

CaseMed-Pregnancy Resource Newsletter

September 2007

Codeine can be toxic to breastfed babies: FDA. CTV.ca, 2007; August 17

The U.S. Food and Drug Administration is warning that nursing babies may be at the risk of morphine overdose if their mothers take codeine and have a genetic mutation that makes them ultra-rapid metabolizers of the painkiller. The agency issued the warning Friday after reviewing information on the subject, including a medical journal report about the death of a 13-day old breastfed infant who died from morphine overdose. The morphine levels in the mother's milk were found to be abnormally high after taking small doses of codeine prescribed to treat pain for an episiotomy. A genetic test showed that the mother was an ultra-rapid metabolizer of codeine, meaning that her body metabolized codeine into morphine much faster and more completely than others. Mothers who are ultra-rapid metabolizers may have higher-than-usual levels of morphine in breast milk, risking a morphine overdose in their babies. Since many doctors are not aware of the risks of breastfeeding for ultra-rapid codeine metabolizers, the FDA is requiring manufacturers of prescription codeine medicines to include information about codeine ultra-rapid metabolism in drug package insert information.

ACOG Committee Opinion No.376: Nalbuphine hydrochloride use for intrapartum analgesia Committee on Obstetric Practice, American College of Obstetricians and Gynecologists Obstet Gynecol, 2007; 110(2 Pt. 1): 449

Safety concerns have been raised regarding the use of nalbuphine hydrochloride during labour. The American College of Obstetricians and Gynecologists find data are insufficient to recommend any changes in nalbuphine hydrochloride administration at this time.

Effects of multiple courses of antenatal betamethasone on the auditory brainstem responses of premature infants Church MW Pediatrics, 2007; 119(3): 450; author reply 450-1

Comments regarding the Amin and Guillet study from Pediatrics, 2007; 119(3): 502-8.

Managing Q fever during pregnancy: the benefits of long-term cotrimoxazole therapy Carcopino X, Raoult D, Bretelle F, et al Clin Infect Dis, 2007; 45(5): 548-55

This study compared the incidence of obstetric and maternal Q fever complications for pregnant women who received long-term cotrimoxazole treatment with that for women who did not receive long-term cotrimoxazole treatment. The researchers found that obstetrical complications (including intrauterine growth retardation, spontaneous abortions, intrauterine fetal death, premature delivery, and oligamnios) occurred in 81.1% of pregnant women who did not receive long-term cotrimoxazole therapy. The women who received long-term cotrimoxazole therapy were protected against maternal chronic Q fever, placental infection and obstetric complications

(especially intrauterine fetal death). In conclusion, the researchers recommend that long-term cotrimoxazole treatment should be used to treat pregnant women with Q fever.

Human granulocytic anaplasmosis during pregnancy: case series and literature review
Dhand A, Nadelman RB, Aguero-Rosenfeld M, et al
Clin Infect Dis, 2007; 45(5): 589-93

The authors describe the clinical and laboratory manifestations and pregnancy outcomes of six women who received a diagnosis of human granulocytic ehrlichiosis during pregnancy. All treated patients had excellent responses to rifampin or doxycycline therapy. Perinatal transmission was documented in one neonate, who responded well to treatment. There do not appear to be any long-term adverse sequelae in children born from these pregnancies.

The safety of antidepressant drugs during pregnancy
Källén B
Expert Opin Drug Saf, 2007; 6(4): 357-70

This article discusses known or suspected effects of maternal use of antidepressants during pregnancy on pregnancy outcome. According to the author, it is unlikely that any marked teratogenic effect occurs with the possible exception of an increased risk for cardiovascular defects after maternal use of clomipramine or paroxetine. An increased risk for preterm birth is seen as well as transient neonatal symptoms after the use of antidepressants in late pregnancy. Selective serotonin re-uptake inhibitor drugs seem to represent a smaller hazard than tricyclic antidepressants. Källén concludes that when a pregnant woman has a major depressive disease and non-pharmacological treatments are not enough, the relatively small risk with drug therapy has to be weighed against the considerable risk for a relapse of the disease if therapy is interrupted. Also, further research to separate the effects of the drug and underlying pathology is urgently needed as are large-scale studies on long-term development.

Lipids and lactate in human immunodeficiency virus-1 infected pregnancies with or without protease inhibitor-based therapy
Livingstone EG, Cohn SE, Yang Y, et al
Obstet Gynecol, 2007; 110 (2 Pt. 1): 391-7

The objective of this study was to evaluate the effect of protease inhibitors on lipid and lactate levels and gastrointestinal symptoms in pregnancy. The researchers found that cholesterol and triglycerides were higher in protease inhibitor-treated women in pregnancy. Lactate and gastrointestinal symptoms were not different. A higher number of low birth weight infants were noted in women with high triglycerides, but other elevated lipid levels did not affect pregnancy outcomes.

Short-term prolactin administration causes expressible galactorrhea but does not affect bone turnover: pilot data for a new lactation agent
Page-Wilson G, Smith PC, Welt CK
Int Breastfeed J, 2007; 2: 10

Medications used to augment lactation increase prolactin secretion but can have intolerable side effects. This study examined the biological activity of recombinant human prolactin (r-hPRL) as preliminary data for its use to augment lactation. The researchers concluded that r-hPRL can cause expressible galactorrhea and that seven days of r-hPRL administration does not adversely

affect bone turnover for menstrual cyclicity. Thus, r-hPRL may be a viable option for short-term lactation augmentation.

A comparison of sulfadoxine-pyrimethamine with chloroquine and pyrimethamine for prevention of malaria in pregnant Nigerian women

Tukur IU, Thacher TD, Sagay AS, et al

Am J Trop Med Hyg, 2007; 76(6): 1019-23

In this study, pregnant Nigerian women were assigned to receive either sulfadoxine-pyrimethamine given twice or presumptive chloroquine treatment followed by weekly pyrimethamine. The researchers concluded that intermittent preventative treatment with sulfadoxine-pyrimethamine is superior to chloroquine and pyrimethamine for prevention of malaria and anemia in pregnant women in Nigeria.

Fetal acid-base and neonatal status after general and neuraxial anesthesia for elective cesarean section

Tonni G, Ferrari B, De Felice C, et al

Int J Gynaecol Obstet, 2007; 97(2): 143-6

The objective of this study was to analyze the relation between fetal acid-base and neonatal status in an observational cohort study of 900 consecutive women with singleton pregnancies at term undergoing elective cesarean section. The authors concluded that if fetal oxygenation is the goal, general anesthesia provides the highest values for partial pressure and saturation of oxygen in umbilical arterial blood. However, epidural anesthesia was associated with better fetal and neonatal status than either spinal or general anesthesia.

Clinical response and tolerability to and safety of saquinavir with low-dose ritonavir in human immunodeficiency virus type 1-infected mothers and their infants

Zorrilla CD, Van Dyke R, Bardeguet A, et al

Antimicrob Agents Chemother, 2007; 51(6): 2208-10

In this study, the researchers found that saquinavir boosted with low-dose ritonavir given with zidovudine and lamivudine was well tolerated by pregnant women and their infants. All mothers had <400 human immunodeficiency virus type 1 RNA copies/ml at delivery. Two had elevated liver transaminases and amylase. Seven infant adverse events were possibly treatment related (anemia, neutropenia, and hyperbilirubinemia).

The safety of prolonged indomethacin therapy

Savage AH, Anderson BL, Simhan HN

Am J Perinatol, 2007; 24(4): 207-13

The purpose of this study was to describe the fetal and newborn safety profile of prolonged indomethacin treatment during pregnancy. A retrospective cohort of 124 pregnant women treated with indomethacin was used to assess the outcomes of oligohydramnios, constriction of the ductus arteriosus, and composite neonatal morbidity. Eight patients (6.5%) developed ductal constriction and nine patients (7.3%) developed oligohydramnios. Composite morbidity occurred in 36 neonates (29%). Ductal constriction, oligohydramnios, and composite morbidity were not associated with duration of therapy, gestational age at start or stop of therapy, time between dosing and delivery, or dose regimen. The authors concluded that prolonged indomethacin therapy rarely is associated with ductal constriction and oligohydramnios.

Umbilical cord plasma concentrations of free morphine following single-dose diamorphine analgesia and their relationship to dose– delivery time interval, Apgar scores and neonatal respiration

Rawal N, Tomlinson AJ, Gibson GJ

Eur J Obstet Gynecol Reprod Biol, 2007; 133(1): 30-3

The objective of this study was to find the effect of dose-delivery interval on cord-blood levels of diamorphine metabolites and its effect on Apgar scores and neonatal respiration. The concentration of free morphine in the umbilical venous blood was significantly associated with the dose-delivery interval (coefficient (95% CI)=1.08(0.99–1.18), $p<0.001$). Twenty neonates had low Apgar score (≤ 7) at 1 min. The odds of such a low score were raised with higher log free morphine in the cord venous plasma, but not statistically significantly (OR (95% CI) =5.3 (0.84–34), $p=0.08$). Fourteen neonates required resuscitation. The odds of requiring resuscitation were significantly raised with higher log free morphine: OR (95% CI) =9.3 (1.0–86), $p=0.05$. The researchers concluded that concentration of free morphine in the umbilical venous blood after delivery was significantly associated with the dose-delivery interval and this had significant effect on the need for resuscitation.