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American Foundation for Maternal and Child Health

http://aimsusa.org

May 4, 2005

THE NATIONAL CHILDREN'S STUDY AS A RESOURCE FOR IMPROVING MATERNAL AND CHILD HEALTH

As many of you know the U.S. has the highest infant mortality rate in the industrialized world despite the millions of dollars poured into prenatal care in this country. While the incidence of prematurity has remained relatively constant throughout the industrialized countries the quality of life for those babies has not. We could improve the outcome of babies, especially those who are born prematurely, if we changed the direction obstetric care has taken over the last few decades.

Maternity care today in many obstetric services appears to be based more on making the mother comfortable and providing learning experiences for the resident, rather than what is best for the long term development of the baby. To my knowledge, most obstetric residents are not required to read the FDA approved labels of all the drugs being administered in their obstetric department- I'm sure most mothers would choose more physiologic means of reducing their discomfort or pain of labor if they understood the inherent risks and the areas of uncertainty regarding the drugs they are offered during labor and birth.

A recent national study carried out by the Maternity Center in New York found that most women received epidurals for the birth of their babies, and that most women were not made aware of the downside of epidural analgesia, i.e. fever in the mother that may require spinal puncture of the newborn to perform a septic workup, oxytocin to counteract dysfunctional labor resulting from the epidural, operative delivery with forceps or vacuum extractor, newborn jaundice requiring separation from her baby, etc. Pitocin was administered to augment contractions in 53% of the labors. Forty-four percent of the mothers were subjected to an induction of labor, and 86% of those mothers received oxytocin to stimulate labor.

Obstetricians, midwives and nurses who care for women during childbirth need to know that there is no obstetric related drug that has been proven safe for the neurologic development of the fetus. **There have been no adequate and well-controlled studies to determine the delayed, long-term effects of bupivacaine or any other epidural drug on pregnant women, or on the neurologic, as well as general, development of children exposed to the drug in utero or during lactation.**

The FDA has not even required such proof for the twelve drugs it has approved for obstetric use. The pharmaceutical companies who make bupivacaine, oxytocin, fentanyl, meperidine, methergine, ritodrine, sufentanil citrate, and terbutaline have removed their respective drugs from the PHYSICIANS DESK REFERENCE, the only source of drug labeling that must print the drug labels exactly as approved by the U.S. Food and Drug Administration.

The maker of naloxone does put the Narcan label in the PDR but states that the drug is not approved for use in obstetric care, and points out in the section covering off-label use that the drug is not effective against respiratory depression due to non-opioid drugs. So let's look at the manufacturer's label for the most commonly used drugs in obstetric care in the United States.

MARCAINE (bupivacaine hcl) **ABBOTT LABORATORIES**

FDA approved Marcaine for use in labor and delivery.

<u>All Information Has Been Omitted From The PDR</u>.

The FDA approved labeling for bupivacaine hcl (Marcaine) reads:

LABOR AND DELIVERY: Local anesthetics rapidly cross the placenta, and when used for epidural, caudal or pudendal block anesthesia, can cause varying degrees of maternal, fetal and neonatal toxicity... Adverse reactions in the parturient, fetus and neonate involve alteration of the central nervous system, peripheral vascular tone and cardiac function..."

Under "ADVERSE REACTIONS. Neurologic" the official labeling continues:

“Neurologic effects following epidural or caudal anesthesia may include spinal block of varying magnitude (including high or total spinal block); hypotension secondary to spinal block; urinary retention; fecal and urinary incontinence; loss of perineal sensation and sexual function; persistent anesthesia, paresthesia, weakness, paralysis of the lower extremities and loss of sphincter control all of which may have slow, incomplete, or no recovery; headache; backache; septic meningitis; meningismus; slowing of labor; increased incidence of forceps delivery; and cranial nerve palsies due to traction on nerves from loss of cerebrospinal fluid Neurologic effects following other procedures or routes of administration may include persistent anesthesia, paresthesia, weakness, paralysis, all of which may have slow, incomplete, or no recovery.”

Epidural analgesia can cause disruptions in normal uterine function that cannot always be completely corrected by the use of oxytocin. The package insert does not mention that such disruption can precipitate the need for forceps or vacuum extraction of the baby, or the use of fundal pressure (external pressure applied to the mother’s lower abdomen) to help push the baby out). Forceps and vacuum extraction carry risks to both mother and baby, as does fundal pressure. Fundal pressure increases the likelihood of uterine inversion, and that an episiotomy will be extended into a rectal tear. Fundal pressure has the potential to increase fetal intracranial pressure if the membranes have ruptured.

The incidence and degree of bupivacaine toxicity depends on the (a) procedure performed, (b) type and amount of drug used, (c) technique of drug administration (d) gestational age of the fetus, (e) condition of the fetus, (f) and previous and concomitant exposure to other drugs. Relative hypoxia and various pathological conditions can affect how a drug given to the mother will affect her fetus during labor, birth and the infant’s development following birth. Hypoxemia and a build up of lactic acid in the fetal blood during labor and birth can increase the uptake of a maternal drug by the fetal brain and heart.

Rosenblatt and her fellow investigators in Britain found that bupivacaine administered to the mother during labor can have prolonged adverse effects on the early development of the exposed offspring. The investigators concluded:

“Significant and consistent effects of bupivacaine throughout the assessment period can be demonstrated. Immediately after delivery, infants with greater exposure to bupivacaine in utero were most likely to be cyanotic and unresponsive to their surroundings. Visual skills and alertness decreased significantly with increases in the cord blood concentration of bupivacaine, particularly on the first day of life, but also throughout the next six weeks. Adverse effects of bupivacaine levels on the infant’s motor organization, his

ability to control his own state of consciousness and his physiological response to stress were also observed."

A similar investigation carried out by Sepkoski, Brazelton and colleagues supports the earlier findings of Rosenblatt et al.

A recent paper by Jevtovic-Todorivic and colleagues published in Neuroscience, (2003;

23 (3); 876-882) entitled "Early exposure to common anesthetic agents caused

widespread neurodegeneration in the developing rat brain and persistent learning

deficits." The paper reads:

"Our data indicate that exposure of infant rats to a clinically relevant anesthesia protocol for 6 hr during synaptogenesis causes not only acute deletion of many neurons from the developing brain but also learning/memory disabilities that persist into adolescence and adulthood. Animals exposed to this anesthesia protocol displayed deficits in spatial reference memory capabilities as manifested by slower pace learning acquisition as juveniles and by significant impairments in both spatial reference and working memory as adults."

PITOCIN

PITOCIN has been approved by the FDA for the medical induction and stimulation of labor. Pitocin has not been approved for the elective induction or stimulation of labor.

All Information Has Been Omitted From The PDR.

Oxytocin crosses the placenta and enters the blood and brain of the fetus within seconds or minutes. There appears to be a correlation between fetal exposure to oxytocin and autism in the exposed offspring.

The manufacturer of oxytocin warns the provider in the package insert:

“Maternal deaths due to hypertensive episodes, subarachnoid hemorrhage, rupture of the uterus, fetal deaths and permanent CNS or brain damage of the infant due to various causes have been reported to be associated with the use of parenteral oxytocic drugs for induction of labor or for augmentation in the first and second stages of labor.”

Because oxytocin is used so commonly to stimulate labor we note here that, in addition to the more benign effects of uterine stimulants, such as nausea and vomiting, the manufacturer of Pitocin (oxytocin) points out in its package insert that oxytocin can cause:

(a) Maternal hypertensive episodes (abnormally high blood pressure)

(b) Subarachnoid hemorrhage (bleeding in area surrounding spinal cord)

(c) Anaphylactic reaction (exaggerated allergic reaction)

(d) postpartum hemorrhage (uterine hemorrhage following birth)

(e) Cardiac arrhythinias (non-normal heart rate)

(f) Fatal afibrinogenemia (loss of blood clotting fibrin)

(g) Premature ventricular contraction (non-normal heart function)

(h) pelvic hematoma (blood clot in the pelvic region)

(1) uterine hypertonicity (excessive uterine muscle tone)

(j) uterine spasm (violent, distorted contraction of the uterus)

(k) tetanic contractions (spasmodic uterine contractions)

(1) uterine rupture

(m) increased blood loss

(n) convulsions (violent, involuntary muscle contraction(s).

(o) coma (unconsciousness that cannot be aroused)

(p) fatal oxytocin-induced water intoxication (undue retention of water marked

by vomiting, depression of temperature, convulsions and coma and may end in death).

Fetal and Newborn Effects

The following adverse effects of maternally administered oxytocin have been reported in the fetus or infant:

(a) bradycardia (slow fetal heart rate)

(b) premature ventricular contractions and other arrhythmias (non-normal heart function)

(c) low 5 minute Apgar scores (non-physiologic neurologic evaluation)

(d) neonatal jaundice (excess bilirubin in the blood of the neonate.

(e) hemorrhage (hemorrhage within the innermost covering of the eyeball)

(f) permanent central nervous system or brain damage

(g) fetal death

Uterine stimulants which foreshorten the oxygen-replenishing intervals between contractions, by making the contractions too long, too strong, or too close together, increase the likelihood that fetal brain cells will die.

The situation is analogous to holding an infant under the surface of the water, allowing the infant to come to the surface to gasp for air, but not to breathe. All of these effects increase the possibility of neurologic insult to the fetus. No one really knows how often these adverse effects occur, because there is no law or regulation in any country which requires the doctor to report an adverse drug reaction to the FDA.

These findings underscore the importance of the midwife managing the woman’s labor in a way that will avoid the need for Pitocin and the pain relieving drugs that are often administered to help the woman cope with the contractions intensified by Pitocin.

DELAYED LONG TERM EFFECTS: There have been no adequate and well-controlled studies to determine the delayed, long-term effects of Pitocin on pregnant women, or on the neurologic, as well as general, development of children exposed to Pitocin in utero or during lactation.

For further information on drugs approved and non-approved by the FDA for use in obstetrics, see the American Foundation for Maternal and Child Health website:

http://aimsusa.org

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