Dr Garsing Wong
Sapphire Appearance Medicine Clinic
Auckland

Dr Murray Hing
Flexa Group
Auckland

Chronic Migraine Treatment with Botox and Physio - Concurrent Workshop Repeated
Sunday, 23 June 2013
Start 8:30am
Start 9:35am
Duration: 55mins
Duration: 55mins
Picasso
Picasso
Chronic Migraine Treatment using Botulinum Toxin Type A
GP CME Workshops 23 June 2013

Dr Garsing Wong
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Disclosures

- Former Exec Member of the New Zealand College of Appearance Medicine
- Former Chairman of the College of Urgent Care Physicians
- Consultancy with Allergan, Sanofi-Adventis, Valeant, GlaxoSmithKline, Merck Sharpe & Dhome, Palomar Medical Technologies, Bayer, Eli Lilly, Lundbeck, Q-med, Ministry of Social Development
- Research Grants from Glaxo Smith Kline & Bayer
Migraine: more than just a headache

- Occasional headaches are common and are often regarded by most people as part of normal life.
- For some, however, headache disorders such as migraine can cause disability and impaired quality of life.
- Globally, it is estimated that 46% of the adult population have an active headache disorder.\(^1\)

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The economic cost of migraine

- Migraine is an important public health problem that is associated with substantial costs\(^1-^3\)

<table>
<thead>
<tr>
<th>Direct costs</th>
<th>Indirect costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication</td>
<td>Absence from work (absenteeism)</td>
</tr>
<tr>
<td>Consultation</td>
<td>Reduced productivity at work (presenteeism)</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>Lost career opportunities</td>
</tr>
<tr>
<td>Diagnostic investigations</td>
<td>Unemployment</td>
</tr>
</tbody>
</table>
The global prevalence of migraine is approximately 10%\(^1\)

### Prevalence by Region

- **Africa**: 4.0 (2 studies)
- **Asia**: 10.6 (6 studies)
- **Europe**: 13.8 (9 studies)
- **N. America**: 12.6 (8 studies)
- **S. America**: 9.6 (10 studies)

**Mean**: 11.2; **Median**: 10.2

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No Prevalence Studies of Chronic Migraine in New Zealand

- Dr Sheena Aurora, Neurologist, Director of the Swedish Headache Centre in Seattle estimates the prevalence in New Zealand to be 1.3%
- 3% episodic migraines->chronic migraine
- Pop 4.4mill -> 80% over age of 15 (Min of Bus Inn)
- estimate 45,814 kiwis suffer from Chronic Migraine!
- Total GP’s 3541 (www.healthworkforce.govt)
- 12.9 Chronic Migraine sufferers per GP
Outline

- Prevalence
- How to diagnose Migraine
- Definition of Chronic Migraine
- What do I do for any headache patient SNOOP4
- Botulinum Toxin type A or OnabotulinumtoxinA
- Safety
- What do I do?
- What can you do
- Role of Physiotherapy & Case Presentation – Hand over to Murray Hing
Preface to IHS-ICHD-2 website

Two years after the publication of the 2nd Edition of The International Headache Classification (ICHD-2), we are now ready to launch a web based edition. This web based version has many facilities that are not present in the printed version or a simple electronic file.

Since a Headache Classification cannot be learned by heart, it is of immense value that doctors all over the world are now able to go on the web and look after whatever question they may have regarding ICHD-2.

Table of Contents

This classification is hierarchical and you must decide how detailed you want to make your diagnosis. This can range from the first-digit level to the fourth. First one gets a rough idea about which group the patient belongs to. Is it for example 1. Migraine or 2. Tension-type headache or 3. Cluster headache and other trigeminal autonomic cephalalgias? Then one obtains information allowing a more detailed diagnosis. The desired detail depends on the purpose. In general practice only the first- or second-digit diagnoses are usually applied whilst in specialist practice and headache centres a diagnosis at the third- or fourth-digit levels is appropriate.
Primary headache disorders: classification according to frequency

- The primary headache disorders are broadly classified based on frequency of headache attack

Migraine: characteristics


- Pain is usually unilateral
- Sensitivity to light, sound or movement
- Moderate-to-severe head pain
- Often accompanied by nausea

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IHS Diagnosis ICD-10

1.1 Migraine without aura G43.0

Previously used terms: Common migraine, hemicrania simplex

Description:
Recurrent headache disorder manifesting in attacks lasting 4-72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia.

Diagnostic criteria:
A. At least 5 attacks fulfilling criteria B-D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)

C. Headache has at least two of the following characteristics:
   1. unilateral location
   2. pulsating quality
   3. moderate or severe pain intensity
   4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)

D. During headache at least one of the following:
   1. nausea and/or vomiting
   2. photophobia and phonophobia

E. Not attributed to another disorder

and revises the International Classification of Headache Disorders.

More

Downloads

ICHD-III Beta
The International Classification of Headache Disorders, 3rd edition, beta version

More

Cephalalgia

Cephalalgia is the official journal of the IHS. It contains original papers on all aspects of headache. The journal provides an international forum for original research papers, review articles and short communications.

More

IHS Discussion Group

Ask questions and share information about the 2nd edition of the IHS...
1.2.1 Typical aura with migraine headache

**Description:**
Typical aura consisting of visual and/or sensory and/or speech symptoms. Gradual development, duration no longer than one hour, a mix of positive and negative features and complete reversibility characterise the aura which is associated with a headache fulfilling criteria for 1.1 **Migraine without aura**.

**Diagnostic criteria:**
A. At least 2 attacks fulfilling criteria B-D

B. Aura consisting of at least one of the following, but no motor weakness:
   1. fully reversible visual symptoms including positive features (eg, flickering lights, spots or lines) and/or negative features (ie, loss of vision)
   2. fully reversible sensory symptoms including positive features (ie, pins and needles) and/or negative features (ie, numbness)
   3. fully reversible dysphasic speech disturbance

C. At least two of the following:
   1. homonymous visual symptoms¹ and/or unilateral sensory symptoms
   2. at least one aura symptom develops gradually over ≥5 minutes and/or different aura symptoms occur in succession over ≥5 minutes
   3. each symptom lasts ≥5 and ≤60 minutes

D. Headache fulfilling criteria B-D for 1.1 **Migraine without aura** begins during the aura or follows aura within 60 minutes

E. Not attributed to another disorder²

**Notes:**
Chronic Migraine

- current practical, clinical definition are headaches of more than 4 hours ≥15 days/month and prior or current diagnosis of migraine, with or without medication overuse, > 3 months

What is medication overuse headache?

- Chronic daily headache syndrome that is either a cause or consequence of a prior headache (usually migraine or tension-type headache)
- Develops through chronic overuse of acute medication taken to treat headache or other pain\(^1\)
- Defined in the 2006 ICHD-IIR guideline as:\(^2\)
  - Headache on ≥15 days in every month
  - Regular overuse for >3 months of acute symptomatic treatment drugs, during which time headaches have developed or worsened markedly
- Overuse of all headache medication taken on an *ad hoc* basis to relieve pain may result in medication overuse headache\(^3\)
- Most commonly associated with regular use of simple analgesics on ≥15 days a month and/or regular use of opioids, ergots or triptans, or any combination of these, on ≥10 days a month\(^3\)

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Medication overuse confounds diagnosis of chronic migraine and other chronic headache disorders

- Medication overuse confounds the diagnosis of chronic daily headache disorders, and is a significant issue\(^1,2\)
- Not all medication-overuse patients improve after discontinuation of medication\(^1\)
- Medication-overuse patients may be responsive to prophylactic medications after withdrawal\(^1\)
- Medication overuse may induce the development of chronic daily headache disorders\(^1,2\)
- Presence of medication overuse may not exclude the diagnosis of chronic migraine\(^3\)


Medication overuse headache is often referred to as ‘rebound’ headache.
Warning signs of secondary headache

- Systemic symptoms and signs (fever, weight loss)\(^1,2\)
- Neurological symptoms and/or signs (pulsatile tinnitus, papilloedema)\(^1,2\)
- Age of transformation approximately 55 years\(^1,2\)
- Recent onset of chronic headache (<6 months)\(^1,2\)
- Different headache pattern/worse severity of headache\(^1,2\)
- Precipitated by valsala or exertion; postural (e.g. worse in upright or recumbent position)\(^1,2\)

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SNOOP4: Ruling Out Secondary Causes of Headache in Migraine

- Systemic symptoms and signs
- Neurologic symptoms or signs
- Onset: peak at onset or <1 minute
- Older: after age 50 years
- Previous headache: pattern change
- Postural, positional aggravation
- Precipitated by valsalva, exertion etc
- Papilloedema

Silberstein SD, Lipton RB in: Silberstein SD et al. eds. Wolff’s Headache and Other Head Pain. 8th ed. New York: Oxford University Press; 2008;315-377
Add a snoop4 shortcut key

- Systemic symp ... Neurologic symp ...
- Onset <1min ... Older > 50 ...
- Previous HA pattern change ...
- Postural, positional aggravation ...
- Precipitated by valsarva ...
- Papilloedema ...
Botulinum Toxin Type A

- Injector since 2004
- Safe
- Actions
- Side Effects
- Bruxism /Facial Shaping/Cosmetic ->Migraine 2005
- Joint program using physiotherapy improves effectiveness of program
- Official validation of use of Botulinum Toxin Type A with the publication of the PREEMPT Clinical Program – RCT - the only proven prophylatic tx for CM
Botulinum Toxin Type A
Onabotulinumtoxin A or Botox®

• is a natural, purified protein that relaxes muscles and inhibits sweat glands
• A simple and quick, minimally invasive non-surgical treatment
• is the only product of its kind with a proven 20-year safety record and effective use in millions of patients worldwide & 20 YEARS of data and experience (Ref: Naumann M et al. Curr Med Res Opin 2004)
• 7 toxin serotypes A to G
• Not interchangeable 3 Aug 2009

• Most common side effect is tenderness or bruising at the site of injection
• Less frequent side effects can include headache, temporary eyelid droop and nausea
• BOTOX® is currently available in approximately 80 countries. http://www.allergan.com/products/neurosciences/index.htm
<table>
<thead>
<tr>
<th>Indication</th>
<th>Date of approval in Australia/New Zealand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal spasticity in adults</td>
<td>2003 (ANZ)</td>
</tr>
<tr>
<td>Strabismus in children (&gt;2 years) and adults</td>
<td>2005/1991</td>
</tr>
<tr>
<td>Focal spasticity of upper &amp; lower limbs, including dynamic equinus foot deformity, due to juvenile cerebral palsy in patients &gt; 2 years</td>
<td>2007/2008</td>
</tr>
<tr>
<td>Blepharospasm</td>
<td>1993/1991</td>
</tr>
<tr>
<td>Cervical dystonia</td>
<td>2000/1993</td>
</tr>
<tr>
<td>Spasmodic dysphonia</td>
<td>2005/(not approved in New Zealand)</td>
</tr>
<tr>
<td>Severe primary hyperhidrosis of the axillae</td>
<td>2001 (ANZ)</td>
</tr>
<tr>
<td>Glabellar lines</td>
<td>2002/2001</td>
</tr>
<tr>
<td>Forehead lines, Crow’s feet</td>
<td>2007/2006</td>
</tr>
<tr>
<td>Chronic migrane</td>
<td>2011 (ANZ)</td>
</tr>
<tr>
<td>Juvenile cerebral palsy</td>
<td>1998/2001</td>
</tr>
</tbody>
</table>

References: 1. BOTOX® Approved Product Information Allergan Australia.
Botulinum Toxin

- It is the most acutely toxic substance known, with a median lethal dose of about 1 ng/kg when introduced intravenously[^1] and 3 ng/kg when inhaled.[^2] This means, depending on the method of introduction into the body, a mere 90–270 nanograms of botulinum toxin could be enough to kill an average 90-kg (200-lb) person, and four kg of the toxin, if evenly distributed, would be more than enough to kill the entire human population of the world.


• 1 microgram = 1000 nanograms
• 1 milligram = 1000 micrograms
• 1 gram = 1000 milligrams
<table>
<thead>
<tr>
<th>SUBSTANCE</th>
<th>ANIMAL/ROUTE</th>
<th>LD50</th>
<th>LD50 g/kg</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Botulinum toxin</strong> <em>(Botox)</em></td>
<td>human, oral, injection, inhalation</td>
<td>1 ng/kg approx 20.8 units (estimated)</td>
<td>0.000000001</td>
<td>Nigam PK et al Botulinum Toxin Indian J Dermatol 2010 Jan-Mar;55(1) 8-14</td>
</tr>
<tr>
<td><strong>Paracetamol</strong> (acetaminophen)</td>
<td>rat, oral</td>
<td>1,944 mg/kg</td>
<td>1.944</td>
<td>[19]</td>
</tr>
<tr>
<td><strong>Coumarin</strong> <em>(benzopyrone, from Cinnamomum aromaticum and other plants)</em></td>
<td>rat, oral</td>
<td>293 mg/kg</td>
<td>0.293</td>
<td>[19]</td>
</tr>
<tr>
<td><strong>Aspirin</strong> <em>(acetylsalicylic acid)</em></td>
<td>rat, oral</td>
<td>200 mg/kg</td>
<td>0.2</td>
<td>[20]</td>
</tr>
<tr>
<td><strong>Caffeine</strong></td>
<td>rat, oral</td>
<td>192 mg/kg</td>
<td>0.192</td>
<td>[21]</td>
</tr>
<tr>
<td><strong>Venom of the Inland Taipan</strong> <em>(Australian snake)</em></td>
<td>rat, subcutaneous</td>
<td>25 µg/kg</td>
<td>0.000025</td>
<td>[41]</td>
</tr>
<tr>
<td><strong>Sarin</strong></td>
<td>mouse, subcutaneous injection</td>
<td>17.23 µg/kg (estimated)</td>
<td>0.0000172</td>
<td>[44]</td>
</tr>
<tr>
<td><strong>Bisoprolol</strong></td>
<td>mouse, oral</td>
<td>100 mg/kg</td>
<td>0.1</td>
<td>[24]</td>
</tr>
</tbody>
</table>
How safe is Botox?

- 1 nanogram of Botox is approx 20 units.
- Average 70kg man needs 1,400 units of Botox to reach a lethal dose = $35,000 of Botox in a 3 month period.
- Average dose for cosmetic area is 20 units.
- Average dose for Chronic Migraine Patients is 130 units.
Irreversible hepatotoxicity occurs with less than 15g i.e. 30 tabs of over the counter paracetamol.
Botulinum Toxin Type A facial shaping
Botulinum Toxin Type A correcting your smile
2 weeks after Botulinum Toxin Type A lower facial lift
2 week after *Botulinum Toxin Type A* lower facial lift (both photos are of the patient doing the same action - grimacing)
What do I do?

- All patients booked into the Migraine Clinic are sent questionnaires which they must return before a booking is made
- Headache diary
- HIT-6
- Becks Depression Score
- Migraine Definition
- Chronic Migraine Definition
- Outline of cost
**Headache Impact Test**

**VERSION 1.1**
This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches. To complete, please circle one answer for each question.

1. **When you have headaches, how often is the pain severe?**
   - Never
   - Rarely
   - Sometimes
   - Very Often
   - Always

2. **How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?**
   - Never
   - Rarely
   - Sometimes
   - Very Often
   - Always

3. **When you have a headache, how often do you wish you could lie down?**
   - Never
   - Rarely
   - Sometimes
   - Very Often
   - Always

4. **In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?**
   - Never
   - Rarely
   - Sometimes
   - Very Often
   - Always

5. **In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?**
   - Never
   - Rarely
   - Sometimes
   - Very Often
   - Always

6. **In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?**
   - Never
   - Rarely
   - Sometimes
   - Very Often
   - Always

**To score, add points for answers in each column.**
- **Total Score**
- **High scores indicate greater impact on your life.**
  - Score range is 36-78.
HEADACHE IMPACT TEST™
What Does Your Score Mean?

If You Scored 60 or More
Your headaches are having a very severe impact on your life. You may be experiencing disabling pain and other symptoms that are more severe than those of other headache sufferers. Don’t let your headaches stop you from enjoying the important things in your life, like family, work, school or social activities.

Make an appointment today to discuss your HIT-6 results and your headaches with your doctor.

If You Scored 56 – 59
Your headaches are having a substantial impact on your life. As a result you may be experiencing severe pain and other symptoms, causing you to miss some time from family, work, school, or social activities.

Make an appointment today to discuss your HIT-6 results and your headaches with your doctor.

If You Scored 50 – 55
Your headaches seem to be having some impact on your life. Your headaches should not make you miss time from family, work, school, or social activities.

Make sure you discuss your HIT-6 results and your headaches at your next appointment with your doctor.

If You Scored 49 or Less
Your headaches seem to be having little to no impact on your life at this time. We encourage you to take HIT-6 monthly to continue to track how your headaches affect your life.
BECKS DEPRESSION INVENTORY FOR MIGRAINE PATIENTS

Name: ___________________________ Age: _____ Sex: ___ Occupation: ___________________________
Marital Status: ________ Education: ___________________________

Instructions: This questionnaire consists of 21 groups of statements. Please read each group carefully, and then pick out ONE statement that best describes the way you are feeling during the past 2 weeks, including today. Please write the number you have chosen in the square provided. If several statements in a group seem to apply equally well, circle the highest number for that group. Be sure you do not choose more than one.

1. 0 I do not feel sad.
   1 I feel sad.
   2 I am sad all the time and I can’t snap out of it.
   3 I am so sad and unhappy that I can’t stand it.

2. 0 I am not particularly discouraged about my future.
   1 I feel discouraged towards my future.
   2 I feel I have nothing to look forward to.
   3 I feel the future is hopeless and that things cannot improve.

3. 0 I do not feel like a failure.
   1 I feel I have failed more than the average person.
   2 As I look back on my life, all I can see is a lot of failures.
   3 I feel I am a complete failure as a person.

4. 0 I get as much satisfaction out of the things I used to.
   1 I don’t enjoy things the way I used to.
Definition of Success

- 50% reduction in frequency of headaches/migraines
- 50% reduction in acute medication

Each visit, HIT-6 and Becks Depression Inventory is compared
Case Presentation

- MA 36y/o female on invalids benefit
- Aged 16 first migraine after seizure
- Recent MRI and CT scan, no intracranial lesion
- Headaches more than 4 hours per day, every day for 15 years.
- Migraines three days per week
- Pethidine inj & tablets, Nortriptyline, Brufen, Codiene, Paracetamol.
- Injected with Botox on 20th June 2013
- Txt today
Case Presentation

- TL 28y/o female, flight attendant.
- Aged 8 first migraine with aura
- Headaches more than 4 hours per day, 16 days a month for years.
- Migraines three days per month
- Brufen, Codeine, Buccastem, Imigran
- Injected with Botox on 4th April 2013
- No headaches since then.
Don’t forget...

- It must not be forgotten however that migraine headache is a phenomenon that has other major contributing factors that contribute to its aetiology;
  - these being a neurovascular component,
  - a hormonal component,
  - and finally the hypersensitivity and or allergenic component [Watson, 2003 #1].
Management of migraine and chronic migraine using Botulinum Toxin Type A
Non-pharmacological treatment: trigger avoidance

- As a first step in the management of migraine, many patients will try to identify their migraine triggers and use avoidance as a treatment strategy¹
- If this is not effective, patients may try, and health professionals may recommend, alternative or approaches to headache care²

Pharmacological treatment options

- Approaches to the pharmacological management of migraine can be either acute (relief) or prophylactic (preventive), depending on the frequency of migraine headache
- The EFNS / BASH guidelines are as follows

<table>
<thead>
<tr>
<th>Acute Treatment</th>
<th>Prophylactic Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>■ Medication taken during a migraine attack to relieve symptoms</td>
<td>■ Medication used to reduce the number of attacks when acute therapy, used appropriately, gives inadequate control of symptoms$^2$</td>
</tr>
<tr>
<td>■ Used when the frequency of the attacks is &lt;2/month$^1$</td>
<td>■ Used when the frequency of attacks is ≥2/month$^1$</td>
</tr>
</tbody>
</table>

Chronic migraine: principles of management

- Accurate diagnosis\(^1\)
- Identification and minimisation/elimination of trigger and aggravating factors\(^1,2\)
- Identification and management of coexistent, comorbid disorders, and other factors that influence prognosis\(^1,2\)
- Thorough understanding of patient’s current medication use\(^2\)
- Establishment of treatment plan\(^1,2\)
  - Non-pharmacological
  - Pharmacological (acute and preventive); establish limits on acute and rescue therapy
- Assessment and monitoring of level of headache-related disability\(^3\)

Establishing realistic goals is key for chronic migraine management

- The main goals for treatment of chronic migraine are to decrease disability and improve health-related quality of life (HRQoL)\(^1\)
- Goals include improvement in headache burden by reducing:
  - Headache days
  - Headache duration
  - Headache intensity and severity
- Benefits occur over time and cannot be expected immediately\(^1\)

Prophylaxis of chronic migraine: the unique role of Botulinum toxin type A

- Prophylactic treatment is recommended in those patients who experience ≥2 migraines/month\(^1\)
- Chronic migraine is classified by the ICHD as ≥15 headache days/month for >3 months, of which ≥8 are migrainous\(^2\)
- Patients with chronic migraine are therefore candidates for migraine prophylaxis
- Few preventive treatments have been investigated for patients with chronic migraine\(^3\)
- BOTOX\(^\circledast\) is currently the only treatment specifically licensed by regulators for prophylaxis of headache in this population\(^4\)

4. BOTOX\(^\circledast\) UK Summary of Product Characteristics. Allergan Ltd.
The PREEMPT clinical programme has established a successful treatment paradigm. Although muscle groups injected in PREEMPT were the same as those injected in the preceding phase 2 trials, there were revisions.
Injection Paradigm
(Fixed-site, Fixed-dose & Modified Follow-the-Pain Models)

Fixed-site, Fixed-dose
- 155 U of BOTOX® (botulinum toxin, type A)
- 31 fixed-sites with fixed-dose (5 U/injection site)
- Injections across 7 specific head/neck muscle areas

Modified Follow-the-Pain strategy
- Up to 40 U of additional BOTOX®
- 8 additional sites (5 U/injection site)
- Maximum total dose of 195 U
- The decision to inject additional BOTOX® is left to the judgment of the injecting physician

Dosing
- For each injection site, the injection volume will be 0.1 mL (5 U)
- Each muscle has a fixed:
  - Total dose
  - Number of injection sites
  - Location of injection sites

Blumenfeld A. et al. Headache 2010; 50:1406-1418
Anatomical Injection Sites Follow Distributions & Areas Innervated by the Trigeminal Sensory System

Auriculotemporal Nerve

Supratrochlear Nerve

Supraorbital Nerve

Greater Occipital Nerve

Lesser Occipital Nerve

Cervical Rami
Injection Sites: Corrugator & Procerus

5 U BOTOX® per injection (0.1 mL injected)

Corrugator: 5 U at each site

Procerus: 5 U at site

5 U BOTOX® per injection (0.1 mL injected)

Blumenfeld A. et al. Headache 2010; 50:1406-1418
Injection Sites: Temporalis

5 U BOTOX® per injection (0.1 mL injected)

Patients may specifically have pain around the temporal artery

Having the patient clench teeth will produce a palpable anterior bulge to the temporalis muscle, directing the anterior injection site

An additional 2 optional follow-the-pain sites may be injected, depending on the patient’s self report of pain or tenderness


Blumenfeld A. et al. Headache 2010; 50:1406-1418
Injection Site: Occipitalis

5 U BOTOX® per injection (0.1 mL injected)

Occipitalis muscles and injection sites*

Sternocleidomastoid muscle

Nuchal ridge

*An additional 2 injections of 5 U can be distributed between the right and left occipitalis muscles in the areas identified as having maximal pain and tenderness.


Blumenfeld A. et al. Headache 2010; 50:1406-1418
Injection Sites: Cervical Paraspinal & Trapezius

5 U BOTOX® per injection (0.1 mL injected)

- Cervical paraspinal: 5 U each*
- Trapezius muscles: 5 U each†
- Semispinalis capitus
- Splenius capitus
- Trapezius
- Levator scapulae

*No additional injections in the cervical paraspinal muscles.
†Up to an additional 4 injections each of 5 U may be distributed between the right and left trapezius muscles based on pain and maximal tenderness. The infero-medial portions of the trapezius muscle should be avoided to limit the possibility of neck weakness.

Blumenfeld A. et al. Headache 2010; 50:1406-1418

Injection Paradigm: Required Dose Using a Fixed-Site, Fixed-Dose Paradigm

<table>
<thead>
<tr>
<th>Order</th>
<th>Muscle</th>
<th>Number of Units (U)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Corrugator</td>
<td>10 (5 each side)</td>
</tr>
<tr>
<td>B</td>
<td>Procerus</td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>Frontalis</td>
<td>20 (10 each side)</td>
</tr>
<tr>
<td>D</td>
<td>Temporalis</td>
<td>40 (20 each side)</td>
</tr>
<tr>
<td>E</td>
<td>Occipitalis</td>
<td>30 (15 each side)</td>
</tr>
<tr>
<td>F</td>
<td>Cervical paraspinal</td>
<td>20 (10 each side)</td>
</tr>
<tr>
<td>G</td>
<td>Trapezius</td>
<td>30 (15 each side)</td>
</tr>
<tr>
<td></td>
<td><strong>Total number of units (U)</strong></td>
<td><strong>155</strong></td>
</tr>
</tbody>
</table>

Dosing and results in these studies are specific to the formulation of BOTOX® manufactured by Allergan, BOTOX® is not interchangeable with other botulinum toxin products and cannot be converted using a dose ratio.

Blumenfeld A. et al. *Headache* 2010; 50:1406-1418
Order of Injection & Patient Position: Fixed-Site Fixed-Dose

The anatomic injection sites follow distributions & areas innervated by the trigeminal nerve complex

**Supine**

- A. Corrugator: 5 U each side
- B. Procerus: 5 U (one site)
- C. Frontalis: 10 U each side
- D. Temporalis: 20 U each side

**Sitting**

- E. Occipitalis: 15 U each side
- F. Cervical paraspinal: 10 U each side
- G. Trapezius: 15 U each side

0.1 mL = 5 U/site

Blumenfeld A. et al. Headache 2010; 50:1406-1418
Dosing for Chronic Migraine Using the PREEMPT Follow-the-Pain Injection Paradigm

<table>
<thead>
<tr>
<th>Order</th>
<th>Muscle</th>
<th>Number of Units (U)*</th>
<th>Additional Units (U), if necessary</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Corrugator†</td>
<td>10 (5 each side)</td>
<td>NA</td>
</tr>
<tr>
<td>B</td>
<td>Procerus</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>C</td>
<td>Frontalis†</td>
<td>20 (10 each side)</td>
<td>NA</td>
</tr>
<tr>
<td>D</td>
<td>Temporalis†</td>
<td>40 (20 each side)</td>
<td>+10 (up to 2 sites)</td>
</tr>
<tr>
<td>E</td>
<td>Occipitalis†</td>
<td>30 (15 each side)</td>
<td>+10 (up to 2 sites)</td>
</tr>
<tr>
<td>F</td>
<td>Cervical paraspinal†</td>
<td>20 (10 each side)</td>
<td>NA</td>
</tr>
<tr>
<td>G</td>
<td>Trapezius†</td>
<td>30 (15 each side)</td>
<td>+20 (up to 4 sites)</td>
</tr>
<tr>
<td></td>
<td><strong>Total number of units (U)</strong></td>
<td><strong>155</strong></td>
<td><strong>195</strong></td>
</tr>
</tbody>
</table>

Dosing and results in these studies are specific to the formulation of BOTOX® manufactured by Allergan, Inc. (Irvine, CA). The Allergan, Inc., formulation is not interchangeable with other botulinum toxin products and cannot be converted using a dose ratio.

*Each IM injection site = 0.1 mL = 5 U BOTOX.
†Dose distributed bilaterally for the minimum 155 U dosing.
NA = no additional

Blumenfeld A. et al. Headache 2010; 50:1406-1418
Order of Injection & Patient Position: Follow-the-Pain

The anatomic injection sites follow distributions and areas innervated by the trigeminal nerve complex

Supine

A. Corrugator: no additional
B. Procerus: no additional
C. Frontalis: no additional
D. Temporals: 5 U/site (up to 2 additional sites)

Sitting

E. Occipitalis: 5 U/site (up to 2 additional sites)
F. Cervical paraspinal: no additional
G. Trapezius: 5 U/site (up to 4 additional sites)

0.1 mL = 5 U/site
Blumenfeld A. et al. Headache 2010; 50:1406-1418
SUMMARY

• Chronic migraine is classified by the ICHD as ≥15 headache days/month for >3 months, of which ≥8 are migrainous
• 45,000 Kiwis, 13 per GP!
• Often suffer in silence
• SNOOP4
• Consider Onabotulinumtoxin A– the only medication specifically licensed by regulators for prophylaxis of headache in this population together with Migraine specific physiotherapy
Take-home message: current practical, clinical definition is headache of more than 4 hours \( \geq 15 \) days/month and prior or current diagnosis of migraine, with or without medication overuse

There is a proven treatment for our 45,000 patients

THANK YOU

Dr Garsing Wong
MBChB, BHB, Dip Comm Em Med, FAMPA, FRNZCGP, FNZCAM

Sapphire Migraine Clinic    Auckland

www.sapphireclinic.co.nz    ph: 09 360 0066
Introduction to migraine

- Migraine distinguished from common headaches in the late 18th century\(^1\)
- Further explored and diagnosed in the 19th century\(^1\)
- Classification of migraine still evolving today
- Ranked by WHO as 19th among all causes of years lived with disability\(^2\)
- Heavy burden of illness for the patient and a high cost for the economy\(^3,4\)
- Treatment options evolving
  - Unmet need still exists for many patients

Migraine: the typical stages of an attack

<table>
<thead>
<tr>
<th>Premonitory phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experienced by only 50% of patients</td>
</tr>
<tr>
<td>Causes irritability, depression, tiredness, food cravings, unusual bursts of energy</td>
</tr>
<tr>
<td>Can be hours or 1–2 days prior to attack</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aura</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lasts 10–30 minutes</td>
</tr>
<tr>
<td>Can affect vision on one side: blank patches, bright or flashing lights or coloured zigzag lines</td>
</tr>
<tr>
<td>Possibly sensory symptoms: pins-and-needles, numbness (starting in fingers, progressing up the arms to the face)</td>
</tr>
<tr>
<td>Difficulty speaking or finding the right words</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can last for a few hours to 2–3 days</td>
</tr>
<tr>
<td>Severe, one-sided headache, most commonly at the front or in the template but can occur on both sides of and anywhere in the head</td>
</tr>
<tr>
<td>Throbbing or pounding headache which is made worse by movement</td>
</tr>
<tr>
<td>Often accompanied by nausea. Vomiting may seem to relieve the headache</td>
</tr>
<tr>
<td>Patient may want to avoid light and noisy situations, preferring to be alone in the dark</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final stage</td>
</tr>
<tr>
<td>Headache fades but may leave the patient feeling tired, irritable, depressed, with difficulty concentrating</td>
</tr>
<tr>
<td>Can take a further day before the patient has fully recovered</td>
</tr>
</tbody>
</table>

Botox Treatment for Chronic Migraine Patient Diary
How is migraine diagnosed and classified?
## FLAG Description/example

<table>
<thead>
<tr>
<th>Description/example</th>
<th>Description/example</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic symptoms or sec. risk factors</strong></td>
<td>Fever, weight loss or known cancer, HIV, immunosuppression, or thrombotic risks.</td>
</tr>
<tr>
<td><strong>Neurological symptoms or abn signs</strong></td>
<td>Confusion, impaired alertness/drowsy, or persistent focal signs (lasting more than 1 hour). ‘First and worst headache’, sudden or abrupt from sleep, or progressively worsening. New onset and progressive, e.g. after 50 years of age for giant cell arteritis.</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>First headache or fundamentally different (i.e. significant change in features, frequency, or severity).</td>
</tr>
<tr>
<td><strong>Older</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Previous headache history Triggered headache By Valsalva activity, exertion, or sexual intercourse</strong></td>
<td></td>
</tr>
</tbody>
</table>
Cost

- Initial consultation charge when referred by their GP
- 30min consult $154
- First treatment subsidised by Allergan total cost $437
- Followup visit at two weeks and at 12 weeks $77
- Additional Botox every 12 weeks $1560
- Physiotherapy strongly recommended for all patients
Publications

- 2011 Journal of Cosmetic Dermatology, Vol 10, pages 93-96 "Phosphatidyl Choline Lipolysis and Hyaluronic Acid Augmentation to Enhance Non-Surgical Lower Facial Contouring Using Botulinum Toxin Type A, Drs Garsing Roger Wong and Wen-Pei Chen".

Patents


- Referred to by Palomar as GET – Garsing Eye Treatment using 1540nm Fractional Erbium Glass Laser.
Migraine and Botulinum Toxin Type A

- Positive effects of Botox on migraine headache were shown in a study by (Brin et al 2002, Blumenfeld et al, 2003) effective prophylactic treatment who conducted a multicenter open-label trial.
- Efficacy was categorised as either complete response with total symptom elimination, partial response with greater than 50% reduction in headache severity and frequency, or no beneficial response.
- Results showed that 51% of patients treated with Botox as a migraine prophylaxis reported a complete response to localised head and neck injections, with a mean duration of 4.1 months.
- An additional 38% reported partial improvement, with a mean response of 2.7 months.
Economic impact of migraine and chronic migraine
What have I observed?

- With respect to migraine headaches, the cortical spreading depression (the cause of aura) has been suggested to activate the trigeminal system (Johnson et al).
- The involvement of the ophthalmic division of the trigeminal nerve and its overlap of structures innervated by branches of C2 nerve roots.
- This explains the typical distribution of migraine over the frontal and temporal regions, and the referral of pain to the parietal, occipital, and high cervicogenic regions.
- It is these factors that could explain the strong relationship between the inflammatory neurogenic and cervicogenic components which seem to be a cause of migraine headaches (Schmitt et al, & Johnson et al).
- And this cervicogenic component may explain the important role that manipulative therapy and postural muscle imbalance correction has in the treatment of cervicogenic headaches and migraine.