PROBLEMS OF DRUG ADHERENCE IN EPILEPSY

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“Taking the exact prescribed amount of medication at the precise times of every day for an extended period of time”

Faught E. Epilepsy and Behavior 2012; 25: 297-302
DRUG ADHERENCE
Methods of measurement

- Direct questioning
- Patient calendars
- Counting pills
- Electronic bottle tops
- Serum drug levels

Faught E. Epilepsy and Behavior 2012; 25: 297-302
MORISKY MEDICATION ADHERENCE SCALE

1. Do you ever forget to take your medication?
2. Do you ever have problems remembering to take your medication?
3. When you feel better do you sometimes stop taking your medication?
4. Sometimes if you feel worse when you take the medicine, do you stop taking it?

YES= 0,  NO=1,  RANGE 0-4,  1-2 LOW ADHERENCE

Morisky PE, DiMatteo MR. J Clin Epidemiology 2011; 64: 255-7
Look the patient straight in the eye at the clinic and ask sweetly –

“How often do you forget to take your tablets?”
Adherence decreases with the number of antiepileptic drugs and drug doses prescribed each day

EVEN ONCE DAILY DOSING DOES NOT RESULT IN PERFECT ADHERENCE!

DRUG ADHERENCE
Teenagers

“If I don’t take my pills regularly, I won’t need to tell people I have epilepsy”.

Melissa, aged 15

“No teenager prescribed 3 antiepileptic drugs is adherent to their treatment schedule”.

Martin, aged 60+
“What is the prospect, in any given case, that an arrest of the fits can be obtained by treatment? The indications of the prognosis have been materially changed by the introduction of the bromides as remedies for epilepsy. Not only do they arrest fits far more frequently than any other remedy, but they are effective in many cases which, according to experience previous to the introduction of these remedies, would have been regarded as most unpromising. Hence, by their use, the conditions of the prognosis have been essentially changed”.

Gowers W R, Epilepsy and Other Chronic Convulsive Diseases, 1881, p201
## NEWLY DIAGNOSED EPILEPSY
Responder rates (%) in an expanding cohort

<table>
<thead>
<tr>
<th>Recruitment</th>
<th>N</th>
<th>One AED</th>
<th>Multiple</th>
<th>Total</th>
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<tbody>
<tr>
<td>1982-1997</td>
<td>470</td>
<td>61</td>
<td>3.0</td>
<td>64.0</td>
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<tr>
<td>1982-2001</td>
<td>780</td>
<td>59</td>
<td>5.4</td>
<td>64.4</td>
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<tr>
<td>1982-2005</td>
<td>1098</td>
<td>62</td>
<td>6.4</td>
<td>68.4</td>
</tr>
</tbody>
</table>

3Brodie MJ et al. Neurology 2012; 78: 1548-54
DRUG-RESISTANT EPILEPSY
SPECIAL REPORT

Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies

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Kwan P et al. Epilepsia 2010; 51: 1069-1077
DEFINITION OF DRUG-RESISTANT EPILEPSY

Failure of adequate trial of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom.

PROPOSAL BY THE AD HOC TASK FORCE OF THE ILAE COMMISSION ON THERAPEUTIC STRATEGIES

Kwan P et al. Epilepsia 2010; 51: 1069-1077
DRUG-RESISTANT EPILEPSY
Newly diagnosed cohort (n=1098)

361 uncontrolled

32 died (SUDEP/suicide etc)
9 antiepileptic drug trials
9 incomplete documentation
311 reviewed

136 (44%) drug-resistant
175 (56%) undefined

Hao X et al. Epilepsy and Behavior 2013; 29: 4-6
DRUG-RESISTANT EPILEPSY
Reasons for being undefined (n=175)

Single agent only
Inadequate drug dosing
Intermittent adherence (34%)
Adverse effects at low dose
Poor patient documentation
Erratic clinic attendance
Alcohol or recreational drug use
Social issues such as imprisonment
Patient choice

Median reasons 2, range 1-4

Hao X et al. Epilepsy and Behavior 2013; 29: 4-6
DRUG ADHERENCE

MW  FEMALE  DOB 16th MARCH 1990

JANUARY 2004  Generalised tonic-clonic seizure at school
              Seen at seizure clinic same week
              Family history + few myoclonic jerks

FEBRUARY 2004  EEG – bursts of polyspikes/photosensitivity
                Started lamotrigine after discussion with family

JULY 2004  Seizure free on lamotrigine 200 mg b.d.

DECEMBER 2004  Still seizure-free – discharged from clinic
DRUG ADHERENCE

MW FEMALE DOB 16th MARCH 1990

JANUARY 2008  -  Mother switched her to homoeopathic remedy

MARCH 2008  -  Found dead in bed with teeth through tongue

WE DISCUSS SUDEP WITH ALL NEWLY DIAGNOSED PATIENTS!
DRUG ADHERENCE
Blood and hair AED levels

Poor adherence

More seizures

? ?

SUDEP

1. Leestma JE et al. Epilepsia 1997; 38; 47-51
2. Davis GG, George JR. J Forens Sci 1998; 43: 598-603
3. Opeskin K et al. Epilepsia 1999; 40: 1795-8
5. Williams J et al. JNNP 2006; 77: 481-4
DRUG ADHERENCE
Study population of 33,658 patients

Nonadherence was associated with

- increased risk of mortality (HR 3.32, 95% CI 3.11 to 3.54)
- more emergency department visits (IRR 1.50, 95% CI 1.49 to 1.52)
- more hospital admissions (IRR 1.86, 95% CI 1.84 to 1.88)
- more motor vehicle accidents (IRR 2.08, 95% CI 1.81 to 2.39)
- greater likelihood of fractures (IRR 1.21, 95% CI 1.18 to 1.23)

RETROSPECTIVE OPEN COHORT DESIGN USING MEDICAID CLAIMS DATA

Faught E et al. Neurology 2008; 71: 472-8
Nonadherence to drug regimens makes epilepsy care much more expensive

- poorer work performance
- higher disability payments
- more emergency department visits
- more hospital admissions
- more antiepileptic drugs at higher doses
  etc, etc, etc.

Zachry WM et al. Epilepsy and Behavior 2009; 16: 268-73
Ivanova JI et al. Pharmacoeconomics 2010; 28: 675-85
“The overall rate of non-adherence in children with epilepsy was 33%. Logistic regression analysis indicated that children with generalised epilepsy (vs focal epilepsy) were more likely (odds ratio 4.7, 95% confidence interval 1.37 to 15.81) to be classified as non-adherent as were children whose parents have depressed mood (odds ratio 3.6%, 95% confidence interval 1.1 to 11.41)”

Shah NH et al. Epilepsia 2013; 1020-7
DRUG ADHERENCE
Survey of 99 patients in capital of Lao PDR

Hospital based – 57.1%
Community based – 58.0%
Total adherence – 57.6%

HIGH LEVEL OF ADHERENCE ASSOCIATED WITH FEW SEIZURES, MONOTHERAPY AND ILLITERACY

Non-adherence was highest in young males with uncontrolled epilepsy taking a complex schedule

NON-ADHERENCE RATE WAS 66.2
MEASURED BY THE MORISKY-GREEN TEST

DRUG ADHERENCE
Prospective study in patients with refractory focal epilepsy admitted for 5 days without drug tapering

18 of 44 (41%) were non-adherent
12 overconsumers/4 underconsumers/2 others

OVERCONSUMPTION WAS THE MOST FREQUENT FORM NONADHERENCE!

DRUG ADHERENCE
Why don’t people with epilepsy take their treatment?

1. They don’t think they have epilepsy
2. They don’t want to have epilepsy
3. They don’t like taking pills in principle
4. They don’t like the prescribed medication
5. They don’t understand the need for treatment
6. The drug schedule is too complicated
7. They are disorganised, unfocused, forgetful
   etc, etc, etc
DRUG ADHERENCE
What can we do to improve it?

1. Discuss history, diagnosis, investigations, and prognosis in detail with patient and family providing written material
2. Give plenty of time for subsequent discussions and answer all questions slowly, honestly and carefully
3. Allow everyone enough time to come to terms with the diagnosis, results of investigations, treatment and prognosis
4. Choose best treatment with specific focus on matching the side effect profile to the patient’s lifestyle and clinical history
5. Ask specifically about individual side-effects such as dizziness, sedation, aggression, depression etc.

KEEP EVERYTHING FLEXIBLE – DON’T BE JUDGEMENTAL!
DRUG ADHERENCE
Causes of refractory nonadherence

- Misinformation on side effects
- Hidden alcohol or drug addiction
- Patient feels better off treatment
- Refusal to accept epilepsy diagnosis
- Inability to prioritise treatment cost

PIGHEADEDNESS IS NOT COMMON!
DRUG ADHERENCE
Antiepileptic drugs

What exactly is he/she taking

Patient?
GP?
Consultant?

ASK PATIENT TO BRING ALL HIS MEDICATION TO EVERY CLINIC APPOINTMENT
DRUG ADHERENCE
What can we do to improve it?

- Involve family in management plan
- Provide dosette box for chronic offenders
- Check plasma levels when possible

IF THE PATIENT DOES NOT TAKE HIS/HER MEDICATION, IT WON'T WORK!