

Migraine and Cardiovascular Disease

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Epilepsy and Headache, 2/4/11

Disclosures

- ▶ Epilepsy Foundation America*
- ▶ American Headache Society
- ▶ American Epilepsy Society

Objectives

- ▶ To define migraine without and with aura
- ▶ To understand the relationship of migraine to stroke
- ▶ To understand the relationship of migraine to CHD
- ▶ To understand the relationship of migraine treatments and CVD

Epidemiology (AMPP)

- ▶ Incidence
 - Males (10–12) > Females (12–14)
 - Aura > Without aura
 - Median age onset 19 M, and 20 F
- ▶ Prevalence
 - F – peaks ~30–39 yo at 24.4%
 - M – peaks ~30–39 yo at 7.4%
- ▶ Migraine aura
 - ~1/3 of people with migraine have aura

Lipton 2007, Hauser 1991, Andermann 1987, Lipton 1994, Markas 1993, Velioglu 1999

Migraine without aura (ICHD-II)

- ▶ A. At least five attacks fulfilling criteria B–D
- ▶ B. HA attack lasting 4–72 hours
- ▶ C. HA has at least 2 of the following characteristics:
 - Unilateral location
 - Pulsating quality
 - Moderate or severe pain intensity
 - Aggravation by or causing avoidance of routine physical activity
- ▶ D. During headache at least one of the following:
 - 1. Nausea and/or vomiting
 - 2. Photophobia and phonophobia
- ▶ E. Not attributable to another disorder

Migraine with aura (ICHD-II)

- ▶ A. At least 2 attacks fulfilling criteria B–D
- ▶ B. Aura consisting of at least one of the following but no motor weakness:
 - Fully reversible visual symptoms including positive features (flickering lights, spots or lines) and/or negative features (loss of vision)
 - Fully reversible sensory symptoms including positive features (pins and needles) and/or negative features (numbness)
 - Fully reversible dysphasic speech disturbance

Migraine with aura (cont'd)

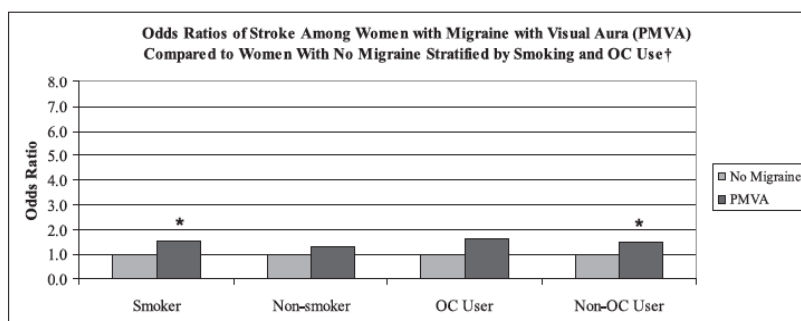
- ▶ C. At least two of the following:
 - Homonymous visual symptoms and/or unilateral sensory symptoms
 - At least one aura symptom develops gradually over >5 minutes and/or different aura symptoms in succession over >5 minutes
 - Each symptom lasts >5 and < 60 minutes
- ▶ D. Migraine without aura begins during the aura or follows aura within 60 minutes
- ▶ E. Not attributable to another disorder

MacClellan 2007

- ▶ Population based (Balto-Wash)
- ▶ Case control
- ▶ 356 women, 15–49 yo
- ▶ Migraine – self-reported
 - No migraine (53% v 59%)
 - Probable migraine without aura (9% v 13%)
 - Probable migraine with visual aura (38% v 29%)
- ▶ Risk factors self reported
- ▶ Neurologists determined stroke type

*Probable Migraine With Visual Aura and Risk of Ischemic Stroke:
The Stroke Prevention in Young Women Study STROKE 2007*

MacClellan 2007



OC indicates oral contraceptive

* $p < 0.05$

† Odds ratios adjusted for age, race, geographic region, and study period

7 fold higher risk of stroke in PMVA, OCP and smoker

MacClellan 2007 – Summary

- ▶ Women – PMVA 1.5 greater odds of ischemic stroke (95% CI, 1.1 to 2.0)
- ▶ Women – PMVA, smokers, OCPs – 7.0-fold higher odds of stroke (95% CI, 1.3 to 22.8) than did women with PMVA, nonsmokers, no OCPs
- ▶ Women – PMVA within the previous year had 6.9-fold higher adjusted odds of stroke (95% CI, 2.3 to 21.2) vs women with migraine
- ▶ The risk was highest in those with NO history of hypertension, diabetes, or myocardial infarction compared to women with no migraine.

Kurth 2005 Women's Health Study

- ▶ Prospective
- ▶ Cohort
- ▶ 39,754 US health professionals age 45+
- ▶ Follow-up 9 years
- ▶ Migraine – self reported ~ ICH 1998
 - Migraine without aura
 - Migraine with aura
- ▶ Stroke – medical records reviewed
 - Ischemic, hemorrhagic, unknown

Migraine, headache, and the risk of stroke in women :
A Prospective Study Neurology 2005

Kurth 2005 Women's Health Study

- ▶ 385 strokes
 - Ischemic (82.3%)
 - Hemorrhagic (18.7%)
- ▶ Migraine (13%)
 - Aura (39%) in prior year
- ▶ Stroke
 - No association with total stroke and all migraine
 - MA – 1.5X risk total and 1.7 X risk ischemic
 - MA no association with hemorrhagic stroke
- ▶ Overall risk small – added 3.8/10,000
- ▶ CV Risk factors
 - Not mentioned

Kurth 2010–Women's Health Study

- ▶ Prospective cohort
- ▶ 27, 860 women >45
- ▶ Objective: Migraine and hemorrhagic stroke
- ▶ Women
 - 18% migraine, 40% of those with aura
- ▶ Stroke
 - No increase in women with any migraine
 - MO – no increased risk
 - MA – active in prior year – 2.25 x risk
- ▶ Low numbers

Migraine and risk of hemorrhagic stroke women BMJ

Migraine and stroke

- ▶ Migraine with aura
- ▶ Women <45
- ▶ Oral contraceptives
- ▶ Smokers

Schurks 2010

Migraine and chest pain

- ▶ Increased rate of chest pain reported in people with migraine (Sternfeld 1995, Rose 2005)
- ▶ Not always correlation with CHD or MI
- ▶ In MO and MA
- ▶ In untreated patients (i.e. no triptan chest tightness)
- ▶ Etiology
 - Vasospasm
 - Referred pain?

Scher 05 GEM (Genetic Epidemiology of Migraine) study

- ▶ Population based, Netherlands
- ▶ Mailed questionnaires, blood samples, VS
- ▶ HA self-reported, confirmed neurologist
- ▶ CV risk factors
- ▶ Results: 42 yo, 53% women
- ▶ MA Women
 - More likely to use OCP, less likely to drink alcohol
 - Higher cholesterol (OR 1.76)
 - Higher BP all migraineurs (OR 1.63), more likely gestational HTN
 - MI < 45 (OR 3.96)

Cardiovascular risks and migraine: The GEM Study Neurology

Kurth 06 – Women's Health Study

- ▶ Prospective, cohort
 - ▶ 27, 840 women
 - ▶ Migraine 18.4%, MA 39.7%
 - ▶ Outcome: Combined endpoint major CVD (nonfatal ischemic stroke, nonfatal MI, death CVD) angina, MI, revascularization, death
 - ▶ 580 major CVD events
 - ▶ MA active vs. nonmigraine
 - ~2 X risk of CVD
 - 1.74 X coronary revascularization
 - 1.71 X angina
- 18 additional CVD events per 10,000

Bigal 2009

- ▶ Population based, AMPP
- ▶ Objective: CVD in migraineurs, CV event rates, MA and MO
- ▶ Questionnaires HA – 120,000 X 5 years
- ▶ Migraine – ICHD-II
- ▶ CV – self-reported (MI, revascularization) and MD diagnosis/medical records, risk factors
- ▶ Results: 67% migraine, 52% controls
- ▶ Mostly F (80%), controls younger (20yo vs 24)

Bigal 2009

- ▶ **Migraine**
 - Heart attack (OR 2.19 1.73–2.77)
 - Stroke (OR 1.61 (1.19–2.18)
 - Claudication (2.86 (2.06–3.96)
 - Higher rates of CV risk factors (OR 1.4)
- ▶ **MO and MA**
 - Heart attack
 - Claudication
- ▶ **MA**
 - Stroke (OR 3.14 2.25–4.38)
 - Significantly associated with all CV risk factors

Limitations/Considerations

- ▶ **Migraine**
 - Heterogeneous (aura, without)
 - Variable diagnosis (ICHD-II, databases, self-ID)
 - Migraine with aura heterogeneous
 - Migraine with aura diagnosis not accurate
 - Treatment not discussed
- ▶ **Stroke**
 - Heterogeneous
 - Diagnosis not accurate
- ▶ **Cardiovascular Disease**
 - Heterogeneous
 - Diagnosis not accurate

Triptans

- ▶ Vasoconstrictive
- ▶ Side effects – chest tightness, flushing, sometimes into jaw or arms
- ▶ Avoid
 - In patients with known CAD
 - Re-consider in those at risk for CAD
 - ‘Complicated’ MA or basilar migraine
- ▶ After 50–60 yo, consider weaning off triptans and change to alternate
- ▶ Event rate
 - 1 in 4 million uses
 - None in 64,000

ASA and migraine

- ▶ Acute treatment
 - Useful, many forms, different preparations
- ▶ Preventative treatment
 - Decreases HA attacks, not as effective as some other preventatives (ie beta-blockers)
- ▶ Long term benefits
 - No good literature on using ASA to prevent stroke, MI in migraine patients
 - Mechanism of MI, stroke, etc. unclear

Case

- ▶ MS is a 52 yo singer with no other PMHx who has had headaches intermittently since 16. She describes them as unilateral throbbing with nausea, rare vomiting and sometimes light sensitivity. She denies visual changes or other neurological features with her headaches. She has managed through the years to treat early enough with triptans and/or NSAIDs to be able to function, but in the past year as she has been having irregular periods, hot flashes, her headaches have become more difficult to treat and have become debilitating on a few occasions.

Case cont'd.

- ▶ She takes only vitamins. She is married, has two children, works part time, rarely drinks, and does not smoke. Her family history is significant for heart disease in 4 male relatives diagnosed in their early 50s. Three had MI before 60. She has been using 100mg sumatriptan at onset to treat her headaches with good relief most of the time. In the past month she used all 9 from her PCP and she even asked her brother (a cardiologist in Georgia) to send her some samples. She denies chest pain or tightness with use of triptans. She has never had a cardiac evaluation.

Case cont'd.

- ▶ Diagnosis
- ▶ Risk factors
- ▶ Evaluation
- ▶ Treatment

Case

- ▶ 28 yo F with headaches, endometriosis and acne. She has had HA since age 5. They are unilateral, pulsating, and at times she has visual changes. She describes them as shimmering lights in her peripheral vision that migrate across both visual fields (~20 min) after which she gets the HA. She has these a few times a year, usually if she is allowed to have a period. She is on continuous OCPs most of the year due to endometriosis. Social and family history are otherwise unremarkable.

Case cont'd.

- ▶ Diagnosis
- ▶ Risk factors
- ▶ Evaluation
- ▶ Treatment

Case

- ▶ 57 yo F with RA and headaches. Patient has been having HA since she was about 17. They are unilateral and severe, with nausea, at times with photophobia. She reports that she may have a few seconds of visual flashes for a few minutes prior to the headache starting. She denies other neurological issues. She is treated with DMARs for her RA. She has been taking triptans regularly up to 15 days of the month for several years since her HA got worse around menopause and she takes naproxen, ibuprofen and butalbital several times a week. She drinks several drinks a week and family history is significant for her father having MI at 70.

Case cont.'d

- ▶ Diagnosis
- ▶ Risk factors
- ▶ Evaluation
- ▶ Treatment

Practical Recommendations

- ▶ MA patients – define
- ▶ Smoking
- ▶ OCPs
- ▶ Vascular risk factors
- ▶ Acute treatments – ? triptans
- ▶ Chronic treatments – ?comorbidities
- ▶ Still slight increase in risk for stroke, MI

Summary

- ▶ Migraine, particularly migraine with aura, is associated with a small but slightly increased risk of stroke
- ▶ Some associated risk factors modify this (OCP, smoking)
- ▶ While less clear, migraine in some cases is also associated with increased risk of CV events, again, seemingly more with MA