Lost in Translation: Making Sense of Clinical Treatment Guidelines

Charles E. Argoff, MD, CPE

Disclosures: Charles Argoff

Financial Disclosure:
– Consultant: Teva, Daiichi Saky, Pfizer, Nektar, Purdue, Depomed, Arbor, Novartis, Quest, Gruenenthal, Braeburn, BDSI, Vertex
– Speaker: Allergan, Depomed, Amgen, Teva, Daiichi Saky, Astra Zeneca, BDSI
– Research Grant: Gruenenthal, Vertex
– Stock Shareholder: Depomed, Pfizer

Drug/Product Off-Label Use Disclosure
– Off-label use of a drug and/or product will be addressed in this presentation. This information will be verbally disclosed both at the beginning of the presentation and at the time of drug/product discussion.
Lost in Translation: Making Sense of Clinical Treatment Guidelines

- Multiple clinical treatment guidelines have been published regarding headache and pain management.
- However, many have questioned the benefit of such clinical guidelines for the treatment of individual patients.
- This course will review key published treatment guidelines for migraine, interventional pain management, chronic opioid use, neuropathic pain, and chronic low back pain.
- The faculty will review the relevant guidelines and discuss their strengths and critical weaknesses when using such guidelines to actually treat people.

Evidence Based Medicine

- Evidence-based medicine (EBM) has been defined as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients."

  Sackett, D. Evidence-based Medicine - What it is and what it isn't. BMJ 1996; 312:71-72

- EBM: The judicious use of the best current available scientific research in making decisions about the care of patients. EBM is intended to integrate clinical expertise with the research evidence and patient value.

Do Published Migraine Guidelines Improve Patient Outcomes?

Learning Objectives

- Using published American Academy of Neurology guidelines for the treatment of certain headache conditions as an example of such guidelines upon attending this symposium, the participant will be able to:
  1. Identify pharmacologic therapies which have strong evidence for their use in the prevention of episodic migraine.
  2. Identify the notable limitations of such recommendations.
Real Patients –
Do Current Treatment Guidelines Help?

- 32 yo female experiencing 2 migraine headaches each week: known FH, worsens around the time of her menstrual cycle, has never been treated
- 18 yo male experiencing postconcussion syndrome and posttraumatic migraine presents to your office
- 28 yo female experiencing 15 headaches monthly, 10 clearly migraine, lasts more than 4 hours, experiencing for more than 3 consecutive months—no response to multiple prophylactic approaches
- 40 yo female experiencing chronic daily headache using OTC analgesics daily

“Discouraging Data on the Antidepressant”
Gabapentin in the treatment of painful diabetic neuropathy*

![Graph showing mean pain score over weeks for Placebo and Gabapentin](image)

*Not approved by FDA for this use
† $P < 0.01$; ‡ $P < 0.05$


---

**Interventional Therapies for Chronic Pain**

- Trigger point injections/botulinum toxin
- Epidural steroid injection
- Sacroiliac joint injection and RFA
- Facet joint injection and RFA
- Discography
- IDET, nucleoplasty, disc RFA
- Spinal cord stimulation
- Spinal drug delivery

RFA, radiofrequency ablation; IDET, intradiscal electrothermal therapy.
How Good is the Evidence?

Evidence Based Medicine

- Evidence-based medicine (EBM) has been defined as "the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients."
  Sackett, D. Evidence-based Medicine - What it is and what it isn't. BMJ 1996; 312:71-72

- EBM: The judicious use of the best current available scientific research in making decisions about the care of patients. EBM is intended to integrate clinical expertise with the research evidence and patient value
EBM Must Be about EBP

Steps in the EBP Process:
- **ASSESS the patient**: Start with the patient—a clinical problem or question arises from the care of the patient
- **ASK the question**: Construct a well built clinical question derived from the case
- **ACQUIRE the evidence**: Select the appropriate resource(s) and conduct a search
- **APPRAISE the evidence**: Appraise that evidence for its validity (closeness to the truth) and applicability (usefulness in clinical practice)
- **APPLY**: talk with the patient, integrate that evidence with clinical expertise, patient preferences and apply it to practice
- **SELF-EVALUATION**: Evaluate your performance with this patient

What is EBP? Introduction to Evidence-Based Practice
[www.hsl.unc.edu/services/tutorials/ebm/whatis.htm](http://www.hsl.unc.edu/services/tutorials/ebm/whatis.htm)

AAN Guidelines: Pharmacologic treatment for episodic migraine in adults

- Authors analyzed published studies from June 1999 through May 2009 using a structured review process developed/published by the AAN
- Recommendations are divided into Level A, Level B, Level C, Level U
AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont’d)

- Level A: established as effective and should be offered
- Level B: probably effective and should be considered
- Level C: possibly effective and may be considered
- Level U: evidence is conflicting or inadequate to support or refute the specific treatment

AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont’d)

- Level A (established as effective and should be offered for migraine prevention):
  1. Anticonvulsants: divalproex sodium, sodium valproate, topiramate
  2. B-blockers: metoprolol, propranolol, timolol
  3. Triptan: frovatriptan for short-term menstrual associated migraine prevention
AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont’d)

- Level B (probably effective and should be considered for migraine prevention):
  1. Antidepressants: amitriptyline, venlafaxine
  2. B-blockers: atenolol, nadolol
  3. Triptans: naratriptan, zolmitriptan for short-term menstrual associated migraine prevention

AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont’d)

- Level C (possibly effective and may be considered for migraine prevention):
  1. ACE inhibitors: lisinopril
  2. Angiotensin receptor blockers: candesartan
  3. A-agonists: clonidine, guanfacine
  4. Anticonvulsant: carbamazepine
  5. B-blockers: nebivolol, pindolol
AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont’d)

- Level U (evidence is conflicting or inadequate to support or refute the use of the medication for migraine prevention):
  1. Anticonvulsant: gabapentin
  2. Antidepressants: SSRI/SNRI, protriptyline
  3. Antithrombotics: acenocoumarol, warfarin, picotamide
  4. B-blocker: bisoprolol
  5. Calcium channel blockers: nicardipine, nifedipine, nimodipine, verapamil
  6. Acetazolamide
  7. Cyclandelate

AAN Guidelines: Pharmacologic treatment for episodic migraine in adults (cont’d)

- Level A NEGATIVE (established as ineffective and should not be offered for migraine prevention): Anticonvulsant: lamotrigine
- Level B NEGATIVE (probably ineffective and should not be considered for migraine prevention: clomipramine
- Level C NEGATIVE (possibly ineffective and may not be considered for migraine prevention): acebutolol, clonazepam, nabumetone, oxcarbazepine, telmisartan
AAN: NSAIDS and other complementary treatments for episodic migraine prevention in adults

- Level A (established as effective and should be offered for migraine prevention): Petasites (butterbur)
- Level B (probably effective and should be considered for migraine prevention): fenoprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium, MIG-99 (feverfew), magnesium, riboflavin, subcutaneous histamine

AAN: NSAIDS and other complementary treatments for episodic migraine prevention in adults (cont’d)

- Level C (possibly effective and may be considered for migraine prevention): cyproheptadine, Co-Q10, estrogen, mefenamic acid, flurbiprofen
- Level U (evidence is conflicting or inadequate to support or refute the use of the medication for migraine prevention): aspirin, indomethacin, omega-3, hyperbaric oxygen
- Level B NEGATIVE (probably ineffective for migraine prevention): montelukast
AAN: Botulinum neurotoxin in the treatment of migraine

- “There is presently no consistent or strong evidence to permit drawing conclusions on the efficacy of BoNT in chronic daily headache (mainly transformed migraine) Level U
- In October 2010, approximately 2 years after that statement was published, the FDA approved onabotulinum toxin A for the treatment of chronic migraine!

“Real” Clinical Considerations NOT Addressed

- No available evidence is sufficient to establish how to choose an optimal therapy for an individual person
- Evidence is NOT available to help the practitioner to choose one treatment over another
- Treatment must be individualized
- No evidence exists for making comparisons among multiple agents within the same class
- For all Level A recommended treatments a large percentage of patients FAILED to benefit
References

- Argoff CE. The Use of botulinum toxins for the management of chronic pain and headache: making the most of an evidence-based approach for these rapidly evolving treatments.  Pain Medicine 2011, 12:1581-82.

Are the CDC Chronic Opioid Guidelines Improving Patient Outcomes?
APS/AAPM Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (2009)

- Patient selection and risk stratification
- Informed consent and opioid management plans
- Initiation and titration of COT
- Methadone
- Monitoring
- High-risk patients
- Dose escalations, high-dose opioid therapy, opioid rotation, indications for discontinuations of therapy

APS, American Pain Society; AAPM, American Academy Of Pain Medicine; COT, chronic opioid therapy

APS/AAPM Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain (2009) (cont’d)

- Opioid-related adverse effects
- Use of psychotherapeutic cointerventions
- Driving and work safety
- Identifying a medical home and when to obtain consultation
- Breakthrough pain
- Opioids in pregnancy
- Opioid policies

APS, American Pain Society; AAPM, American Academy Of Pain Medicine
CDC Guidelines-1

- Determining when to initiate or continue opioids for chronic pain outside end-of-life care
- Selection of opioid therapy, nonpharmacologic therapy, nonopioid pharmacologic therapy
- Establishment of treatment goals
- Discussion of risks and benefits of therapy with patients

http://www.cdc.gov/drugoverdose/prescribing/guideline.html- accessed 11/1/15

CDC Guidelines-2

- Opioid selection, dosage, duration, follow-up, and discontinuation
- Selection of extended-release and long-acting opioids
- Dosage considerations
- Duration of treatment for acute pain and chronic opioid use
- Considerations for follow-up and discontinuation of opioid therapy

http://www.cdc.gov/drugoverdose/prescribing/guideline.html- accessed 11/1/15
CDC Guidelines-3

- Assessing risk and addressing harms of opioid use
- Evaluation of risk factors for opioid-related harms and integration into the management plan
- Review of prescription drug monitoring program data
- Use of urine drug testing
- Considerations for concurrent use of opioids and benzodiazepines
- Arrangement of treatment for opioid use disorder

http://www.cdc.gov/drugoverdose/prescribing/guideline.html- accessed 11/1/15