

Early Amniotomy Shortens Labor in Nulliparas

BY SUSAN LONDON

FROM THE ANNUAL MEETING OF
THE SOCIETY FOR MATERNAL-FETAL
MEDICINE

SAN FRANCISCO – Early amniotomy appears safe and efficacious for shortening labor at term in nulliparous women having an indication for labor induction, according to results of a randomized controlled trial.

Among the 585 women studied, the average time from induction to delivery was 2.3 hours, or 11% shorter with early amniotomy vs. standard care, investigators reported at the meeting. This benefit was achieved without an increase in rates of maternal or neonatal infections.

“Based on this clinical trial, it would seem that early amniotomy may be a useful adjunct for nulliparous labor inductions,” said Dr. George A. Macones,

the Mitchell and Elaine Yanow Professor and chair of the department of ob.gyn. at Washington University in St. Louis.

Many studies have evaluated different methods of labor induction, he noted. “However, surprisingly, there are very few data on the timing of amniotomy in labor induction and how this may improve or worsen outcomes.”

Amniotomy is easy and inexpensive and may shorten labor, according to Dr.

Macones. But it also may be associated with rare complications such as umbilical cord prolapse, and possibly with an increased infection risk resulting from a longer duration of ruptured membranes.

Women were eligible for the trial if they were nulliparous, had a singleton pregnancy, were at term (37 weeks’ gestation or later), and needed induction as determined by their treating physician. They were excluded if they were HIV positive or had cervical dilatation exceeding 4 cm at the time of admission to labor and delivery.

The women were randomly assigned in a 1:1 ratio to nonblinded management with either early amniotomy (defined as artificial rupture of membranes

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DR. MACONES

performed when cervical dilatation was equal to or less than 4 cm) or standard care (defined as artificial rupture of membranes performed when cervical dilatation was greater than 4 cm). The primary method of induction (misoprostol, cervical Foley catheter, oxytocin, and/or prostaglandin gel) was left to the treating physician’s discretion. “Just to be clear, we did not study the timing of amniotomy as a primary method of induction, but rather as an adjunct to other methods,” Dr. Macones noted.

All other decisions about intrapartum and postpartum care were similarly left up to the treating physicians. The 585 women randomized were 23 years old on average, and the majority (70%) was black. Almost a third had gestational hypertension or preeclampsia, and another third were positive for group B streptococcus. The mean gestational age was about 39.5 weeks, and the mean cervical dilatation was 1.1 cm on admission. The leading indications for induction were a gestation past 40 weeks (39%) and gestational hypertension or preeclampsia (28%).

The primary methods of induction used were similar across groups. In nearly three-fourths of women, the treating physicians used multiple methods.

Most women received epidural analgesia, with no difference between groups, according to Dr. Macones.

Median cervical dilatation at the time of rupture of membranes was 4 cm less in the early amniotomy group, compared with the standard care group (3.0 vs. 7.0 cm; $P = .001$). In intent-to-treat analyses, the time from induction to delivery was 2.3 hours shorter with early amniotomy (19.0 vs. 21.3 hours; $P = .004$). “This difference in the length of labor occurred mainly and not surprisingly in the first stage of labor, but not in the second stage,” Dr. Macones noted. In addition,

Continued on following page

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• XERESE is indicated for the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and adolescents (12 years of age and older).

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• Topically apply XERESE 5 times per day for 5 days. Therapy should be initiated as early as possible after the first signs and symptoms (i.e., during the prodrome or when lesions appear). • For each dose, topically apply a quantity of XERESE sufficient to cover the affected area, including the outer margin. Avoid unnecessary rubbing of the affected area to avoid aggravating or transferring the infection. For adolescents 12 years of age and older, the dosage is the same as in adults.

WARNINGS AND PRECAUTIONS

General: • XERESE is intended for cutaneous use only for herpes labialis of the lips and around the mouth. XERESE should not be used in the eye, inside the mouth or nose, or on the genitals. • There are other orofacial lesions, including bacterial and fungal infections, which may be difficult to distinguish from a cold sore. Patients should be encouraged to seek medical advice when a cold sore fails to heal within 2 weeks. • XERESE has a potential for irritation and contact sensitization [see *Adverse Reactions*].

ADVERSE REACTIONS

Overall Adverse Reaction Profile: • The safety data derived from XERESE clinical studies reflect exposure to XERESE in 1002 subjects with recurrent herpes labialis treated 5 times daily for 5 days. The majority of the adverse reactions were local skin reactions and occurred in the area of the application site.

Adverse Reactions in Clinical Studies: • Because clinical studies are conducted under widely varying conditions, the adverse reaction rates observed cannot be directly compared to rates in other clinical studies and may not reflect the rates observed in clinical practice. The majority of the adverse reactions were local and occurred in the area of the application site.

Skin and Subcutaneous Tissue Disorders: • The following most common adverse reactions (<1%) were local skin reactions and occurred in the area of the application site: Drying or flaking of the skin; burning or tingling following application; erythema; pigmentation changes; application site reaction including signs and symptoms of inflammation. • Contact dermatitis following application has been observed when applied under occlusion in dermal safety studies. Where contact sensitivity tests have been conducted, the reactive substances were hydrocortisone or a component of the cream base. • A study enrolling 225 healthy adults was conducted to evaluate the contact sensitization potential of XERESE using repeat insult patch testing methodology. Of 205 evaluable subjects, one confirmed case (0.5%) of sensitization to hydrocortisone and 2 additional cases (1.0%) of possible sensitization to the XERESE base were identified. Additionally, one subject developed a contact allergy in the photosafety study to propylene glycol, one of the inactive ingredients of the cream base. • Dermal tolerance was assessed in a 21-day cumulative irritation study in 36 healthy subjects. XERESE, its cream base, and Zovirax® (acyclovir) Cream 5% all showed a high and cumulative irritation potential under occlusive and semi-occlusive conditions. Photoallergic potential and phototoxicity were assessed in two studies in 50 and 30 healthy volunteers, respectively. No photoallergic or phototoxicity potential was identified for XERESE.

DRUG INTERACTIONS

• No drug interaction studies have been performed with XERESE.

USE IN SPECIFIC POPULATIONS:

Pregnancy Category B

Teratogenic Effects: • Acyclovir was not teratogenic in the mouse, rabbit, or rat at exposures greatly in excess of human exposure. There are no adequate and well-controlled studies of systemic acyclovir in pregnant women. A prospective epidemiologic registry of acyclovir use during pregnancy between 1984 and 1999 followed 749 pregnancies in women exposed to systemic acyclovir during the first trimester of pregnancy resulting in 756 outcomes. The occurrence rate of birth defects approximated that found in the general population. However, the size of the registry was insufficient to evaluate the risk for less common defects or to permit reliable or definitive conclusions regarding the safety of acyclovir in pregnant women and their developing fetuses. • Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. • Animal reproduction studies have not been conducted with XERESE. No studies have been performed in pregnant women. Systemic exposure of acyclovir and hydrocortisone following topical administration of XERESE is minimal.

Nursing Mothers: • It is not known whether topically applied acyclovir or hydrocortisone is excreted in breast milk. Systemic exposure following topical administration of either drug is expected to be below detection limits. Because many drugs are excreted in human milk, caution should be exercised when XERESE is administered to a nursing woman.

Pediatric Use: • Safety and effectiveness in pediatric subjects less than 12 years of age have not been established.

Geriatric Use: • In clinical studies, there were insufficient subjects above 65 years of age to reach a firm conclusion regarding safety and efficacy of XERESE in this group, although the available results were similar to lower age subjects.

Immunocompromised Subjects: • Even though the safety of XERESE has been studied in immunocompromised subjects, data are insufficient to support use in this population. Immunocompromised subjects should be encouraged to consult a physician concerning the treatment of any infection. • Benefit has not been adequately assessed in immunocompromised patients. • A randomized, double-blind study was conducted in 107 immunocompromised subjects with stable HIV infection and recurrent herpes labialis. Subjects had, on average, 3.7 episodes of herpes labialis in the previous 12 months. The median age was 30 years (range 19 to 64 years), 46% were female, and all Caucasian. Median CD4+ T-cell count at screening was 344/mm³ (range 100–500/mm³). Subjects were treated with XERESE or 5% acyclovir in XERESE vehicle. The primary objective was to exclude a doubling of the healing time in either treatment arm. The mean healing time for cold sores was similar between the two treatment groups: 6.6 days for XERESE and 6.9 days for 5% acyclovir in XERESE vehicle.

OVERDOSAGE

• Overdosage by topical application of XERESE is unlikely because of minimal systemic exposure [see *Clinical Pharmacology–Pharmacokinetics*].



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Universal MRSA Screening at L&D: Little Benefit

BY NEIL OSTERWEIL

FROM THE INTERSCIENCE CONFERENCE
ON ANTIMICROBIAL AGENTS AND
CHEMOTHERAPY

BOSTON – Active surveillance testing for methicillin-resistant *Staphylococcus aureus* colonization of pregnant women who were admitted to labor and delivery units costs a lot of bucks for only a little bang.

Over a 20-month period, a universal methicillin-resistant *S. aureus* (MRSA) screening program, required by Illinois law, cost \$90,950 but had no apparent impact either on MRSA disease in the postpartum period or on nosocomial MRSA infections in a postpartum ward and newborn nursery, said Naseem Helo, a fourth-year medical student at Loyola University Medical Center in Maywood, Ill.

Continued from previous page

these women were more likely to deliver within 24 hours of labor induction (68% vs. 56%; $P = .002$).

The early amniotomy group did not differ significantly from the standard care group with respect to rates of cesarean delivery (41% vs. 40%), cord prolapse (0.7% vs. 0%), and abruption (0.4% vs. 0.6%).

Fetal heart rate data were not analyzed, but rates of amnioinfusion (a “reasonable proxy” for variable decelerations) were similar, according to Dr. Macones.

The two groups also had statistically indistinguishable rates of infectious outcomes, including chorioamnionitis (11.5% vs. 8.5%) postpartum fever (10.4% vs. 9.4%) in the mother, and NICU admission (13.6% vs. 15.0%) and suspected or confirmed sepsis (9.7% vs. 11.1%) in the neonate.

In questions posed after the presentation, one attendee asked how the 4-cm threshold was selected for early amniotomy, and whether the findings would be similar with, say, a 2-cm threshold instead. “We chose 4 cm based on some earlier work in spontaneous labor with rupturing membranes,” Dr. Macones explained. “I agree that we could dial that down a bit.” However, within the early amniotomy group, the efficacy and safety findings appeared similar regardless of the timing of the procedure, he said.

When asked if the study was mixing cervical ripening with labor induction, Dr. Macones said, “I think the lines between ripening and induction are actually quite gray.” He contended that the study’s aim was to assess the impact of amniotomy when the intention was to perform it as early as possible.

An alternative approach would be to look at women once their cervix is ripened and then ask what the role of amniotomy is, he acknowledged. “But I think that’s a little bit different question than we actually had.”

Dr. Macones did not report any relevant financial disclosures. ■

Among 2,254 pregnant women who were admitted to the labor and delivery unit, 1,819 (81%) received a nasal MRSA test at a cost of \$50 each and 39 women (2%) screened positive, for a cost of more than \$2,300 per positive screen, Mr. Helo said at the meeting, which was sponsored by the American Society for Microbiology.

Of the 39 MRSA-colonized women, 13 went on to have a cesarean section, 21

had vaginal delivery, 2 had miscarriages, and 3 were lost to follow-up because they did not deliver at the center.

When investigators looked at the effect of the positive results on practice, they found that although 9 of 13 (69%) women who had cesareans had positive test results available before the surgery, only 3 of the 9 (33%) received vancomycin prophylaxis.

“During the newborn stay, no new-

borns had complications of MRSA disease, and there were no nosocomial infections in our labor and delivery service, postpartum ward, and newborn nursery during the 20-month study period or 2 years prior to the study,” Mr. Helo said.

The investigators suggested that the decision to implement universal MRSA surveillance should be driven by MRSA colonization rates in specific geographic populations. ■

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Reference: 1. Sinatra RS, Jahr JS, Reynolds LW, Viscusi ER, Groudine SB, Payen-Champenois C. Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery. *Anesthesiology*. 2005;102:822-831.

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