

Survey of Provider Preferences Regarding the Route of Misoprostol for Induction of Labor at Term

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Abstract

Objective To survey obstetrical provider preferences regarding use of misoprostol for induction of labor (IOL).

Methods An anonymous 25-question survey was distributed at an American College of Obstetricians and Gynecologists (ACOG) joint District V and VII Meeting in 2014 to obstetrics providers. The same survey was sent electronically to local providers. A separate survey was emailed to the labor and delivery nurses at two of the teaching hospitals in Indianapolis. The surveys queried provider demographics, dosing practice for misoprostol, opinions regarding different dosing strategies, and instructions on buccal administration.

Results A total of 113 (46.5%) providers responded. Of these, 92.9% used misoprostol for IOL, 73% preferred the vaginal route, 20% preferred buccal administration, and 7% oral administration. Only resident physician and midwife providers endorsed buccal route preference. Being a midwife independently predicted a preference for using buccal misoprostol (odds ratio [OR]: 125.8, 95% confidence interval [CI]: 7.9–1992.3). Additionally, 44 nurses completed the survey regarding administration techniques of buccal misoprostol. Also, 54.5% of nurses correctly instructed their patients on buccal administration techniques.

Conclusion Although not extensively studied, one-fifth of providers, particularly nurse midwives, prefer buccal administration of misoprostol for IOL. The majority of nurses correctly administered buccal misoprostol. There may be a need for further study and education about buccal administration of misoprostol for IOL.

Keywords

- ▶ misoprostol
- ▶ labor induction
- ▶ provider preference
- ▶ buccal
- ▶ vaginal

In the United States, the rate of induction of labor (IOL) has significantly increased from 9% in 1990 to just over 23% in 2012.¹ There are many medicinal and mechanical options available to induce labor, including dinoprostone inserts, misoprostol, balloon catheters, and oxytocin. The goal in selecting which agent and route to use should depend on the safety profile and efficacy. Additionally, the woman's preference should be considered.²

Although used off-label, misoprostol is frequently used in obstetrics for IOL. Its safety and efficacy have been extensively supported by research.^{2–4} The oral and sublingual routes are easily administered and considered less invasive. However, they are often associated with more adverse side-effects, such as chills, nausea, vomiting, and diarrhea, when compared with the vaginal route.⁵ The oral and sublingual routes have the shortest time to peak serum concentration

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and the highest peak serum concentration,⁶ which may contribute to these adverse side-effects. The vaginal route is typically more uncomfortable for the woman and usually requires a provider to administer; however, it has fewer side-effects due to its longer time to peak concentration and lower peak concentration.⁷ Vaginal misoprostol has a higher bioavailability (a greater area under the concentration–time curve) that contributes to its longer duration of action than the oral or sublingual routes requiring less frequent dosing.⁶ Clinically, we have noticed a trend toward more use of buccal misoprostol for IOL, even though there are few data comparing the different routes of administration.⁸

The objective of this study was to survey obstetrical providers' preferences regarding the route and dosing of misoprostol as an induction agent for a live, singleton, term fetus. Additionally, this study sought to evaluate provider thoughts and comfort level with buccal administration of misoprostol. A secondary objective was to assess the instructions given by labor and delivery nurses regarding buccal misoprostol.

Materials and Methods

This study was approved by the Indiana University Institutional Review Board (IRB).

Survey of Providers

The study population consisted of obstetric providers in attendance at the April 2014 American College of Obstetricians and Gynecologists (ACOG) combined Annual District V and VII Meeting in Indianapolis, IN, and faculty, residents, and nursing staff affiliated with the Indiana University School of Medicine (IUSM). Study data were collected and managed using the Research Electronic Data Capture (REDCap) software hosted at the Indiana University. REDCap is a secure, web-based application.⁹

The survey to the providers consisted of 25 questions, 7 of which were questions on demographics. A mid-level provider was defined as a nurse practitioner, certified nurse midwife, or a physician's assistant. Most questions were single-selection answer choices with occasionally free text answers (see ► **Appendix A**). For the electronic version, if a provider answered "no" to the question "As part of your normal practice, do you use misoprostol for induction of labor of a live fetus?" then the REDCap logic commands would skip to the applicable questions and terminate the survey early. The survey questions were developed with experts in survey methodology but were not formally validated. They were pilot tested with a small group of providers and wording revised to the final form in ► **Appendix A**.

Four weeks prior to the meeting, the electronic version of the survey was emailed to the obstetric providers associated with IUSM as a convenience sample. There were instructions to complete the survey at first attempt, although due to the anonymity of the process, duplications were unable to be detected. After approved by the District V Advisory Council, the identical paper survey was distributed to those in attendance at the District Meeting as a voluntary and anon-

ymous survey with instructions to return it to a collection container. No surveys were electronically submitted after the paper surveys were distributed.

Survey of Nursing Staff

Nurses were surveyed if they were associated with the IUSM obstetrics and gynecology residency program and worked at either Eskenazi Hospital or Methodist Hospital in Indianapolis. This shorter survey consisted of six questions that focused on the administration of buccal misoprostol (see Appendix B). The nurses were emailed through each hospital's list-serve, and the data were collected with the REDCap software.

Analysis

Collated surveys were summarized with descriptive statistics. Comparisons between physician and midlevel providers were performed with chi-squared test for discreet variables and *t*-tests for continuous variables as applicable.

Results

Provider Survey

At the ACOG District Meeting, 177 people were documented to be in attendance, of whom, 124 were physicians/obstetric providers. Of the 106 paper surveys distributed at this meeting, 60 surveys were returned (56.6%), all completed by the providers. Additionally, 137 email solicitations were sent yielding 53 surveys submitted electronically (38.7%). Thus, there were a total of 113 provider surveys completed for an overall response rate of 46.5%.

Of the providers surveyed, 96 (85%) were physicians, 14 (12%) were mid-level providers, and 3 selected as "other" (left blank or stated that they no longer practiced obstetrics, ► **Table 1**) Of the physicians, 39 (41%) were still in training, either residency or fellowship. A total of 93 (97%) physicians were trained in obstetrics and gynecology. The remaining physicians were either family practitioners ($n = 2$) or were double boarded in both ($n = 1$). Half of the providers (50.4%) stated they were in academic medicine, 24.5% in private group practice, 11.8% still in training, 6.2% associated with a hospital-owned group practice, 2.7% were solo practitioners, and 0.9% worked for a government-affiliated hospital. Seventy percent of the participants were females (► **Table 1**). Most respondents (67%) had been in practice < 10 years or were in residency.

The majority of participants responded that they use misoprostol as an agent of induction of labor (92.9%). Of the eight providers who did not use misoprostol, reasons given included "no longer practicing obstetrics," "preferring other agents like a Foley bulb," "it is not FDA approved," and "the nurses are uncomfortable." Most providers (73%) preferred to administer misoprostol vaginally, with 20% responding that they preferred the buccal route, and 7% preferred oral administration. No one endorsed preferring the sublingual or rectal routes for labor induction. Of those who preferred the buccal route, half were midlevel providers and the other half were obstetrics and gynecology resident physicians in varying years of training.

Table 1 Comparison of characteristics of providers preferred route of misoprostol administration

Characteristic	Overall (n = 113)	Prefer vaginal (n = 75)	Prefer buccal (n = 20)	Prefer oral (n = 7)	p-Value ^a
Age category					0.07
< 30 y	23 (21%)	14 (64%)	7 (32%)	1 (4%)	
31–40 y	43 (39%)	26 (63%)	11 (27%)	4 (10%)	
41–50 y	19 (17%)	15 (88%)	2 (12%)	0 (0%)	
51–60 y	14 (13%)	9 (82%)	0 (0%)	2 (18%)	
61–70 y	10 (9%)	10 (100%)	0 (0%)	0 (0%)	
Gender (female)	76 (70%)	46 (62%)	19 (95%)	5 (71%)	0.018
Gender (male)	37 (30%)	28 (90%)	1 (3%)	2 (6.5%)	
Type of practitioner					<0.001
Physician	96 (85.0%)	73 (83%)	10 (11%)	5 (6%)	
Midlevel provider	14 (12.4%)	1 (8%)	10 (77%)	2 (15%)	
Other	3 (2.6%)	1 (100%)	0 (0%)	0 (0%)	
In practice <10 y	73 (67%)	46 (67%)	18 (26%)	5 (7%)	0.042
In practice ≥10 y	36 (33%)	28 (90%)	2 (6.5%)	1 (3%)	
Practice setting					0.008
Academic/University	56 (51%)	36 (67%)	16 (30%)	2 (4%)	
Solo practice	3 (2.7%)	1 (100%)	0 (0%)	0 (0%)	
Group private practice	27 (24.5%)	22 (92%)	1 (4%)	1 (4%)	
VA/Government affiliate	1 (1%)	0 (0%)	0 (0%)	1 (100%)	
Resident physician	13 (11.8%)	9 (69%)	2 (15%)	2 (15%)	
Other ^b	10 (9.1%)	6 (75%)	1 (12.5%)	1 (12.5%)	

Abbreviation: VA, veteran affairs.

Note: Results are presented as n (%).

^ap-Values for comparisons are between the three preference groups.

^bOther category included mostly providers who commented that they were in a hospital owned-practice or worked as hospitalists/laborists.

The majority of providers (77%) routinely calculated a Bishop score prior to starting an induction of labor, and of those who did, a score of 6 to 8 was most often deemed favorable to start oxytocin rather than a cervical ripening agent such as misoprostol. The majority (93%) selected a starting dose of misoprostol at 25 µg for IOL. The rate of beginning with a dose of 25 µg was somewhat lower for those preferring the oral route (71 vs. 95% each for vaginal and buccal, $p = 0.12$). Twenty-nine percent of those endorsing the oral route began at a dose of 50 µg. When asked if they would increase the subsequent dose of misoprostol, 52% considered doing so (either routinely or if there was no response from the initial dose). Of these, all opted for a 50 µg dose to be given either vaginally or buccally. The maximum comfortable single dose of misoprostol to be given was noted as 50 µg by 75% of providers; however, eight individuals felt comfortable administering 100 to 200 µg with varied routes of administration (oral, buccal, and vaginal). A total of 92.3% providers responded that they administered misoprostol every 4 hours as per ACOG guidelines.³ Three responded that an hourly dose was used; these providers administered misoprostol orally at 25 µg as the

starting dose. The mean total maximum number of doses of misoprostol that providers felt comfortable administering was 5.8; however, 30% did not have a cutoff. When asked if there was a maximum total cumulative dose of misoprostol, providers felt comfortable administering the median dose as 250 µg, but 56% of providers did not have a maximum. For those who used both vaginal and buccal administration of misoprostol, 42.6% used the same dose for each route, whereas 11.9% increased the dose when given buccally.

When questioned about which route was more effective, 5% thought the buccal route was more effective than the vaginal route, 36% considered them equal, and 24% thought the buccal route was less effective; the remaining 34% responded that they were unaware of any studies comparing the effectiveness between the two routes. According to the survey, the most persuasive sources to change a provider's use of buccal misoprostol for IOL would have to come from the ACOG practice bulletins (78%), peer-reviewed journal articles (53%), or data presented at a conference (46%). Additionally, 80% of providers said they would consider enrolling patients in a study that used buccal misoprostol for IOL at term.

Of the providers who administered buccal misoprostol, the majority (55.6%) gave instructions to the patients to keep the medicine in their cheek until completely dissolved versus moving it around if not dissolved (3.7%), swallowing it if not dissolved (24.1%), or no specific instructions given (16.7%).

—**Table 1** also displays the characteristics of providers who endorsed preference to start induction with vaginal, buccal, or oral misoprostol. Preference for buccal misoprostol was associated with being female, a midlevel provider, in practice < 10 years, and at an academic/university-affiliated practice. Female providers more often preferred to begin inductions with buccal misoprostol compared with male providers (34.3 vs. 9.7%, $p = 0.018$). In a multivariable logistic regression controlling for gender, age category, type of practitioner, and practice setting, only being a midlevel provider predicted a preference for starting inductions with a nonvaginal route of misoprostol (OR: 125.8, 95% CI: 7.9–1992.3).

Nurse Survey

There were 44 responses to the nursing survey of the total pool of 179 nurses approached (response rate was 24.6%, although we were unable to verify if all nurses actually received and read the email). The questions focused on the instructions given to the patients when administering buccal misoprostol. Among the nurses surveyed, 41 (93.2%) had previously administered buccal misoprostol; the surveys from the other 3 nurses were left blank. All but two nurses instructed the patients to place the medication in the correct anatomical location between the lip and mucosa of the gums. The remaining two nurses indicated that they gave the medication sublingually. The majority of nurses (54.5%) instructed patients to wait for the medicine to completely dissolve; one recommended massaging the medicine in the cheek. If instructions were given involving time, a range from 20 to 60 minutes was recommended before either swallowing or massaging the pill.

The majority of nurses reported receiving instructions on buccal administration from another nurse (50%), a physician (33%), or from a variety of other sources including reading it on their own (7.5%) in nursing school (5%), from a midwife (2.5%), or from written directions on the order (2.5%). Of note, the two nurses that incorrectly administered the misoprostol sublingually reported learning their technique from a physician and from the written order.

Discussion

Our study revealed that most of the practitioners surveyed utilized misoprostol for IOL of a term, live, singleton fetus and preferred the vaginal route of administration. The dose and timing of misoprostol was consistent with the practice trends and guidelines from ACOG of 25 µg doses every 4 hours.³ Additionally, our results were similar to results from a survey of providers in Switzerland.¹⁰ That survey also found that the most frequent route of administration was intravaginal (86%) but that most providers preferred a 50 µg dose (94%) with similar dosing intervals.¹⁰ It was interesting that

the only providers who completed the survey that used the buccal route of administration were mid-level providers or physicians in their residency training. Also, being a mid-level provider independently predicted a preference for the buccal route, controlling for age, practice setting, and gender. One possible explanation for this is the appeal of the patient for the less-invasive route; most mid-level providers participating in the study were certified nurse midwives who often care for patients who prefer minimal interventions and limited cervical exams making the buccal route of drug administration an appealing option. Another possible explanation is that there was a recent education session from a guest lecturer discussing the advantages of buccal administration of misoprostol for miscarriage management and IOL at the IUSM. The survey in Switzerland only questioned obstetricians.¹⁰

From the study results, most participants stated that they were unaware of the evidence regarding the use of buccal misoprostol for induction of labor. To our knowledge, there are only limited data on the topic. One randomized control trial compared buccal to vaginal misoprostol and one Cochrane Review combined buccal and sublingual study.^{8,11} However, there are multiple studies supporting efficacy and safety of sublingually administered misoprostol when compared with the vaginal and oral routes for IOL.^{12–16}

The buccal mucosal administration of misoprostol is a less studied route in obstetrics, but it has some favorable properties. Similar to the oral and sublingual routes, it is easily administered and minimally invasive. Similar to the vaginal route, it has a longer time to peak serum concentration and lower peak serum concentration.⁶

The limitations of the current study include those common to survey studies. We experienced a low rate of return of completed paper surveys, although our return rate is on par with many other provider practice surveys. One explanation for the low return of provider surveys at the District Meeting may be due to the high proportional attendance of nonobstetrical subspecialists (i.e., gynecology, oncology, and female pelvic medicine) no longer practicing obstetrics. Additionally, medical students present at the meeting received the survey included in the meeting materials but were instructed not to participate. Another possible explanation is the providers associated with IUSM most likely completed the emailed electronic version prior to receiving a paper version at the ACOG District Meeting, which could account for some of the 46 paper surveys not returned. We were unable to control for duplicated survey completions; however, we did instruct providers at the meeting who may have already completed the survey to not complete attempt it again. The study was also limited in its generalizability in that the District Meeting took place in Indiana, potentially leading to an over-representation of providers from the Midwest. To improve generalizability, we evaluated the feasibility of distributing the survey through the ACOG Collaborative Ambulatory Research Network, through the ACOG list-serve, or via residency program coordinators but were concerned with potentially lower response rates with these methods.

Additionally, the survey of nurses was local to the hospitals associated with the department. Thus, these results may not be generalizable. Repeating the survey to a national office may be needed. As the surveys asked different questions to the two groups, we were unable to compare the results between the physician and nursing practices.

The results from this study suggest that most obstetrical providers are comfortable with the use of misoprostol for induction of labor of a live, term fetus. Although vaginal misoprostol is currently the favored route, one fifth of the providers surveyed preferred the buccal route. The preference for the buccal route was particularly seen with midlevel providers. As there are little data directly comparing vaginal to buccal administration of misoprostol for IOL, direct comparison of clinical trials is required. These trials should include patient satisfaction measures so that if clinical and adverse event findings are equivalent, patient preference may help guide care. According to our results, the majority of providers that participated in this survey would be comfortable involving their patients in such a study.

Conflict of Interests

There exists no financial conflict of interests.

Note

This research was presented at the Annual District V Meeting of ACOG, from September 18 to 20, 2015, Denver, CO.

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