epilepsy therapy project

A non-profit (501-c-3) organization advancing new therapies for people living with epilepsy

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http://EpilepsyTherapyProject.org

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www.Epilepsy.com

Suicidality Following the Initiation of Antiepileptic Drug Monotherapy

A study of the Dept of Veterans Affairs database

Van Cott, Pugh, Cramer, et al (privileged communication)

- Factors associated with an increase risk of suicidality among adults:
  - Epilepsy
  - Older age Conwell et al, Biol Psychiatry 2002;52:193–204
  - Previous suicide attempt

METHODS

HIPPA compliant access to de-identified data

- Newly Treated – AED monotherapy
  - Identified a cohort of patients ≥66 years who had received VA care for at least one year prior to being treated with any AED for any condition.
- All Diagnoses
  - Demographic and clinical conditions were identified with ICD-9-CM codes validated by chart abstraction
  - Identified co-morbid conditions before AED treatment
- Primary outcome:
  - Suicide, suicidal attempt or ideation after initiation of an AED (hereafter suicidality)

All VA patients ≥ 66 years old with at least 1 AED during FY00-FY04
N = 449,269

↓

with new AED prescriptions, all Dx
N = 114,333

↓

AED monotherapy only [defined cohort, all Dx]
N = 112,096

New Epilepsy Dx
N = 7,445

Not Epilepsy Dx
N = 104,651

6 cases = .08%

Suicidality rates
raw bivariate:
p = .3797

58 cases = .06%

for multivariable models, a 1:12 suicidality cases (64) - controls matching schema for the New Epilepsy Dx and Not Epilepsy Dx groups yielded a total N = 832 [matched for prior suicide attempt, epilepsy diagnosis, and year of AED prescription] (privileged communication)

RESULTS

- 64 suicidality cases were compared to 768 controls

- Primary predictor of suicidality:
  - Diagnosis of depression before treatment with an AED
    - OR 4.42, 95% CI 2.30-8.49
  - No significant differences among different AEDs
  - Epilepsy, dementia, chronic pain and numerous co-morbid medical conditions were not more common in the suicidality group
    - (privileged communication)

What to change (if anything) in future RCTs?

The problem may be epilepsy & comorbid psychiatric disorder - not the AED

- Clinical trials in epilepsy are already using adequate tools to detect mood-depressant effects of AEDs
  - PRO screening tools to observe effects on mood (pre-post)
  - MEDDRA collects spontaneous reports of suicidal ideation

Example

Prospective self-report reveals no excess suicidality

- Clinical trials of a new AED esclicarbazepine
  - Included a Patient Reported Outcome assessment with a depression screener
    - QOLIE-31 with MHI-5 mood items from MOS/SF-36
  - Included a physician –assessed depression rating
    - Montgomery-Asberg Depression Rating Scale
    - Item #10 asks specifically about suicidality
- Both scales improved with the addition of ESL to standard AEDs
  - No signal of suicidality in this population

Example

Suicidality may be related to lack of treatment response

- Analysis of the entire levetiracetam database of self-reported adverse effects by COSTART terms
  - » Cramer et al, Incidence of behavioral adverse events among epilepsy patients. Epilepsy & Behavior 2003; 4: 118-123.

Responder = ≥50% seizure reduction	Tx Responder N=229	Tx Non-Responder N=430
All suicidal behavior	0	3 (0.7%)

Screening tools for epilepsy clinical trials (?)

- Importation of a suicide screening tool developed for psychiatry may not be useful in epilepsy
  - Validation is an iterative process
    - Per 2006 FDA PRO Guidelines: *Instruments must be validated in the target population*

- Please don't complicate clinical trials with instruments for which the data might not be interpretable (AED vs epilepsy?).
  - Depression screening in epilepsy is a Practice Guideline issue
  - Risk of suicidality related to epilepsy is not appropriate for labeling