UNIVERSITY OF COPENHAGEN

Faculty of Health and Medical Sciences

Do we need drug holidays - pro

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Disclosures

Honoraria for lectures and member of advisory board for AbbVie, Pfizer and Teva

Case

- 52-year-old woman
- Four years ago, 18 headache days per month of which 9 were migraine
- Started CGRP-mAbs treatment
- Significant improvement: after the first 3 months, only 3 days with headache per month, 2 of these were migraine
- Attacks successfully treated with triptans
- She recently moved to your area; you are seeing her for the first time
- She has never taken a drug holiday
- Will you pause treatment (i.e., introduce a drug holiday)?

Drug holiday

- How should drug holidays for chronic migraine patients treated with CGRP-mAbs be designed?
- In many countries, drug holidays of 1-3 months are mandatory for each 6-18 months of treatment. Is this optimal?
- Danish experience: A drug holiday for 2 months for every 12 months was initially required by the authorities. This was a disaster; many patients experienced much worsening of migraine. We convinced the authorities to allow drug holidays for only 1 month for every 18 months of treatment
- This works well for most, but not all, of our patients
- How to optimize drug holidays for chronic migraine patients treated with CGRP mAbs?

Drug holiday

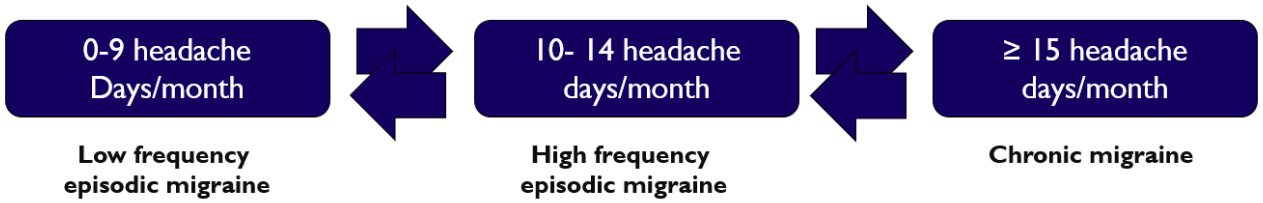
- Problem: If the patient still has frequent migraine, which is reduced by an effective treatment, then the migraine will worsen significantly during the drug holiday, and it may take some time before migraines are back to baseline. How to deal with this?
- Learn from our many years of experience with chronic migraine treated with botulinum toxin type A
  - Botox: If there is no worsening in the last weeks before next treatment cycle, then we increase intervals between treatment cycles,
  - CGRP-mAbs: Every 18-24 months, the patient should pause treatment and start again, if migraines gets worse. Explain reason for drug holiday for the patient
  - The patient might learn that treatment, e.g., every 5 weeks is sufficient
- Drug holidays should be tailored to the individual patient

Drug holiday

- Why do we need drug holidays at all?
- A significant number of patients experience remission over time
- A lower migraine burden compared to before start of treatment might possibly be due to spontaneous improvement and not to sustained effect of preventive treatment

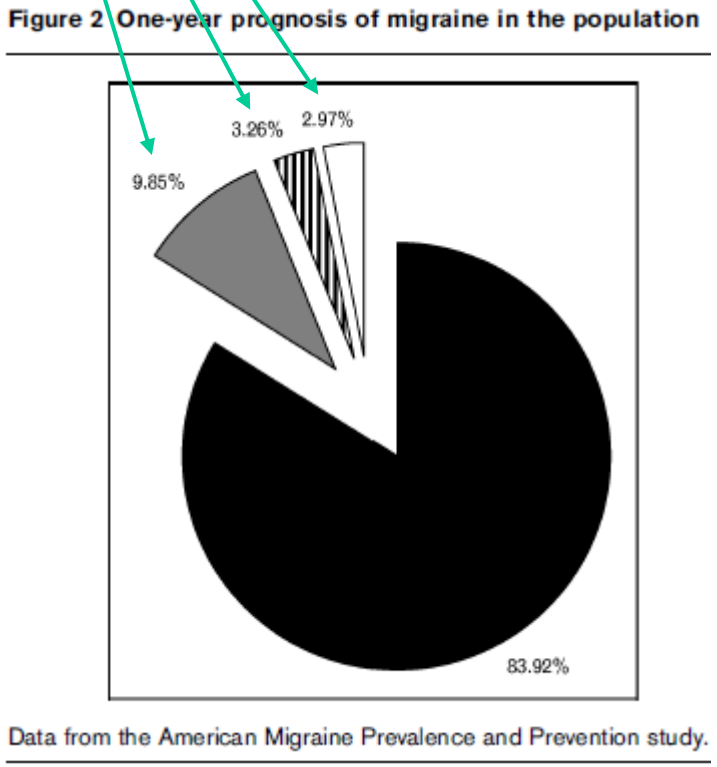
From episodic to chronic migraine and visa versa

- Every year, between 2.5 and 4.6% of people with episodic migraine experience progression to chronic migraine
- Approximately *the same proportion* regress from chronic migraine to episodic migraine spontaneously



Lipton RB. Neurology 2009; Munakata J et al. Headache 2009

Within 1 year:
Complete remission 10%
Partial remission 3%
Worsening 3%



Bigal and Lipton, Curr Op Neurol 2008

Why should we avoid giving CGRP-mAbs to patients that do not benefit from treatment?

- No evidence that treatment with CGRP-mAbs is disease modifying
- Minimize exposure to drugs to reduce risk of adverse events, e.g.,
  - known adverse effects such as hypertension and constipation
  - exposure during future events in the patient's life where treatment could be problematic such as pregnancy, acute myocardial infarction, stroke, Raynaud syndrome, etc.
  - potential adverse effects of long-term treatment, yet unknown, could be serious

Why should we avoid giving CGRP-mAbs to patients that do not benefit from treatment?

- To avoid pathologizing patients
- To optimize use of health care resources
  - we can take better care of all the other patients with headache and facial pain, who currently do not get the treatment they deserve
- Think green
  - avoid unnecessary use of resources, e.g., production of medications, injectors, plastic, transport of medications and patients, etc.

Why should we use drug holidays?
Summary

- A significant proportion of patients experience remission over time
- We should avoid treating with CGRP-mAbs in patients, who do not need it
  - to minimize drug exposure to avoid current known adverse effects; to avoid risks of serious adverse effects with future comorbidity; and to avoid risks of yet unknown adverse effects from long-term treatment
  - to avoid pathologizing patients
  - to optimize use of health care resources and to reduce environmental impact
- Drug holidays should be tailored to the individual patient
- This will ensure the best possible treatment of each of our unique patients

Questions?

Danish Headache Centre