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Editorial

Is it safe to use pharmacological agents for induction of labor?

The risk of perinatal morbidity or mortality for pregnant women with oligohydramnios is higher than that for pregnant women with normal amniotic fluid index, and is often secondary to various kinds of medical or obstetric disorders such as preeclampsia and systemic lupus erythematosus.[1−3] When continuation of the pregnancy might jeopardize patient health and possibly result in subsequent life-threatening catastrophic circumstances for pregnant women or their babies, delivery may be a better choice compared to continuing the pregnancy.[4] Therefore, labor induction is often used in such critical situations, a common obstetric intervention that artificially initiates the process of effacement of the cervix, dilatation of the cervix, and uterine contractions as well as routinely results in successful vaginal delivery. However, induction of labor itself, especially applied at an inappropriate time, may increase the risk of perinatal morbidity and/or cesarean delivery, which is already common in this high-risk group.[5] Additionally, cesarean delivery occurs much more frequently in women with an unfavorable cervix condition who have scheduled labor induction.[4]

Induction of labor starting with cervical ripening through the Foley catheter method has been a generally accepted technique and believed to be the safest method to manage pregnant women with an unfavorable cervix because it avoids exogenous uterine stimulants and relies on the local and endogenous prostaglandin release.[6] This mechanical method utilizes a simple Foley catheter bulb that is passed through the cervix and inflated in the potential space between the amniotic sac and the uterus.[6] In recent decades, following the introduction of pharmacological agents such as prostaglandin E1 (misoprostol) or E2 analogues (dinoprostone),[6−9] these drugs have given the medical community and patients promising and exciting drug treatments. Typically, these drugs are widely used after a promotional budget becomes continuous. In addition, the results of a multicenter randomized controlled noninferiority trial that compared oral misoprostol versus a Foley catheter for induction of labor at term (PROBAAT-II) supported a similar safety and effectiveness between the two methods in the induction of labor for women with an unfavorable cervix at term.[4] Although the PROBAAT-II study favored the benefits of misoprostol, such as low price, ease of storage, extended shelf life at room temperature, and suitability for use in low-resource settings, as well as the countries where there are reservations about induction owing to a high prevalence of infection, and the risk of vertical transmission is present,[4] there are still many uncertainties that should be clarified. For example, the oral administration of misoprostol to induce labor has a higher risk of postpartum hemorrhage, elevated frequency of asphyxia, and a 3.8 times greater incidence of spontaneous rupture of the membrane compared with the Foley catheter method in other studies.[4,6]

One systematic review and network meta-analysis was conducted to compare the use of Foley catheters, misoprostol, and dinoprostone for cervical ripening in labor induction; the results showed that no method of labor induction revealed overall superiority when all outcomes (rates of failure to achieve vaginal delivery within 24 hours, incidence of uterine hyperstimulation with fetal heart rate changes, and rates of cesarean delivery) were considered, because the following results were found: (1) vaginal misoprostol is most likely to achieve vaginal delivery within 24 hours; (2) vaginal misoprostol is most likely to be the worst treatment for increased uterine hyperstimulation; and (3) Foley catheter is least likely to cause hyperstimulation, but is the worst treatment in achieving vaginal delivery within 24 hours.[10] However, it is interesting that the authors who conducted this systematic review and meta-analysis still suggested that oral misoprostol for the induction of labor is safer than vaginal misoprostol and has the lowest rate of cesarean delivery.[10] In fact, misoprostol has been recommended to be used for induction of labor by the World Health Organization (WHO) and the American College of Obstetricians and Gynecologists, but misoprostol remains unapproved for induction or labor.[4] Unlike misoprostol, dinoprostone is generally more acceptable and has been widely used for cervical ripening. Therefore, it is not surprising that Kansu-Celik and colleagues[9] used dinoprostone as an agent for induction of labor in their study published in this issue of the *Journal of Chinese Medical Association*.

The study by Kansu-Celik and colleagues[9] investigated 40 pregnant women, with a singleton live cephalic presentation between 37 and 42 gestational weeks, intact amniotic membrane, oligohydramnios, reassuring fetal heart rate, and unfavorable uterine cervix (Bishop score $\leq$ 5) without other remarkable obstetric or surgical history. These women visited

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the Sekai Tahir Burak Women's Health, Research, and Education Hospital between April 2009 and August 2009. Kansu-Celik and colleagues[9] attempted to evaluate the efficacy and safety of dinoprostone for cervical ripening and labor induction in pregnant women with term oligohydramnios and unfavorable uterine cervix.[9] In the same study, 64 pregnant women with normal amniotic fluid index were included as controls.[9] The results showed that there was no statistically significant difference in induction time to delivery between the two groups, and the perinatal and neonatal outcomes were also similar between the two groups.[9] Therefore, Kansu-Celik and colleagues[9] concluded that dinoprostone is a safe alternative for induction of labor in women with oligohydramnios with term pregnancies. This study reconfirmed the safety of dinoprostone; however, fetal distress manifested more frequently in the oligohydramnios group than in the normal control group (20% vs. 4.7%), contributing to a higher cesarean delivery rate in the oligohydramnios group, although uterine hyperstimulation occurred in 10% (4/40) of pregnant women with oligohydramnios. In fact, neonatal intensive care unit admission within 24 hours after delivery was also higher in the oligohydramnios group (7.5% vs. 3.1%). Therefore, the use of vaginal dinoprostone for induction of labor in women with oligohydramnios at term might be applied overenthusiastically. Kansu-Celik and colleagues[9] might overlook the potential risk if dinoprostone is used as an agent for labor induction for pregnant women with oligohydramnios at term. We would encourage researchers to replicate this study in a future investigation[9] to reevaluate the safety and effectiveness of either prostaglandin E1 or E2 for cervical ripening and labor induction in pregnant women who need induction of labor, regardless of whatever indication is noted.

Conflicts of interest

The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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