PRESCRIBING HORMONAL CONTRACEPTIVES TO WOMEN WITH MIGRAINE (CON)

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Disclosures
- Advisory Boards: Eli Lilly, Dr. Reddy’s
- Common Stock: J&J, Stryker
- Associate Editor: Headache

Objectives/Discussion Points
- Risk of stroke associated with contraceptives
- Risk of stroke associated with migraine, specifically migraine with aura
- Risk of stroke in woman with migraine using OCP
- Guidelines addressing use of OCP in women with migraine with aura
OCP use is associated with ischemic stroke, MI, and VTE

Risk of Stroke with OCP. Meta-analysis 2000

• More than 10 million women on low dose OCP (< 50 mcg) in U.S.

• Meta-analysis: 16 studies were analyzed using random effects modeling

• Ischemic stroke risk (controlling for HTN and smoking):
  
  RR 1.93 (95% CI 1.36-2.74) for <50 mcg EE/day

  • Increase from 4.4 to 8.5 strokes per 100,000 women
     1 additional stroke per 24,000

  • Increase of 425 strokes per year

Gillum LA, et al. JAMA 2000;284:72-78

Risk of Stroke with OCP. Meta-analysis 2013

<table>
<thead>
<tr>
<th>Authors, year of publication</th>
<th>Year of recruitment</th>
<th>Type of study</th>
<th>Number of women</th>
<th>RR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARO collaboration, 1996</td>
<td>1989-1993</td>
<td>Case control</td>
<td>141,073</td>
<td>1.3(0.97-1.7)</td>
</tr>
<tr>
<td>Holstein et al., 1997</td>
<td>1991-1995</td>
<td>Case control</td>
<td>229,775</td>
<td>2.0(1.20-3.4)</td>
</tr>
<tr>
<td>Holtz et al., 1998</td>
<td>1991-1998</td>
<td>Case control</td>
<td>144,788</td>
<td>0.7(0.3-1.8)</td>
</tr>
<tr>
<td>Schulte et al., 1998</td>
<td>1991-1995</td>
<td>Case control</td>
<td>175,191</td>
<td>0.7(0.3-1.5)</td>
</tr>
<tr>
<td>Kooperman et al., 1997</td>
<td>NA</td>
<td>Case control</td>
<td>140,136</td>
<td>4.1(1.7-10.8)</td>
</tr>
<tr>
<td>Lefebvre et al., 1998</td>
<td>1991-1998</td>
<td>Case control</td>
<td>626,482</td>
<td>0.7(0.4-1.1)</td>
</tr>
<tr>
<td>Tonsil et al., 1995</td>
<td>1996-1997</td>
<td>Case control</td>
<td>72,173</td>
<td>3.1(1.2-8.2)</td>
</tr>
<tr>
<td>Knott et al., 1998, 2002</td>
<td>1991-1995</td>
<td>Case control</td>
<td>203,225</td>
<td>2.1(1.5-3.1)</td>
</tr>
<tr>
<td>Steinh et al., 2004</td>
<td>1991-1998</td>
<td>Case control</td>
<td>236,282</td>
<td>1.8(0.8-3.9)</td>
</tr>
<tr>
<td>Nightingale et al., 2004</td>
<td>1991-1998</td>
<td>Menedez case</td>
<td>180,139</td>
<td>2.3(1.2-4.5)</td>
</tr>
<tr>
<td>Mustelin et al., 2004</td>
<td>1994-1995</td>
<td>Case control</td>
<td>105,283</td>
<td>2.3(1.4-3.8)</td>
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<tr>
<td>Peruzzi et al., 2007</td>
<td>NA</td>
<td>Case control</td>
<td>108,256</td>
<td>4.0(2.5-6.5)</td>
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<tr>
<td>Yang et al., 1999</td>
<td>1991-2004</td>
<td>Cohort</td>
<td>153,069</td>
<td>3.1(1.9-5.3)</td>
</tr>
<tr>
<td>Gallagher et al., 2013a</td>
<td>1989-2000</td>
<td>Cohort</td>
<td>699,267,400</td>
<td>0.9(0.7-1.2)</td>
</tr>
</tbody>
</table>

RR: Risk ratio. CI: Confidence interval.

* Not available.
* Mortality events.
* Not included in the meta-analysis because the risk accounted for comparison of even cases with severe cases.

Plu-Bureau G. Best Practice & Research Clinical Endocrinology & Metabolism 27 (2013) 35-45
Cochrane Review of MI and Stroke risk with OCP use. Meta-analysis 2015

- 28 publications included, moderate quality of evidence
- Risk of ischemic stroke was 1.7-fold (95% CI 1.5-1.9) increase in OCP users
- Risk of myocardial infarction was 1.6-fold (95% CI 1.2-2.1) increase in OCP users
- Risk increased with higher dose of estrogen
- Risk did not vary clearly according to the generation of progestagen or according to progestagen type.


Risk of Stroke with OCP. Meta-analysis 2015

<table>
<thead>
<tr>
<th>Estrogen dose</th>
<th>Study #</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 50 mcg</td>
<td>9</td>
<td>3.3 (2.5-4.3)</td>
</tr>
<tr>
<td>&lt; 50 mcg</td>
<td>11</td>
<td>2.0 (1.6-2.4)</td>
</tr>
<tr>
<td>30-40 mcg</td>
<td>5</td>
<td>1.8 (1.6-1.9)</td>
</tr>
<tr>
<td>20 mcg</td>
<td>3</td>
<td>1.6 (1.4-1.8)</td>
</tr>
<tr>
<td>Progestin only pills</td>
<td>4</td>
<td>0.99 (0.7-1.4)</td>
</tr>
</tbody>
</table>

Summary OR for first-ever ischemic stroke risk associated with current use of OCPs

Risk of Stroke with OCP

15 year Danish cohort study of 1.6 million women, 15-49 yo, 5036 events/9,336,662 person years

Although the absolute risks of thrombotic stroke and myocardial infarction associated with the use of hormonal contraception were low, the risk was increased by a factor of 0.9 to 1.7 with oral contraceptives that included ethinyl estradiol at a dose of 20 μg and by a factor of 1.3 to 2.3 with those that included ethinyl estradiol at a dose of 30 to 40 μg, with relatively small differences in risk according to progestagen type. (Funded by the Danish Heart Association.)

Study CHCs:
- Drospirenone (3.0 mg)/ethinyl estradiol (30 mcg) tablets
  - ATE—HR=2.01 (95% CI 1.06-3.81)
  - VTE—HR=1.77 (95% CI 1.33-2.35)
- Norelgestromin (6.0 mg)/EE (750 mcg) transdermal patch
- Etonogestrel (11.7 mg)/EE (2700 mcg) vaginal ring

Comparator CHCs
- Levonorgestrel (0.10 mg)/EE (20 mcg) tabs
- Levonorgestrel (0.15 mg)/EE (30 mcg) tabs
- Norethindrone (1 mg)/EE (20 mcg) tabs
- Norgestimate (0.18–0.25 mg)/EE (35 mcg) tabs

Risk of Venous thromboembolism (VTE)
- VTE = deep venous thrombosis, pulmonary embolus
- Rate of 10 per 100,000 women-years among non-pregnant women not using COCs
- The adjusted odds ratio (OR) for VTE associated with current low estrogen OCP use was 4.07 (95% CI 2.8–6.0)

Hormonal contraceptive—Summary
- Arterial disease, including coronary heart disease and stroke, is one of the major harmful effects of hormonal contraceptives. It is less common than venous thrombosis
- Reducing the daily dose of ethinyl-estradiol leads to a decrease in the risk of arterial disease
- The risk of arterial disease is similar among users of second and third generation pills
- Non-oral hormonal contraceptives are no safer than oral hormonal contraceptives
- Progestogen only pills appear not to be associated with an increased risk of myocardial infarction and stroke
OCP use is associated with thrombophilia
Balance of Hemostasis

ATIII, Protein C, Protein S  \[\downarrow\]  COAGULATION  \[\uparrow\]
PAI-1, TAFI  \[\downarrow\]  FIBRINOLYSIS  \[\uparrow\]
Alpha 2 Antiplasmin

PLATELETS, VWF, FIBRINOGEN, CRP
FACTORS II, VII, VIII

PLASMIN, TPA, UPA


Effect of OCP use on thrombotic risk

<table>
<thead>
<tr>
<th>Deleterious change</th>
<th>OCP-related change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen [\uparrow] = CV risk</td>
<td>[\uparrow]</td>
</tr>
<tr>
<td>PAI-1 [\uparrow] = CV risk</td>
<td>[\downarrow]</td>
</tr>
<tr>
<td>AT III [\downarrow] = VTE risk</td>
<td>[\downarrow]</td>
</tr>
<tr>
<td>Protein S [\downarrow] = VTE risk</td>
<td>[\downarrow]</td>
</tr>
<tr>
<td>CRP [\uparrow] = CV risk</td>
<td>[\downarrow]</td>
</tr>
</tbody>
</table>


Migraine is associated with ischemic stroke, MI and VTE
Migraine and Ischemic Stroke Meta-analyses
Of Relative Risk

  - All studies: 1.73 [1.13-2.29]
  - Migraine with Aura: 2.16 [1.53-3.03]
  - All studies: 2.04 [1.72-2.43]
  - Migraine with Aura: 2.25 [1.53-3.33]
  - All studies (prospective cohort): 1.64 [1.22-2.20]
  - Migraine with Aura: 2.14 [1.33-3.34]

Association between stroke and migraine with and without aura

Meta-analyses Results

- Stroke risk is double in women and likely NOT elevated in men
  - Women: RR, 95% CI 2.08 (1.13-3.84)
  - Men: RR, 95% CI 1.37 (0.89-2.11)
- Stroke risk is elevated in persons < 45 years old, especially women
  - Age <45: RR, 95% CI 2.65 (1.41-4.97)
  - Age <45, Women RR, 95% CI 3.65 (2.21-6.04)

Migraine and Ischemic Stroke
Nationwide population-based study in Taiwan
Peng KP, et al., Cephalalgia 2016; April 26
Two cohorts (migraine/no migraine) of 120K each followed 3.6 years
• Stroke risk is elevated in women <45 yo with migraine
  • aHR, 95% CI 3.48 (2.20-5.39)
• Stroke risk is elevated in women <45 years old, with migraine with aura
  • aHR, 95% CI 4.58 (2.45 – 8.56)

Migraine and Risk factors profiles in persons with stroke
• Advanced age: NO
• Male sex: NO
• CVD risk profile: NO
• Health Behaviors: YES
  • Smoking 9.03 (4.22-19.34)
  • OCP users 7.02 (1.51-32.68)

OCP use increases stroke risk in persons with migraine
Evidence from Case-Control Studies

<table>
<thead>
<tr>
<th>Author, year</th>
<th>Study Pop.</th>
<th>Do COCs?</th>
<th>ischemic stroke risk in migraine?</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collaborative Group, 1975</td>
<td>598 cases &amp; controls 15-44y</td>
<td>No OCs</td>
<td>No Migraine</td>
<td>No standard mig criteria, self-report of COC use</td>
</tr>
<tr>
<td>Lidegaard 1993, 1995, 1996</td>
<td>320 cases 1357 controls</td>
<td>COC 30-50 mg, without migraine OR 1.8 COC use and migraine, estimated OR 5.0</td>
<td>No standard mig criteria, self-report of COC use</td>
<td></td>
</tr>
<tr>
<td>Toronto et al, 1995</td>
<td>72 cases 173 controls</td>
<td>No OCs</td>
<td>No Migraine</td>
<td>Self report COC use</td>
</tr>
<tr>
<td>Siwek et al, 1999</td>
<td>175 cases, 173 controls</td>
<td>Low dose COCs vs no COCs</td>
<td>No standard mig criteria, self-report of COC use</td>
<td></td>
</tr>
<tr>
<td>Chang et al, 1999</td>
<td>295 cases 736 controls</td>
<td></td>
<td>No standard mig criteria, self-report of COC use</td>
<td></td>
</tr>
<tr>
<td>Nightingale Farme, 2004</td>
<td>190 cases 1294 controls</td>
<td>Current COC use History of migraine</td>
<td>No standard mig criteria, didn't report joint effects</td>
<td></td>
</tr>
</tbody>
</table>

Curtis KM et al, Contraception 2006;73:189-94

Impact of risk factors on OCP-related risk of ischemic stroke

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 35 yo</td>
<td>3.08 (1.82-5.23)</td>
</tr>
<tr>
<td>&lt; 35 yo</td>
<td>1.82 (1.38-2.39)</td>
</tr>
<tr>
<td>Migraine Yes</td>
<td>6.32 (2.35-17.05)</td>
</tr>
<tr>
<td>No</td>
<td>2.55 (1.10-5.91)</td>
</tr>
<tr>
<td>Hypertension Yes</td>
<td>8.02 (5.53-11.64)</td>
</tr>
<tr>
<td>No</td>
<td>2.73 (2.22-3.37)</td>
</tr>
<tr>
<td>Current Smoking Yes</td>
<td>4.90 (3.17-7.57)</td>
</tr>
<tr>
<td>No</td>
<td>2.59 (1.96-3.43)</td>
</tr>
<tr>
<td>Obesity Yes</td>
<td>1.78 (0.24-13.26)</td>
</tr>
<tr>
<td>No</td>
<td>2.03 (1.43-2.87)</td>
</tr>
</tbody>
</table>


Stroke risk with migraine based on OCP use

- Systematic review of case-control studies, all deemed of fair to poor quality
- Reference group is non users w/o migraine
- Limited evidence suggests a 2 to 4-fold increased risk of stroke among women with migraine (not separated by subtype) who use COCs compared with nonuse.

Tepper NK, Contraception 94 (2016) 630–640
Potential Mechanisms of stroke

- **Arteries**
  - Vasculopathy, endothelial dysfunction

- **Blood**
  - Hypercoagulability, arterial and venous thrombosis

- **Cardioembolism**
  - Patent foramen ovale

Migraine and stroke in migraine are associated with thrombophilia

### Endothelial Activation Markers in Pre-menopausal women with migraine

<table>
<thead>
<tr>
<th>Variable</th>
<th>MA vs controls</th>
<th>MO vs control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxidative stress</td>
<td>OR=6.6 (2-21)</td>
<td>OR=3.0 (0.9-10)</td>
</tr>
<tr>
<td>vWF %</td>
<td>OR=6.5 (2-22)</td>
<td>OR=4.6 (1.4-15)</td>
</tr>
<tr>
<td>CRP mg/L</td>
<td>OR=8.0 (2-28)</td>
<td>OR=2.6 (0.7-9)</td>
</tr>
</tbody>
</table>

Logistic regression adjusted for age, BMI, smoking, OCP, HTN

Tietjen GE, et al. Stroke 2009
**Endothelial Activation Markers**
in Pre-menopausal women with migraine

- Migraine was associated with:
  - TGF-β 1 OR=4.1  (95% CI, 3 -7.2)
  - IL-6 OR=5.0  (95% CI, 2 -13)
  - TNF α OR=11.9  (95% CI, 3.5-30.2)

Levels correlate with headache frequency, and with BMI.

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**Migraine and Vascular Disease Biomarkers. CAMERA Study**

<table>
<thead>
<tr>
<th>Unadjusted comparisons</th>
<th>Migraine</th>
<th>MA</th>
<th>MO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR OR OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>1.89</td>
<td>1.97</td>
<td>1.79</td>
</tr>
<tr>
<td>hsCRP</td>
<td>1.59</td>
<td>1.74</td>
<td>1.43</td>
</tr>
<tr>
<td>Factor II</td>
<td>1.76</td>
<td>2.03</td>
<td>1.48</td>
</tr>
<tr>
<td>vWF Ag</td>
<td>0.76</td>
<td>0.69</td>
<td>0.86</td>
</tr>
<tr>
<td>D-dimer</td>
<td>1.02</td>
<td>1.22</td>
<td>0.91</td>
</tr>
</tbody>
</table>

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**Migraine and Vascular Disease Biomarkers. CAMERA Study**

<table>
<thead>
<tr>
<th>WOMEN</th>
<th>Migraine with Aura High frequency</th>
<th>Migraine with Aura Low frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>hsCRP</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Factor II</td>
<td>+++</td>
<td>-</td>
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<tbody>
<tr>
<td>Fibrinogen</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>hsCRP</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Factor II</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

Adjusted for age, municipality, education level, smoking status, BMI, hypertension.
### Migraine and Vascular Disease Biomarkers. CAMERA Study

- Fibrinogen, hs CRP, vWF Ag, and d-dimer
  - **DID** correlate with frequency and with duration of **aura**
  - **DID NOT** correlate with frequency and duration of **headache**

### CAMERA Study

**Deep White Matter Lesions**
- In women, OR=2.1
- No association with migraine in men
- ≥1 attack/mos, OR 2.6

**Biomarkers linked to WML**
- Biomarkers linked to migraine
  - Aura, aura frequency, aura duration, and female sex

- Kruit et al, *JAMA* 2004
- Tietjen et al, *Cephalalgia* 2017

### Migraine and Thrombophilia

- Associations with Migraine, especially with aura:
  - **DEFINITE**—high levels of estrogen states, platelets, RBCs, vWF antigen, fibrinogen, prothrombin, IPA antigen, and EMP
  - **POSSIBLE**—high levels of aPL, homocysteine, Protein S, and the MTHFR C677 T polymorphism (evidence conflicting)
  - **UNLIKELY**—Factor V Leiden, Prothrombin gene mutation (negative evidence in meta-analyses)

- Tietjen GE, Collins SA. Hypercoagulability and Migraine. *Headache* 2017
Migraine and Thrombophilia

- Migraine may cause a hypercoaguable state during and between attacks
- Ictal rise in platelet reactivity, vWF levels, cytokine levels
- EMP release may have lasting effects
- A hypercoaguable state may cause migraine with aura
- Aura (CSD) resulting from clot-induced brain ischemia, a TIA equivalent

Migraine Aura as a TIA Variant

Migraine aura is associated with PFO and with cardioembolic stroke

Patent Foramen Ovale

- Conduit for venous clots
- Enables serotonin (5HT) to avoid pulmonary filtration
- 5HT is prothrombotic
  - Causes oxidative stress
  - Activates the cerebral endothelium
  - Activates platelets
- PFO Closure
  - Decrease in left atrial 5 HT
  - Decrease in left atrial MMP 9

Review of 21 eligible studies with 5572 participants
- Odds Ratios for PFO-Migraine
  - Migraine with Aura: 3.4, p<.00001
  - MA+MO: 2.5, p=.0001
  - Migraine without Aura: Non-significant
Migraine and CV Risk factors in persons with stroke

The Italian Project on Stroke in Young Adults: 981 subjects, <45 y (mean 36 y), 51% women, migraine with aura was associated with:
- low cardiovascular disease risk profile
- Underlying pro-coagulant state (eg OCP)
- Cardiac right-to-left shunt (PFO)

Pezzini et al, Stroke. 2011;42:17-21

| Table 2. Migraine-Covariate Interaction OR of Age, Gender, Right-to-Left Shunt, Proatherosclerotic Risk Profile, and Thrombophilic Defects According to Multinomial Logistic Regression Model |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | MA vs No Migraine | MC vs No Migraine | MA vs MO |
|                 | OR    | 95% CI | OR    | 95% CI | OR    | 95% CI |
| Age*            | 1.06  | (0.90-1.25) | 1.06  | (0.94-1.19) | 1.00  | (0.83-1.21) |
| Women           | 2.37  | (1.42-3.95) | 2.72  | (1.88-3.94) | 0.87  | (0.48-1.58) |
| Right-to-left shunt | 2.41  | (1.47-3.95) | 0.93  | (0.63-1.39) | 2.58  | (1.45-4.59) |
| Proatherosclerotic risk profile (<1 factor) | 0.50  | (0.26-0.99) | 0.71  | (0.44-1.14) | 0.71  | (0.30-1.66) |
| Combined thrombophilic defects (at least 1) | 2.21  | (1.05-4.68) | 0.78  | (0.37-1.63) | 2.83  | (1.13-7.07) |

*OR changes by 5-year units step.

Pezzini et al, Stroke. 2011;42:17-21

Patent Foramen Ovale

- Shared pathogenesis: same condition which causes migraine also causes stroke
- PFO leads of stroke via shunting of venous thrombi
- PFO leads to migraine via shunting of venous vasoactive substance
- Causative: Paradoxical cardioembolism causes ischemia-generated cortical spreading depression (aura)
- Congenital link between PFO and migraine
### Presentation

| MA, +/− history of other endotheliopathies | CBC, tc CRP, VWF antigen, fibrinogen, and fasting lipid profile, glucose level, glycosylated hemoglobin, homocysteine |
| MA, personal or family history of thrombosis | CBC, to CRP, VWF antigen, fibrinogen, and fasting lipid profile, glucose level, glycosylated hemoglobin, homocysteine, Protein C, Protein S, Antithrombin deficiencies APC, Prothrombin (Factor II), Antiphospholipid antibodies: LA, aCL, β2GP1 |
| MA, + subcortical white matter abnormalities on brain MRI | CBC, tc CRP, VWF antigen, fibrinogen, and fasting lipid profile, glucose level, glycosylated hemoglobin, homocysteine, Antiphospholipid antibody profile: LA, aCL, β2GP1, CADASIL genetic testing if pattern is suggestive |
| MA, + stroke-like lesions on brain MRI | CBC, tc CRP, VWF antigen, fibrinogen, and fasting lipid profile, glucose level, glycosylated hemoglobin, homocysteine, Protein C, Protein S, Antithrombin deficiencies, APC, Prothrombin (Factor II), Antiphospholipid antibody profile: LA, aCL, β2GP1, Evaluation for PFO: TCD/TEE with agitated saline/TEE |

### Evaluation

- CBC, tc CRP, VWF antigen, fibrinogen, and fasting lipid profile, glucose level, glycosylated hemoglobin, homocysteine
- Protein C, Protein S, Antithrombin deficiencies APC, Prothrombin (Factor II)
- Antiphospholipid antibodies: LA, aCL, β2GP1
- CADASIL genetic testing if pattern is suggestive
- Evaluation for PFO: TCD/TEE with agitated saline/TEE

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![Diagram of ENVIRONMENT, GENETICS, RISK FACTORS, PFO with R to L shunt, Transient Ischemic Attack, Migraine and Stroke: Shared Pathogenesis]

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![Diagram of ENVIRONMENT, GENETICS, RISK FACTORS, PFO with R to L shunt, Transient Ischemic Attack, Migraine and Stroke: Shared Pathogenesis]
Summary

• Migraine, particularly migraine with aura, increases risk of stroke (OR 2-6)
• COC use increases risk of stroke (OR 2), risk being dependent on patient age and estrogen dose
• Risk of stroke in women with migraine using COC appears to be elevated by 2 to 4 fold c/t migraine w/o COC and (OR 5-17)
• Absolute stroke risk is low

Consensus Guidelines for OCP Use in Migraine

<table>
<thead>
<tr>
<th></th>
<th>WHO</th>
<th>ACOG</th>
<th>IHS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine w/o aura</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>&lt; 35 yo</td>
<td>generally should not use</td>
<td>generally should not use</td>
<td>Yes</td>
</tr>
<tr>
<td>Migraine w/o aura</td>
<td>No</td>
<td>No</td>
<td>+/− case-by-case</td>
</tr>
<tr>
<td>&gt;35 yo</td>
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<td>Any age</td>
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Grades of existing Evidence

• WHO: Low or intermediate
  • Intermediate: Strong, consistent association and no plausible confounders
  • Low: No serious flaws in study quality
• ACOG: Level B
  • Based on limited or inconsistent scientific evidence
• IHS: Level C
  • Evidence based on observational studies

* World Health Organization, Reproductive Health and Research 2004
Recommendations

- Women with migraine should minimize other vascular risks
- Women with migraine with aura should not use hormonal therapy
- Women with migraine without aura on hormone therapy should stop if aura develops or headache worsens
- Efficacy as primary stroke preventive unproven

“Certainly, if all the patient needs is reliable contraception, there are multiple other options: tubal ligation, vasectomy, IUD, progestin-only pills – a discussion that could be held with the patient’s PCP or gynecologist. The need for this discussion here is that our patients – women with migraine – often have hormonally mediated headaches that require certain CHCs for prevention.”

Anne Calhoun

Hormonal Contraceptives and Migraine With Aura—Is There Still a Risk? Headache 2017;57:184-193
THE END