Obstetrical Use of Misoprostol (Cytotec®)

[August 2022 (replaces September 2021)]

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Summary

The BCM OB/Gyn Perinatal Guidelines Committee therefore makes the following recommendations:[1]

1. If misoprostol is used for cervical ripening in the third trimester, 25 mcg intravaginally or 100 mcg orally should be considered; the route of administration should remain consistent throughout the cervical ripening process.
2. Intravaginal 25 mcg doses should be administered every 3-4 hours, with clinical correlation (i.e. taking into account the uterine contraction pattern and maternal-fetal status at the time), up to a maximum of 8-6 total doses, respectively.
3. Oxytocin should not be administered less than 4-6 hours after the last misoprostol dose, with clinical correlation (i.e. taking into account the uterine contraction pattern and maternal-fetal status at the time).
4. Misoprostol should not be used in the third trimester for cervical ripening in those patients with previous transmural hysterotomy (e.g. cesarean section), non-reassuring fetal status or oligohydramnios.
5. For midtrimester induction of labor for fetal demise or for a medically indicated termination of pregnancy, misoprostol 400 mcg vaginally or sublingually every 3 hours for up to 5 doses or a vaginal loading dose of 600-800 mcg followed by 400 mcg vaginally or sublingually every 3 hours is an appropriate option. This regimen may be safely used in people with a prior cesarean delivery, although these people are likely at increased risk for uterine rupture with any termination method employed. Osmotic cervical dilators (e.g. laminaria) do not provide added benefit to induction with prostaglandin analogues.[2]
6. Following midtrimester induction of labor with misoprostol, 10 units of IM oxytocin into the upper thigh should be administered after fetal delivery since it significantly increases placental expulsion rates and decreases short-term postpartum blood loss.
7. For postpartum hemorrhage from uterine atony, misoprostol 400 mcg can be safely used sublingually, orally, or rectally.

Dosing

The optimal dose and timing interval of intravaginal misoprostol, synthetic PGE1 analogue, are unknown. A randomized double-blind trial found that a dose of 50 mcg every 3 hours was associated with a shorter start-to-delivery interval and a higher incidence of vaginal delivery after one dose, but that 25 mcg every 3 hours was effective as well and associated with a lower incidence of tachysystole and cord pH values < 7.16.[3] In comparing the 25 mcg dose given every 3 hours vs. every 6 hours, patients with the 6 hour dosing schedule had longer intervals to delivery, more frequently required oxytocin augmentation and had more failed inductions.[4]

With orally administered misoprostol, the plasma concentration peaks earlier and higher than with vaginal administration, however, the plasma concentrations are detectable for longer after vaginal administration.[5] **Giving 100 mcg of misoprostol orally every 4 hours has been shown to be as effective as vaginal administration of 25 mcg every 4 hours, with no differences in maternal or neonatal outcomes.**[6]

Nonviable pregnancies

For midtrimester induction of labor in the setting of fetal demise or a medically indicated termination of pregnancy (eg, previable preeclampsia with severe features), high doses of misoprostol have been employed. A dosing regimen of 400 mcg intravaginally every 6 hours has been shown to be effective.[7] When this regimen was compared to 400 mcg orally every 3 hours, the vaginal route was found to be superior.[8] ACOG now recommends either of the following regimens: 1) 400 mcg administered vaginally or sublingually every 3 hours for up to 5 doses. If delivery is not effected after 5 doses, the woman may be allowed to rest for 12 hours before starting the cycle again. The vaginal dosage is superior to sublingual dosage for nulliparous people; or 2) a vaginal loading dose of 600-800 mcg followed by 400 mcg vaginally or sublingually every 3 hours.[2] In a randomized clinical trial of third-stage management after misoprostol second-trimester pregnancy termination, a single intramuscular injection of 10 units of oxytocin was superior in terms of achieving a significant reduction in the need for operative placental removal and postpartum blood loss compared with a single 600 mcg oral dose of misoprostol or a nonpharmacologic approach to the management of the third stage. Interventions to facilitate placental removal if it has not occurred spontaneously by 2 hours after delivery is recommended as the likelihood of spontaneous expulsion after this time is low.[9]

History prior CD

Misoprostol has not been recommended for cervical ripening in patients who have had prior cesarean delivery or major uterine surgery because of the risk of uterine rupture.[10] However, in a review of 101 people with at least one prior cesarean delivery undergoing abortion at 14 - 28 weeks' gestation with misoprostol, there was no case of uterine rupture or hysterectomy. During the study, 6 dosage regimens of misoprostol were used, with the most frequent dose was 400 mcg intravaginally every 6 hours.[11]

Uterotonic

Finally, misoprostol can be used as a uterotonic for postpartum hemorrhage due to uterine atony. The time to onset of misoprostol is longer than other uterotonics, so it should be considered after methergine, hemabate, and pitocin. Recommended dose ranges are 400 mcg - 1000 mcg, and the routes of administration are oral, rectal and buccal. After oral administration, uterine tonus develops, which is not followed by uterine contractions unless repeated doses are given. Studies have shown that doses higher than 400 mcg increase side effects and may not increase effectiveness.[1,5]

Route	Onset of Action	Duration of Action
Oral	8 min	~2 hrs
Sublingual	11 min	~3 hrs
Vaginal	20 min	~4 hrs
Rectal	100 min	~4 hrs

References

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