting.[10] We noted that the

Table 3. Side Effects Reported by Participants Randomized to Cabergoline or Placebo After Second-Trimester Abortion or Pregnancy Loss

	No. of Participants With Side Effects		
Side Effect	Cabergoline (n=36)	Placebo (n=37)	*P*
Nausea or vomiting	5 (13.9)	2 (5.4)	.261
Headache	12 (33.3)	9 (24.3)	.395
Dizziness or lightheadedness	7 (19.4)	7 (18.9)	.955
Constipation	14 (38.9)	18 (48.6)	.401
Acid reflux	3 (8.3)	2 (5.4)	.674
Fatigue	12 (33.3)	11 (29.7)	.704
Lower extremity edema	4 (11.1)	4 (10.8)	>.99
Hot flushes	2 (5.6)	9 (24.3)	.025
Palpitations	1 (2.8)	1 (2.7)	>.99
Anxiety	4 (11.1)	3 (8.1)	.711
Insomnia	8 (22.2)	11 (29.7)	.465
Visual disturbance	1 (2.8)	2 (5.4)	>.99
Total reporting side effects	29 (80.6)	26 (70.3)	.308

Data are n (%) unless otherwise specified.

Table 4. Bother* From Side Effects Reported by Participants Randomized to Cabergoline or Placebo After Second-Trimester Abortion or Pregnancy Loss

	Cabergoline	Placebo	*P*
Day 2	(n=34)	(n=29)	
Bother rating	0 (0–3)	0 (0–2)	.348
Significant bother	0 (0)	0 (0)	–
Day 3	(n=33)	(n=27)	
Bother rating	0 (0–3)	0 (0–6)	.079
Significant bother	0 (0)	1 (3.7)	>.99
Day 4	(n=35)	(n=33)	
Bother rating	0 (0–3)	0 (0–6)	.019
Significant bother	2 (5.7)	6 (18.2)	.144
Day 7	(n=31)	(n=30)	
Bother rating	0 (0–6)	0 (0–4)	.234
Significant bother	2 (6.5)	4 (13.3)	.425
Day 14	(n=33)	(n=27)	
Bother rating	0 (0–4)	0 (0–4)	.616
Significant bother	2 (6.1)	1 (3.7)	.614

Data are median (range) or n (%) unless otherwise specified.
* Bother on facial pain score (0=none, 6=extremely); significant bother 4 or higher.

proportion of people reporting hot flushes was significantly higher for those who received placebo compared with cabergoline; although there is physiologic plausibility to support this side effect in those who received placebo (elevated prolactin levels suppress the hypothalamic-pituitary-ovarian axis, resulting in decreased estrogen levels and causing the hypothalamus to be more sensitive to temperature change), this may also reflect type 1 error from multiple testing.

We selected a dose of 1 mg of cabergoline based on existing formulary options of 0.5 mg tabs and prior dose-finding studies that supported higher efficacy with higher doses. In a dose-finding study at term, comparing cabergoline 400 micrograms, 600 micrograms, and 800 micrograms, the frequency of reported breast symptoms differed significantly among doses of cabergoline but serum prolactin levels did not differ,[18] which suggests that the frequency of breast symptoms may not be wholly explained by cabergoline's dopaminergic action in the anterior pituitary to suppress the release of prolactin. Future studies may consider the comparison of 0.5 mg with 1 mg in the second trimester, particularly in those who are at less than 20 weeks of gestation, as this may be cost-effective if similarly efficacious.

Strengths of our study include the randomized controlled design, a diverse participant population surveyed with preferred language questionnaires, and lack of industry sponsorship. Our primary outcome of breast symptoms was both clinically meaningful and person-centered, allowing broad generalizability of results. Study limitations include low trial acceptance (66%). It is unclear from this study if patients do not desire a pharmacologic intervention, are unaware of the potential discomfort, or simply did not want to participate in a clinical trial in an otherwise emotionally challenging life event. It will be important to follow up after implementation if acceptance remains low. Other limitations include being underpowered to detect small differences in side effects, lack of gestational age stratification in original randomization scheme, and restricted external validity inherent to a randomized trial. Participants in the substudy collecting serum prolactin levels were not randomly selected, and, with a small sample, results should be taken with caution.

We found cabergoline to be an effective, well-tolerated pharmacologic intervention to prevent bothersome breast symptoms after second-trimester abortion or pregnancy loss. Given the current lack of evidence-based interventions to prevent breast symptoms in this population, these findings support routine use of cabergoline after second-trimester abortion or pregnancy loss.

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Authors' Data Sharing Statement

Will individual participant data be available (including data dictionaries)? *No.*

What data in particular will be shared? *Not applicable.* What other documents will be available? *Not applicable.*

When will data be available (start and end dates)? *Not applicable.*

By what access criteria will data be shared (including with whom, for what types of analyses, and by what mechanism)? *Not applicable.*

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