Induction Ups Risk of Amniotic Fluid Embolism

BY MARY ANN MOON Contributing Writer

edical induction of labor appears to double the risk of amniotic Lfluid embolism, reported Dr. Michael S. Kramer of Montreal Children's Hospital and his associates.

Findings from their retrospective cohort study of approximately 3 million hospital births throughout Canada between 1991 and 2002 "support the long-

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standing, but heretofore unsubstantiated, suspicion that labour induction increases the risk of this rare but serious maternal complication.

"Although the small absolute risk of amniotic fluid embolism is unlikely to affect the decision to induce labour in the presence of compelling clinical indications, women and physicians should be aware of this risk if the decision is elective," the researchers said in the Oct. 21 issue of the Lancet.

"We should emphasise that the absolute risk increase of amniotic fluid embolism for women undergoing medical induction of labour is very small: 4 or 5 total cases and 1 or 2 fatal cases per 100,000 women induced.

"However, with 4 million births per year and induction rates approaching 20% in the [United States], this practice could be causing amniotic fluid embolism in 30-40 women per year in the [United States] alone (including 10-15 deaths)," Dr.

findings of minimal risk may be related to the use of oral contraceptive formulations containing lower hormonal doses of estrogens and progestogens. 8. Carbohydrate and Lipid Metabolic Effects: Oral contraceptives have been shown to cause glucose intolerance in a significant percentage of users. Oral contraceptives contraining greater than 7. S microgens or elevatores estrogens cause estrogens cause estimates and transmission and create insulin resistance, this effect varying with different progestational agents. However, in the nondiabelic vortan or contraceptives cause of these of estrogens cause estimates estimates and dabate vortanes of these of estrogens cause estimates and contraceptive users. 9. 9. Evaluet Bloop Perseare: Woman with significant typeritorismic should not be started on hormorase in blood pressure last been reported in cal contraceptive users. 9. 9. Evaluet Bloop Perseare: Woman with significant typeritorismic should not be started on hormoral contraceptive users. 9. 9. Evaluet Bloop Perseare: Woman with significant typeritorismic should not be started on hormoral contraceptive users. 9. 9. Evaluet Bloop Perseare: Woman with significant typeritorismic should not be started on hormoral contraceptive users. 9. 9. Evaluet Bloop Perseare: Woman taxionized this increase is more likely in older cal contraceptive increase in bodo pressure las been reported in man contraceptive users. 9. 9. Evaluet Bloop Perseare: Woman taxionized this increase is should be monitored (base), and 15 significant devalion of bloop pressure occurs, oral contraceptives, and the is contraceptives, they should be monitored (base), and 15 significant devalion of bloop pressure occurs, oral contraceptives, and the is no difference in the occurrence of hypertension among ever- and never-users. 10. Headacte: the nest or exaction of microare to 28 (28%) of the contrace development of hardened exacting with a this recurrent, persistent, or severe requires discontinuation of real contraceptives and evaluation of th SEASONIQUE^{IM} (levonorgestrel / ethinyl estradiol tablets) 0.15 mg / 0.03 mg and (ethinyl estradiol tablets) 0.01 mg Brief Summary. See full package brochure for complete information. Patients should be counseled that this product does not protect against INI-infection (AIDS) and other sexually transmitted diseases. CONTRAINDICATIONS: Oral contraceptives should not be used in women who currently have the following conditions: • Thrombophebitis or throm-beembolic disorders • A past history of deep vein thrombophebitis or thromboembolic disorders • Cerethovascular or coronary artery disease (current or history) • Valvular heart disease with thrombogenic complications • Uncontrolled hypertension • Diabetes with vascular involvement • Headaches with local neurological symptoms • Major surgery with prolonged immobilization • Known or suspected carcinoma of the energy of paraletal bleeding • Cholestatic jaundice of pregnancy or jaundice with prior pil use • Hepatic adenomas or carcinomas, or active liver disease • Known or suspected pregnancy • Hypersensitivity to any component of this product <u>WARNINGS</u> <text><text><text><text><text>

Figure: Percentage of Women Taking Seasonique™ Reporting Intermenstrual Bleeding and/or Spotting.



As in any case of bleading irregularities, nonhomonal causes should always be considered and adequate diagnostic measures taken to rule out malignancy, or pregnancy. In the event of amenorhea, pregnancy should be ruled out. Some women may encounter post-pill amenorhea or oligomenorhea (possibly with anoulation), especially when such a condition was preexistent. PRECAUTIONS 1. Secually Transmitted Diseases: Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually trans-mitted diseases.

mitted diseases,
2. Physical Examination and Follow-up: A periodic history and physical examination are appropriate for all women, including women using oral contraceptives. The physical examination hower may be deferred until after initiation of oral contraceptives if requested by the woman and judged appropriate by the clinician. The physical examination should include special reference to blood pressure, breasts, abdomen and pelvic organs, including cervical cytology, and relevant bloom of ward and ware to the second bloom periodic bloom events. In case of undiagnosed, persistent or recurrent ahnormal vaginal bleeting, appropriate diagnostic measures should be conducted to rule out malignance, Vomen with a strong many history of these cases cancer or who have breast conducted with particular care.
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In your event a Use set of the control of hyperinidemias more difficult. (See WARNING 2016 S14) in patients with amilal detects of ligorotem metabolism receiving estrogen-containing preparations, there have been case reports of significant elevations of plasma triglycerides leading to pancreatitis.
4. Liver Function: If jauncide develops in any woman receiving such drugs, the medication should be discontinued. Steroid hormones may be poorly metabolized in patients with conditions, which might a edugated by fluid retention. They should be prescribed with caution, and only with careful monitoring, in patients with conditions, which might a edugated by fluid retention. They should be prescribed with caution, and only with careful monitoring, inplatents with conditions, which might a edugated by fluid retention. They should be prescribed with caution, and only with careful monitoring, inplatents with conditions, which might a bagravated by fluid retention. They should be prescribed with caution, and only with careful monitoring in patients with conditions, which might a bagravated by fluid retention. They should be prescribed with caution, and only with careful monitoring in patients with conditions, which might a bagravated by fluid retention. They should be prescribed with caution, and only with careful monitoring in patients with conditions, which might a bagravated by fluid retention.
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Ing, in patients with containeds, which might be aggravated by liub retention. **6. Enviroional Disorders:** Women with a history of depression should be carefully observed and the drug discontinued if depression recurs to a serious depree. Patients becoming significantly depressed while taking oral contraceptives should stop the medication and use an alternate method of contraception in an attempt to determine whether the symptom is drug related. **7. Orate Lenses:** Contact-lens weares who develop visual changes or changes in test betarates should be assessed by an onthalmologist. **8. Orug Interactions:** Changes in contraceptive effectiveness associated with or-doministration of other products. • A. Arti-rifictive agents and other drugs that increase the metalodism of contraceptive stroids. This could result in unintended pregnancy or treaktivrough bleding. Examples includer flampin, Ler-tip and the antibiotics, anticons, increase and deverse on the betwere combine of a contraceptive and cost as ampioillin and test results. • b. Anti-HV protease inhibitors: Several of the anti-HV protease inhibitors thate been studied with or-administration of and contraceptive and costase, The staff with administration of anti-HV protease inhibitors: Several of the anti-HV protease inhibitors is contained splute and deverase) in the devena combine of and contraceptive and encores. The staff with develop indicates of the administration of anti-HV protease inhibitors contained splute and elevase (to the target) and play optication hate second to any relate the effectiveness of contraceptive and the antibility of the administration of anti-HV protease inhibitors in the administration of anti-HV protease inhibitors in the staff of the administration of anti-HV protease inhibitors in the staff of the administration of anti-HV protease inhibitors and the administration of anti-HV protease inhibitors in the staff of the administration of anti-HV protease inhibitors in the staff orelation is the administrating of a staff admini

OVERDOSAGE: Serious ill effects have not been reported following acute ingestion of large doses of oral contraceptives by young children. Overdosage may cause nausea, and withdrawal bleeding may occur in females.

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Kramer and his associates added (Lancet 2006:368:1444-8).

Despite being rare, amniotic fluid embolism is one of the leading causes of maternal mortality in developed countries, ahead of postpartum hemorrhage and other pulmonary embolisms. The cause of this catastrophic complication is not well understood. "It is thought to arise from a simultaneous tear in the fetal membranes and uterine vessels, through which amniotic fluid can pass into the uterine venous circulation and hence to the maternal pulmonary arterial circulation," the researchers said.

Strong uterine contractions are believed to raise the risk of amniotic fluid embolism, and induction and augmentation of labor have been proposed as possible contributing factors.

In their epidemiologic study of the association between drug-induced labor and amniotic fluid embolism, there were 180 cases of this condition, including 24 fatal cases, yielding a total rate of 6/100,000 singleton deliveries and a fatal rate of 0.8/100,000 singleton deliveries.

The rate was almost twice as high in women who had undergone medical induction of labor as in those who had not. This association remained robust after the data were adjusted to account for many other potential risk factors, such as maternal age, presentation, delivery method, previous cesarean delivery, pregnancy complications, and labor complications.

This finding "should be a cause for concern in view of the increasing tendency for clinicians to induce labour, and especially for routine induction at term or after term," the investigators said.

They also found that multiple pregnancy, older maternal age, cesarean delivery, forceps- or vacuum-assisted delivery, eclampsia, polyhydramnios, placenta previa, placental abruption, cervical laceration, uterine rupture, and fetal distress all raised the risk of amniotic fluid embolism, though not to the degree that drug-induced labor did. Many of these risk factors could be directly related to "the presumed causal roles of strong uterine contractions, excess amniotic fluid, and disruption of the uterine vasculature," the researchers noted.

Moreover, the link between amniotic embolism on the one hand and cesarean or instrumental vaginal delivery on the other "might simply reflect the difficult labours that led to these procedures, rather than true effects of the procedures themselves."

In particular, "the very strong association with caesarean delivery could also indicate reverse causality (i.e., the caesarean could have been a consequence of the signs and symptoms of amniotic fluid embolism," Dr. Kramer and his associates pointed out.

The rates of total and fatal amniotic fluid embolism did not increase over time in this study, even though the rate of medically induced labor did increase. This probably reflects the rarity of the disorder, or it could be because of the concomitant decrease in other risk factors, such as forceps delivery, they added.