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Induction of labour in the third trimester: review of outcomes with intravaginal misoprostone gel at a rural hospital in British Columbia

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Objective: To evaluate the efficacy and safety of intravaginal misoprostol for induction of labour in the third trimester at a rural northern British Columbia community hospital where misoprostol was used for such purposes up until September 2001. The evaluation was done by examining the need for tocolysis, the need for oxytocin augmentation, the incidence of failed induction, the incidence of uterine rupture, and the neonatal Apgar score. Results were compared with those of an historical group that underwent induction of labour using dinoprostone gel.

Design: Retrospective chart audit of the method of induction of labour, the need for intervention, and outcomes.

Setting: A 64-bed community hospital where approximately 480 babies per year are delivered.

Patients: 162 women who had induction of labour with intravaginal misoprostol between Jan. 1 and Dec. 31, 1998, and 60 women who had induction of labour with dinoprostone gel between Jan. 1 and Dec. 31, 1995.

Outcome measurements: The need for tocolysis, the need for oxytocin augmentation, the incidence of failed induction (cesarean section) and neonatal Apgar scores.

Results: Tocolysis was required by one woman in the dinoprostone group and none in the misoprostol group. The percentage of women who required augmentation was the same in the 2 groups (11.7%). The incidence of failed induction was lower in the misoprostol group (12.3% v. 16.7%), but this was not statistically significant. The median neonatal Apgar score at 5 minutes was 10 in both groups.

Conclusions: Experience at Fort St. John Hospital & Health Centre suggests that intravaginal administration of misoprostol is a reliable and safe method of induction of labour in the third trimester. The large body of supportive evidence could be used to promote the licensing of misoprostol for this indication.

Objet : Évaluer l'efficacité et l'innocuité du misoprostol intravaginal pour déclencher le travail au cours du troisième trimestre dans un hôpital communautaire rural du nord de la Colombie-Britannique où l'on a utilisé le misoprostol à ces fins jusqu'en septembre 2001. On a effectué l'évaluation en examinant le besoin de tocolyse, le besoin d'augmenter l'oxytocine, l'incidence d'inductions infructueuses, l'incidence de ruptures de l'utérus et l'indice d'Apgar des nouveau-nés. On a comparé les résultats à ceux d'un groupe historique de patientes chez lesquelles on a déclenché le travail au moyen d'un gel de dinoprostone.

Concept : Vérification rétrospective des dossiers portant sur la méthode d'induction du travail, le besoin d'intervention et les résultats.

Contexte : Hôpital communautaire de 64 lits où quelque 480 bébés naissent chaque année.

Patientes : Cent soixante-deux femmes chez lesquelles on a déclenché le travail au moyen de misoprostol intravaginal entre le 1er janvier et le 31 décembre 1998, et 60 femmes chez lesquelles on l'a provoqué au moyen de dinoprostone entre le 1er janvier et le 31 décembre 1995.

Mesures de résultats : Le besoin de tocolyse, le besoin d'augmenter l'oxytocine, l'incidence d'inductions infructueuses (césariennes) et les indices d'Apgar des nouveau-nés.

Résultats : Il a fallu une tocolyse chez une femme du groupe de celles qui ont reçu la dinoprostone et chez aucune de celles qui ont reçu le misoprostol. Le pourcentage des femmes chez lesquelles il a fallu augmenter la dose a été le même dans les deux groupes (11,7 %). L'incidence d'inductions infructueuses a été moins élevée chez celles qui ont reçu du misoprostol (12,3 % c. 16,7 %), mais elle n'était pas significative sur le plan statistique. L'indice d'Apgar médian des nouveau-nés à cinq minutes s'établissait à 10 dans les deux groupes.

Conclusions : L'expérience du Fort St. John Hospital & Health Centre indique que l'administration intravaginale de misoprostol constitue une façon fiable et sans danger de déclencher le travail au cours du troisième trimestre. La masse importante de données d'appui pourrait servir à promouvoir l'autorisation du misoprostol pour cette indication.

Introduction

Misoprostol, a synthetic analogue of prostaglandin E1, is approved in Canada only for the

prevention and treatment of nonsteroidal anti-inflammatory drug-induced gastroduodenal ulcers and the treatment of duodenal ulcers caused by peptic ulcer disease.1 However, because of its uterotonic and cervical-ripening activity it has gained widespread use in obstetrics, and clinical studies support this use.2 Using the US Preventive Services Task Force classification, misoprostol 25 µg intravaginally every 4–6 hours is graded as A for efficacy (good and consistent scientific evidence to support the recommendation) and C for safety (rare adverse outcomes).2 Indeed, the use of misoprostol for induction of labour had become so standard that in 1999 the Obstetric Practice Committee of the American College of Obstetricians and Gynecologists (ACOG) issued an opinion and a practice guideline regarding the appropriate use of misoprostol for this indication.3 Sanchez-Ramos and Kaunitz4 performed a meta-analysis of randomized, controlled trials of cervical ripening and induction of labour (5735 women in the misoprostol group and 2945 in the control group, who received placebo, oxytocin, dinoprostone gel, or other) and found that the mean time to delivery was shorter, augmentation was required less frequently, and the rate of cesarean section was lower in the misoprostol group.

Reports of adverse events, specifically uterine rupture, associated with the off-label use of misoprostol in pregnant women prompted discussions between the US Food and Drug Administration (FDA) and G.D. Searle, the manufacturer of Cytotec® (misoprostol) tablets; Searle subsequently issued a letter in August 2000 to obstetricians and other physicians stating that misoprostol should not be administered to any pregnant woman and, specifically, that it was not approved for the induction of labour or abortion.3 This raised great concern among administrators, doctors, nurses and pharmacists regarding litigation. In response, the ACOG reaffirmed to its members that use of misoprostol for cervical ripening and induction of labour is safe and effective when used appropriately. Searle has responded that it does "support the role of physicians, using their professional judgement, to prescribe an approved pharmaceutical product for a use outside of its FDA-approved indication in the best interest of their patients."5 The Society of Obstetricians and Gynaecologists of Canada (SOGC) currently has no position paper regarding induction of labour.

Misoprostol tablets have been used intravaginally for induction of labour in the third trimester for over 7 years at Fort St. John Hospital & Health Centre. Based on legal advice from the BC Health Care Risk Management Society, the Continuing Quality Improvement Committee at our hospital stopped the use of misoprostol for this indication in September 2001. The perception of the physicians who commonly prescribed misoprostol tablets intravaginally for induction of labour and the maternity nurses who monitored the patients, is that this method is more effective than dinoprostone gel (i.e., shorter time to delivery and less frequently requiring oxytocin augmentation) without additional adverse effects.

We performed a retrospective chart review of induction of labour in the third trimester using intravaginal misoprostol in 1998, focussing on the need for tocolysis, the need for oxytocin augmentation, the incidence of failed induction, the incidence of uterine rupture, and the neonatal Apgar scores. We compared the results with induction of labour using dinoprostone gel in 1995.

Methods

Study site

Fort St. John Hospital & Health Centre is a 64-bed community hospital. The city of Fort St. John, BC, has a population of approximately 16 000 and serves as the regional referral centre for the entire North Peace region of BC (pop. 31 000). There is a high birth rate per capita (15.9/1000), with approximately 480 babies delivered each year. Between 1995 and 1998 there was a turnover of the obstetrician and of 3 of the 10 family practitioners who practised obstetrics

Study population

Contraindications to induction through the use of misoprostol include transverse lie, absolute cephalopelvic disproportion, placenta previa, active genital herpes, presence of uterine scar, and vaginal birth after cesarean section (VBAC). Contraindications to dinoprostone gel include all of these except VBAC, although recent evidence raises concerns about even its use in the presence of a uterine scar.6

A retrospective chart review was performed to identify all women who had induction of labour in the third trimester by intravaginal use of misoprostol tablets between Jan. 1 and Dec. 31, 1998. Similarly, a retrospective chart review was conducted to identify all women who had induction through the use of dinoprostone gel between Jan. 1 and Dec. 31, 1995. The year 1998 was chosen because we initially decided in 1999 to look at our use of misoprostol, and 1995 was chosen as the historical control because it was the closest year chronologically during which dinoprostone was predominantly used. The need for tocolysis, the need for oxytocin augmentation, the incidence of failed induction, the incidence of uterine rupture, and the neonatal Apgar scores were noted for each woman.

Table 1 contains the standard procedures at Fort St. John Hospital & Health Centre for the use of misoprostol (instituted in 1996) and dinoprostone gel for induction of labour.

Statistics

The need for tocolysis was compared using Fisher's exact test, and the need for oxytocin augmentation was compared using the chi-squared test.

Results

Study population

There were a total of 481 deliveries in 1995 and 484 deliveries in 1998. During 1995, 133 women had induction of labour: 60 received dinoprostone gel, 22 received intravaginal misoprostol and 51 received intravenous oxytocin alone. During 1998, 188 women had induction of labour: 162 received intravaginal misoprostol and 26 received intravenous oxytocin alone.

The mean patient age was 27.1 years in the dinoprostone group (year studied, 1995) and 26.2 (range 35–42) years in the misoprostol group (year studied, 1998). The mean gestational age in both groups was 41 (range 36–42) weeks, and the most common reason for induction was because term had been exceeded. The median number of misoprostol tablets used was 1 (range 1 to 4). The total number of doses of dinoprostone gel was not captured. Results are summarized in Table 2. The need for tocolysis was not significantly different (Fisher's exact test, $p = 0.27$). The need for augmentation was the same in the 2 groups ($\chi^2 = 0.0$, $p = 0.99$). Although not statistically significant ($\chi^2 = 0.7$, $p = 0.040$), failed induction was less common in the misoprostol group (12.3% v. 16.7%) and 1- and 5-minute neonatal Apgar scores were similar in the 2 groups (median = 9 at 1 min, median = 10 at 5 min).

Discussion

A limitation of our study is its retrospective nature and the use of an historical control group. The misoprostol and dinoprostone populations were similar with respect to mean patient age and reason for induction. Other variables such as patient weight and Bishop's scores could not be compared because they were not consistently recorded.

For the total obstetric population, there was a higher rate of induction in 1998 compared to 1995. We suspected that this was because in March of 1997, the SOGC published a Clinical Practice Guideline recommending that women with an uncomplicated pregnancy who reach 41 to 42 weeks gestation should be offered elective delivery.7 However, the fact that the median gestational age was the same in the 2 groups does not support this.

The medical staff was similar between the 2 time periods so any differences in individual practices should not have influenced the outcome.

Our experience suggests a low incidence of adverse effects when misoprostol is used for induction of labour. In their 2000 review, Sanchez-Ramos and Kaunitz noted an incidence of uterine hyperstimulation in 5.8% of the misoprostol groups and 3.4% of controls.4 Thus we were expecting to see the number of cases of hyperstimulation in our groups to be in the vicinity of 9 for the misoprostol group and 2 for the dinoprostone group. Our numbers do not concur with reports of hyperstimulation associated with misoprostol and, in fact, our anecdotal experience locally is that the use of dinoprostone has required more tocolysis for hyperstimulation than misoprostol has.

Rowlands and coworkers conducted a multicentre, prospective, randomized, controlled trial comparing intravaginal dinoprostone (n = 63) with intravaginal misoprostol 100 µg (n = 63) and found a significantly shorter mean time from insertion of priming agent to vaginal delivery and shorter duration of active labour in the misoprostol group.8 Moreover, women who received misoprostol were less likely to need a second dose of prostaglandin or oxytocin for augmentation of labour. Neonatal outcome was similar in the 2 groups.

The main reason Searle elaborated its warning regarding off-label use of misoprostol was in response to reports of uterine rupture associated with its use. Uterine rupture appears to be a particular concern in cases where there is a uterine scar.9 Because previous cesarean section was a contraindication to its use in our hospital, this was not seen as a concern. The meta-analysis performed by Sanchez-Ramos and Kaunitz suggests that there is a higher incidence of hyperstimulation when using 50 µg as compared to 25 µg;4 however, we have found the 50-µg dose to be well tolerated. This may be because we practise relatively low-risk obstetrics and the patients selected for induction with misoprostol are generally low-risk patients being induced for post dates. We believe that our experience supports the usefulness of misoprostol in the rural setting, as this is predominantly the type of obstetrics being practised.

Cost is a concern with any treatment. Compared to dinoprostone gel, misoprostol tablets are cheaper in terms of drug acquisition price. The cost of half of a misoprostol 100-µg tablet is 13.6 cents versus $44.79 and $53.85 for the 1- and 2-mg doses of dinoprostone gel, respectively.

In our study, more women in the dinoprostone group required cesarean section. The meta-analysis by Sanchez-Ramos and Kaunitz supports this finding.4 Although only misoprostol and dinoprostone inductions were examined in the study, the number of inductions initiated solely with oxytocin was noted. In 1998, fewer women received oxytocin as the initial drug for induction (26/188 in 1998 v. 51/133). We speculate that this is because as physicians gained more experience with misoprostol they perceived it to be a more effective method of labour induction requiring less intensive nursing care. Thus, although the use of oxytocin augmentation was similar in the 2 groups, the overall use of oxytocin in 1998 was much lower than in 1995.

Conclusions

The warning by Searle and the subsequent advice from the BC Health Care Risk Management Society, while understandable, is disappointing and a concern to the staff of Fort St. John. It has been our experience that the use of intravaginal misoprostol has been a safe and useful method of induction of labour. The restriction of its use for this has significant implications for rural hospitals the size of ours, as it inevitably will lead to the use of more oxytocin and more failed inductions with the subsequent problems of decreased patient satisfaction and increased drug acquisition, staffing and operating room costs. There is a large body of evidence supporting the safe use of misoprostol for the induction of labour and this should be used to promote the licensing of misoprostol for this indication.

Competing interests: None declared.

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for induction of labour.

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