Unraveling the mystery –
the case for neuropathic pain

University of Waterloo
School of Optometry & Vision Science
Continuing Education Programme
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Complex Dry Eye Disease – Unraveling the Mystery

The case for neuropathic pain
Lyndon Jones | Richard Maharaj | C. Lisa Prokopich

Abstract

While many aspects of dry eye disease are being elucidated, the spectrum of disease remains a mystery in many ways. This course will use a case format to highlight the diagnosis and management of challenging cases of dry eye disease (DED) specifically one of the most challenging form of ocular complaint, that of neuropathic pain.
Objectives

• Case review format highlighting the diagnosis and management of challenging cases of dry eye disease (DED) using DEWS II approach; specifically neuropathic pain

• Review symptomatic versus asymptomatic patient pathway in the context of DEWS II

• Follow the diagnostic clues to build a DED diagnosis using homeostasis markers for diagnosis (i.e. TFBUT, osmolarity, vital dye staining)

• Know when to use other diagnostic testing (e.g. MMP-9, meibography, others) for subcategory assessment

• Determine from diagnostic clues (e.g. anesthetic, scleral lens) if neuropathic pain may be the cause; interpreting confocal microscopy

• Identify peripheral and central neuropathic features

• Discuss possible systemic factors in neuropathic pain and the psychosocial impact

• Review treatment options for neuropathic pain
Complex Dry Eye Disease – Unraveling the Mystery

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**Disclosures**

<table>
<thead>
<tr>
<th>Lyndon Jones</th>
<th>Richard Maharaj</th>
<th>C. Lisa Prokopich</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the past 3 years, members of CORE have received research funding and/or honoraria from Alcon, Allergan, Contamac, Coopervision, GL Chemotec, Inflamax Research, Johnson &amp; Johnson Vision, Menicon, Nature’s Way, Novartis, PS Therapy, Santen, Shire, SightGlass, Visioneering and NSERC, CIHR, CAO</td>
<td>Consultancies with Labtician-Thea, Takeda (formerly Shire), Johnson and Johnson Vision, I-MED pharma, Allergan, Novartis/Alcon, InMode Aesthetics, Santen, Bayer</td>
<td>Speakers bureau or consultations with Allergan, Novartis/Alcon, iMed, Innova, Santen, Purdue, Takeda, Labtician-Thea, Bausch + Lomb</td>
</tr>
</tbody>
</table>
CASE # 1

28-year-old African-Canadian man (lawyer)
## History & Clinical Findings

<table>
<thead>
<tr>
<th>History</th>
<th>Symptom score</th>
<th>Clinical tests</th>
</tr>
</thead>
</table>
| Trained as lawyer but stopped work due to eye pain 2 years ago | VAS pain score: 10/10 OU | • TMH: OD 0.20 OU  
  • Schirmer: 30 mm OU |
| GH: suffers from depression and insomnia as a result of continuous eye pain | Osmolarity: OD 270; OS 265 mOsm/L | |
| Meds: None at the moment | FTBUT: >10 secs OU | |

### Symptoms:
- Seen multiple practitioners
- Diagnosed with blepharitis, allergy, dry eye
- Multiple treatments for last 4 years; “Costing me a lot of money”
- Eyes are constantly painful; worse at end of day
- Cornea: No staining OU
- Eyelid margins: Normal
- MG: clear expression OU
Clinical Impression & Discussion

• Clinical impression
  • Not DED
  • Symptoms far exceed clinical signs?

• Options?
  • Malingering?
  • Psychological?
    • Time off work? Insurance claim?
  • Neuropathic pain\textsuperscript{1-8}
    • Central vs ‘peripheral’ (surface) initiation of pain
      - Confirm with topical anesthetic or scleral lens
        o Topical anesthetic caused no change in symptoms, nor did trial scleral lens

What is Neuropathic Pain?
Neuropathic Pain (Neuralgia)

• Neuropathic pain
  • Caused by a lesion or disease of the somatosensory nervous system
• Neuropathic pain is a clinical description
  • Commonly referred to as pathological pain or pain without biological value
  • Often associated with normally “non-painful” stimuli
  • Pain often described as burning, shooting, stabbing, or electric-like
• 5%-10% of the population report chronic pain in many Western countries

Prevalent Forms of Neuropathic Pain

- Trigeminal neuralgia
- HIV-associated pain
- Post-stroke pain
- Phantom limb pain
- Multiple sclerosis
- Reflex sympathetic dystrophy
- Spinal cord injury
- Cancer-related pain
- Postherpetic neuralgia
- Diabetic peripheral neuropathy

W5 investigates a rare but painful side effect of laser eye surgery

It's one of the most popular elective procedures in the world.

CASE # 2

27-year-old Caucasian man (banker)

CASE # 2
# History & Clinical Findings

<table>
<thead>
<tr>
<th>History</th>
<th>Symptom score</th>
<th>Clinical tests</th>
</tr>
</thead>
</table>
| LASIK surgery 2 years ago | OSDI: 46/100 | • TMH: OD 0.20 OU  
|  |  | • Schirmer: OD 7 mm; OS 8 mm |
| GH: good | Osmolarity: OD 301; OS 303 mOsm/L | FTBUT: 10 secs OU  
| Meds: “Pain doctor” prescribed gabapentin 300 mg po qd 1 month ago. No effect on ocular pain |  | • Cornea: Trace SPK; LASIK scars OU  
|  |  | • Eyelid margins: Normal  
|  |  | • MG: clear expression OU |

## Symptoms:
- Eyes are very light sensitive and constantly ached for 2 months after LASIK surgery
- Aching pain continues; varies around 5/10 most of the time
Clinical Impression & Discussion

- Clinical impression
  - Mildly depressed tear production typical of post-LASIK
  - ADDE?
    - But symptoms far exceed clinical signs?
      - Minimal staining
      - Minor reduction in tear production

- Options?
  - Neuropathic pain secondary to LASIK?¹⁻⁵
  - Confirm with in vivo confocal microscopy⁵⁻⁷

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Clinical diagnostic testing to rule in or rule out NOP?
1. DEWS Definition and Classification Subcommittee. The definition and classification of dry eye disease: report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2017)
Osmolarity and Chemistry Testing

TearLab® Osmolarity System

i-Pen® Tear Osmolarity

By Labtician-Thea

By i-Med Pharma

By Labtician-Thea
Ocular Surface Assessment

Tear Break-Up Time

Tear film break up is indicated by the dark areas that appear on the cornea.

Meibography: Upper and Lower Eyelid Images

Upper Lid:
Normal

Upper Lid:
Shortening of glands

Upper Lid:
Irregular/Tortuous Glands

Upper Lid:
Drop Out & Shortening

Lower Lid:
Normal

Lower Lid:
Hypertrophy and shortening of glands

Lower Lid:
Drop Out & Shortening, Hypertrophic glands
CASE # 3

27-year-old Caucasian woman (professional)
## History & Clinical Findings

**CASE # 3**

<table>
<thead>
<tr>
<th>History</th>
<th>Symptom score</th>
<th>Clinical tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>LASIK surgery 2 years ago OU (~-7.00)</td>
<td>OSDI: 71/100</td>
<td>• TMH: normal height</td>
</tr>
<tr>
<td>PRK enhancement 1 year ago OS only</td>
<td></td>
<td>• Phenol red: OD 17mm; OS 16mm (lowest values OU; after plugs)</td>
</tr>
<tr>
<td>GH: good</td>
<td></td>
<td></td>
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<tr>
<td>Meds: (all ~6 months)</td>
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<tr>
<td><strong>NEURONTIN (gabapentin)</strong> 300 mg po TID</td>
<td></td>
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<tr>
<td><strong>PAXIL (paroxetine)</strong> 20mg/day</td>
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<tr>
<td><strong>Omega 3</strong> 2000mg/day x 7 months</td>
<td></td>
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<tr>
<td>Thealoz Duo +/- HYLO prn; Liposic ung qhs</td>
<td></td>
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<tr>
<td><strong>Autologous serum 30%</strong> + hyaluronate 6-8x/day</td>
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<tr>
<td><strong>Xiidra (lifitegrast 5%)</strong> BID x 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lacrimal occlusion (3-month LT dissolvable intracanalicular)</td>
<td></td>
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<tr>
<td><strong>Symptoms:</strong></td>
<td></td>
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<tr>
<td>• Dry eye increased after LASIK OU, but since PRK in OS, much worse</td>
<td></td>
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<tr>
<td>• <strong>Burning/stinging</strong> pain OS (baseline 1 to 2/10)</td>
<td></td>
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<tr>
<td>(eye patch decreases pain)</td>
<td></td>
<td></td>
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<tr>
<td>• Increases to deep ache behind the eye with computer, driving</td>
<td></td>
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<tr>
<td>(7 to 8/10)</td>
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<td></td>
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<tr>
<td>FTBUT: 5 secs OU</td>
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<td></td>
</tr>
<tr>
<td>Cornea: SPK; LASIK scars OU; scleral show</td>
<td></td>
<td></td>
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<tr>
<td>Eyelid margins: MGD, notching</td>
<td></td>
<td></td>
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<tr>
<td>MG: clear expression OU</td>
<td></td>
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</tr>
</tbody>
</table>

**CASE # 3**
• Clinical impression
  • Findings very similar to Case #2

• Options?
  • Neuropathic pain secondary to PRK on top of LASIK?1-5
    • Confirm with in vivo confocal microscopy5-7
Treatment for Neuropathic Pain?
Second order neurons (red dashed line) decussate and join the contralateral spinothalamic pathways and synapse in the thalamus. The thalamus is the beginning of the perception of pain.

Third-order neurons (red dashed line) then relay information to the supra-spinal centers, including the somatosensory cortex.

Nociceptors detect noxious stimuli; ion channels activate and change the stimulus to electrical energy causing action potentials to the somatosensory cortex and the paralimbic structures. It is here that the pain is characterized. Emotional and additional facets of pain are perceived and interpreted.

First order neuron (red solid line) with nerve ending in the cornea, cell body in the trigeminal ganglion, and synapse in the subnucleus caudalis.

In actuality, however, there are multiple synapses for each nociceptor in the trigeminal subnucleus interpolaris/subnucleus caudalis (IV/Vc) transition zone, and in the subnucleus caudalis/upper cervical transition zone (Vc/C1–2).
Second order neurons (red dashed line) decussate and join the contralateral spinothalamic pathways and synapse in the thalamus. The thalamus is the beginning of the perception of pain.

Third-order neurons (red dashed line) then relay information to the supra-spinal centers, including the somatosensory cortex.

Nociceptors detect noxious stimuli; ion channels activate and change the stimulus to electrical energy causing action potentials to the somatosensory cortex and the paralimbic structures. It is here that the pain is characterized. Emotional and additional facets of pain are perceived and interpreted.

Peripheral Sensitization

In actuality, however, there are multiple synapses for each nociceptor in the trigeminal subnucleus interpolaris/subnucleus caudalis (VI/Vc) transition zone, and in the subnucleus caudalis/upper cervical transition zone (Vc/C1–2).

First order neuron (red solid line) with nerve ending in the cornea, cell body in the trigeminal ganglion, and synapse in the subnucleus caudalis.

The alldynia characteristic of neuropathic pain thought to originate here with the recruitment of Aβ and C fibers and phenotypic switch from innocuous touch to pain transmission.

Central sensitization

Central sensitization may initially be reversible, but often becomes permanent.

Neuroplastic changes

Central sensitization ‘hallmark’ is pain that is disconnected from ongoing peripheral input (e.g. after LASIK when symptoms >> ocular surface findings, or “pain without stain”).

Central sensitization may initially be reversible, but often becomes permanent.

Intermediary (Trigeminal nucleus)

The allodynia characteristic of neuropathic pain thought to originate here with the recruitment of Aβ and C fibers and phenotypic switch from innocuous touch to pain transmission.

After treatment with 20% autologous serum tears (reduced tortuosity, beading, reflectivity, as well as reduced symptom scores)
Confocal Scanning laser

CASE # 3

OD LASIK

OS LASIK + PRK
Treatments for Neuropathic Pain (NP)

• Difficult condition to treat effectively; invariably requires **polypharmacy** given the number of systems, pathways, receptors, processes

• Medications for peripheral NP are mostly consistent across various NP pain guidelines. 1\textsuperscript{st} and 2\textsuperscript{nd} line drugs include:
  • TCA (amitriptyline)
  • SNRI (duloxetine, venlafaxine)
  • Gabapentinoids (or Ca+ channel delta ligands) (pregabalin, gabapentin)

• Non-narcotic pain relievers are generally not helpful
• Narcotic pain relievers may have some success
• ADR profiles and cost are drivers for prescribing, but individuality and complexity of NP makes this challenging in all but hands of pain specialists
Current Treatment Options: NP

- **Gabapentinoids, TCAs and SNRIs (not SSRIs)** individually are considered 1st line treatments. If a 1st line agent only provides partial relief, it is reasonable to add another 1st line agent for combination [RxTx]

- **Tramadol** and opioid analgesics are 2nd line agents. Caution should be used because of their extensive ADRs, including addiction/misuse/abuse risk; monitoring needs to be diligent, including consultation with the Canadian Guidelines *

- **Cannabinoids** are considered a 3rd line agent for NP, but require more study

- **Topical agents** are 4th line agents for NP. (For parts of the body other than the eye, agents include lidocaine, methadone, tapentadol, lacosamide, lamotrigine and topiramate)

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*Canadian Pain Society (CPS)*

- **Canada**
- **Published 2014**

**First-line pharmacotherapy**

- Gabapentin
- Pregabalin
- Tricyclic antidepressants (TCAs)
- Serotonin norepinephrine reuptake inhibitors (SNRIs) *(DULOXETINE most studied SNRI and recommended)*

**Second-line pharmacotherapy**

- Tramadol
- Controlled-release opioids

**Third-line pharmacotherapy**

- Cannabinoids

**Fourth-line pharmacotherapy**

- Topical lidocaine

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*Duloxetine is the most studied SNRI and, therefore, recommended.*

**Doses ≥75mg of amitriptyline, imipramine or dopamine are not recommended for patients ≥65 years.**

***Long-term use of tramadol should not be used in non-specialist settings unless advised by a specialist.***

****Long-term safety of repeated applications of high-concentration capsaicin patches has not been established.

* Cdn Guidelines for the Safe and Effective Use of Opioids for Chronic Noncancer Pain

<table>
<thead>
<tr>
<th>Medication (class)</th>
<th>Mechanism of action</th>
<th>Starting dosage</th>
<th>Maximum dosage</th>
<th>Side Effects</th>
<th>Precaution and contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TCA</strong></td>
<td></td>
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</tr>
<tr>
<td>(Tricyclic Antidepressants)</td>
<td>Monoamine reuptake inhibition, sodium channel blockade and anticholinergic effects</td>
<td>10–25 mg at bedtime</td>
<td>100 mg at bedtime</td>
<td>Dry mouth, constipation, somnolence, anticholinergic effects, weight gain</td>
<td>Cardiac disease, prostatic adenoma and seizure disorder High doses should be avoided in adults &gt; 65 years of age</td>
</tr>
<tr>
<td>Nortriptyline, Desipramine</td>
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<tr>
<td>Use a tertiary amine TCA only if a secondary are not available Ref. 112–119</td>
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<tr>
<td>Nortriptyline/Desipramine are FDA-approved for treatment of symptoms of depression</td>
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<tr>
<td>Carbamazepine (Anticonvulsant) Ref. 120,121</td>
<td>Sodium channel– blocker</td>
<td>200 mg daily</td>
<td>400–800 mg/day, divided in 2–3 doses</td>
<td>Hyponatremia, Drowsiness, headache, Dizziness, rash and nausea</td>
<td>Concomitant use of MAO inhibitors Cardiac or hepatic disease Renal failure Prostatic hyperplasia</td>
</tr>
<tr>
<td>FDA-approved for epilepsy, trigeminal neuralgia, and manic and mixed episodes of bipolar disorder</td>
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<tr>
<td><strong>Anti-convulsant</strong></td>
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<tr>
<td><strong>Opioid antagonist</strong></td>
<td>At low doses has an antiinflammatory effect, reducing the preinflammatory cytokines</td>
<td>1.5 mg at bed time</td>
<td>4.5 mg/bedtime</td>
<td>Headache, vivid dreams, nightmares, tachycardia and anxiety</td>
<td>Past organ transplant and use of immunosuppressive drugs</td>
</tr>
<tr>
<td>Low-Dose Naltrexone (Opioid Antagonist) Ref. 122–124</td>
<td>Modulating microglial activity</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>FDA-approved at higher doses (50 mg to 300 mg) for treatment of drug and alcohol addiction</td>
<td>Opioid antagonist - μ-opioid and κ-opioid receptors</td>
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</tr>
<tr>
<td><strong>Opioid agonist</strong></td>
<td>μ-receptor agonist and monoamine reuptake inhibitor</td>
<td>50 mg/day</td>
<td>100 mg/day in divided doses every 3–7 days as tolerated</td>
<td>Nausea, vomiting, constipation, dizziness, and somnolence</td>
<td>History of substance abuse, suicide risk and antidepressant in elderly patients</td>
</tr>
<tr>
<td><strong>Tramadol</strong> (Opioid Agonist) Ref. 110,111,125</td>
<td></td>
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<tr>
<td>FDA-approved for treatment of moderate to moderately severe pain</td>
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<tr>
<td><strong>Third-Line Agents</strong></td>
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</tr>
<tr>
<td><strong>Anti-convulsant (Ca channel alpha2 delta ligands)</strong></td>
<td>Act on the α,δ subunit of voltage-gated calcium channels, which decrease central sensitization</td>
<td>100–300 mg three times/day</td>
<td>2400 mg/day</td>
<td>Sedation, dizziness, peripheral edema</td>
<td>Reduced dose in renal insufficiency</td>
</tr>
<tr>
<td>Calcium channel α-2-δ ligands - Gabapentin (Anticonvulsants) FDA-approved for treatment of post-herpetic neuralgia Pregabalin (Anticonvulsant) Ref. 113, 126–136</td>
<td></td>
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</tr>
<tr>
<td>FDA-approved for treatment of neuropathic pain and fibromyalgia</td>
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</tr>
<tr>
<td><strong>SNRI</strong></td>
<td>Serotonin-noradrenaline reuptake inhibitors</td>
<td>30 mg/day</td>
<td>60 mg twice/day</td>
<td>Nausea, abdominal pain, constipation</td>
<td>Hepatic disorders Use of tramadol hypertension</td>
</tr>
<tr>
<td>(Serotonin-noradrenaline reuptake inhibitors) Duloxetine Ref. 137–139</td>
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</tr>
</tbody>
</table>

## Current Treatment Options

Monoamine uptake inhibition, norepinephrine reuptake inhibition in the spinal dorsal synapses, secondary activity at sodium channels

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose</th>
<th>Effective Dose</th>
<th>Common A/E</th>
<th>Major A/E</th>
<th>CI/Precautions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antidepressant – TCA</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
| ELAVIL (amitriptyline) | 10–25mg/day | 25–75mg/day | Somnolence, anticholinergic effects (e.g. xerostomia, Urinary retention, constipation, blurred vision, mydriasis), fatigue, weight gain | Somnolence, anticholinergic effects (e.g. xerostomia, Urinary retention, constipation, blurred vision, mydriasis), fatigue, weight gain | Contraindicated in patients with recent MI or cardiac rhythm disorders, severe liver disease | Initiate dose at bedtime
Dose can be increased 10–25mg every 3–7 days as tolerated. Effect usually in 2–4 weeks.
Doses above 100mg should be used with caution
Doses can be taken once or divided into two administrations. A single dose above 75mg is not recommended
Risk for discontinuation syndrome if abruptly stopped |
| (nortriptyline) | 25mg/day then gradually adjust levels to therapeutic benefit | 75–100mg/day | | | | | **Doses ≥75mg of amitriptyline, imipramine or dopamine are not recommended for patients ≥65 years.**

Current Treatment Options
sodium channel blocker commonly used for trigeminal neuralgia (1st line for trigeminal neuralgia)

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose</th>
<th>Effective Dose</th>
<th>Common A/E</th>
<th>Major A/E</th>
<th>CI/Precautions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-convulsant - carbamazepine</td>
<td>NOP start with 200mg hs and increase by 200mg eery 7 days until reach effective dose</td>
<td>Final effective dose of 400-1200 mg/day, in 2-3 divided doses (can be tapered after response achieved) (this dose may be higher for NP that is not ocular)</td>
<td>drowsiness, headache, and dizziness, hyponatremia</td>
<td></td>
<td>Concomitant use of MAO inhibitors, cardiac or hepatic disease, renal failure, prostatic hyperplasia</td>
<td></td>
</tr>
</tbody>
</table>

TEGRETOL (carbamazepine)

Initial dose: 200mg hs and increase by 200mg every 7 days until reach effective dose

Effective dose: 400-1200 mg/day, divided

Final effective dose: 400-1200 mg/day, in 2-3 divided doses (can be tapered after response achieved) (this dose may be higher for NP that is not ocular)

## Current Treatment Options

block the presynaptic serotonin and norepinephrine transporter proteins, which inhibits the reuptake of these neurotransmitters

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Dose</th>
<th>Effective Dose</th>
<th>Common A/E</th>
<th>Major A/E</th>
<th>CI/Precautions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYMBALTA (duloxetine)</td>
<td><strong>20–30mg/day or 60mg/day</strong></td>
<td><strong>Titrate up to 60mg BID</strong></td>
<td>Nausea, drowsiness, dizziness, constipation, dyspepsia, diarrhea, xerostomia, anorexia</td>
<td>Stevens-Johnson syndrome, hepatotoxicity, hypertensive crisis, GI haemorrhage, delirium, MI, cardiac arrhythmias, glaucoma, suicidal thoughts and behaviour, mania or hypomania in patients with bipolar disorder, seizures, severe hyponatraemia, fragility bone fractures, neuroleptic syndrome, serotonin syndrome</td>
<td>Contraindicated in patients with liver disease that results in hepatic impairment, severe renal impairment (CrCL &lt;30mL/min) and uncontrolled HT. Do not use concurrently or within 14 days of d/c of an MAOI</td>
<td>Dose-adjust in renal and hepatic impairment. May lower seizure threshold</td>
</tr>
<tr>
<td>EFFEXOR (venlafaxine)</td>
<td>37.5mg or 75mg each day. Increase by 75mg weekly until desired effect (max dose of 225mg/daily; adequate trial 4-6 weeks)</td>
<td>75–225mg/day</td>
<td></td>
<td></td>
<td></td>
<td>Gradual tapering is recommended</td>
</tr>
</tbody>
</table>

*Duloxetine is the most studied SNRI and, therefore, recommended.*

---

## Current Treatment Options

Bind to the calcium channel α2-δ subunit resulting in decreased central sensitization and nociceptive transmission

<table>
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<tr>
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<th>Major A/E</th>
<th>CI/Precautions</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LYRICA</strong> (pregabalin)</td>
<td>150mg/day, given in either 2 or 3 divided doses (75mg BID or 50mg TID)</td>
<td>300–600mg/day</td>
<td>Somnolence, peripheral oedema, weight gain</td>
<td>Angioedema, hepatotoxicity, rhabdomyolysis, suicidal thoughts and behaviour, seizures with rapid d/c, thrombocytopenia</td>
<td>Caution in elderly patients who are cardiovascular compromised. Post-marketing reports of CHF. CNS depression (caution with activities requiring mental alertness and elderly at risk for falls)</td>
<td>Adverse effects may be more severe in older patients, lower starting doses and more gradual titration recommended. Dose adjust in renal impairment</td>
</tr>
<tr>
<td>NEURONTIN (gabapentin)</td>
<td>Day 1 — 300mg QD</td>
<td>900–3600mg/day</td>
<td>Sedation, peripheral edema, weight gain</td>
<td>Drug rash with eosinophilia and systemic symptoms (DRESS), suicidal thoughts and behaviour, seizures with rapid d/c</td>
<td>CNS depression (caution with activities requiring mental alertness and elderly at risk for falls)</td>
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Management:
What can we do as optometrists?
## Staged Management of DED: Neuropathic Ocular Pain

<table>
<thead>
<tr>
<th>Step 1</th>
<th>Step 2</th>
<th>Step 3</th>
<th>Step 4</th>
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</thead>
<tbody>
<tr>
<td>• <strong>Education</strong></td>
<td>• <strong>Non-preserved ocular lubricants to minimize preservative-induced toxicity</strong>&lt;br&gt;• <strong>Tea tree oil treatment for Demodex (if present)</strong>&lt;br&gt;• <strong>Tear conservation</strong>&lt;br&gt;• <strong>Overnight treatments (such as ointment or moisture chamber devices)</strong>&lt;br&gt;• <strong>In-office, physical heating and expression of the meibomian glands (including device-assisted therapies)</strong>&lt;br&gt;• <strong>In-office intense pulsed light therapy for MGD</strong>&lt;br&gt;• <strong>Prescription drugs to manage DED</strong></td>
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<td>• <strong>Environmental / dietary modifications</strong></td>
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<td>• <strong>Eliminate offending systemic medications</strong></td>
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<tr>
<td>• <strong>Artificial tear substitutes, gels / ointments</strong></td>
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<tr>
<td>• <strong>Eyelid therapy</strong></td>
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</tbody>
</table>

If *Stage 1* options are inadequate, consider:

- Non-preserved ocular lubricants to minimize preservative-induced toxicity
- Tea tree oil treatment for Demodex (if present)
- **Tear conservation**
- Overnight treatments (such as ointment or moisture chamber devices)
- In-office, physical heating and expression of the meibomian glands (including device-assisted therapies)
- In-office intense pulsed light therapy for MGD
- **Prescription drugs to manage DED**

If *stage 2 treatments are inadequate, add*:

- Oral secretagogues
- **Autologous/allogeneic serum eye drops**
- Therapeutic contact lens options (soft bandage lenses; rigid scleral lenses)

If *stage 3 treatments are inadequate, consider*:

- **Topical corticosteroid for longer duration**
- Amniotic membrane grafts
- Surgical punctal occlusion
- Other surgical approaches (eg, tarsorrhaphy, salivary gland transplantation)
Dx: Central Neuropathic Ocular Pain (presumed)

Management

✓ Education
  • Not primarily a dry eye problem (pain without stain)
  • Use objective tests and photos to show healthy ocular surface
✓ Referral to pain clinic via general practitioner
✓ Full ocular diagnostic work-up for DED/OSD
✓ Greatest challenge with these cases?
  • Diagnosis is missed; refer appropriately
✓ Patients often told they are crazy (in their head)!
  • Validate patient complaints
  • They will thank you for confirming that they have a “genuine” problem
Dx: Surface (Peripheral) Neuropathic Ocular Pain

Management

✓ Evaluate meds to determine ADRs, and if dosing is appropriate (advocate)
  • Did not appear to be effective; dosing?
✓ Systemic anti-inflammatory
  • Nutrition?
✓ Topical steroid to decrease inflammation
✓ Lacrimal occlusion to optimize tear film retention
✓ Topical agents containing nerve growth factor
  • Autologous serum tears 8x/day
Person-centred Management: What can we do as optometrists?

Manage the PAIN

- Pain specialist referral
- Advocate for and support your patient!
- Consider the classes of meds used for NP pain, that central pain is multi-modal and requires polypharmacy

Manage the EYE

- Diligently treat any DED/OSD present
- Consider nociceptor stimulation (Scleral lenses, goggles, lubricants, new agents) and Nerve regeneration (autologous serum, anti-inflammatories)

Identify/diagnose

- NP pain can be very challenging to manage, but early diagnosis is key to arresting the cycle
- Optometrists are perfectly placed as primary eyecare practitioners to treat, but also support and advocate for patients with NP pain
Unraveling the mystery – the case for neuropathic pain

University of Waterloo
School of Optometry & Vision Science
Continuing Education Programme
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Thank you!