

CaseMed-Pregnancy Resource Newsletter

April 2008

MEDICAL STUDIES

ACOG Practice Bulletin No.92: Use of psychiatric medications during pregnancy and lactation

Authors not listed

Obstet Gynecol, 2008; 111(4): 1001-20

No abstract available.

Management of severe antepartum depression: an update

[Article in French]

Alberque C, Bianchi-Demicheli F, Andreoli A, et al

Rev Med Suisse, 2008; 4(144): 392, 394, 396-7

In this article, the authors update the epidemiology, diagnostic process, and significant clinical features as well as the main treatment and prevention issues in the field of antepartum depression. The strengths and limitations of psychotherapy, antidepressant medication, and psychiatric hospitalization are reviewed with a special accent on the specific ethical and scientific issues associated with the clinical dilemma of risks balance evaluation and medication treatment choice with these patients

Outpatient use of cardiovascular drugs during pregnancy

Andrade SE, Raebel MA, Brown J, et al

Pharmacoepidemiol Drug Saf, 2008; 17(3): 240-7

The purpose of this study was to provide information on the prevalence of use of cardiovascular drugs, some of which may have fetotoxic or teratogenic effects, in the outpatient setting among pregnant women in the United States. The researchers conclude the prevalence of use of cardiovascular drugs that are suspected to be fetotoxic or teratogenic (ACE inhibitors, ARBs, and statins) was low in this cohort of pregnant women. Differing patterns of use across health plans suggests that further research is needed to evaluate the potential differential effects of cardiovascular drugs to assist prescribers and patients in making informed treatment decisions.

Increase in use of selective serotonin reuptake inhibitors in pregnancy during the last decade, a population-based cohort study from the Netherlands

Bakker MK, Kölling P, van den Berg PB, et al

Br J Clin Pharmacol, 2008; 65(4): 600-6

Recent case-control studies suggest a relationship between the use of selective serotonin reuptake inhibitors (SSRIs) and the occurrence of birth defects and other adverse pregnancy outcomes. The aim of this study was to determine the extent of the use of SSRIs before and during pregnancy and its trend over the years 1995-2004 in the Netherlands. The authors conclude that there has been a significant increase in the use of SSRIs among pregnant women in the Netherlands over

the last 10 years, parallel with the increase in exposure in women of fertile age. In light of the recent warnings about the use of SSRIs in pregnancy, healthcare professionals should be careful in prescribing SSRIs to women planning a pregnancy.

Oxytocin-ergometrine co-administration does not reduce blood loss at caesarean delivery for labour arrest

***Balki M, Dhumne S, Kasodekar S, et al
BJOG, 2008; 115(5): 579-84***

The objective of this study was to determine if intravenous infusion of a combination of oxytocin and ergometrine maleate is better than oxytocin alone to decrease blood loss at caesarean delivery for labour arrest. Balki and colleagues conclude that in women undergoing caesarean delivery for labour arrest, the co-administration of perometrine with oxytocin does not reduce intraoperative blood loss, despite apparently superior uterine contraction.

Antibiotic treatment from the obstetrician's point of view

[Article in German]

Baltzer J

Dtsch Med Wochenschr, 2008; 133(11): 516

No abstract available.

Increasing exposure to angiotensin-converting enzyme inhibitors in pregnancy

***Bowen ME, Ray WA, Arbogast PG, et al
Am J Obstet Gynecol, 2008; 198(3): 291.e1-5***

The objective of this study was to identify angiotensin-converting enzyme (ACE) inhibitor prescription-filling trends in pregnant women. Results showed that despite evidence of fetal complications associated with ACE inhibitor use during pregnancy, the number of pregnant women with pregnancy-related ACE inhibitor exposures increased steadily from 1986 to 2003. Bowen and Ray conclude that better methods are needed to reduce fetal exposure to potentially teratogenic prescribed medications.

Seizure control and pharmacokinetics of antiepileptic drugs in pregnant women with epilepsy

Brodtkorb E, Reimers A

Seizure, 2008; 17(2): 160-5

The main concerns associated with epilepsy during pregnancy consist of maternal and fetal risks from uncontrolled seizures, and harmful effects of the treatment on the development of the offspring. Although seizure control is maintained in the majority of cases, worsening occurs in a fraction of childbearing women with epilepsy. According to the authors, the serum concentrations of almost all antiepileptic drugs decrease during pregnancy, particularly those which are metabolized by glucuronidation. The inter-individual variability is pronounced. In highly protein-bound drugs, such as phenytoin and valproate, unbound drug is less affected than total concentrations. Lamotrigine and levetiracetam concentrations may decrease by more than 50% in the course of pregnancy, while monohydroxyoxcarbazepine may decrease by up to 30-40%. Brodtkorb and Reimers conclude that appropriate clinical follow-up tailored to individual needs and supported by therapeutic drug monitoring should be performed in pregnant women with epilepsy.

Laboratory abnormalities among HIV-1-infected pregnant women receiving antiretrovirals in Latin America and the Caribbean

***Ceriotto M, Harris DR, Duarte G, et al
AIDS Patient Care STDS, 2008; 22(3): 167-71***

No abstract available.

Validation of neural tube defects in the full featured-general practice research database

***Devine S, West SL, Andrews E, et al
Pharmacoepidemiol Drug Saf, 2008; Mar 17 [Epub ahead of print]***

The General Practice Research Database (GPRD) has been used to identify associations between pregnancy medication exposures and birth defects, but experts have argued that databases such as this one cannot provide detailed information for the valid identification of complicated congenital anomalies. The objective of this study was to determine if the GPRD could be used to identify cases of neural tube defects (NTDs). The authors found that their identification algorithm was useful in identifying three of the four types of the NTDs studied. However, additional information is necessary to accurately identify cases of spina bifida.

Clozapine use in two women with schizophrenia during pregnancy

***Duran A, Ugur MM, Turan S, et al
J Psychopharmacol, 2008; 22(1): 111-3***

In this study the researchers report on clozapine use during pregnancy in two women. The first woman had two deliveries while she was receiving clozapine treatment for schizophrenia. Both her deliveries were term, uncomplicated vaginal deliveries, and the clozapine dose was reduced throughout pregnancy. The second woman developed schizophrenia after her first child was born. She became pregnant after clozapine initiation. She delivered twins by term, uncomplicated vaginal delivery. In these cases, no specific risks for the mothers and their children can be attributed to the use of clozapine. Duran and colleagues conclude that mothers receiving clozapine treatment should not be advised to breastfeed their children.

Antiepileptic drugs as human teratogens

***Eadie MJ
Expert Opin Drug Saf, 2008; 7(2): 195-209***

The aim of this study was to assess the better-quality evidence concerning the fetal hazards from exposure to antiepileptic drug monotherapy during human pregnancy. Results showed there is reasonable evidence to suggest that valproate is a significant teratogen during therapeutic use in women. Older antiepileptic drugs (such as phenobarbitone, phenytoin, and carbamazepine) probably have some teratogenic potential, but less than valproate. According to Eadie, the situation remains unclear regarding the more recently marketed antiepileptic drugs.

Evaluation of the risk of congenital cardiovascular defects associated with the use of paroxetine during pregnancy

***Einarson A, Pistelli A, Desantis M, et al
Am J Psychiatry, 2008; Apr 1 [Epub ahead of print]***

The objective of this study was to determine whether paroxetine was associated with an increased risk of cardiovascular defects in infants of women exposed to the drug during the first trimester of pregnancy. From teratology information services around the world, the authors collected

prospectively ascertained, unpublished cases on infants exposed to paroxetine early in the first trimester of pregnancy and compared them with an unexposed cohort. The authors also contacted the authors of published database studies on antidepressants as a class to determine how many of the women in those studies had been exposed to paroxetine and the rates of cardiovascular defects in their infants. Einarson and colleagues conclude that paroxetine does not appear to be associated with an increased risk of cardiovascular defects following use in early pregnancy, as the incidence in more than 3,000 infants was well within the population incidence of approximately 1%.

Use of 5-HT₁ agonists in pregnancy

Evans EW, Lorber KC

Ann Pharmacother, 2008; Mar 18 [Epub ahead of print]

The objective of this study was to report and evaluate available data on the use of serotonin 5-HT₁ agonists (triptans) during pregnancy. Evans and Lorber conclude that sumatriptan appears to be a safe treatment alternative for pregnant women who experience new-onset or worsened migraines in the first trimester. Based upon available data, the other agents in this class cannot be recommended for use during pregnancy at this time.

Fetal safety profile of drugs used in the treatment of inflammatory rheumatic diseases

[Article in Portuguese]

Falcão S, Mourão AF, Pimentão JB, et al

Acta Reumatol Port, 2007, 32(4): 323–31

The high prevalence of inflammatory rheumatic diseases in women of childbearing age increases the risk of exposure to antirheumatic agents during conception, pregnancy and breast feeding. According to the authors, the decision for pharmacological treatment initiation maintenance should be the result between the severity of maternal disease and the risk benefits with treatment. This aim of this paper was to review recent literature about drug fetal safety profile, emphasize the importance of monitoring the pregnancy in patients with inflammatory rheumatic diseases, and stress the need for further research in this area.

Infant safety with antipsychotic therapy in breast-feeding: a systematic review

Gentile S

J Clin Psychiatry, 2008; Mar 18: e1-e8 [Epub ahead of print]

The purpose of this study was to analyze the literature for information regarding the safety of first- and second-generation antipsychotics for breast-fed infants in order to individuate the safest treatment option for women who need such medications during puerperium. Gentile found that no conclusions could be drawn regarding the risk/benefit profile of the majority of antipsychotic medications in breast-feeding. Hence, when clinicians are forced to start antipsychotic treatment in drug-naive patients, the choice of the safest option should be based on the general effectiveness profile of each agent, with 2 possible exceptions: clozapine (the drug should be considered contraindicated during breast-feeding because of its liability of inducing potential life-threatening events in the infant), and olanzapine (the drug seems to be associated with an increased risk of inducing extrapyramidal reactions in the breast-fed babies). Conversely, in patients who need to continue antipsychotic therapy during breast-feeding, it is suitable to maintain the previous pharmacologic regimen, if known as effective.

Is the use of letrozole to induce ovulation teratogenic?

Gill SK, Moretti M, Koren G

Can Fam Physician 2008; 54(3): 353-4

This article answers the following question: A patient of mine has been prescribed letrozole to induce ovulation; however, a recent release from the FDA contraindicates the use of letrozole in premenopausal women owing to teratogenicity. Does the use of letrozole increase the risk of a child being born with a birth defect? According to the authors, the use of letrozole to induce ovulation has not been associated with an increased risk of a child being born with a birth defect; in contrast, the use of clomiphene citrate in pregnancy is associated with intrauterine growth restriction.

Management of inflammatory bowel disease in the pregnant patient

Habel FM, Ravindran NC

World J Gastroenterol, 2008; 14(9): 1326-32

This article presents an approach to the management of inflammatory bowel disease (IBD) in the pregnant patient, including counseling and investigation, and summarizes existing data on the safety of medications used to treat IBD in pregnancy and breastfeeding.

Antibiotic therapy in pregnancy

[Article in German]

Haas A, Maschmeyer G

Dtsch Med Wochenschr, 2008; 133(11): 511-5

Infections are one of the causes of abortion during the first trimester, whereas during second and third trimester, they represent the primary cause of preterm birth. In this article, the various antibiotic treatment options in pregnancy are discussed. According to Haas and Maschmeyer, when antimicrobial agents are indicated, beta-lactam antibiotics are generally safe and effective. With respect to penicillins, an approximately 10 per cent maternal allergy rate should be taken into consideration, and first-generation cephalosporins may be a suitable alternative. Among the macrolide antibiotics, erythromycin should be preferred. Clindamycin, metronidazole, sulfonamides and chloramphenicol may be used as second-line agents, however, sulfonamides and chloramphenicol should be avoided during the prepartal period. Glycopeptide and aminoglycoside antibiotics should be reserved for life-threatening maternal infections refractory to other antibiotics. Tetracyclins may only be used before the 12 (th) week of gestation. Quinolones should be strictly avoided due to potential toxicity for the unborn children.

The pharmacists request that pregnant women consult physicians prior to GraviFrisk use

[Article in Danish]

Jacobsgaard H

Ugeskr Laeger, 2008; 170(10): 867

No abstract available.

Failure to lactate: a possible late effect of cranial radiation

Johnston K, Vowels M, Carroll S, et al

Pediatr Blood Cancer, 2008; 50(3): 721-2

This article provides a retrospective review of the lactation experience of female survivors who received 24 Gy cranial radiotherapy as CNS prophylaxis for acute lymphoblastic leukemia in

childhood prior to 1982 and who attend the Long-Term Follow-Up Clinic at Sydney Children's Hospital, Randwick, Australia. Ten of the twelve women who produced offspring reported minimal or no breast changes during pregnancy and failure to lactate postpartum. The data suggests a high risk of failure of lactation in women treated during childhood with 24Gy cranial irradiation. Johnston and colleagues conclude that awareness of this possibility can assist in counseling.

Antimicrobial therapy associated with preterm birth

[Article in Hungarian]

Kazy Z, Puhó E, Czeizel E

Orv Hetil, 2008; 149(10): 449-56

In this study, the effect of 51 antimicrobial drugs was evaluated for the reduction of preterm birth. The use of 51 antimicrobial drugs in the mothers of 38,151 newborn infants including at least ten pregnant women was evaluated. Ampicillin and clotrimazole showed an obvious preterm birth preventive effect, mainly after the use during the first trimester of pregnancy. Kazy and colleagues conclude that ampicillin and particularly clotrimazole may be effective for the reduction of preterm birth associated with infectious diseases of pregnant women.

Pregnancy and tuberculosis: to assess tuberculosis cases in pregnancy in a developing region retrospectively and two case reports

Keskin N, Yilmaz S

Arch Gynecol Obstet, 2008; Feb 14 [Epub ahead of print]

Since tuberculosis (TB) cases activated by HIV infection during pregnancy are well reported in the literature, the researchers aimed to investigate the aggressiveness of pulmonary TB among pregnant women and to assess the effects of TB on the fetus in Kutahya, an area where HIV positive cases are not seen. Generally, TB is expected to be more aggressive during pregnancy. Since the cases studied were HIV negative, the TB may not have progressed as aggressively. Results also showed there was less aggressiveness and non-resistance to TB treatment in HIV-negative pregnant women when compared with HIV-positive women. The authors conclude that HIV infection results in greater mortality than the triple combination of human immunodeficiency virus, mycobacterium TB, and pregnancy. Furthermore, the advance of TB in pregnant women was not different from that in non-pregnant women in Kutahya. The fetus and the newborn were not affected. Isoniazid, rifampin, ethambutol, and pyrazinamide were used for therapy.

Anaesthetics and breast feeding

[Article in Norwegian]

Khiabani HZ, Spigset O

Tidsskr Nor Laegeforen, 2008; 128(6): 704-5

Many women undergo anaesthetic procedures related to childbirth or during the period of lactation. Most anaesthetic drugs are lipophilic and are thus excreted into breast milk. This article summarizes available knowledge regarding anaesthetics, their excretion into breast milk and possible effects on the suckling infant. The consequences of such an exposure are discussed in terms of whether breast-feeding should be allowed or not after anaesthetic procedures.

Decreased cord blood IL-4, IL-13, and CCR4 and increased TGF-beta levels after fish oil supplementation of pregnant women

Krauss-Etschmann S, Hartl D, Rzehak P, et al

J Allergy Clin Immunol, 2008; 121(2): 464-470.e6

The objective of this study was to investigate how supplementation of pregnant women with a fish oil (FO) preparation modulates allergy-related immune parameters in mothers and offspring. Results revealed that supplementation with FO during pregnancy is associated with decreased mRNA levels of T(H)2-related molecules in the fetus and decreased maternal inflammatory cytokines. The authors speculate that both effects are mediated by TGF-beta.

An autopsy case of acute multiple sclerosis (Marburg's type) during pregnancy
Letournel F, Cassereau J, Scherer-Gagou C, et al
Clin Neurol Neurosurg, 2008; Mar 12 [Epub ahead of print]

Letournel and colleagues report a case of a 9-month pregnant woman who presented acute psychiatric and neurological symptoms with extensive involvement of the white matter on MRI and no oligoclonal bands on CSF examination. Despite high doses of intravenous steroids, plasmapheresis and immunosuppressive drugs, a fatal outcome (coma) was noted 8 months later. A neuropathological examination confirmed the diagnosis of Marburg's type of multiple sclerosis showing sharp-edged lesions of demyelination, giant astrocytes, numerous macrophages and little perivascular inflammation. The definition and limits of the Marburg entity with reference to acute disseminated encephalomyelitis, the impact of pregnancy, unusual MRI features, neuropathology and treatment are discussed in this article.

Managing headache during pregnancy and lactation
Marcus DA
Expert Rev Neurother, 2008; 8(3): 385-95

Headache patterns for both primary and secondary headaches are often modified in women during pregnancy. Although approximately two thirds of women with migraines experience headache improvement during pregnancy; women who continue to suffer from migraine or other headaches during pregnancy need effective clinical care to include appropriate diagnostic studies, counseling about expectations during pregnancy and lactation, and modifications in therapeutic regimens to minimize risk to the fetus and nursing baby. This review describes the epidemiology of headache during pregnancy and lactation, to include both effects of these conditions on headache activity and possible concerns about how a maternal headache diagnosis may influence the course and outcome of pregnancy. Although restrictions in diagnostic testing and medication interventions are often necessary during pregnancy and breastfeeding, this review describes evaluation and management strategies that provide effective clinical care while minimizing risk to the developing baby

Depression, antidepressant medication, and functioning outcomes among pregnant women
Marcus SM, Flynn HA
Int J Gynaecol Obstet, 2008; 100(3): 248-51

The objective of this study was to describe prenatal patterns of antidepressant use and their relationship to depression in pregnancy. The researchers interviewed 276 high risk women to investigate their use of antidepressant medication. Of the women interviewed, 13% reported current use of antidepressant medication. There were no differences in depression or health functioning outcomes between women taking antidepressants and those not using them. Marcus and Flynn conclude that monitoring the depressive symptoms of women using pharmacotherapy during pregnancy is important to optimize their treatment.

Emerging therapeutic options for breast cancer chemotherapy during pregnancy
Mir O, Berveiller P, Ropert S, et al
Ann Oncol, 2008; 19(4): 607-13

In their study, Mir and colleagues conducted a comprehensive review of reports documenting the use of taxanes, vinorelbine, trastuzumab and lapatinib during pregnancy in the English literature, in order to evaluate their safety profile in pregnant patients. They found the administration of recent drugs taxanes and vinorelbine to be feasible during the 2nd and 3rd trimesters of pregnancy, with a favorable toxicity profile. In contrast, anti-HER-2 agents may obscure the normal development of the fetal kidney, and should be avoided during pregnancy.

Pharmacokinetics of oral zidovudine administered during labour: a preliminary study
Mirochnick M, Rodman JH, Robbins BL, et al
HIV Med, 2007; 8(7): 451-6

The aim of this study was to determine whether oral zidovudine (ZDV) given during labour would provide a similar systemic exposure to the established intravenous regimen used to prevent mother-to-child transmission in HIV-infected pregnant women. While ZDV exposure improved with the increased dosing regimen, Mirochnick and colleagues conclude that their sample size was small and larger studies are needed to establish whether oral ZDV administration during labour can consistently provide equivalent exposure to intravenous administration.

Safety of glyburide for gestational diabetes: a meta-analysis of pregnancy outcomes
Moretti ME, Rezvani M, Koren G
Ann Pharmacother, 2008; Mar 18 [Epub ahead of print]

The objective of this study was to determine the safety of glyburide use in pregnancy in the treatment of gestational diabetes compared with insulin therapy by analyzing all available human studies. An increased perinatal risk was not found with glyburide use. However, Moretti and colleagues conclude that the effectiveness and safety of glyburide does require further evaluation, as most studies to date were not randomized.

Pregnancy and breastfeeding in patients with Crohn's disease
Mottet C, Juillerat P, Pittet V, et al
Digestion, 2007; 76(2): 149-60

Available data on Crohn's disease and pregnancy show that women with Crohn's disease can expect to conceive successfully, carry to term, and deliver a healthy baby. Control of disease activity before conception and during pregnancy is critical, to optimize both maternal and fetal health. Generally speaking, pharmacological therapy for Crohn's disease during pregnancy is similar to pharmacological therapy for nonpregnant patients. Patients maintained in remission by way of pharmacological therapy should continue it throughout their pregnancy. Sulfasalazine, mesalazine and corticosteroids are safe, azathioprine and 6-mercaptopurine are reasonably safe with few discordant data, infliximab seems safe as well, whereas methotrexate is contraindicated during pregnancy. During breastfeeding, mesalazine and prednisone are considered safe, azathioprine/6-mercaptopurine, budesonide and infliximab probably safe and methotrexate is contraindicated.

Steady-state nevirapine plasma concentrations are influenced by pregnancy
Nellen JF, Damming M, Godfried MH, et al
HIV Med, 2008; 9(4): 234-8

Optimal plasma concentrations of antiretroviral drugs are required during pregnancy to treat maternal HIV infection and prevent mother-to-child transmission. In this study, Nellen and colleagues investigated the effect of pregnancy on nevirapine (NVP) plasma concentrations. Results revealed that pregnancy has a moderate but significant lowering effect on NVP plasma concentrations and being of African descent compensates for the lowering effect of pregnancy on NVP concentrations.

Treatment of breast cancer with trastuzumab during pregnancy

Pant S, Landon MB, Blumenfeld M, et al

J Clin Oncol, 2008; 26(9): 1567-9

No abstract available.

Hypoechoic thyroid nodules on ultrasound 4 years after prenatal exposure to radioiodine: resolution with thyroxine therapy

Perry RJ, Ainine A, Butler S, et al

Acta Paediatr, 2008; 97(4): 509-12

Perry and colleagues describe the case of an infant inadvertently exposed to radioiodine at 17 weeks gestation. The mother had received 400 MBq of (131)I for hyperthyroidism (total T4 178 nmol/L, thyroid stimulating hormone (TSH) <0.1 mU/L, 4-h (131)I uptake 16%). Following cordocentesis at 27 weeks (free T4 12.7 pmol/L, TSH 35.4 mU/L) intra-amniotic thyroxine was withheld and a male infant was born at 39 weeks gestation, birthweight 3520 g. The cord TSH was low (0.1 mU/L), total T4 151 nmol/L on day 4, the mother having received no medication during pregnancy. Postnatal follow-up showed mild TSH elevation (11.0-19.4 mU/L) but normal free T4 (9-12.7 pmol/L) during the first 2 years of life following which the child was discharged still untreated. On recall at 4.3 years, TSH elevation persisted (15.4 mU/L) and ultrasound showed several hypoechoic thyroid nodules within the left lobe that disappeared after thyroxine treatment. The authors conclude that in the event of inadvertent exposure to radioiodine in utero, the infant should receive thyroxine therapy from birth in order to protect the thyroid gland from TSH over-stimulation, however mild.

Dihydroartemisinin-piperaquine rescue treatment of multidrug-resistant Plasmodium falciparum malaria in pregnancy: a preliminary report

Rijken MJ, McGready R, Boel ME, et al

Am J Trop Med Hyg, 2008; 78(4): 543-545

Dihydroartemisinin-piperaquine (DHA-PPQ) is a promising new artemisinin combination treatment. There are no published data on the intentional use of the drug in pregnancy. Between June 2006 and January 2007, 50 Karen pregnant women with recurrent *P. falciparum* infections, despite 7-day treatments with quinine or artesunate (+/-clindamycin) or both, were treated with DHA-PPQ. This rescue treatment was effective and well tolerated and there was no evidence of toxicity for the mothers or the fetus.

Treatment of foetal supraventricular tachycardia with antiarrhythmic medication administered through the umbilical vein

[Article in Dutch]

Roest AA, Vandenbussche FP, Klumper FJ, et al

Ned Tijdschr Geneeskd, 2008; 152(7): 389-92

Foetal supraventricular tachycardia (SVT) with hydrops foetalis is associated with a high morbidity and mortality rate. If SVT with hydrops foetalis persists despite transplacental therapy, direct foetal treatment can be initiated. One foetus was found to have SVT with hydrops foetalis during the 29th week of pregnancy, and the condition persisted despite transplacental treatment. Amiodarone was administered directly via the umbilical vein, and the SVT resolved. A second foetus was found to have SVT with hydrops foetalis during the 28th week of pregnancy. The condition persisted despite maternal antiarrhythmic medication. Direct treatment of the foetus with amiodarone was successful. Amiodarone is the treatment of choice for direct foetal therapy for SVT, and can be administered safely via the umbilical vein. Direct foetal therapy should be considered for the treatment of foetal SVT with hydrops foetalis that occurs in the first 31 weeks of pregnancy and persists despite adequate transplacental therapy.

The risk of postpartum hemorrhage with selective serotonin reuptake inhibitors and other antidepressants

***Salkeld E, Ferris LE, Juurlink DN
J Clin Psychopharmacol, 2008; 28(2): 230-234***

Limited evidence suggests that selective serotonin reuptake inhibitor (SSRI) antidepressants can hinder platelet aggregation and can increase the risk of hemorrhage. Because antenatal depression is common and is often treated with antidepressants, the authors sought to determine if exposure to SSRI antidepressants in late pregnancy is associated with an increased risk of postpartum hemorrhage compared with non-SSRI antidepressants. Salkeld and colleagues conclude that SSRI antidepressants confer no disproportionate risk of postpartum hemorrhage at the time of delivery compared with non-SSRI antidepressants. This information may help guide decisions regarding pharmacotherapy for depression during pregnancy.

Comparison of maternal and fetal outcomes, in epileptic and non-epileptic women

***Saleh AM, Abotalib ZM, Al-Ibrahim AA, et al
Saudi Med J, 2008; 29(2): 261-6***

The objective of this study was to assess maternal and fetal outcomes, in epileptic and non-epileptic pregnant women. There were no significant differences between either group in total length of labor, labor induction and oxytocin augmentation, need for labor analgesia, total blood loss and the need for blood transfusion, mode of delivery, and the length of hospital stay. There were no significant differences in all maternal complications between either of the groups. There was an increase in the mean dose of the antiepileptic medications needed during pregnancy. However, 4 women in the epileptic group had major seizures during pregnancy. All of these women needed addition of a second antiepileptic medication. Major congenital malformations occurred in 2 newborns of epileptic women, and none occurred in the control group. Both newborns were from women who received polytherapy. Saleh and colleagues conclude that women with epilepsy are not at increased risk for obstetric and neonatal complications, provided there is a combined team management approach by a neurologist and an obstetrician.

Nifedipine concentration in maternal and umbilical cord blood after nifedipine gastrointestinal therapeutic system for tocolysis

***Silberschmidt AL, Kühn-Velten WN, Juon AM, et al
BJOG, 2008; 115(4): 480-5***

The purpose of this study was to determine nifedipine concentrations in maternal plasma at steady state, and maternal and umbilical cord plasma at delivery, after tocolysis with nifedipine gastrointestinal therapeutic system (GITS) tablets. The researchers conclude that steady-state

plasma nifedipine concentrations after repeated dosing with nifedipine GITS 30-150 mg/day in pregnant women with preterm labour do not exceed 100 micrograms/l; fetal levels are 77% of maternal levels.

Transfer of isoniazid from circulation to breast milk in lactating women on chronic therapy for tuberculosis

Singh N, Golani A, Patel Z, et al

Br J Clin Pharmacol, 2008; 65(3): 418-22

Isoniazid is considered safe during lactation; however, limited data is available on the transfer of isoniazid from circulation to milk in lactating women. The aim of this study was to determine milk to plasma (M: P) ratios and infant dose (absolute and relative) for isoniazid in lactating women on antituberculosis therapy. Singh and colleagues found that the mean relative dose of isoniazid (1.2%) transmitted to the infant via breast milk is below the 10% notional level of concern. Based on this data, the researchers conclude that isoniazid therapy is safe during breastfeeding.

Pharmacological aspects of neonatal antidepressant withdrawal

Ter Horst PG, Jansman FG, van Lingen RA, et al

Obstet Gynecol Surv, 2008; 63(4): 267-279

This article discusses the importance of antidepressant therapy during pregnancy and postpartum, summarizes the important neonatal effects of antidepressants, and describes the potential teratogenic effects of antidepressants.

Motor and mental development of infants exposed to antiepileptic drugs in utero

Thomas SV, Ajaykumar B, Sindhu K, et al

Epilepsy Behav, 2008; Mar 15 [Epub ahead of print]

Thomas and colleagues evaluated the mental (MeDQ) and motor (MoDQ) developmental quotients of 395 infants of mothers with epilepsy (IME) (mean age: 15 months) enrolled in the Kerala Registry of Epilepsy and Pregnancy between 1998 and 2004. The same developmental pediatricians, blinded to antiepileptic drug (AED) exposure, evaluated the children using the Indian adaptation of the Bayley Scale of Infant Development. Results revealed that infants not exposed to AEDs had a higher MeDQ and MoDQ than those exposed to AEDs. Those exposed to polytherapy had significantly lower developmental quotients than those exposed to monotherapy. Cumulative AED scores during pregnancy had an inverse relationship with developmental quotients. On multiple regression analysis, polytherapy was a stronger predictor of lower developmental quotients than dosage. Compared with carbamazepine monotherapy, valproate monotherapy was associated with significantly lower MeDQ and MoDQ in IME, but the differences between other AEDs were not significant for IME exposed to valproate monotherapy. The authors conclude that one limitation of the study is that the influence of maternal intelligence on developmental quotients was not evaluated

Optimization of anesthetic service during abdominal delivery of pregnant women with gestosis [Article in Russian]

Tiukov VL, Pyregov AV, Shepetovskaia NL, et al

Anesteziol Reanimatol, 2007; 6: 25-9

Differential preoperative preparation of pregnant women with gestosis, by using calcium antagonists is an effective preventive measure against a circulatory hyperdynamic response to

transportation to the operating suite. In pregnant women who had all hemodynamic types at baseline, the eukinetic type achieved during the preparation is retained. The patients with gestosis who did not receive calcium antagonists were found to have a circulatory hyperdynamic response with increased myocardial oxygen uptake (during surgery in particular). The use of calcium antagonists, ketonal, tranexamic acid, and hydroxyethyl starch-130/04 solution in the anesthetic appliance promoted the preservation of eukinetic hemodynamics in all those operated on, without increasing myocardial oxygen demands. The better reaction of the circulatory system and myocardial oxygen demands to surgical injury (the second mediatory wave of the systemic inflammatory response syndrome) correlated with higher neonatal Apgar scores in this category of puerperas with gestosis.

Teratogenic effects of antiepileptic drugs

Tomson T, Battino D

Seizure, 2008; 17(2): 166-71

The use of older generation antiepileptic drugs (AEDs) during pregnancy is known to be associated with a two- to threefold increased risk of birth defects in the offspring and possible also other adverse outcomes in the exposed infant. Much less is known about newer generation AEDs in this respect. Recent studies based on national registries as well as specific epilepsy and pregnancy registries are beginning to provide information on comparative teratogenic effects of different AEDs. As a result, the prevalence of birth defects appears to be higher with exposure to valproate compared with carbamazepine and possibly also in comparison with lamotrigine. Tomson and Battino conclude that further studies based on larger cohorts are needed to compare AEDs at different dosages and to analyse the possible impact of confounding factors. Furthermore, data is insufficient to assess the human teratogenic potential of other newer generation AEDs than lamotrigine. Retrospective and a few small prospective studies suggest that exposure to valproate may also be associated with a lower verbal IQ at school age, but further prospective studies are required to draw firm conclusions.

Prescribing of sulfasalazine, azathioprine and methotrexate round pregnancy--a descriptive study

Vroom F, van Roon EN, van den Berg PB, et al

Pharmacoepidemiol Drug Saf, 2008; 17(1): 52-61

In their study, Vroom and colleagues report prescribing patterns round pregnancy of sulfasalazine (SSZ), azathioprine (AZA), methotrexate (MTX) and co-medications among women to whom one of these disease modifying anti-rheumatic drugs (DMARDs) were prescribed before pregnancy. Results showed that DMARDs and co-medication are received before, during and after pregnancy, although no specific prescription patterns were found. Administrative databases, such as the pregnancy-interaction database (IADB.nl, 1994-2004), are useful in describing drug-prescribing patterns for better understanding of drug prescribing around pregnancy in daily practice. Based on these data, the authors conclude that the prescribing of DMARDs and related co-medication is based on the individual patient.

Serum concentration/dose ratio of levetiracetam before, during and after pregnancy

Westin AA, Reimers A, Helde G, et al

Seizure, 2008; 17(2): 192-8

The purpose of this study was to investigate changes in levetiracetam (LEV) serum concentration/dose ratio (C/D-ratio) in relation to pregnancy. Results revealed that serum

concentrations of LEV declined significantly in the third trimester of pregnancy and increased rapidly after delivery.

Comparison of clomiphene citrate, metformin, or the combination of both for first-line ovulation induction, achievement of pregnancy, and live birth in Asian women with polycystic ovary syndrome: a randomized controlled trial

Zain MM, Jamaluddin R, Ibrahim A, et al

Fertil Steril, 2008; Mar 3 [Epub ahead of print]

The objective of this study was to determine the first-line medication to be used in anovulatory patients with polycystic ovary syndrome (PCOS) for ovulation induction and pregnancy achievement. Results showed that the ovulation rate was 23.7% in the metformin group, 59% in the CC group, and 68.4% in the combination treatment group. This was translated into a similar pregnancy and live birth rate, which were higher in the clomiphene citrate and combination groups compared to the metformin group, although statistically the differences were not significant. There were no multiple pregnancies and the rate of spontaneous first trimester loss was similar to the general population. Zain and colleagues conclude that clomiphene citrate should be the first-line treatment for ovulation induction in ovulatory patients with PCOS

LAY PRESS NEWS

Birth Defect link to acne treatment

Evening Herald, 2008; March 10

A warning about a drug for treating acne, which can cause severe birth defects, premature birth and death in babies, has been issued by the Irish Medicines Board. Isotretinoin (sold under the brand names Accutane and Roaccutane) can cause babies in the womb to suffer severe defects including malformation of the head and face, mental retardation and severe internal defects of the brain, heart glands, and nervous system. It should not be taken either during breastfeeding. The warning says that women prescribed the anti-acne drug should use “at least one and preferably two” forms of contraception and medically supervised pregnancy tests “before, during and five weeks after the end of treatment.” The warning emphasizes the need for women to “understand the need for rigorous follow-up on a monthly basis” and accept the need for effective contraception “without interruption” for a month before starting treatment right through to a month after the treatment has finished.

Body building pill may prevent baby brain damage

Schultz N

New Scientist.com, 2008; March 11

A food supplement used by athletes and body builders to boost muscle power might help to prevent brain damage and death of newborn babies from oxygen starvation. Problems with the placenta and umbilical cord before or during birth can reduce the fetal oxygen supply. One in 300 babies in developed countries suffers birth injuries as a result and one in 20 babies in the UK are born by emergency caesarean section because doctors worry they may not be getting enough oxygen. Zoe Ireland and David Walker’s study examines the effects of maternal creatine supplementation on the health of the fetus using spiny mice (which are more comparable to human babies at birth). Theo Wallimann, a cell biologist at the Swiss Federal Institute of Technology (ETH) in Zürich, agrees the results may well hold true for humans. “I am a strong advocate for creatine supplementation during pregnancy. However, the creatine dose used in

these experiments was very high, and although preliminary trials suggest that even premature babies can tolerate high doses well, we obviously need more research", he says. Patrick O'Brien, of the Royal College of Obstetricians and Gynaecologists in London believes that creatine supplementation could become a potentially safe and easy protective intervention, much like folic acid supplementation, which is now recommended to prevent neural tube defects such as spina bifida. "Because such defects are thankfully rare, it also takes very large studies to show a protective effect in humans, so we still have a long way to go."

UPDATE: Acid-blockers in pregnancy up kids' asthma risk

Kerr M

Reuters Health E-Line, 2008; March 21

Children whose mothers took stomach acid-blocking medication during pregnancy have increased odds of developing asthma. Dr. Elizabeth H. Yen of Children's Hospital in Boston presented her team's findings at the annual meeting of the American Academy of Allergy, Asthma and Immunology. The study covered three types of stomach acid-suppressing drugs: histamine-2-receptor antagonists, such as Pepcid and Zantac; proton pump inhibitors, like Nexium or Prilosec; and other anti-ulcer drugs, e.g., sucralfate. Over-the-counter antacids, such as Maalox, Mylanta, Tums, Rolaids, etc., "could not be analyzed in our study because their use by mothers in this Swedish birth cohort was not ascertained," Yen added. Maternal intake of acid-blocking medication was associated with a 51 percent increased likelihood of asthma in children. "This was seen with asthma only," Yen pointed out. There was no increase in the odds of other allergic diseases, such as eczema, food allergies, or hay fever. It made no difference which of type of acid-reducing medication women took, Yen said, or when they took it during pregnancy, or if they had a history of allergies. "This provides the first evidence of a novel potential risk factor for the development of allergic diseases in children," she concluded. Yen does note that the study is presently under review, and has not yet been published. "Therefore, it has not yet undergone the peer-review process," which ensures that the data and findings are accurate.

Babies' soft skull due to Moms' lack of vitamin D

Reuters.com, 2008; March 31

The softening of the skull bones in normal-appearing newborns is tied to a vitamin D deficiency in the womb, according to Japanese researchers. In their study published in the Journal of Clinical Endocrinology and Metabolism, Dr. Tohru Yorifuji and colleagues found that the rate of soft skull bones, also known as craniotabes, "was influenced by the daylight hours approximately 4 months prior to delivery," thus suggesting "the condition is associated with vitamin D deficiency in utero." Low vitamin D levels and other abnormalities at 1 month of age were more common in babies who were breast-fed than in those who were fed formula at least part of the time. As a result, they recommend "treating breast-fed infants with craniotabes with vitamin D, or preferably, treating all pregnant women with vitamin D."

Medical Reporter

Branswell H

The Canadian Press, 2008; April 2

Women who are pregnant when the next flu pandemic strikes will find themselves with special needs, concerns and risks - and very little science to help decide whether it's safe to take flu drugs or necessary to wear medical masks in public. Recognizing this group's vulnerability, the U.S. Centre for Disease Control is gathering experts (with backgrounds that vary from drug metabolism in pregnancy to baby delivery) to create special guidelines for pregnant women. This

article discusses how little studied therapeutic and preventative agents in pregnancy are and how the immune system of the pregnant woman is altered to allow the fetus to grow. This alteration can cause her to experience an increased risk of infection or increased morbidity or mortality with different infections. Little is known regarding the impact of a mother's bout of influenza on her developing fetus. Fever in pregnancy has been linked to an increased rate of neural tube defects; however, there are safe, relatively well-studied medicines that can be used to treat such a fever.

No link found in Paxil use, baby heart defects
CTV.ca, 2008; April 3

This news item discusses the study conducted by the Motherisk program at the Hospital for Sick Children and the University of Toronto. Data from women and babies who took Paxil was compared with the outcomes of women whose infants were not exposed. The rate of cardiovascular defects was 0.7 per cent in each group. The incidence of heart defects in the general population is about one per cent. "This drug does not increase the risk of cardiovascular defects, heart defects," lead author Adrienne Einarson said in an interview after the findings were published online this week in the American Journal of Psychiatry. Einarson began the study after GlaxoSmithKline, the maker of Paxil, published information on its website in 2005 comparing its drug to another antidepressant. The study based on the outcomes of 815 infants indicated an incidence of cardiovascular malformations of two per cent among the babies of women who had used Paxil. Two other small studies showed rates of two per cent and 1.9 per cent. Einarson indicated that "based on this rather preliminary information" regulatory authorities in Canada and the U.S. advised women to avoid the drug if possible during pregnancy. "So everyone got in a panic," she said, noting that the incidence for the GlaxoSmithKline study was later adjusted downward to 1.5 per cent. Motherisk had calls from women who were already taking Paxil when they found out they were pregnant, and it prompted this new study. "We know that 50 per cent of pregnancies are unplanned, so if you've already taken it and you're six weeks pregnant, I can tell you also that the heart is one of the first organs to develop. Right after the woman misses her period," she explained. "By the time they're six weeks pregnant, there's not really much point stopping it anyway, right. It's like closing the barn after the horse is gone. The heart is already developed then, so if there was going to be any problem - not that we ever felt there was - but if there was, to tell somebody at that point you should stop taking it, it's not going to be helpful." The study notes that untreated depression in pregnancy is associated with a sixfold increase in the risk of postpartum depression.

Seizures and societal outlook
Arjun G
The Hindu, 2008; April 3

This article discusses whether women with epilepsy can have a normal pregnancy and baby. The author suggests that both the neurologist and the obstetrician need to be involved in reviewing the anti-epileptic drug that the woman is on and in deciding whether there is need for a change in medication prior to the beginning of a pregnancy. According to the author, it is best to be on a single drug. While there is a slightly increased risk of certain abnormalities in the baby due to anti-epileptic drugs, these problems can be prevented by taking folic acid supplementation prior to conception and in the first three months. Dr Arjun states that a good quality ultrasound in the fifth month can ensure the foetus does not have a birth defect. There may be also a need to increase the dose of the anti-epileptic drug in pregnancy. Dr. Arjun believes that women on a single drug can safely breast feed their babies after consulting with their pediatrician

Rate of birth defects in Korea remains steady

Chang-gyu K

JoongAng Daily, April 7

The Korea Food and Drug Administration announced that birth defects are present in 2.98 percent of all newborn babies and fetuses. The rate has been stable in recent years but it is about double the 1.53 percent recorded in 1999. The researchers said the steady increase of congenital heart defects is due to advanced diagnostic techniques. According to an official report of 18 hospitals nationwide issued by the College of Medicine at the Catholic University of Korea, a total of 932 out of 31, 272 babies, including newborn and stillborn babies as well as fetuses in the womb for more than 16 weeks, had birth defects last year. Shin Jong-chul, leader of the research team, says an average of 15.69 of 10, 000 babies are born with Down syndrome which is the most frequently found defect. Japan has a rate of 10.28 while the United States has a rate of 17.23. “Compared to other countries in the world, Korea’s rate of Down Syndrome is not high,” said Shin Jong-chul. The second most frequent birth defect is the cleft lip and palate, followed by two congenital heart defects: the tetralogy of Fallot and transposition of the great arteries, which can bring about a heart murmur, fast breathing, low weight gain in infants, and shortness of breath.