Oral Misoprostol and Intracervical Dinoprostone for Cervical Ripening and Labor Induction: A Randomized Comparison. Bartha JL, Comino-Delgado R, Garcia-Benasach F, Martinez-Del-Fresno P, Moreno-Corral L. Obstet and Gynecol 2000;96:465–9.

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Background and Study Design

The reported study was a randomized study conducted in Cadiz, Spain at University Hospital of Puerto Real. It compared the efficacy, safety, and tolerance of labor induction and cervical ripening using a single dose of 200-mcg oral misoprostol with the research hospital's protocol of dosing with intracervical dinoprostone. Excluded from the study were women who had nonvertex presentations, uterine scars other than a prior low transverse cesarean, multiple gestations, premature rupture of membranes, and a Bishop score of at least six. Study subjects were comprised of 200 women who met study criteria who were consecutively admitted for induction. Subjects were randomly assigned to one of the two induction method groups: induction with 200-mcg oral misoprostol or induction with .5-mg dinoprostone intracervically every 6 hours for a maximum four doses. If cervical ripening was not achieved within 24 hours for women in both groups, oxytocin infusion commenced and proceeded for 12 hours. If the women were not in active labor after the oxytocin, a cesarean delivery was performed. Oxytocin was used in both groups if a woman was in active labor and labor progress had arrested for more than 1 h. Continuous fetal monitoring was used to assess fetal well-being for all study participants.

Study variables included: labor time intervals (from start of induction protocol to start of active phase, spontaneous rupture of membranes, and birth), number of women with a Bishop score of at least six at 6, 12, and 24 h, success of induction (defined as delivery within 24 h of administration of study drug protocol), route of delivery, need for oxytocin augmentation, and rate of cesarean birth for failed induction.

Results

All three study time intervals were significantly shorter for women in the misoprostol group as compared to the dinoprostone group, with the following time intervals from administration of the drug protocol to: start of the active phase of labor (11.05 h versus 15.8 h), spontaneous rupture of membranes (10.0 h versus 15.6 h), and birth (14.02 h versus 20.23 h). In the dinoprostone group, higher rates of women who required oxytocin was found (68% versus 52%) and higher rates of women giving birth by cesarean due to failed induction (9% versus 1%). Additionally, for women in the misoprostol group who gave birth vaginally, the time interval from protocol to birth was shorter (12.26 h versus 14.52 h); also, these women were more likely to reach a Bishop score of at least six by 6 h (43% versus 27%) when compared to the dinoprostone group women. There were no significant differences between groups in the rates of tachysystole, hypertonus, and hyperstimulation.

The authors compared their findings with several other similar studies. Adair (1) used a 200-mcg dose of oral misoprostol in a comparison of oral versus vaginal dosing. A significantly higher rate of hyperstimulation was found with oral dosing, resulting from repetitive oral dosing every 6 h for up to a total of three doses. Nagai (2) also used 200-mcg oral misoprostol and did not report hyperstimulation syndrome. Bartha and colleagues recommend the use of continuous electronic fetal monitoring and uterine contraction monitoring.

Discussion

By concluding that a single dose of 200-mcg oral misoprostol was more effective than intravaginal dinoprostone for cervical ripening and induction, this study addresses several key issues currently in debate within hospitals, birth centers, and pharmaceutical companies. Although informed consent was obtained from all subjects, it is not clear if women were aware that at the onset of the study the pharmaceutical company responsible for the manufacture of misoprostol *does not* advocate its use for induction of labor, due to the risk of maternal or fetal death, uterine hyperstimulation, rupture or perforation, hysterectomy, amniotic fluid embolism, severe vaginal bleeding, retained placenta, shock, fetal bradycardia, and pelvic pain. Studies of this kind, which compare a drug with known hazards to a relatively safe drug, call into question the ethical standards by which all women's and perinatal clinical research should be conducted.

Important factors that were not addressed by this study and its design included maternal activity before and during labor (walking, eating, drinking), the incidence of bed-restricted fetal monitoring or telemetry, and the incidence of prescribed narcotics or epidurals. Additionally, the study did not examine other variables that could account for shorter labors in the misoprostol group. For example, if more pain medication was given in the misoprostol group, it could have allowed for greater relaxation and hence a shorter labor. Cultural factors that

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could limit the study's generalizability were also omitted. The cost-effectiveness of the use of misoprostol, however, is not in debate because inducing 100 women with misoprostol is estimated to cost $30 as compared to the $3,456.80 needed for induction for 100 women using dinoprostone.

If a dose were proven to effectively and safely ripen a cervix and induce labor, there would be clear advantages for its use. At this point however, the use of misoprostol for cervical ripening and induction is not sufficiently supported by scientific evidence. The new protocol also has the potential to compromise a woman's experience of labor and birth through the need for additional technology; moreover, especially with a drug that has known hazardous side effects and whose definitive dosages and safety measures have not yet been confirmed by its manufacturer, this study brings into view the broader matter of the necessity for labor induction itself.

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