Sudden Unexpected Death in Epilepsy (SUDEP) Check List

&

Cornwall SUDEP study

Dr Rohit Shankar
Consultant Neuropsychiatrist
Cornwall Partnership NHS Foundation Trust
& Hon. Associate Professor
Exeter Medical School
MBBS, DPM, MRCPsych, CCT, PGC –Cl. research, PGC-Aspergers
Co- Investigators

- Dr David Cox – Consultant Neuropsychiatrist
- Dr Brendan McLean - Consultant Neurologist
- SUDEP Action – Mrs Jane Hanna OBE - Study Sponsors
- Professor Matthew Walker – Consultant Neurologist and Chair of Institute of Neurology
- Mrs Caryn Jory & Mr Mike Tripp – Epilepsy Specialist Nurses
- Dr Richard Laugharne – Lead for R & I - CFT
- Dr Emma Carlyon – HM Coroner Cornwall
Does Epilepsy Kill?

• largely neglected in earlier literature
• sudden unexpected death in epilepsy (SUDEP) is the most important epilepsy-related mode of death
• is the leading cause of death in people with chronic uncontrolled epilepsy
SUDEP

- Epilepsy - 600,000 people in UK
- SUDEP - 500 epilepsy deaths/year
- No exact cause
- Cannot accurately predict
- Extensive research
- Potential risk factors
The Big Debate

• To tell or not to tell
• When to tell
• How to tell
• What to Tell
To Tell Or Not To Tell & If So, When?

• The Fatal Accident Inquiry in Scotland judicial process

• ‘Real or lively possibility’ that the death might have been avoided by the reasonable precaution
Inquiry Recommendations

• The risk of SUDEP should be advised to patients and carers unless in the case of a particular patient there is a risk of serious harm

• The information and advice about SUDEP should be provided directly by the consultant in charge of the patient’s case or, where appropriate, by an epilepsy specialist nurse

• But we knew that and was a NICE recommendation
In contrast ..... 

- Morton et al 2006
- 387 replies
- 351 neurologists
- 288 consultants
  - 82% of neurology consultants in UK
- Epilepsy nurses survey – around 50%
- Not following NICE guidelines
- The right ‘not to know’?
- Waddell et al Are we discussing SUDEP
  – a retrospective case note series
  Seizure October 2012 14/345 (4%)
How & What To Tell?

• No clarity or guidelines

• Dependent on communication skills, time and patient understanding

• Concerns of not being person centered
Strategy- for trying to reduce the risk

• Variations in rates of reported SUDEP suggest a potential for modifying risk

• A literature search for top 20 risk factors concentrating on population based studies

• Be pragmatic: some guidance from the best available data is likely to help us focus our efforts in combating the risks. This is likely to be better than not using the data because its incomplete or imperfect

• Develop a one page screening tool for risk factors that can be used at point of referral, in clinics for discussion and to monitor our risk management progress – employed into Excel – 5 minutes to complete
Checklist items:

- Risk factors found consistently in the literature and of strong effect when examined in quantitative studies
  - modifiable factors
    - Presence of GTCS (high frequency a strong risk factor in many studies)
  - Non-modifiable factors
    - Early onset of epilepsy
    - Young age
Checklist items:

- Risk factors where evidence is present, but weak or some contradictory evidence:
  - Non-modifiable factors
    - Duration of epilepsy
    - Presence of intellectual disability
    - Presence of structural brain lesion

- The reason it is weak is that it has not been explored!
Checklist items:

- Risk factors where evidence is present, but weak or some contradictory evidence:
  - modifiable factors
    - Unclear treatment history
    - Polytherapy with 3 or more AEDs
    - Suboptimal compliance with AEDs
    - Frequent AED changes
    - Subtherapeutic AED levels
    - Prone position at night
    - No surveillance at night
    - Treatment for depression
    - Alcohol problem
The SUDEP Safety Checklist

- The Boston Surgical Safety Checklist
- Aeroplane Industry
- Patient risk – ‘do they hear what we hear’?
- Clinician risk – NICE 2004 – 2012 still 4%
- Corporate Risk
Cornwall 9 year SUDEP study

• This study is the first epidemiological study in England occurring in a whole population identifying systemically all deaths

• First large scale review in UK of SUDEP deaths since 2005

• Systemically inspected all epilepsy and epilepsy related deaths in Cornwall UK 2004 to 2012 –HM coroner

• Of a total 93 cases, 48 cases met the criteria for SUDEP and we elicited associated relevant risk factors using the SUDEP checklist template
Salient Findings

• Many findings from our study are comparable to what has been reported in previously

• Novel findings:
  – SUDEP is not as ‘Sudden’ – 42/48 had a clinically identifiable increase in seizure intensity and/or frequency 3-6 months prior to death
  – only 9/48 of patients had definitely met a specialist 1 year prior to death and 21/48 had contact with the GP for an epilepsy medication review in the last year
  – Cumulative risk of the various modifiable factors
Epilepsy and ID

- Cornwall unique in having an ID specialist community based epilepsy service
- 3 out of 48 in the 9 year sample
- None known to the local ID services
- 6.25% Versus 23%
SUDEP

• Over representation of ID in Epilepsy (26%)

• Moderate – profound ID - 50% Seizures

• Of this 50% treatment resistant

• Risk factors over represented

• Higher SUDEP representation
EPILEPSY & ID

• Complex issues affect health outcomes

• Quality of life
• Safety
• Community access

• Communication via 3rd party often difficult

• Epilepsy reviews can cause distress and affect health outcomes

• Treatment resistant epilepsy
What do we do different?

• Clinically – no different!

• Some expertise around Autism, complex ID behaviours, reasonable adjustments, MCA

• Closer and regular contact

• SUDEP checklists, Epilepsy Radars, MIRS, tele – welfare checks

• Working from GP surgeries and DGH – home visits

• Identifying the OTHER causes – abuse, family, training, location
Moral of the story

- Population which died noted deterioration in either/and/or
  - core epilepsy factors
  - social factors
  - psychological factors
  - other biological factors

- Leading to a possible cumulative increase in risk
Recommendations for SUDEP prevention-sharing information

- Share information with patients and families/carers
- Identify modifiable and unmodifiable risks
- Map cumulative risk especially if noted worsening if there is - of Alcohol, lifestyle (work, relationship, bereavement) & Mental Health
- Impact of concordance
- Surveillance when alone
- What else can we do to enhance quality viz. a viz. cost?
New pilot project in Cornwall

• Recognition of the tension of offering more face to face reviews
• Tele-health
• Newquay – 2 GP practices
  Dr Tamsyn Anderson/Dr Brendan Mclean/Dr Richard Laugharne/ Professor Ley Sanders
• Epilepsy + Project
• 3 monthly phone contact to check on Holistic health
• Using a modified checklist
WHY?

Quality of Life:
Psychological Social

Seizures

Biological factors

Epilepsy management is about balance
Conclusions

- Talking about SUDEP can be facilitated by the use of the safety checklist which could reduce risk to patients/clinicians/organizations

- SUDEP might not be ‘unexpected’

- Modifiable factors including lifestyle/social factors, psychological factors/biological factors could influence seizure outcomes – addressing this will improve patient outcomes and costs

- Pro-active measures like tele-health might be a way forward in delivering better outcomes at reduced costs

- The learning from projects in epilepsy could be transferable to other long term conditions
References


Antipsychotic medication in Pregnancy register

Presenting
Clare Dale - Research Manager

Project Team
Zoe Doran¹, Rohit Shankar¹,², Richard Laugharne¹,², Darren Mackintosh¹, Adrian Flynn¹, Mike Metcalfe¹, John Craig³

¹. Cornwall NHS Partnership Foundation Trust, 2. Exeter Medical School 3. Belfast Health and Social Care Trust, UK Epilepsy and Pregnancy Register
Background

3000-4000 pregnancies in the UK are exposed to antipsychotic medication

This figure has risen by 5% between 1998 and 2010. (Abel 2013)

There is a need to balance risk of taking antipsychotic medication with risk of stopping it.

A 2004 Cochrane review of antipsychotic medication in pregnancy found no studies met the inclusion criteria and this resulted in 'serious clinical and ethical problems' [Webb et al. 2004].
### Current Evidence Summary

#### Lit review reference

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Number of subjects</th>
<th>Medication</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brunner <em>et al.</em> [2013]</td>
<td>Prospective observational study</td>
<td>610</td>
<td>Olanzapine</td>
<td><strong>No difference</strong> in pregnancy and neonatal outcome compared with general population data.</td>
</tr>
<tr>
<td>Habermannet <em>et al.</em> [2013]</td>
<td>Prospective cohort study</td>
<td>1967</td>
<td>Typical antipsychotics ($n = 284$), atypical antipsychotics ($n = 561$), controls ($n = 1122$)</td>
<td><strong>Higher rate of major malformations</strong> in neonates exposed to atypical antipsychotics. Higher rates of postnatal disorders in neonates observed in groups exposed to typical and atypical antipsychotics. Preterm birth and low birth weight more common with exposure to typical antipsychotics.</td>
</tr>
<tr>
<td>Boden <em>et al.</em> [2012]</td>
<td>Population-based cohort study</td>
<td>358 203</td>
<td>Olanzapine/clozapine (169), other antipsychotics (338) or none (357,696)</td>
<td>Exposure to antipsychotics <strong>increased the risk of gestational diabetes</strong>. No increased risk of SGA. Olanzapine/clozapine associated with macrocephaly</td>
</tr>
</tbody>
</table>
### Current evidence summary Cont.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>N</th>
<th>Medication</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johnson <em>et al.</em> [2012]</td>
<td>Prospective case control</td>
<td>309</td>
<td>Exposed to antipsychotics (22), antidepressants (202) or no psychotropics (85)</td>
<td>A history of <em>in utero</em> antipsychotic exposure was associated with <strong>lower scores on a standardized test of neuromotor performance</strong> in 6 month olds compared with antidepressant or no psychotropic exposure.</td>
</tr>
<tr>
<td>Babu <em>et al.</em> [2010]</td>
<td>Prospective cohort study</td>
<td>70</td>
<td>Olanzapine</td>
<td>Olanzapine may be associated with <strong>higher birth weight.</strong></td>
</tr>
<tr>
<td>Lin <em>et al.</em> [2010]</td>
<td>Birth data</td>
<td>4176</td>
<td>Typical and atypical antipsychotics</td>
<td>Higher <strong>risk of preterm birth</strong> for mothers prescribed typical antipsychotics. No significant difference in rates of low birth weight, LGA or SGA.</td>
</tr>
<tr>
<td>Wichman [2009]</td>
<td>Retrospective case file review</td>
<td>16</td>
<td>Aripiprazole (2), quetiapine (10), risperidone (4), ziprasidone (1)</td>
<td>One major malformation with ventriculomegaly and hydrocephalus in an infant exposed to aripiprazole. Shortened gestational age.</td>
</tr>
</tbody>
</table>
Epilepsy Pregnancy Register

Dr Craig visited Cornwall for a CPD event

Epilepsy Pregnancy Register has lead to significant development in understanding of safely of AE medications in pregnancy

Currently a large proportion of people on AE drugs in pregnancy are on this register and the evidence is now informing prescribers of the safest route.
Study Objective

The main objective of the antipsychotics in pregnancy register is to collate and publish relevant information relating to the frequency of major congenital abnormalities, perinatal abnormalities and adverse birth outcomes such as low birth weight (LBW), spontaneous abortion and gestational diabetes amongst women who are exposed to antipsychotic medication during the course of their pregnancy.
Identification

- Identified by the CFT Perinatal Team
- Inclusion: Taking antipsychotic medication and pregnant with capacity

Approach

- Treating clinician approaches the potential participant as part of normal clinical discussion
- Participant consents to details being passed to Researcher

Consent

- Researcher contacts potential participant
- Sends out a consent form to be returned if interested
- Data collected via telephone interview and notes review
Baseline

- Maternal demographic information
- Psychiatric History/Diagnosis
- Antipsychotic treatment before/during pregnancy (Type and Dates)
- Details of any other treatment 3M prior to conception

Follow up

- Previous obstetric history
- Details about the pregnancy inc abnormalities and outcome
- Date of pregnancy completion
- Details of any birth defects
- Infants APGAR score
<table>
<thead>
<tr>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collecting data on obesity and smoking</td>
<td>Will take time to gather sample size needed</td>
</tr>
<tr>
<td>Collecting information on specific antipsychotics and doses</td>
<td></td>
</tr>
<tr>
<td>Collecting data on trimester of exposure</td>
<td></td>
</tr>
<tr>
<td>Data collected from patient and healthcare professionals</td>
<td></td>
</tr>
</tbody>
</table>
The future:

Peninsula collaboration

Cardiff collaboration

The world!
Developing a screening tool for co-morbid depression and pain in chronic conditions

Dr Karen A Cocksedge
CT1 Psychiatry
Cornwall Foundation Trust

Co-Researchers:
Dr Rohit Shankar, Prof Anthony Woolf, Dr Chantal Simon, Prof Ian Jones
Pain in Depression

- In ICD10/DSM IV on depression, pain is a possible symptom
- But not defined as a key symptom/somatic symptom
- SUPRISING!!
- Pain and depression commonly co-exist:
  - 41-65% of patients with depression experiencing chronic pain\(^1\)–\(^4\)

\(^1\)Ohayon & Schatzzberg 2003
\(^2\)Bair et al. 2003
\(^3\)Arnow et al. 2006
\(^4\)Demyttenaere et al. 2010
Depression in Pain

- Depression is also a common finding in chronic pain:
  - 13-85% of patients with chronic pain have depression\(^1\)
  - Pain in diabetes strongly associated with depression with \(P<0.001\)^2
  - Change in pain is a strong predictor of subsequent depression with \(P<0.001\)^3

- Hence clear association between depression and pain

---

\(^1\)Bair et al. 2003  
\(^2\)Bair et al. 2010  
\(^3\)Kroenke et al. 2011
Why the Link?

- Depression: reduction in neurotransmitters (5-HT, NA, D)
- Pain pathway is ascending
- Descending pain pathway which is controlled by 5-HT and NA neurons
- If reduced 5-HT and NA then more pain
Why Does it Matter?

- Depressed patients are more likely to present with pain than affective symptoms\(^1\)
- When both depression and pain are recognised, clinicians focus on pain, and depression is often undertreated\(^1\)
- When both are recognised and depression is fully treated, it seems harder to treat\(^2\text{-}^4\)

\(^1\)Bair et al. 2003  
\(^2\)Bair et al. 2004  
\(^3\)Karp et al. 2005  
\(^4\)DeVeaugh-Geiss et al. 2010

- Depression and pain together costs a lot more
What do we do if we find it?

- If both depression and pain together:
  - Need an MDT approach to address physical, psychological and social factors
  - Treatments to include lifestyle measures, psychological therapy and drug treatments
  - Evidence that SNRI antidepressants work better for both pain and depression than SSRIs
    - Target both the pain and depression by increasing 5-HT and NA
    - Duloxetine – recent Cochrane review 2014
Importance in Chronic Illness

- Depression affects 20% of people with chronic illness: 2-3 x level in those with good health\(^1\)
- Chronic illness + depression have worse outcomes than chronic illness alone\(^2\)
- Hence in GP, recommended by NICE to screen for depression in all chronic illness\(^3\)

\(^1\)Health Survey for England 2009
\(^2\)Lustman et al. 2007
\(^3\)NICE Clinical Guideline 91

- But, given the association between depression and pain, should be screening for pain too
Searching for a Suitable Screening Tool

- Lots of screening tools for depression:
  - PHQ-9
  - HADS
  - Beck
  - NICE: 2 simple questions

- Lots of screening tools for pain:
  - Visual Analogue Scale
  - Numerical Rating Scale
  - Verbal Rating Scale

- Full literature search for screening tools for both:
  - No validated tools!
A New Screening Tool

During the last month, have you often been bothered by:
- feeling down, depressed or hopeless?
- having little interest or pleasure in doing things?

YES

During the last month have you often been bothered by:
- feelings of worthlessness?
- poor concentration?
- thoughts of death?

How long have you felt like this?
How does it affect your day-to-day functioning and relationships?
Do you feel isolated?
Is there any history of psychiatric problems?

NO

During the last month, have you often been bothered by pain?

YES

-Where is the pain?
-How severe is your pain on a scale of 0-10 with 0 being “no pain” and 10 being “the worst possible pain”
Testing the Feasibility of the Tool

- Is the screening tool able to correctly identify previously undiagnosed pain and/or depression in chronic illness?
  - Sample with diabetes
  - Sample with COPD
- Patients in two GP surgeries in Cornwall:
  - Narrow Cliff Surgery
  - Newquay Health Centre
- Total of 2500 patients ≥ 18 years
Testing the Feasibility of the Tool 2

- Screening tool to be administered by Practice Nurse as part of annual review of diabetes/COPD
- Screening over 6 months, so see half the patients (1250)
- Expect 20% depression – 250 patients
- Expect chronic pain in approx 50% - 125 patients
- Everyone who screens positive, further exploration by nurse (with training)
- See GP if treatment needed
Testing the Feasibility of the Tool 3

- For everyone who screens positive, further questioning will allow determination of the sensitivity of the tool.
- Everyone who screens positive with previously unknown pain/depression has been newly identified by the tool, leading to earlier treatment/referral.
- Feedback from tool usage will allow re-design/improvement as needed before further work.
Further Work

• Once we have a feasible screening tool:
  
  • Use in a larger sample of GP practices across South-West
  
  • Plan to study outcomes in this larger study:
    • What treatments were given to those screened positive?
    • What were the outcomes of these?

• What are the cost implications of earlier diagnosis?
Publications in this Work

• Currently:
  • Cocksedge KA, Simon C, Shankar R. “A difficult combination: chronic physical illness, depression and pain”, Br J Gen Pract, 2014. Accepted (as an Editorial)

• Planned:
  • Feasibility study to be submitted 2015
  • Larger outcome study thereafter
Conclusions

- Strong association between pain and depression
- In chronic health conditions we commonly screen for depression
- There are no screening tools to screen for pain and depression simultaneously
- Screening for both is strongly indicated in chronic health conditions, hence we have developed a new tool
- A feasibility study of this tool is underway, with further studies planned
- We believe this will improve patient outcomes and provide efficiency savings in general practice