MIGRAINE PREVENTION
Revolutionary
New Therapy

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Migraine – a Disease Process

- Migraine is a chronic disease process similar to many other chronic medical conditions
- Migraine has a low mortality but high morbidity
- 38 million Americans suffer with migraines
  - Only 60% are treated
  - 15 million U.S. Citizens are suffering needlessly
- Migraines are widely undertreated
- Most common medical cause of temporary, total disability in the U.S.
- Worldwide 1 billion migraine sufferers –
  - Top 10 on World Health Organization of cause of disability

Migraine Prevalence

- Female Predominate Disease
- Annually 1 out of 5 US females will have migraine
  - 6% of US males will have migraine
- Chronic migraine: 3+ million migraineurs in U.S. alone
- CM puts a greater social, financial and emotional burden on patients than does EM
- CM with higher rates of disability
  - Annual medical costs 4 times higher
- CM with higher comorbidities: HTN, CAD, Lipids, COPD
  Psychiatric Ds., Suicide

Diagnosing Migraine

- International Classification of Headache Disorders (ICHD)
  - Recurrent Headaches – at least 5 lifetime attacks
  - Duration: 4 – 72 hours
  - At least **two** of the following:
    1. Unilateral
    2. Pulsating
    3. Moderate or severe intensity
    4. Aggravated by routine physical activity.
  - Additionally **one** of:
    - Photophobia and phonophobia
    - Nausea and/or vomiting

Episodic Migraine (EM)

- Less than 15 headache/migraine days a month
- Have typical migraine features
  - Photophobia
  - Phonophobia
  - Nausea and/or vomiting
  - Pulsatile
  - Made worse with movement
- Triggered by weather, alcohol, stress, menses, others…
- Needs to meet ICHD criteria for migraine headaches

Chronic Migraine (CM)

- Fulfill the ICHD criteria for migraine headaches
  - Headache symptoms for over 3 months
  - **15 or more headache days a month**
  - 8 out of 15 days must have classic migraine features
  - Migraine attacks aborted with triptan treatment – but have lack of adequate headache control
- Need to exclude Analgesic Overuse Headaches
  - **Common in most CM sufferers**
- Exclude Occipital Neuralgia
- Chronic Daily Headache is NOT Chronic Migraine

Progression to Chronic Migraine

- EM progresses to CM at 3% annually
- Risk Factors:
  - Head Injuries
  - Obesity
  - Sleep Apnea
  - Depression
  - Stressful Life Events: divorce, job or job changes
  - Major Life Changes
  - Controlled substance analgesic overuse

Migraine – Major Life Burden

- WHO – World Health Organization ranks migraine as one of the most debilitating medical illnesses
- Only 10% of patients on preventative medications
  - 3.8 million of 38 million migraine sufferers
- Migraine is associated with:
  - Personal disease burden – poor Quality of Life
  - Societal burden of chronic, recurrent pain
  - Chronic disability
  - High financial costs
- Chronic Migraine remains under-diagnosed and under-treated
  - Only 5% of CM patients receive correct diagnosis/treatment

Comprehensive Treatment

- Identify what types of headaches patient has:
  - **<u>Multiple headache disorder is common</u>**
    - Migraines
    - "Sinus" – really migraines
    - Tension-type
    - Occipital Neuralgia
    - Analgesic Overuse
    - Cervicalgia
- Eliminate Causes
  - Stop analgesics, treat occipital neuralgia/cervicalgia
  - Educate patient about "sinus" headaches = "Unicorns"
- **Headache Diary** – important clinical tool for all CM

Comprehensive Treatment (cont.d)

- Patient Education on Realistic Expectations
  - They have a chronic medical condition
  - 3-4 months of aggressive preventative treatment needed to get headaches controlled
  - "Quick Fix" Interventions
    - Wean off analgesics and **ALL** narcotics
    - Occipital nerve blocks
    - Start preventative therapy immediately
  - Explain that Headache Diary is important for both the patient and you to monitor their progress
  - Patient may be 50-70% better but tell you nothing has changed. Diary helps patient to recognize improvement

Comorbid Conditions

- Depression is common in migraine population
  - Start aggressive depression therapy immediately
- Blood pressure control
  - Low normal range only
- Screen for Sleep Apnea
- Obesity Counseling – dietary consultation
- Get your patient to do some type of exercise
  - **Sitting is the new smoking**.
- Cardiac, diabetes, lipid screening

Depression & Anxiety

- Prevalence of Neuropsychiatric Disorders is 3X Higher in Migraine Population
  - Depression – up to 50%
  - Anxiety – 30-40%
  - Other Phobias
  - Suicide
- Common comorbidity in all headache patients
- Patient may not be aware of condition
- High index of suspicion in All Chronic Migraine
  - Treat with effective SSRI or SNRI

Obesity

- Obesity is a national epidemic in the U.S.
- Higher in the CM population
- Multiple Medical Complications
  - Hypertension
  - Cardiac disease
  - Hyperlipidemia
  - Sleep apnea – not a benign condition
  - Chronic Insomnia
  - Metabolic Syndrome
- Get Dietary Consultation and Counseling

Sleep Apnea

- Frequently not recognized
  - Insomnia
  - Daytime Fatigue
  - Not always easy to diagnose
- Get a sleep study – Untreated Sleep Apnea is **NOT** benign
- Untreated Sleep Apnea Morbidity
  - Obesity – Metabolic Syndrome
  - Diabetes
  - Hypertension
  - Hyperlipidemia
  - Cardiac disease – MI, arrhythmias
  - Sudden Death

Insomnia & Apnea

- Chronic insomnia is common in CM
- Sleep deprivation leads to poor health & medical disease
- Excessive daytime sleepiness
  - Increase risk for MVA
  - Risk of losing job
  - Drop out of school
- Migraine patients typically have poor sleep hygiene
  - Counsel on good sleep habits
  - Computer, TV, news, video games, eating late

Botox for Chronic Migraine

- Botox has been demonstrated to be effective in the long term treatment of **Chronic Migraine only**
  - The only headache type approved for Botox by FDA
- No clinical evidence that Botox is effective for:
  - Episodic Migraine or High Frequency EM
  - Chronic Tension-type Headaches
  - Chronic Daily Headaches (Persistent Daily Headache)
- Need to see a $\geq$50% reduction in migraines to say Botox was effective for a given patient with CM
  - Maximum benefit after 3 treatments – 9 months
  - Headache diary – Check at every visit
- Placebo rate in migraine studies is about 40%

Botox for Chronic Daily Headache

- No scientific evidence of therapeutic efficacy
- Insurance & Medicare have multiple restrictions on approval of use of Botox for CM
  - Meet ICHD criteria for ***chronic migraine*** headaches
  - Need adequate documentation of trial/failure of multiple **preventative agents**
    - Anticonvulsants, SSRIs, SNRIs, beta-blockers, verapamil, muscle relaxants
    - Some response to triptan therapy is needed
  - Document migraines ≥15 days with headache diary
  - Failed physical therapy and "other modalities"

Insurance Companies Lie

- Many patients want Botox for their headaches
- Media hype – "Botox is ***the treatment*** for headaches"
- "My friend had it and it worked great."
- Insurance companies tell patients they will cover Botox
  - What they don't tell patients is under what conditions
  - Complete failure to inform public under what criteria Botox will be paid for – "Just have your doctor call."
  - "I'm entitled to Botox because my insurance told me they will cover it."
    - Authorization – time-consuming, painful prior authorization
    - Cost: A single treatment with Botox for CM: $1250
    - Most do not meet necessary criteria for Migraine Botox therapy

Botox for Chronic Migraine

- Botox may work for your CM patient
  - Typically adjunctive therapy
- Careful patient selection is important
- Meets ICHD classification for CM
- Eliminate other causes of headache
- Meets Medicare/Insurance requirements
- Response Rate: 3 out of 4 CM patients respond to Botox
- Need experienced physician giving Botox
  - Follow the published Botox Migraine Protocol

Migraine - Prevention is Key

- Prevention of headache is key in all migraine & headache treatment
- Preferred therapy – antidepressants
  - Prozac, Lexapro, Celexa
  - Effexor XR, Savella
  - Amitriptyline, nortriptyline, imipramine
- Other Migraine preventatives
  - Topiramate
  - Valproic Acid
- Baclofen
- Beta-blockers

Preventative Therapies

- Start at first visit
- Pick initial drug depending on comorbidities
- Use therapeutic dosages
  - SSRIs – 40-80 mg
  - SNRIs – 75-400 mg
  - Tricyclics – up to 75 mg nightly
  - Baclofen 20-80 mg daily
  - Topiramate – 200-600 mg daily
    - Effects OCP therapy over 200 mg daily dose

21st Century Migraine Therapy

- Total shift in Migraine Treatment paradigm
- CGRP Monoclonal Antibodies – for Migraine Prevention
  - 1st new anti-migraine drug developed in over 25 years
- Designed from the ground up to block initiation of the migraine cascade
- CGRP (calcitonin gene related peptide)
  - Inflammatory neuropeptide – released from the trigeminal nerve terminals
  - Modulates pain and vasodilation
  - Involved in the early migraine cascade to headache
- New MABs block effect of CGRP in migraine genesis

CGRP Blockers for Migraine

- New class of drug therapy for **Migraine Prevention**
  - Indicated for both Episodic and Chronic Migraine
- CGRP Monoclonal Antibodies
  - Attach at the CGRP Receptor site blocking CGRP-R

  Or:
  - Attach to the CGRP ligand, prevention receptor binding
- Mechanism of Action
  - Inhibit pain transmission
  - Decrease artery dilation
  - Block neurogenic inflammation
- High safety profile
  - No drug-drug interaction
  - Do not have any immunomodulatory effect
  - Not renally or hepatically metabolized

CGRP Blockers For Migraine

- Use in patients with 4 or more migraine days a month
  - High frequency Episodic Migraines
  - Chronic Migraine
  - Prolonged episodic migraines
- Self-injected, once a month therapy
  - TEVA has a once every 3 month protocol
- Have all Migraine patients keep headache diary

CGRP-R Blocker

- **Aimovig**™ - (erenumab-aooe) – Amgen
  - The only CGRP Receptor Blocker
    - 100% human IgG_2 MAB
    - FDA approved May 17, 2018
  - Specifically blocks only the CGRP receptor
    - 70 mg & 140 mg sub-q monthly dosing
    - No CGRP receptor agonist activity
  - Approved for both EM & CM
    - 4 or more migraine days a month
  - Side effects: injection site reaction, constipation

CGRP Ligand Blocker

- **Ajovy**™ - (fremanezumab) – TEVA
  - CGRP ligand blocker – humanized IgG_2 MAB
  - Targets CGRP(calcitonin gene-related peptide)
    - FDA Approval pending – PDFUA Sept. 16, 2018
  - Approvals for EM and CM pending
  - Dosing:
    - Monthly: initial 675 mg sub-q then 225 mg monthly
    - Quarterly: 675 mg sub-q every 90 days
  - Side effects: injection site reaction

CGRP Ligand Blocker

- **Emgality**™ - (Galcanezumab-gnlm) – Eli Lilly
  - CGRP ligand blocker - fully humanized IgG_4 MAB
    - Targets CGRP(calcitonin gene-related peptide)
    - FDA Approval pending – PDFUA Oct. 11, 2018
  - Approvals for EM and CM pending
  - Has been studied in Botox Failure migraine patients
  - Dosing:
    - 120 mg or 240 mg sub-q monthly
  - Side effects: injection site reaction

CGRP Ligand Blocker

- **Eptinezumab** – Alder
  - CGRP blocker - fully humanized IgG_1 MAB
    - Targets CGRP(calcitonin gene-related peptide)
    - FDA Approval pending – PDFUA (est.) late 2019
  - Approvals for EM and CM pending
  - Unique Dosing:
    - 100 mg or 300 mg IV infusion quarterly
  - Side effects (>2% over placebo)
    - nasopharyngitis (6.3%), URI (4.0%), nausea (3.4%), UTI (3.1%), arthralgia (2.3%), dizziness (2.6%), anxiety (2.0%), fatigue (2.0%)

Abortive Migraine Therapy

- Secondary concern for most migraine patients
- Therapeutic goal is 4 headache days or less a month
- Need to avoid Analgesic Overuse Headaches
- Triptans are the mainstay in acute migraine treatment
  - Tablets
  - Sumatriptan Injections
  - Onzetra Nasal System (sumatriptan)
- NSAID therapy
  - Gel cap preparations
  - Cambia – uniquely different diclofenic acid therapy
- Anti-emetic therapy
  - Tablets – Zofran, Reglan, Phenergan
  - Suppositories
    - Phenergan, Compazine

Quality of Life for Migraineurs

- Keep your patients out of the Emergency Room
  - Equip them all with **Migraine Rescue Kit**
    - **Injectables**
      - Sumatriptan
      - Toradol
      - DHE-45
    - **Anti-emetics**
      - Tablets
      - Suppositories
- **AVOID NARCOTICS ALL TOGETHER**

Summary – Migraine

- Migraine disease contributes significantly to the burden of disease-related disability in the U.S. & worldwide
- CM is associated with multiple system disease
  - Higher morbidity
  - Higher incidence of neuropsychiatric illness
- Screen patients carefully for comorbid conditions
- Treat aggressively with Preventative Therapy
  - 21st Century Preventative Agents – CGRP Blockers
  - Do not use narcotics
- Dramatic improvement in Quality of Life of your patients

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