Trigeminal Neuralgia
Future directions

Prof Joanna M. Zakrzewska
18th International Leksell Gamma Knife Society
Amsterdam 2016
Aims and Objectives

Phenotyping

Imaging

Outcomes

Decisions

Drugs vs surgery
Primary Headaches
Trigeminal Autonomic Cephalalgias
TAC

Cluster
SUNCT
SUNA
PHC

short unilateral neuralgiform headache with conjunctival redness tearing/autonomic symptoms

Paroxysmal hemicrania

ICHDI beta Version 2013
Trigeminal neuralgia (part I): Revisiting the clinical phenotype

Y Haviv¹, J Khan², A Zini³, G Almoznino¹,⁴, Y Sharav¹ and R Benoliel²

DOI 10.1007/s11916-015-0493-0

Do Trigeminal Autonomic Cephalalgias Represent Primary Diagnoses or Points on a Continuum?

Larry Charleston IV¹

DOI 10.1007/s11916-014-0473-9

Tic Versus TAC: Differentiating the Neuralgias (Trigeminal Neuralgia) from the Cephalalgias (SUNCT and SUNA)

Juliana VanderPluym • Lawrence Richer
<table>
<thead>
<tr>
<th>Feature</th>
<th>SUNCT/SUNA</th>
<th>TN classical type 1</th>
<th>TN + concomitant pain Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency (day)</td>
<td>3-200</td>
<td>3-200</td>
<td>3-200</td>
</tr>
<tr>
<td>Duration</td>
<td>5-240 secs</td>
<td>5-120 secs</td>
<td>5-120sec + mins - hrs</td>
</tr>
<tr>
<td>Background pain</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Autonomics</td>
<td>++</td>
<td>rare</td>
<td>rare</td>
</tr>
<tr>
<td>Migrainous features</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Triggers</td>
<td>Cold wind ++ Touch</td>
<td>Touch</td>
<td>Touch</td>
</tr>
<tr>
<td>Management</td>
<td>Lamotrigine MVD</td>
<td>Carbamazepine MVD, Ablative</td>
<td>Carbamazepine Gabapentin</td>
</tr>
</tbody>
</table>
Stories have

- A teller
- A listener
- A language
- Characters
- A plot
- Time
Communication
We’re not great at it....

• 77% of patients are interrupted after 12 seconds and not allowed to complete their opening statement of concerns
• 69% of patients are interrupted and directed toward a specific concern
• 37% of patients were not asked about their agenda for the appointment
• 70% of patients leave wanting to ask more questions
• Female patients are interrupted more often than male patients
• Male HCPs interrupt more frequently than female HCPs
Effects of TN

loss of identity
Loneliness – isolation – how can you go to social activities when you cannot eat,

how can you be intimate when you cannot bear your face to be touched

How do you get across the message that despite looking normal you have one of the most suicide pain

Depression is common, suicide
Depression

During the last month have you often been bothered by:

1. Feeling down, or depressed or hopeless?
2. Having little interest or pleasure in doing things?

Pilling BMJ 2009
NICE guidelines
Psychological areas of the brain activated in non evoked pain

Functional brain imaging of trigeminal neuralgia

Xavier Moisset a, Nicolas Villain b, Denis Ducreux c, Alain Serrie d, Gérard Cunin d, Dominique Valade e, Bernard Calvino f, Didier Bouhassira a,*

The IASP definition of trigeminal neuralgia (TN) is “sudden, usually unilateral, severe, brief, stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve.”

Here’s now one sufferer describes the pain: “Supper with friends. Candles and wonderful food. Suddenly my face is split apart—the bones feel as though they are shattering and the flesh naked aside by red-hot claws. I lean forward, the food falls from my mouth. The guests stare, concerned and appalled. I cannot explain why the tears stream down my face. I cannot even swallow, my own saliva dripping onto my plate. All I can do is try not to scream. If I look into a mirror I cannot believe that there is no sign of injury, no blood pouring out of my eye.”

The personal experience of TN pain, illustrating the suffering and fear accompanying the first attack, which many patients remember because of its dramatic onset.

TN has an enormous psychological impact, but few scholarly papers highlight the ways it can affect the quality of life. TN is a neuropathic condition with a unique clinical manifestation; it is also one of the few chronic pain conditions in which sufferers can be rendered 100% pain-free either with medications or surgery. For this reason, correct diagnosis is crucial so that patients can then follow a generally acknowledged care pathway, as soon

TN specialists Joanna Zakrzewska invited patients with TN to attend focus groups in the United Kingdom and United States. Sessions were recorded and transcribed. Patients in the U.S. support group also emailed their stories to relate their route of diagnosis, their symptoms, and the impact of the condition on their lives and those of the people closest to them.

Another important source of information was the collaborative art and medicine project Face2Face, based in London. Photographer Deborah Padfield worked individually with a group of facial pain patients, including three with TN, to
REZ NVC + anatomical changes

Antonini et al. Pain 2014: 155; 1464-1471
Tractography pre and post Gamma Knife Surgery

Hodaie et al 2012
DTI and tractography

- Promising results
- Potential biomarker
- Utility needs evaluating in all forms of surgery
Outcomes

Therapy

% pain relief

Decreased intensity frequency

Character of pain Provoking factors

Objective measures

Side effects

Beliefs concerns

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Quality of life BPI
n=82

Tolle et al Pain Practice 2006
Development of and psychometric testing for the Brief Pain Inventory–Facial in patients with facial pain syndromes

Clinical article

John Y. K. Lee, M.D.,¹ H. Isaac Chen, M.D.,¹ Christopher Urban, B.S.,¹ Anahita Hojat, B.S.,¹ Ephraim Church, B.A.,¹ Sharon X. Xie, Ph.D.,² and John T. Farrar, M.D., Ph.D.²

Brief Pain Inventory–Facial minimum clinically important difference

Sukhmeet K. Sandhu, BA,¹ Casey H. Halpern, MD,¹ Venus Vakhshori, BS,¹ Keyvan Mirsaedi-Farahani, BS,¹ John T. Farrar, MD, PhD,² and John Y. K. Lee, MD¹
|   |   |   |   |   |   |   |   |   |   |   |
|---|---|---|---|---|---|---|---|---|---|
| 8. Eating a meal | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
| 9. Touching your face (including grooming) | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
| 10. Brushing or flossing your teeth | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
| 11. Smiling or laughing | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
| 12. Talking | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
| 13. Opening your mouth widely | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
| 14. Eating hard foods like apples | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| Does not interfere | | | | | | | | | Completely interferes |
New Survey on Quality of Reporting

Proposal for evaluating the quality of reports of surgical interventions in the treatment of trigeminal neuralgia: the Surgical Trigeminal Neuralgia Score


(http://thejns.org/doi/abs/10.3171/2013.6.FOCUS13213)

Neurol Focus 2013

59 surgical studies 2008-2010
STNS maximum score 30
Scores 6-24
**Trigeminal neuralgia**

**Search date September 2013**

Joanna Zakrzewska and Mark E. Linskey

**ABSTRACT**

INTRODUCTION: Trigeminal neuralgia is a sudden, unilateral, brief, stabbing, recurrent pain in the distribution of one or more branches of the fifth cranial nerve. Pain occurs in paroxysms, which can last from a few seconds to several minutes. The frequency of the paroxysms ranges from a few to hundreds of attacks a day. Periods of remission can last for months to years, but tend to shorten over time. The condition can impair activities of daily living and lead to depression.

METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of ongoing treatments in people with trigeminal neuralgia? We searched: Medline, Embase, The Cochrane Library, and other important databases up to September 2013 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found seven studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: baclofen; carbamazepine; gabapentin; lamotrigine; oxcarbazepine; microvascular decompression; and destructive neurosurgical techniques (radiofrequency thermocoagulation, glycerol rhizolysis, balloon compression, and stereotactic radiosurgery).

**QUESTIONS**

What are the effects of ongoing treatments in people with trigeminal neuralgia?

<table>
<thead>
<tr>
<th>INTERVENTIONS</th>
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<tbody>
<tr>
<td><strong>TREATMENTS</strong></td>
</tr>
<tr>
<td>🌟 Likely to be beneficial</td>
</tr>
<tr>
<td>Carbamazepine</td>
</tr>
<tr>
<td>Oxcarbazepine*</td>
</tr>
<tr>
<td>Baclofen (in people with multiple sclerosis who develop trigeminal neuralgia)*</td>
</tr>
<tr>
<td>🌟 Trade off between benefits and harms</td>
</tr>
<tr>
<td>Microvascular decompression*</td>
</tr>
<tr>
<td>Non-percutaneous destructive neurosurgical techniques (stereotactic radiosurgery)*</td>
</tr>
<tr>
<td>Percutaneous destructive neurosurgical techniques (radiofrequency thermocoagulation, glycerol rhizolysis, or balloon compression)*</td>
</tr>
<tr>
<td>🌟 Unknown effectiveness</td>
</tr>
<tr>
<td>Lamotrigine</td>
</tr>
<tr>
<td>Gabapentin</td>
</tr>
<tr>
<td>Footnote</td>
</tr>
<tr>
<td>*Categorisation based on observational studies and/or consensus.</td>
</tr>
</tbody>
</table>
Adverse effects of AEDs

- disturbed sleep
- memory problems
- depression
- sleepiness
- dizziness
- weight gain
- shaky hands
- trouble with mouth or gums
- difficulty in concentrating
- upset stomach
- double or blurred vision
- problems with skin
- hair loss
- headache
- nervousness +/- aggression
- feelings of aggression
- restlessness
- tiredness
- unsteadiness

161 patients

New drug for TN

Zakrzewska et al. Trials 2013, 14:402
http://www.trialsjournal.com/content/14/1/402

STUDY PROTOCOL

Novel design for a phase IIa placebo-controlled, double-blind randomized withdrawal study to evaluate the safety and efficacy of CNV1014802 in patients with trigeminal neuralgia

Diagram:
- **Period 1**
  - 7 day Run-in
  - 21 day Open-label CNV1014802 150mg tid OR 350mg bid

- **Period 2**
  - 28 day DB CNV1014802 150mg tid OR 350mg bid
  - 7 day Follow-up
  - 7 day Follow-up

Randomisation
Conclusions

• Fewer treatment failures with raxatrigine 33.3% vs placebo 64.3%
• Greater reductions in number/ severity of paroxysms raxatrigine 45% vs 26% placebo
• Both clinicians and patients reported a greater proportion of improvements with the raxatrigine
• Very well tolerated with no significant adverse events
Medical vs surgical treatments

Evidence free zone
Natural history and outcome of 200 outpatients with classical trigeminal neuralgia treated with carbamazepine or oxcarbazepine in a tertiary centre for neuropathic pain

Giulia Di Stefano, Silvia La Cesa, Andrea Truini and Giorgio Cruccu

7% referred for surgery
Trigeminal neuralgia

Primary care
Carbamazepine
Initial good control but now failing
Refer pain clinic
Neurology headache

Idiopathic TN
MRI
Blood tests

Drug therapy

Symptomatic TN

Tumours etc

MS Drug therapy

Psychology CNS

Poor quality of life

Carbamazepine
Oxcarbazepine
Lamotrigine
Baclofen
Pregablin
Gabapentin

Joint neurosurgery clinic

Neurosurgery

Neurovascular compression

Microvascular decompression

Ablative procedures Gasserian ganglion
Gamma knife

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Decision analysis of medical and surgical treatments for trigeminal neuralgia: How patient evaluations of benefits and risks affect the utility of treatment decisions

A.L. Spatz a,1, J.M. Zakrzewska a,1, E.J. Kay b,*

As surgical techniques narrowly offer the highest chance of maximising patient quality of life, all patients with TN should consider surgery.
Ottawa Personal Decision Guide

1. Clarify the decision.
   - What decision do you face?
   - When do you need to make a choice?
   - How far along are you with making a choice?
   - Are you leaning toward one option?

2. Explore the decision.
   - List the options and main benefits and risks that you already knew.
   - Understand the benefits and risks that you think are most likely to happen.
   - Use stars (*) to show how much each benefit/risk matters to you. 5 stars means it matters a lot; 0 stars means not at all.

<table>
<thead>
<tr>
<th>Benefits</th>
<th>Options</th>
<th>How much it matters (*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Option #1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Option #2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Option #3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Identify the decision making needs.
   - Knowledge: Do you know the benefits and risks of each option?
   - Values: Are you clear about which benefits and risks matter most to you?
   - Support: Do you have enough support and advice to make a choice?
   - Certainty: Do you feel sure about the best choice for you?

4. Plan the next steps based on the needs.
   - Knowledge: (If you feel you do not have enough facts)
   - Values: (If you are not sure what matters most to you)
   - Support: (If you feel pressure from others)
   - Other plans: Describe


Decision guide for patients
Choice, Option, Decision

“COD”

- Deliberation

Prior Preferences → Informed Preferences

Choice Talk + Options Talk = Decision Talk

Good Decision

Decision Support
Brief - During
Long - External

http://www.advancingqualityalliance.nhs.uk/SDM
Support groups TN
US, UK, Australia, Canada, Denmark
Web sites: www.tna-support.org/
Summary

Phenotyping

Outcomes

Imaging

Decisions

Drugs vs surgery
Trigeminal Neuralgia

Doctors are men who prescribe medicines of which they know little to cure diseases of which they know less in human beings of whom they know nothing. Voltaire 1694-1778

“There is science in what we do, yes, but also habit, intuition and sometimes plain old guessing.

The gap between what we know and what we aim for persists. And this gap complicates everything we do.”

Complications: A Surgeon’s Notes on an Imperfect Science, Gawande