

Nitrous Oxide Underused in U.S. for Labor Pain

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — A simple technique to help manage labor pain is used commonly in the United Kingdom, Scandinavia, and Canada, but is offered to few U.S. women—nitrous oxide, or so-called “laughing gas.”

Administered as a 50/50 blend of oxygen and nitrous oxide, the gas has proved safe for mothers, their babies, and health care personnel in the vicinity of use, Judith T. Bishop said at a meeting on antepartum and intrapartum management sponsored by the University of California, San Francisco.

Simple and fast, nitrous oxide is particularly useful through the second stage of labor for multiparous women who arrive too late to get an epidural.

It's relatively weak as an analgesic, yet useful. One woman who delivered at the university described how it felt to use nitrous oxide during labor by saying, “It still hurts, but I don't care,” recalled Ms. Bishop, a certified nurse-midwife

and professor of ob.gyn. and reproductive sciences at the university.

“I've heard that more than once. It's not too dissimilar from some reports from women who are using nonpharmacologic methods,” she noted. “They may have rated their pain somewhat highly, but their satisfaction and their ability to cope was improved.”

Her institution has large holding tanks of oxygen and nitrous oxide that get piped into every labor and delivery room. Three cables control the flow—one for each gas, and one to scavenge the gas from the environment and remove it from the room.

The mother controls the application of the gas. She's given a mask and some instructions on its use by the anesthesiologist, midwife, or obstetrician, with ongoing supervision by a nurse. The full effect of nitrous oxide can be felt in 50 seconds.

Because it's simple and fast to start or stop, nitrous oxide is particularly useful through the second stage of labor for multiparous women who arrive in time to deliver but too late to get an epidural, she said. Nitrous oxide also can be used dur-

ing perineal repair of women who didn't get an epidural.

Very few U.S. medical centers offer nitrous oxide during labor, for reasons that are unclear. “Many, many places are asking us for information about nitrous oxide. We have a protocol for nurses and certified nurse-midwives to administer” nitrous oxide, Ms. Bishop said. The University of Washington is the only other medical center that she knows of that offers nitrous oxide for labor pain.

Dr. Mark A. Rosen, director of obstetric anesthesia at the university and author of a review of nitrous oxide during labor, said in an interview that he has taken informal polls while lecturing at other institutions and conferences. When he asks how many physicians have nitrous oxide available during deliveries at their hospitals, he said, very few raise their hands.

His systematic review of 11 randomized controlled trials of nitrous oxide for labor pain reported that more than half of la-

boring women in the United Kingdom and Finland use nitrous oxide, which is widely employed and considered safe in Canada, Australia, New Zealand, and many other parts of the world when supervised by physicians, nurses, or midwives (*Am. J. Obstet. Gynecol.* 2002;186:S110-26).

He also assessed eight controlled trials and eight observational studies for potential adverse outcomes and performed a nonsystematic review of studies on occupational exposure. Potential side effects

SHE'S BEEN SEARCHING FOR A HORMONE THERAPY THAT SUITS HER

ACTIVELLA is a registered trademark of Novo Nordisk FemCare AG.

www.activella.com

© 2007 Novo Nordisk Inc.
132182 June 2007 Printed in the U.S.A.

FDA Has Consumer Health Web Page

The U.S. Food and Drug Administration has launched a Web page, Consumer Health Information for You and Your Family (www.fda.gov/consumer), and a related e-newsletter, FDA Consumer Health Information (www.fda.gov/consumer/consumernews.html). The Web page provides links to information about the various products that FDA regulates, including food, human and animal drugs, medical devices, and vaccines. The e-newsletter replaces the agency's print magazine. ■

from nitrous oxide include maternal nausea, vomiting, or poor recall of labor, but it does not seem to affect the fetus, as seen with narcotics.

"Nitrous oxide is not a potent labor analgesic, but it is safe for parturient women, their newborns, and health care workers in attendance during its administration. It appears to provide adequately effective analgesia for many women," he concluded.

An estimated 6% of U.S. women in labor used nitrous oxide in the decade leading up to 1986, but by the 1990s the use of nitrous oxide in labor had nearly disappeared in the United States, his report

noted. "I really don't understand why this simple but weakly effective analgesic doesn't have more use in the United States," Dr. Rosen said.

Ms. Bishop suggested that habit and tradition have more to do with its use than science. "We develop our own routines within practices, institutions, and countries. It is really not in most cases about what's 'right' or 'best,' just what the decision-makers decide," she said.

Before she and Dr. Rosen arrived at the university, the director of obstetric anesthesia was an Englishman.

"I imagine he had good experience with nitrous oxide and was comfortable with

it," she speculated. Dr. Rosen trained under his predecessor and also spent some time in England.

A midwife colleague at the University of Michigan told Ms. Bishop that use of nitrous oxide for labor started in Michigan in 1978 when a British physician became chair of obstetric anesthesia. "Its use became quite popular," but the chair's successor in 1995 removed it as an option, she said.

"We tend in the United States to go with the higher-tech approach to health care—doctors, not midwives, and epidurals, not nitrous oxide—dropping off lower-tech options even though they may still serve a purpose," Ms. Bishop noted.

Market forces also may play a role in the demise of U.S. use of nitrous oxide for labor, midwife and epidemiologist Judith Rooks suggested in a recent editorial (*Birth* 2007;34:3-5). "Obstetric use of nitrous oxide in America is similar to that of any older, inexpensive, off-patent, unglamorous, safe and reasonably effective but not highly potent drug. Nitrous oxide is like an 'orphan' drug—little known outside of dentistry, lacking elan and pizzazz, with no companies or influential professional groups that stand to profit by its greater use," she wrote.

"There is no 'nitrous lobby,'" Ms. Bishop added. ■

YOU'VE BEEN SEARCHING FOR ONE THAT'S A GOOD FIT ALL AROUND

Introducing **ACTIVELLA® 0.5 mg/0.1 mg**—
a new lower-dose hormone therapy option*

Now there is a hormone therapy
that may suit you both

You can provide what her body is missing with what you want for her in a hormone therapy.

- The lowest 17 β -estradiol and norethindrone acetate (NETA) combination commercially available
 - 50% less 17 β -estradiol*
 - 80% less NETA*
- An estrogen identical to the one her body once made^{1,2}
- Rapid relief from moderate to severe vasomotor symptoms within 3 to 4 weeks^{1,3}
- Similar bleeding profile when compared with placebo^{1,3,4}
 - 88% of women were amenorrheic after 6 months^{1,4}
- Favorable tolerability and safety^{1,3,4}
 - Clinical symptoms of breast discomfort, breast pain, and breast tenderness were similar to those with placebo after 6 months⁴
 - FDA approved as safe and effective

Activella 0.5 mg/0.1 mg is indicated in women who have a uterus for the treatment of moderate to severe vasomotor symptoms associated with menopause and the prevention of postmenopausal osteoporosis. When prescribing solely for the prevention of postmenopausal osteoporosis, therapy should only be considered for women at significant risk of osteoporosis and non-estrogen medications should be carefully considered.

0.5 mg/0.1 mg
ACTIVELLA®
(estradiol/norethindrone acetate) tablets

NEW LOWER DOSE*

*When compared with ACTIVELLA 1.0 mg/0.5 mg.

IMPORTANT SAFETY INFORMATION

Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Dementia in prescribing information.)

The estrogen plus progestin substudy of the Women's Health Initiative (WHI) reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thrombosis in postmenopausal women (50 to 79 years of age) during 5.6 years of treatment with oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) per day, relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders and Malignant neoplasms, *Breast cancer* in prescribing information.)

The estrogen-alone substudy of the WHI reported increased risks of stroke and deep vein thrombosis (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with oral conjugated estrogens (CE 0.625 mg) per day, relative to placebo. (See CLINICAL STUDIES and WARNINGS, Cardiovascular disorders in prescribing information.)

The Women's Health Initiative Memory Study (WHIMS), a substudy of the WHI study, reported increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 4 years of treatment with CE 0.625 mg combined with MPA 2.5 mg and during 5.2 years of treatment with CE 0.625 mg alone, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See CLINICAL STUDIES, WARNINGS, Dementia and PRECAUTIONS, Geriatric Use in prescribing information.)

Other doses of oral conjugated estrogens with medroxyprogesterone acetate and other combinations and dosage forms of estrogens and progestins were not studied in the WHI clinical trials and, in the absence of comparable data, these risks should be assumed to be similar. Because of these trials, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

Other warnings include: gallbladder disease, hypercalcemia, and visual abnormalities.

Activella should not be used in women with any of the following conditions: undiagnosed abnormal genital bleeding; known, suspected, or history of cancer of the breast; known or suspected estrogen-dependent neoplasia; active deep vein thrombosis, pulmonary embolism, or history of these conditions; active or recent (e.g., within the past year) arterial thromboembolic disease (e.g., stroke, myocardial infarction); liver dysfunction or disease; known hypersensitivity to the ingredients of Activella 0.5 mg/0.1 mg; known or suspected pregnancy.

In a clinical trial, the most commonly reported adverse events (reported at a frequency of $\geq 5\%$) were back pain, headache, pain in extremity, nausea, diarrhea, nasopharyngitis, endometrial thickening, and vaginal hemorrhage.

REFERENCES: 1. Activella [package insert]. Princeton, NJ: Novo Nordisk Inc; 2007. 2. Loose-Mitchell DS, Stancel GM. Estrogens and progestins. In: Hardman JG, Limbird LE, eds. *Goodman & Gilman's The Pharmacological Basis of Therapeutics*. 10th ed. New York, NY: McGraw-Hill; 2001:1598. 3. Panay N, Ylikorkala O, Archer DF, Gut R, Lang E. Ultra-low-dose estradiol and norethisterone acetate: effective menopausal symptom relief. *Climacteric*. 2007;10:120-131. 4. Data on file. CTR. Novo Nordisk Inc, Princeton, NJ.

Please see brief summary of prescribing information on following page.