West Middlesex University Hospital

SSRI'S and Aspirin

Date of Search: 27/06/2016 & 28/06/2016
Sources Searched: Medline, Embase, PsycINFO, BNF, NICE Evidence

Summary

The results from most, but not all observational studies suggest that there is an association between the use of SSRIs and upper GI bleeds. Several studies have found the use of SSRIs with concomitant NSAIDs to increase the risk of upper GI bleeding further. Being over the age of 80 or having a previous history of GI bleeding may also add to the risk of upper GI bleeding with SSRIs. There is also evidence that the risk is higher in patients who have just started taking SSRIs, in those taking SSRIs with a high/intermediate affinity for the serotonin receptor, and in male patients. If an SSRI is required in a patient at high risk of an upper GI bleed then the use of a gastro-protective agent could be considered. Studies have shown the use of acid suppressing drugs, e.g. PPIs, to be protective against upper GI bleeds in patients receiving single-therapy SSRI or combined NSAID and SSRI treatment. Current NICE guidance on depression recommends considering a gastroprotective drug in older people on SSRIs who are also taking NSAIDs or aspirin. Another source recommends that patients taking multiple drugs that could cause bleeding seek informed medical advice before starting regular use of non-prescription drugs such as ibuprofen.

Source: *What is the risk of gastrointestinal bleeding associated with selective serotonin reuptake inhibitors (SSRIs)?* (March 2015) UK Medicine's Information http://www.medicinesresources.nhs.uk/GetDocument.aspx?pageId=795809 [Accessed 27/06/2016]

Manufacturers advise avoid SSRI'S during pregnancy unless the potential benefit outweighs the risk.

Source: BNF June 2016 https://www.medicinescomplete.com/mc/bnf/current/PHP2421-citalopram.htm#PHP69017-contraindications-topic [Accessed 27/06/2016]

Risks of SSRI use in pregnancy:

- **General risks**
  - **First trimester exposure to selective serotonin reuptake inhibitors (SSRIs)** may be associated with:
    - An increased risk of congenital malformations, especially cardiovascular malformations. These are most consistently demonstrated with paroxetine but have also been reported for citalopram, fluoxetine, and sertraline.
    - Increased risks of other specific malformations. These have been reported in some studies but findings are inconsistent and causality cannot be determined. Available data are too limited to establish or exclude an association between prenatal SSRI exposure and risk of fetal loss.
  - **Use of any SSRI later in pregnancy** (after 20 weeks) may be associated with:
    - An increased risk of persistent pulmonary hypertension (PPHN) of the newborn (absolute risk less than 0.5%). There are inadequate data to quantify the risk of PPHN with any specific SSRI and there are no data on the effect of different doses.
    - Neonatal withdrawal symptoms (following near term or chronic use).
  - Some studies have suggested that exposure to SSRIs and other antidepressants during pregnancy may be associated with an increased risk of spontaneous abortion, low birth weight, and intrauterine growth restriction. However, there is evidence to suggest that the maternal condition may contribute to these adverse effects.
- **The UK Teratology Information Service (UKTIS) reviewed the evidence for paroxetine, citalopram, fluoxetine, and sertraline and concluded that:**
  - **For paroxetine:** use in early pregnancy has been associated with an increased risk of congenital malformations, especially those affecting the heart. However, available data are conflicting and the teratogenic potential of paroxetine remains unproven.
  - **For citalopram, fluoxetine, and sertraline:** data on the risk of congenital malformations following their use in early pregnancy are conflicting.
    - Several studies have demonstrated no statistically significant increase in risk; however, one large study has suggested an increased risk of cardiovascular malformations following their use in pregnancy. Due to the conflicting data the teratogenic potential of these drugs cannot be proved; however, if exposure in pregnancy does cause cardiovascular malformations, the absolute risk appears to be small.
  - **For escitalopram:** data on its safety in pregnancy are extremely limited; however, considering data for other SSRIs in pregnancy, the risk of congenital malformations following use in early pregnancy cannot be ruled out.
- **Based on the available data:**

- The UK Teratology Information Service (UKTIS) states that:
  - Although a risk of cardiovascular malformations was initially reported with only paroxetine, more recent data has indicated that there may be risks associated with all four of the most commonly prescribed SSRIs (citalopram, fluoxetine, paroxetine, and sertraline) though data are conflicting. Since the published data are contradictory, the teratogenic potential of SSRIs remains unproven.
  - Although associated with risks, some of which are severe, SSRIs may still need to be prescribed in pregnancy where alternative treatments are not considered clinically appropriate.
  - There is currently insufficient evidence to warrant additional fetal monitoring in women taking SSRIs, and exposure to citalopram, fluoxetine, sertraline, escitalopram, or paroxetine at any stage in pregnancy would not usually be regarded as medical grounds for termination of pregnancy.
- The Medicines and Healthcare products Regulatory Agency (MHRA) advises that when prescribing fluoxetine to treat depression during pregnancy, prescribers should be aware that there may be a small increased risk of congenital cardiac defects in infants exposed in early pregnancy, similar to that seen with paroxetine.

Source: *CKS Depression and antenatal* (September 2015) http://cks.nice.org.uk/depression-antenatal-and-postnatal#!scenariorecommendation:17 [last accessed 27/06/2016]

Search History:
1. Medline; "Selective serotonin reuptake inhibitor*".ti,ab; 9116 results.
2. Medline; "serotonin-specific reuptake inhibitor*".ti,ab; 91 results.
3. Medline; SSRI*1.ti,ab; 5360 results.
4. Medline; exp SEROTONIN UPTAKE INHIBITORS/; 32933 results.
5. Medline; "Serotonin Uptake Inhibitor*".ti,ab; 523 results.
6. Medline; 1 OR 2 OR 3 OR 4 OR 5; 36885 results.
7. Medline; aspirin*.ti,ab; 40776 results.
8. Medline; exp ASPIRIN/; 40158 results.
9. Medline; 7 OR 8; 58186 results.
10. Medline; 6 AND 9; 121 results.
11. Medline; pregn*.ti,ab; 404201 results.
12. Medline; exp PREGNANCY/; 787739 results.
13. Medline; 11 OR 12; 870043 results.
14. Medline; 10 AND 13; 2 results.
15. Medline; exp PRE-ECLAMPSIA/; 25883 results.
16. Medline; 6 AND 9 AND 15; 0 results.
17. Medline; exp AGE FACTORS/; 439200 results.
18. Medline; 10 AND 17; 9 results.
19. Medline; young*.ti,ab; 510978 results.
20. Medline; 10 AND 19; 5 results.
21. EMBASE; "Selective serotonin reuptake inhibitor*".ti,ab; 12493 results.

22. EMBASE; "serotonin-specific reuptake inhibitor*".ti,ab; 131 results.
23. EMBASE; SSRI*1.ti,ab; 13210 results.
24. EMBASE; exp SEROTONIN UPTAKE INHIBITORS/; 158931 results.
25. EMBASE; "Serotonin Uptake Inhibitor*".ti,ab; 591 results.
26. EMBASE; 21 OR 22 OR 23 OR 24 OR 25; 160696 results.
27. EMBASE; aspirin*.ti,ab; 57961 results.
28. EMBASE; exp ASPIRIN/; 170513 results.
29. EMBASE; 27 OR 28; 177949 results.
30. EMBASE; 26 AND 29; 4509 results.
31. EMBASE; pregn*.ti,ab; 502767 results.
32. EMBASE; exp PREGNANCY/; 620412 results.
33. EMBASE; 31 OR 32; 794743 results.
34. EMBASE; 30 AND 33; 155 results.
35. EMBASE; *SEROTONIN UPTAKE INHIBITOR/; 9954 results.
36. EMBASE; *ACETYLSALICYLIC ACID/; 46615 results.
37. EMBASE; 33 AND 35 AND 36; 0 results.
38. EMBASE; 35 AND 36; 31 results.
39. EMBASE; exp AGE/; 703522 results.
40. EMBASE; young*.ti,ab; 644562 results.
41. EMBASE; 39 OR 40; 1258040 results.
42. EMBASE; 38 AND 41; 3 results.
43. EMBASE; exp ECLAMPSIA AND PREECLAMPSIA/; 47669 results.
44. EMBASE; 30 AND 43; 18 results.
45. EMBASE; 33 AND 35; 597 results.
46. EMBASE; exp BLEEDING/; 676934 results.
47. EMBASE; 33 AND 36 AND 46; 216 results.
48. EMBASE; 33 AND 36 AND 46; 216 results.
49. EMBASE; 32 AND 36 AND 46; 151 results.
50. EMBASE; 30 AND 41; 277 results.
51. EMBASE; 29 AND 35 AND 41; 13 results.
52. EMBASE; exp ANTIINFLAMMATORY AGENT/; 1343213 results.
53. EMBASE; 33 AND 35 AND 52; 25 results.
54. EMBASE; 26 AND 43 AND 52; 53 results.
55. EMBASE; 35 AND 43; 15 results.
56. EMBASE; MATERNAL HYPERTENSION/; 12469 results.
57. EMBASE; 26 AND 29 AND 56; 8 results.
58. Medline; 6 AND 17; 899 results.
59. EMBASE; bleed*.ti,ab; 235631 results.
60. Medline; bleed*.ti,ab; 157729 results.
61. Medline; 58 AND 60; 15 results.
62. PsycInfo; "Selective serotonin reuptake inhibitor*".ti,ab; 6053 results.
63. PsycInfo; "serotonin-specific reuptake inhibitor*".ti,ab; 66 results.
64. PsycInfo; SSRI*1.ti,ab; 3757 results.
65. PsycInfo; "Serotonin Uptake Inhibitor*".ti,ab; 181 results.
66. PsycInfo; 62 OR 63 OR 64 OR 65; 7490 results.
67. PsycInfo; pregn*.ti,ab; 37506 results.
68. PsycInfo; exp PREGNANCY/; 20754 results.

69. PsycInfo; 67 OR 68; 39863 results.
70. PsycInfo; 66 AND 69; 260 results.
71. PsycInfo; 66 AND 69; 260 results.
72. PsycInfo; aspirin*.ti,ab; 2388 results.
73. PsycInfo; exp ASPIRIN/; 433 results.
74. PsycInfo; 72 OR 73; 2477 results.
75. PsycInfo; 71 AND 74; 2 results.
76. PsycInfo; bleed*.ti,ab; 2039 results.
77. PsycInfo; 66 AND 74 AND 76; 11 results.
78. PsycInfo; 66 AND 74 AND 76; 11 results.
79. Medline; exp HEMORRHAGE/; 286840 results.
80. Medline; 60 OR 79; 380297 results.
81. Medline; 6 AND 13 AND 80; 25 results.
82. EMBASE; exp BLEEDING/; 676934 results.
83. EMBASE; 33 AND 35 AND 82; 28 results.
84. EMBASE; exp DRUG INTERACTION/; 294787 results.
85. EMBASE; 30 AND 46 AND 84; 163 results.
86. EMBASE; exp RISK FACTOR/; 753313 results.
87. EMBASE; 85 AND 86; 24 results.
88. EMBASE; 30 AND 84 AND 86; 46 results.
89. EMBASE; (without adj2 "risk factor*").ti,ab; 4701 results.
90. EMBASE; 30 AND 89; 3 results.
91. EMBASE; age.ti,ab; 2463750 results.
92. EMBASE; 30 AND 91; 546 results.
93. EMBASE; age.ti; 175736 results.
94. EMBASE; 92 AND 93; 14 results.
95. EMBASE; exp YOUNG ADULT/; 141528 results.
96. EMBASE; 30 AND 95; 10 results

Title: Postpartum Hemorrhage and Use of Serotonin Reuptake Inhibitor Antidepressants in Pregnancy

Citation: Obstetrics and Gynecology, March 2016, vol./is. 127/3(553-561), 0029-7844;1873-233X (01 Mar 2016)

Author(s): Hanley G.E., Smolina K., Mintzes B., Oberlander T.F., Morgan S.G.

Language: English

Abstract: OBJECTIVE: To examine whether using selective serotonin reuptake inhibitors and selective serotonin-norepinephrine reuptake inhibitors in pregnancy is associated with an increased risk of postpartum hemorrhage. METHODS: We conducted a population-based cohort study including 225,973 women with 322,224 pregnancies in British Columbia, Canada, between 2002 and 2011. Women were categorized according to whether they had late-pregnancy exposure (at least 15 of the last 30 days of pregnancy), midpregnancy exposure (in the last 5 months of pregnancy but not the final 30 days), or no exposure.

Postpartum hemorrhage was identified using International Classification of Diseases (9th and 10th Revisions) codes in data on all hospitalizations. RESULTS: We found an increased risk of postpartum hemorrhage associated with exposure to an serotonin-norepinephrine reuptake inhibitor in the final month of pregnancy after adjustment for potential confounders (n51,390; adjusted odds ratio [OR] 1.76, 95% confidence interval [CI] 1.47-2.11, respectively) corresponding to 4.1 (95% CI 2.4-5.7) additional cases of postpartum hemorrhage per 100 people treated. There was no significant relationship between selective serotonin reuptake inhibitor use in the final month of pregnancy and postpartum hemorrhage (n56,637; adjusted OR 1.09, 95% CI 0.98-1.21), except when confining the cohort to women with complete body mass index (BMI) information (n5235,031 [73%]) and controlling for BMI (adjusted OR 1.14, 95% CI 1.01-1.28) or when controlling for variables that are possibly on the causal pathway (adjusted OR 1.13, 95% CI 1.02-1.26). Midpregnancy exposure to a serotonin-norepinephrine reuptake inhibitor (n5242) or a selective serotonin reuptake inhibitor (n51,507) was not associated with an increased postpartum hemorrhage risk. CONCLUSION: Serotonin-norepinephrine reuptake inhibitor exposure in late pregnancy was associated with a 1.6-to 1.9-fold increased risk of postpartum hemorrhage.

Publication Type: Journal: Article

Source: EMBASE

Full Text:
Available from *Obstetrics and Gynecology* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital
Available from *Ovid* in Obstetrics and Gynecology

Title: Is third trimester serotonin reuptake inhibitor use associated with postpartum hemorrhage?

Citation: Journal of Psychiatric Research, February 2016, vol./is. 73/(79-85), 0022-3956;1879-1379 (February 01, 2016)

Author(s): Kim D.R., Pinheiro E., Luther J.F., Eng H.F., Dills J.L., Wisniewski S.R., Wisner K.L.

Language: English

Abstract: As serotonin reuptake inhibitor (SRI) use may decrease platelet function, previous research has shown a relationship between SRI use and an increased risk for bruising and bleeding. The literature regarding the association between SRI use during pregnancy and increased bleeding at delivery, referred to as postpartum hemorrhage (PPH), is mixed. In secondary analyses from two prospective observational studies of pregnant women with mood disorders, 263 women were exposed to an SRI (n = 51) or not (n = 212) in the third trimester. To be precise, we used the terminology estimated blood loss (EBL) >600 cc rather than the term PPH because the current definition of PPH differs. The occurrence of EBL >600 cc was determined using the Peripartum Events Scale (PES) completed from obstetrical records by a blinded medically trained member of the study team. EBL >600 cc occurred in 8.7% of women in this cohort. There was no statistically significant difference in the rates of

EBL >600 cc in the 24 h after delivery in women taking SRIs during the third trimester (9.8%) compared to non-exposed women (8.5%). Utilizing generalizing estimating equations, the odds of EBL >600 cc in each group were not significantly different (OR 1.17, CI-0.41-3.32, p = 0.77). When the SRI group was limited to women with exposure at the time of delivery, the difference in the odds of EBL >600 cc was unchanged (OR 1.16, CI = 0.37-3.64, p = 0.79). In population, both third trimester and use at delivery of SRIs during pregnancy was not associated with an increased risk of excessive blood loss.

Publication Type: Journal: Article

Source: EMBASE

Title: Antidepressants during pregnancy and postpartum hemorrhage: a systematic review.

Citation: European journal of obstetrics, gynecology, and reproductive biology, Jun 2015, vol. 189, p. 38-47, 1872-7654 (June 2015)

Author(s): Bruning, Andrea H L, Heller, Hanna M, Kieviet, Noera, Bakker, Petra C A M, de Groot, Christianne J M, Dolman, Koert M, Honig, Adriaan

Abstract: The use of antidepressants in pregnancy is increasing. Concerns have risen about the use of antidepressants during pregnancy and the risk of postpartum hemorrhage (PPH). The aim of this systematic review is to summarize evidence on the association between use of antidepressants during pregnancy and the risk of PPH. An Embase and Pubmed search was conducted. English and Dutch language studies reporting original data regarding bleeding after delivery associated with exposure to antidepressants during pregnancy were selected. Quality appraisal was conducted using the Newcastle Ottawa Scale (NOS). Out of 81 citations, 4 studies were included. Based on the NOS, 3 were considered of good quality and 1 was considered of satisfactory quality. Two studies reported an increased incidence of PPH in women who used antidepressants during pregnancy. The other two studies identified no overall increased risk of PPH among pregnant women exposed to antidepressants. The existing evidence remains inconclusive whether use of antidepressants during pregnancy is associated with an increased risk of postpartum hemorrhage. If there is such an association the absolute increased risk will be low and the clinical relevance needs to be further examined.

Source: Medline

Title: Risk-benefit balance assessment of SSRI antidepressant use during pregnancy and lactation based on best available evidence

Citation: Expert Opinion on Drug Safety, March 2015, vol./is. 14/3(413-427), 1474-0338;1744-764X (01 Mar 2015)

Author(s): Weisskopf E., Fischer C.J., Bickle Graz M., Morisod Harari M., Tolsa J.-F., Claris O., Vial Y., Eap C.B., Csajka C., Panchaud A.

Language: English

Abstract: Introduction: Psychiatric disorders are among the leading causes of disability in Western societies. Selective serotonin reuptake inhibitors (SSRIs) are the most frequently prescribed antidepressant drugs during pregnancy and the postpartum period. Over the last decade, conflicting findings regarding the safety of SSRI drugs during pregnancy and lactation have questioned whether such treatments should be used during this period.Areas covered: We discuss the main criteria that should be considered in the risk/benefit assessment of SSRI treatment in pregnant and/or breastfeeding patients (i.e., risks associated with SSRI use and with untreated depression as well as therapeutic benefits of SSRI and some alternative treatment strategies). For each criterion, available evidence has been synthesized and stratified by methodological quality as well as discussed for clinical impact.Expert opinion: Currently, it is impossible for most of the evaluated outcomes to distinguish between the effects related to the mother's underlying disease and those inherent to SSRI treatment. In women suffering from major depression and responding to a pharmacological treatment, introduction or continuation of an SSRI should be encouraged in order to prevent maternal complications and to preserve maternal-infant bonding. The choice of the right drug depends above all on individual patient characteristics such as prior treatment response, diagnoses and comorbid conditions.

Publication Type: Journal: Review

Source: EMBASE

Title: Selective serotonin reuptake inhibitor (SSRI) use during pregnancy increases risk of postpartum hemorrhage and anemia: A hospital-based cohort study

Citation: Thrombosis Research, February 2015, vol./is. 135/(S70), 0049-3848 (February 2015)

Author(s): Lindqvist P.G., Nasiell J., Gustafsson L.L., Nordstrom L.

Language: English

Abstract: Background: Selective serotonin reuptake inhibitors (SSRIs) are known to increase the risk of gastrointestinal bleeding. Objective: Study the risk for bleeding complications in relation to SSRI in pregnancy. Patients and methods: A hospital-based cohort study. All delivered women at Karolinska University Hospital in Stockholm over a five-year period (2007 to 2011) were included in the study. Those women who the electronic maternal health record indicated were using SSRI (n=500) were considered exposed, and all other delivered women formed a control population (n=39,594). Main outcome measures: Blood loss, postpartum hemorrhage (PPH), PP anemia, and length of hospitalization. Results: The absolute risk of PPH and PP anemia for the 1.2% exposed to SSRI were 18.0% and 12.8%,

respectively. Among women with vaginal non-surgical delivered who reported use of SSRI during pregnancy had approximately a two-fold increased risk of both PPH (OR 2.6, 95% CI: 2.0-3.5) and PP anemia (OR 2.1, 95% CI: 1.5-2.9), as compared to controls. Blood loss and length of hospitalization were significantly higher among women using SSRI than non-users (arithmetic mean 484 mL vs. 398 mL, 3.8 d vs. 2.4 d, respectively). Conclusion: The use of SSRI during pregnancy increases blood loss and doubles the risk of PPH and PP anemia in a setting where SSRI had not been considered a risk factor for increased blood loss. Since PPH is a leading cause of maternal mortality and morbidity the awareness of bleeding complications is important both in relation to pregnancy and to surgery in general.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: The use of antidepressants in pregnancy: focus on maternal risks.

Citation: Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstétrique et gynécologie du Canada : JOGC, Jan 2015, vol. 37, no. 1, p. 56-63, 1701-2163 (January 2015)

Author(s): Gadot, Yifat, Koren, Gideon

Abstract: Studies have consistently reported a decrease in the use of antidepressants during pregnancy compared with the pre-pregnancy period. Multiple recent studies have focused on the potential fetal risks of selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs), with very little attention paid to maternal risks. The maternal risks of these medications are the focus of this review. Untreated depression is associated with increased risks of maternal morbidity, both somatic and psychiatric. In contrast, use of antidepressants has been associated with increased risks of hypertension, preeclampsia, and bleeding. In this review we present the evidence for maternal risks in an attempt to develop a risk-benefit ratio.

Source: Medline

Title: Risk of upper gastrointestinal bleeding from different drug combinations

Citation: Gastroenterology, October 2014, vol./is. 147/4(784-792.e9), 0016-5085;1528-0012 (01 Oct 2014)

Author(s): Masclee G.M.C., Valkhoff V.E., Coloma P.M., De Ridder M., Romio S., Schuemie M.J., Herings R., Gini R., Mazzaglia G., Picelli G., Scotti L., Pedersen L., Kuipers E.J., Van Der Lei J., Sturkenboom M.C.J.M.

Language: English

Abstract: Background & Aims Concomitant use of nonsteroidal anti-inflammatory drugs (NSAIDs) and low-dose aspirin increases the risk of upper gastrointestinal bleeding (UGIB). Guidelines suggest avoiding certain drug combinations, yet little is known about the magnitude of their interactions. We estimated the risk of UGIB during concomitant use of nonselective (ns)NSAIDs, cyclooxygenase -2 selective inhibitors (COX-2 inhibitors), and low-dose aspirin with other drugs. Methods We performed a case series analysis of data from 114,835 patients with UGIB (930,888 person-years of follow-up) identified from 7 population-based health care databases (approximately 20 million subjects). Each patient served as his or her own control. Drug exposure was determined based on prescriptions of nsNSAIDs, COX-2 inhibitors, or low-dose aspirin, alone and in combination with other drugs that affect the risk of UGIB. We measured relative risk (incidence rate ratio [IRR] during drug exposure vs nonexposure) and excess risk due to concomitant drug exposure (relative excess risk due to interaction [RERI]). Results Monotherapy with nsNSAIDs increased the risk of diagnosis of UGIB (IRR, 4.3) to a greater extent than monotherapy with COX-2 inhibitors (IRR, 2.9) or low-dose aspirin (IRR, 3.1). Combination therapy generally increased the risk of UGIB; concomitant nsNSAID and corticosteroid therapies increased the IRR to the greatest extent (12.8) and also produced the greatest excess risk (RERI, 5.5). Concomitant use of nsNSAIDs and aldosterone antagonists produced an IRR for UGIB of 11.0 (RERI, 4.5). Excess risk from concomitant use of nsNSAIDs with selective serotonin reuptake inhibitors (SSRIs) was 1.6, whereas that from use of COX-2 inhibitors with SSRIs was 1.9 and that for use of low-dose aspirin with SSRIs was 0.5. Excess risk of concomitant use of nsNSAIDs with anticoagulants was 2.4, of COX-2 inhibitors with anticoagulants was 0.1, and of low-dose aspirin with anticoagulants was 1.9. Conclusions Based on a case series analysis, concomitant use of nsNSAIDs, COX-2 inhibitors, or low-dose aspirin with SSRIs significantly increases the risk of UGIB. Concomitant use of nsNSAIDs or low-dose aspirin, but not COX-2 inhibitors, with corticosteroids, aldosterone antagonists, or anticoagulants produces significant excess risk of UGIB.

Publication Type: Journal: Article

Source: EMBASE

Title: Risk of vaginal bleeding and postpartum hemorrhage after use of antidepressants in pregnancy: a study from the Norwegian Mother and Child Cohort Study.

Citation: Journal of clinical psychopharmacology, Feb 2014, vol. 34, no. 1, p. 143-148, 1533-712X (February 2014)

Author(s): Lupattelli, Angela, Spigset, Olav, Koren, Gideon, Nordeng, Hedvig

Abstract: This study aimed to examine obstetric bleeding outcomes after exposure during pregnancy to selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), tricyclic (TCAs), and other antidepressants (OADs).The

Norwegian Mother and Child Cohort Study and the Medical Birth Registry of Norway constituted the data source for the present study. We included 57,279 pregnant women, of which 1.02% reported use of antidepressants during pregnancy, mostly SSRIs/SNRIs (0.92%). We categorized exposure according to antidepressant use in pregnancy (SSRIs/SNRIs, n = 527; TCAs/OADs, n = 59; nonexposed, nondepressed, n = 55,411) with inclusion of a disease comparison group (nonexposed, depressed, n = 1282). We used logistic regression to estimate adjusted odds ratio (aOR) and 95% confidence interval (CI) for vaginal bleeding outcomes in pregnancy and postpartum hemorrhage.Compared with nonexposed subjects, first trimester exposure to SSRIs/SNRIs or TCAs/OADs did not confer any increased risk of vaginal bleeding in early pregnancy (aOR, 0.91; 95% CI, 0.72-1.16 and aOR, 0.83; 95% CI, 0.36-1.92, respectively). No increased risk for vaginal bleeding in midpregnancy was observed among users of SSRIs/SNRIs (aOR, 0.81; 95% CI, 0.50-1.31) or TCAs/OADs (aOR, 0.96; 95% CI, 0.26-3.53) in second trimester. Exposure to SSRIs/SNRIs during gestational week 30 to childbirth did not confer any increased risk of postpartum hemorrhage after vaginal (aOR, 0.90; 95% CI, 0.47-1.74) or cesarean (aOR, 1.47; 95% CI, 0.51-4.22) delivery. Women in the disease comparison group presented a significant moderate increased risk of vaginal bleeding in early pregnancy (aOR, 1.22; 95% CI, 1.06-1.39) and midpregnancy (aOR, 1.28; 95% CI, 1.07-1.55) but not postpartum.Among this Norwegian cohort of pregnant women, use of antidepressants in pregnancy was not associated with any obstetrical bleeding outcome.

Source: Medline

Full Text:
Available from *Ovid* in Journal of Clinical Psychopharmacology
Available from *Ovid* in Journal of clinical psychopharmacology.

Title: Short-term use of serotonin reuptake inhibitors and risk of upper gastrointestinal bleeding.

Citation: The American Journal of Psychiatry, Jan 2014, vol. 171, no. 1, p. 54-61, 0002-953X (Jan 1, 2014)

Author(s): Wang, Yen-Po, Chen, Yung-Tai, Tsai, Chia-Fen, Li, Szu-Yuan, Luo, Jiing-Chyuan, Wang, Shuu-Jiun, Tang, Chao-Hsiun, Liu, Chia-Jen, Lin, Han-Chieh, Lee, Fa-Yauh, Chang, Full-Young, Lu, Ching-Liang

Abstract: Objective: The association between selective serotonin receptor inhibitors (SSRIs) and risk of upper gastrointestinal bleeding remains controversial. Previous studies have generally evaluated the issue for approximately 3 months, even though the SSRI-mediated inhibition of platelet serotonin concentrations occurs within 7–14 days. The authors explored the risk of upper gastrointestinal bleeding after short-term SSRI exposure by a case-crossover design. Method: The records of psychiatric inpatients with upper gastrointestinal bleeding were retrieved from the Taiwan National Health Insurance Database (199822009). Rates of antidepressant use were compared for case and control periods with time windows of 7, 14, and 28 days. The adjusted self-matched odds ratios from a conditional logistic regression model were used to determine the association

between SSRI use and upper gastrointestinal bleeding. Results: A total of 5,377 patients with upper gastrointestinal bleeding were enrolled. The adjusted odds ratio for the risk of upper gastrointestinal bleeding after SSRI exposure was 1.67 (95% CI = 1.23–2.26) for the 7-day window, 1.84 (95% CI = 1.42–2.40) for the 14-day window, and 1.67 (95% CI = 1.34–2.08) for the 28-day window. SSRIs with high and intermediate, but not low, affinity for serotonin transporter were associated with upper gastrointestinal bleeding. An elevated risk of upper gastrointestinal bleeding after SSRI exposure was seen in male but not female patients. Conclusions: Short-term SSRI use (7–28 days) is significantly associated with upper gastrointestinal bleeding. Gender differences may exist in the relationship between SSRI use and upper gastrointestinal bleeding. Physicians should carefully monitor signs of upper gastrointestinal bleeding even after short-term exposure to SSRIs, as is done with nonsteroidal anti-inflammatory drugs and aspirin. (PsycINFO Database Record (c) 2014 APA, all rights reserved)(journal abstract)

Source: PsycInfo

Full Text:
Available from *Free Access Content* in American Journal of Psychiatry

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Title: Use of antidepressants near delivery and risk of postpartum hemorrhage: Cohort study of low income women in the United States

Citation: BMJ (Online), August 2013, vol./is. 347/7922(no pagination), 1756-1833 (24 Aug 2013)

Author(s): Palmsten K., Hernandez-Diaz S., Huybrechts K.F., Williams P.L., Michels K.B., Achtyes E.D., Mogun H., Setoguchi S.

Language: English

Abstract: Objective: To determine whether use of serotonin or non-serotonin reuptake inhibitors near to delivery is associated with postpartum hemorrhage. Design: Cohort study. Setting: 2000-07 nationwide Medicaid data (Medicaid Analytic eXtract). Population 106 000 pregnant women aged 12-55 with a diagnosis of mood or anxiety disorder. Women were categorized into four mutually exclusive exposure groups according to pharmacy dispensing data: current (delivery date), recent (1-30 days before delivery date), past (1-5 months before delivery date), and no exposure (reference group). Main outcome measures: Risk of postpartum hemorrhage by timing of exposure and by serotonin or non-serotonin reuptake inhibitors, classes of antidepressant, and antidepressant types. Relative risks and 95% confidence intervals adjusted for delivery year, risk factors for postpartum hemorrhage, indicators of severity of mood/anxiety disorder, other indications for antidepressants, and other drugs. High dimensional propensity score (hdPS) methods were used to empirically identify and adjust for additional factors. Results: 12 710 (12%) women had current exposure to serotonin reuptake inhibitor monotherapy, and 1495 (1.4%) women had current exposure to non-serotonin reuptake inhibitor monotherapy. The risk of postpartum hemorrhage was 2.8% among women with mood/anxiety disorders but no exposure to antidepressants, 4.0% in the current users of serotonin reuptake inhibitors, 3.8% in the

current users of non-serotonin reuptake inhibitors, 3.2% in the recent users of serotonin reuptake inhibitors, 3.1% in the recent users of non-serotonin reuptake inhibitors, 2.5% in the past users of serotonin reuptake inhibitors, and 3.4% in the past users of non-serotonin reuptake inhibitors. Compared with no exposure, women with current exposure to serotonin reuptake inhibitors had a 1.47-fold increased risk of postpartum hemorrhage (95% confidence interval 1.33 to 1.62) and women with current non-serotonin reuptake inhibitor exposure had a 1.39-fold increased risk (1.07 to 1.81). Results were similar with hdPS adjustment. Women with current exposure to serotonin reuptake inhibitors had an adjusted excess risk of 1.26% (0.90% to 1.62%), with a number needed to harm of 80, and for women with current exposure to non-serotonin reuptake inhibitors the excess risk was 1.03% (0.07% to 1.99%), with a number needed to harm of 97. For exposure to serotonin reuptake inhibitors the relative risk was 1.19 (1.03 to 1.38) for recent exposure and 0.93 (0.82 to 1.06) for past exposure; for non-serotonin reuptake inhibitors the figures were 1.17 (0.80 to 1.70) and 1.26 (1.00 to 1.59), respectively. Current exposure to selective serotonin reuptake inhibitor monotherapy was also associated with postpartum hemorrhage (1.42, 1.27 to 1.57), as was current serotonin norepinephrine (noradrenaline) reuptake inhibitor (1.90, 1.37 to 2.63) and tricyclic monotherapy (1.77, 0.90 to 3.47). All types of selective serotonin reuptake inhibitors available for analysis and venlafaxine, a serotonin norepinephrine reuptake inhibitor, were significantly associated with postpartum hemorrhage. Conclusions: Exposure to serotonin and non-serotonin reuptake inhibitors, including selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclics, close to the time of delivery was associated with a 1.4 to 1.9-fold increased risk for postpartum hemorrhage. While potential confounding by unmeasured factors cannot be ruled out, these findings suggest that patients treated with antidepressants during late pregnancy are more likely to experience postpartum hemorrhage.

Publication Type: Journal: Article

Source: EMBASE

Title: Selective serotonin reuptake inhibitors and pregnancy: A review of maternal, fetal and neonatal risks and benefits

Citation: Obstetric Medicine, 2013, vol./is. 6/4(155-158), 1753-495X;1753-4968 (2013)

Author(s): Marchocki Z., Russell N.E., Donoghue K.O.

Language: English

Abstract: Depression is common in women of childbearing age. Whereas non-pharmacological interventions are recommended as first line interventions, pharmacological

treatment may be required. Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants in pregnancy. Ideally, discussion of the risks and benefits of SSRI use in pregnancy should occur prior to pregnancy. The potential risks of psychotropic medications need to be balanced against the risks associated with untreated psychiatric conditions and the discontinuation of necessary medications. © The Author(s) 2013 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav.

Publication Type: Journal: Review

Source: EMBASE

Title: Selective serotonin reuptake inhibitors in pregnancy

Citation: Current Medicinal Chemistry, 2012, vol./is. 19/27(4554-4561), 0929-8673;1875-533X (2012)

Author(s): Bellissima V., Ververs T.F.F., Visser G.H.A., Gazzolo D.

Language: English

Abstract: The use of antidepressant drugs, such as selective serotonin reuptake inhibitors (SSRIs), during pregnancy is rapidly increasing. To date, the effects of SSRI on pregnant women and fetuses are controversial and still a matter of debate. Although a number of studies have shown that these antidepressants are not teratogenic, some of them have reported an increase of congenital malformations after antenatal exposure to SSRIs. Moreover, fetal behavior is affected by these drugs, 30% of infants suffer from neonatal withdrawal symptoms and long term sequelae have not yet been excluded. Since there are no clear guidelines for SSRI treatment in pregnancy, potential risks must be balanced against the effects of untreated maternal depression. Treatment with SSRIs before and during pregnancy should only be considered in case of real necessity. Milder forms of depression should be treated with alternative methods. In this paper we have reviewed the literature on effects of SSRIs on embryonic, fetal and infant development.

Publication Type: Journal: Article

Source: EMBASE

Title: Serotonin reuptake inhibitor antidepressants and abnormal bleeding: a review for clinicians and a reconsideration of mechanisms.

Citation: The Journal of clinical psychiatry, Dec 2010, vol. 71, no. 12, p. 1565-1575, 1555-2101 (December 2010)

Author(s): Andrade, Chittaranjan, Sandarsh, Surya, Chethan, Kumar B, Nagesh, Koregala S

Abstract: It is generally believed that selective serotonin reuptake inhibitor (SSRI) drugs increase the risk of abnormal bleeding and decrease the risk of ischemic heart disease events by blocking the uptake of serotonin into platelets, leading to an impairment in the platelet hemostatic response. To perform a detailed qualitative review of existing literature on the association of abnormal bleeding with the use of SSRIs. We conducted a PubMed search during June 2009 using the search terms antidepressants and SSRIs (including the names of individual SSRIs: fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram) in association with bleeding, platelets, hemostasis, nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin, antiplatelet drugs, proton pump inhibitors, peptic ulcer, premenstrual dysphoric disorder, menstruation, pregnancy, postpartum hemorrhage, surgery, tooth extraction, dental bleeding, stroke, ischemic heart disease, and other terms related to the field. We then searched the reference lists of identified studies. We provide a qualitative discussion of all studies that would inform clinicians about the mechanisms of bleeding and bleeding risks associated with these drugs in different clinical contexts. Epidemiologic studies show that SSRI use is associated with roughly doubled odds of upper gastrointestinal (GI) bleeding; bleeding at other sites has been less commonly described, as has a possibly increased risk of bleeding associated with surgical procedures. The risk of SSRI-associated GI bleeding is increased with the concurrent use of NSAIDs, anticoagulants, and antiplatelet agents and is decreased by concurrent proton pump inhibitors. The risk of bleeding is increased in patients with cirrhosis of the liver or liver failure. There is, curiously, little literature on use of SSRIs and menstrual or postpartum blood loss. Selective serotonin reuptake inhibitors appear protective against ischemic heart disease events. The data are too limited to allow interpretations about influences on ischemic and hemorrhagic stroke. On the basis of the findings of our literature search, we suggest that SSRI-induced increase in gastric acid secretion may explain the GI bleeding risk and that SSRI-related effects on platelet reactivity, endothelial reactivity, and inflammatory markers may explain the ischemic heart disease protective effect. Because the absolute risk of GI bleeds with SSRIs is low, precautions are probably necessary only in high-risk patients, such as those with acid-peptic disease and those with a history of bleeds. We discuss management issues and areas for future research.

Source: Medline

Title: An Association Between Selective Serotonin Reuptake Inhibitor Use and Serious Upper Gastrointestinal Bleeding

Citation: Clinical Gastroenterology and Hepatology, December 2009, vol./is. 7/12(1314-1321), 1542-3565 (December 2009)

Author(s): Dall M., Schaffalitzky de Muckadell O.B., Lassen A.T., Hansen J.M., Hallas J.

Language: English

Abstract: Background & Aims: In vitro studies have shown that selective serotonin reuptake inhibitors (SSRIs) inhibit platelet aggregation. It is controversial whether use of SSRIs is a cause of clinically important bleeding; results from observational studies have been

equivocal. Methods: A population-based case-control study was conducted in Denmark. The 3652 cases all had a first discharge diagnosis of serious upper gastrointestinal bleeding (UGB) from 1995 to 2006. Controls (n = 36,502), matched for age and sex, were selected by risk-set sampling. Data on drug exposure and medical history were retrieved from a prescription database and the county's patient register. Confounders were controlled for by conditional logistic regression and the case-crossover design. Results: The adjusted odds ratio (OR) of UGB among current, recent, and past users of SSRIs was 1.67 (95% confidence interval [CI], 1.46-1.92), 1.88 (95% CI, 1.42-2.5), and 1.22 (95% CI, 1.07-1.39). The adjusted OR for concurrent use of SSRI and nonsteroidal anti-inflammatory drugs (NSAIDs) was 8.0 (95% CI, 4.8-13). The adjusted OR for the concurrent use of NSAID, aspirin, and SSRI was 28 (95% CI, 7.6-103). Of the UGB cases, 377 were current users of SSRI; the adjusted OR for UGB in the case crossover analysis was 2.8 (95% CI, 2.2-3.6). The adjusted OR among users of proton pump inhibitors was 0.96 (95% CI, 0.50-1.82). Conclusions: Use of SSRI was associated with UGB, consistent with its antiplatelet effects. SSRIs should be prescribed with caution for patients at high risk for UGB. © 2009 AGA Institute.

Publication Type: Journal: Article

Source: EMBASE

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

Citation: Journal of clinical psychopharmacology, Apr 2008, vol. 28, no. 2, p. 230-234, 0271-0749 (April 2008)

Author(s): Salkeld, Erin, Ferris, Lorraine E, Juurlink, David N

Abstract: 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, we 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. This was a population-based nested case-control study of women aged 16 to 45 years in Ontario, Canada, who received government-funded prescription coverage within 2 years before delivery. We identified case patients with postpartum hemorrhage and matched controls (1:10) without postpartum hemorrhage from the same cohort. Controls were matched to cases on age, mode of delivery, parity, and calendar time. We linked prescription claims data to hospital and physician records for the study period (January 1999 to March 2005). Exclusion criteria included drugs and medical conditions that predispose to hemorrhage, and receipt of multiple antidepressants in the 6 months preceding delivery. Antidepressant drug exposure was classified as SSRI or other agents within 90 days before delivery. There were 2460 postpartum hemorrhage cases and 23,943 matched controls. The adjusted odds ratio for the association between postpartum hemorrhage and exposure to SSRIs within 90 days before index date was 1.30 (95% confidence interval, 0.98-1.72) as compared with 1.12 (95% confidence interval, 0.62-2.01) for non-SSRIs. Selective serotonin reuptake inhibitors

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.

Source: Medline

Full Text:
Available from *Ovid* in Journal of Clinical Psychopharmacology

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Title: Selective serotonin reuptake inhibitors and risk of upper GI bleeding: confusion or confounding?

Citation: The American journal of medicine, Sep 2006, vol. 119, no. 9, p. 719-727, 1555-7162 (September 2006)

Author(s): Yuan, Yuhong, Tsoi, Keith, Hunt, Richard H

Abstract: Selective serotonin reuptake inhibitors (SSRIs) represent a relatively new class of antidepressants. Several studies have reported bleeding disorders associated with the use of SSRIs, which are considered the result of a decrease in platelet serotonin leading to a defect in platelet aggregation. To what extent the use of SSRIs increases the risk of gastrointestinal bleeding is unclear. A comprehensive literature search for studies addressing SSRI use and upper gastrointestinal tract bleeding (UGIB) was conducted using Medline, EMBASE, and Cochrane databases with a recursive manual reference search up to May 2005. Any observational and interventional studies were systematically reviewed, and critical appraisal was conducted on available studies. Published clinical evidence on the relationship between SSRI use and gastrointestinal bleeding is limited to observational studies without any clinical trials. Three cohort studies and one case-control study met inclusion criteria. These studies combined different affinity SSRIs in the class and had differing control groups with conflicting conclusions. Both a cohort study and a case-control study investigating the concurrent use of nonsteroidal anti-inflammatory drugs (NSAIDs) or low-dose aspirin found that combined use with an SSRI increased the risk of UGIB. Only a few epidemiology studies have investigated the association between SSRIs and UGIB. They provide weak evidence to support the hypothesis of a link between SSRIs and UGIB at a population level. Available evidence shows that concurrent use of NSAIDs or aspirin with SSRIs greatly increases the risk of UGIB. The preventive strategy should be considered in those SSRI users at high risk, especially the elderly or those with a history of UGIB and taking nonselective NSAIDs or aspirin.

Source: Medline

Full Text:
Available from *American Journal of Medicine* in Patricia Bowen Library and Knowledge Service West Middlesex university Hospital

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Title: Interaction between selective serotonin reuptake inhibitors and nonsteroidal antiinflammatory drugs: review of the literature.

Citation: Pharmacotherapy, Sep 2006, vol. 26, no. 9, p. 1307-1313, 0277-0008 (September 2006)

Author(s): Mort, Jane R, Aparasu, Rajender R, Baer, Rebecca K

Abstract: To evaluate the evidence of an interaction between selective serotonin reuptake inhibitors (SSRIs) and nonsteroidal antiinflammatory drugs (NSAIDs) producing an increased risk for gastrointestinal adverse outcomes such as bleeding. We searched MEDLINE for English-language literature published between 1966 and August 2005. All studies examining gastrointestinal adverse effects from an SSRI-NSAID combination were included. Four retrospective studies examined gastrointestinal adverse outcomes from the combination of SSRIs and NSAIDs. The risk ratio for an upper gastrointestinal bleed from this drug combination (compared with not receiving either agent) ranged from 3.3-15.6, and the risk ratio for gastrointestinal adverse effects was 12.4. Two studies found that the risk for an upper gastrointestinal bleed from the drug combination exceeded the additive risk of the agents alone. The risk ratio for an upper gastrointestinal bleed from an SSRI-aspirin interaction was 1.9-7.2. In addition, the number needed to harm in terms of an upper gastrointestinal bleed from an SSRI-NSAID combination ranged from 62-75 patient-years, and the number needed to harm for gastrointestinal adverse effects was 2 patient-years. Concurrent use of an SSRI and NSAID increases the risk of gastrointestinal adverse outcomes such as bleeding. Clinicians must take care to avoid these negative outcomes by altering NSAID or SSRI therapy, or by providing ulcer-protective drugs.

Source: Medline

Full Text:
Available from *John Wiley and Sons* in Pharmacotherapy, The Journal Of Human Pharmacology And Drug Therapy
Available from *John Wiley and Sons* in Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy

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Title: Antidepressants and risk of upper gastrointestinal bleeding.

Citation: Basic & clinical pharmacology & toxicology, Mar 2006, vol. 98, no. 3, p. 304-310, 1742-7835 (March 2006)

Author(s): de Abajo, Francisco J, Montero, Dolores, Rodríguez, Luis A García, Madurga, Mariano

Abstract: Selective serotonin reuptake inhibitors (SSRIs) are nowadays the most widely used antidepressants in the world, mainly because they have a better adverse reaction profile and a higher safety margin in overdoses, when compared to other antidepressants. These drugs recently have been the target of important debates concerning safety issues, among them the possibility that they may increase the risk of bleeding. Over the 1990s, an increasing number of individual cases of bleeding disorders were reported in the literature and to the pharmacovigilance programmes which prompted several epidemiological and

pharmacological studies. In this review we have examined all available data. The whole evidence supports the hypothesis that antidepressants with a relevant blockade action on serotonin reuptake mechanism increase the risk of bleeding. Such disorders may have different degrees of severity and may be located anywhere in the body. The epidemiological evidence is, however, more robust for upper gastrointestinal bleeding. It has been estimated that upper gastrointestinal bleeding may occur at a frequency ranging from 1 in 100 to 1 in 1,000 patient-years of exposure to high-affinity drugs (the SSRIs), with the very old patients being in the highest part of the range. The increased risk may be of particular relevance when the SSRIs are associated with NSAIDs as well as low-dose aspirin.

Source: Medline

Full Text:
Available from *John Wiley and Sons* in Basic and Clinical Pharmacology and Toxicology
Available from *John Wiley and Sons* in Basic and Clinical Pharmacology and Toxicology

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Title: Which patients taking SSRIs are at greatest risk of bleeding?

Citation: The Journal of family practice, Mar 2006, vol. 55, no. 3, p. 206-208, 0094-3509 (March 2006)

Author(s): Mansour, Ahmed, Pearce, Mark, Johnson, Benjamin, Sey, Michael Sai Lai, Oda, Ninos, Collegala, Natasha, Krishnadev, Upasana, Bhalerao, Shree

Abstract: For patients at high risk of abnormal bleeding, consider prescribing an antidepressant with low serotonin reuptake inhibition, which may lower risk. For patients taking high-serotonin reuptake inhibition antidepressants, recommend avoidance or minimal use of nonsteroidal anti-inflammatory drugs and aspirin.

Source: Medline

Title: SSRIs and upper gastrointestinal bleeding: what is known and how should it influence prescribing?

Citation: CNS drugs, Jan 2006, vol. 20, no. 2, p. 143-151, 1172-7047 (2006)

Author(s): Dalton, Susanne O, Sørensen, Henrik T, Johansen, Christoffer

Abstract: SSRIs have achieved a high usage rate in the treatment of depression because of a similar efficacy to TCAs and a favourable safety and tolerability profile. However, SSRI use has been associated with bleeding. We reviewed the epidemiological evidence on the association between SSRI use alone and the risk of upper gastrointestinal bleeding, and on synergistic effects reported with other commonly used drugs that can also cause bleeding.A literature search identified four studies of SSRI use and risk for upper gastrointestinal bleeding and a further two studies of SSRI use and bleeding in general, including upper gastrointestinal bleeding. The available evidence indicates quite convincingly that SSRI use

may play a causal role in upper gastrointestinal bleeding and that these drugs may act synergistically with other bleeding risk-increasing medications such as NSAIDs or low-dose aspirin. Assuming a causal role of SSRIs, reported excess gastrointestinal bleedings attributable to SSRI use was reported to be 3.1 per 1000 treatment years, 4.1 per 1000 treatment years among octogenarians and 11.7 per 1000 treatment years among persons with prior upper gastrointestinal bleeding. These non-negligible risks warrant that prescribing doctors consider strategies on the individual level to reduce the likelihood of an upper gastrointestinal adverse event. Patients at particular risk include those with previous ulcers or gastrointestinal bleeding, the elderly and those with certain concurrent illnesses and/or high-risk comedications. Suggested strategies include alternatives to SSRI use, prescribing of less gastrotoxic NSAIDs or co-prescribing of gastroprotective drugs. Patients should be informed about the likelihood of possible upper gastrointestinal bleeding and high-risk patients should be followed closely.

Source: Medline

Title: Safety of selective serotonin reuptake inhibitors in pregnancy.

Citation: Current drug safety, Jan 2006, vol. 1, no. 1, p. 17-24, 1574-8863 (January 2006)

Author(s): De las Cuevas, Carlos, Sanz, Emilio J

Abstract: Psychiatric treatment with selective serotonin reuptake inhibitors (SSRIs) may be desirable or necessary during pregnancy; however, the benefit of these treatments must balance the benefits to the mother with any risk to the developing foetus. At the present time, the role of serotonin in normal central nervous system development, as well as the effects of altering serotonin transmission at critical periods of embryo development, remains to be further clarified. Depression has a high prevalence in pregnant women (around 10%) and approximately one-half of the pregnancies are unplanned, making necessary that physicians have to know the risks associated with the decision to use this kind of antidepressants during pregnancy. The effects of antidepressants in pregnancy could be classified in several main categories: the teratogenic possible effects; the effects on the normal development of the brain and neuropsychological functions; the effects on birth weight and/or early delivery; the risk of increased bleeding on the mother during delivery; the neuropsychological behaviour and adaptation after delivery, including not only neonatal withdrawal syndromes but also pain reactivity and increased parasympathetic cardiac modulation during recovery after an acute noxious event and in a wide range of neurobehavioural outcomes; and medium- to long-term effects in neurocognitive functions in those children. These areas are reviewed according to the most recent published cohort-controlled studies and prospective surveys regarding SSRIs use in pregnancy. The review tries to clarify the blurred aspects of the use of SSRI during pregnancy and to give sensible and up-to-dated guidelines for the treatment of psychiatric disorders with SSRI during pregnancy.

Source: Medline

Title: Maternal selective serotonin reuptake inhibitor intake does not seem to affect neonatal platelet function tests.

Citation: Acta haematologica, Jan 2006, vol. 115, no. 3-4, p. 157-161, 0001-5792 (2006)

Author(s): Maayan-Metzger, A, Kuint, J, Lubetsky, A, Shenkman, Boris, Mazkereth, R, Kenet, G

Abstract: Recently, concerns have been raised regarding the potential impairment of neonatal platelet function and the potential risk of bleeding in neonates born to mothers treated with selective serotonin reuptake inhibitors (SSRI). Our aim was to test whether the platelet function of neonates born to SSRI-treated mothers was impaired when compared to non-SSRI-exposed neonates. In a single-center prospective study, platelet function was evaluated using a cone and platelet analyzer (CPA) device and compared between mother-infant pairs as well as normal non-SSRI-exposed infants. Twenty-seven SSRI-exposed and 27 non-SSRI-exposed full-term neonates and their 23 mothers were tested. No correlation was found between SSRI exposure among either neonates or mothers and parameters of surface coverage (SC) and average size (AS), manifesting platelet function as tested by CPA. SC was similar among SSRI-exposed babies as compared to those in the control group, whereas the size of platelet aggregates (AS) was higher among controls. Neither maternal diseases nor SSRI intake were associated with impaired platelet function and lower SC values, nor were any perinatal conditions. None of the babies suffered from bleeding. We conclude that maternal SSRI therapy does not impair whole-blood CPA-tested platelet function of healthy full-term neonates.

Source: Medline

Title: Paroxetine use during pregnancy associated with neonatal intracerebral bleeding.

Citation: Primary Psychiatry, Jul 2004, vol. 11, no. 7, p. 21-22, 1082-6319 (Jul 2004)

Author(s): Ginsberg, David L.

Abstract: In studies evaluating the safety of Selective serotonin reuptake inhibitors (SSRIs) during pregnancy, while no increase in major anomalies has been reported, several studies have found a greater risk of neonatal complications, including premature delivery, lower Apgar scores, and neurobehavioral effects, such as tremulousness, erratic motor activity, and underarousal. The article presents a case report of neonatal intracerebral hemorrhage in association with maternal use of paroxetine throughout pregnancy. Recently, there have been reports of neonatal intracerebral hemorrhage in association with maternal use of paroxetine throughout pregnancy. In evaluating the potential adverse effects of prenatal exposure to SSRIs and in deciding whether to use these medications during pregnancy, physicians and parents must balance these concerns against the seriousness of depression and its risks both to mother and baby, and should consider the effectiveness of other nonmedication treatments, such as psychotherapy. In the interim, clinicians who prescribe

SSRIs during pregnancy ought to be aware of the possibility of precipitating bleeding in the neonate, particularly in patients who have a past personal or family history of bleeding. In all pregnant women taking SSRIs during pregnancy, consideration should be given to advising against concomitant use of aspirin, NSAIDs, or other medications which may impair clotting.

Source: PsycInfo

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