WHMC311

Session 14

Nervous System Disease Part I

Naturopathic Medicine Department
Topic Overview

- Overview of principles and considerations in herbal management of the nervous system condition pain.

- Review of herbal actions, indications, applications and contraindications of: analgesics, sedatives, hypnotics, tranquilisers, anti-spasmodics, relaxants, nerve tonics, nerve trophorestoratives, cognition enhancers and neuroprotectives.
Naturopathic Diagnostics: NS

- Dysfunction of the Central Nervous System can be seen in abnormalities in the size and shape of the pupil.
- Also at the following regions: cerebral (brain) area, spinal area, adrenal area, nerve rings and iris fibre signs.
- Dysfunctions of the Autonomic Nervous System may also be seen in Autonomic Nervous Wreath size, shape, colour and texture abnormalities.

(Jensen, 1952)
Herbal Medicine for the NS

Receptor Activity
- Herbal remedies are not directly comparable to conventional drugs in terms of direct action.
- It is most likely that the primary effect of plant constituents on the nervous system is on the synaptic junctions.
- Communication junctions are in receptor sites on pre and post synaptic membrane.

(Bone & Mills 2013, p.270)
Receptor Activity

- Ca channel activity – opioid alkaloids, ginseng saponins, coumarin, scopolamine (Capillaris) etc.
- Adrenergic effects – Ephedra, ephedrine, pseudoephedrine, Angelica sinesis and Cnidium monnieri (Beta-2-adrenergic)
- Acetylcholine – Solanacea family - Nicotiana tabacum (tobacco) etc.
- GABA and benzodiazepine – Valeriana officinalis, Salvia miltiorrhiza
- Dopaminergic – Mucuna pruriens, Polygala tenuifolia, Corydalis ambigua

(Bone & Mills 2013, p.270-271)
Pain

- Pain is a disagreeable subjective physiological and psychosocial experience that often serves a biological purpose (warning of injury)

- Highly subjective, pain does not necessarily correlate with the degree of tissue damage

(Sinclair, 2014, p.803)
Pain Classification

- Somatogenic (direct physiological mechanism or insult)
  - Nociceptive (ongoing activation)
  - Neuropathic (neurological dysfunction)

Or

- Psychogenic (non organic origin)

  - Acute (lasting less than 4 weeks)

Or

  - Chronic (longer than 12 weeks)

(Sinclair, 2014, p.803-6)
Pain Management

- Classify/asses the pain
- Identify the cause
- Pain amelioration
- Address the underlying cause
- Address comorbidities (depression, insomnia etc.)
- Enhance mental resilience
- Lifestyle modifications
- Close patient monitoring
- Address social factors

(Sinclair, 2014, p.806-7)
Treatment Considerations

- Ameliorate pain and reduce suffering
  - *Eschscholzia californica* (GABA binding and anxiolytic, possibly inhibit catecholamine degradation, synthesis of adrenaline and bind to opiate and benzodiazepine receptors)
  - *Corydalis ambigua* (tetrahydropalmatine – sedative, analgesic, dopamine receptor antagonist)
  - *Passiflora incarnate* (anxiolytic, hypnotic and mild sedative – possibly secondary clinical benefit)
  - *Piper methysticum* (anxiolytic, hypnotic, sedative and skeletal muscle relaxant, lactones DHK and DHM shown analgesic effect via non-opiate pathways)

(Sinclair, 2014, p.809)
Treatment Considerations

- Ameliorate pain and reduce suffering
  - *Harpagophytum procumbens* (iridiod glycosides – anti-inflamm and analgesic, possible iNOS and COX-2 expression through inhibiting NF-kB and reducing COX-1 activity)
  - *Salix alba* (Acetyl group to salicylic acid led to NSAID and Asprin development; hyaluronidase/lipoxygenase inhibition, free radical scavenging may contribute to anti-inflammatory and analgesic action)
  - *Piscidia erythrina* (central analgesic activity)  
    (Sinclair, 2014, p.810)
Indications for Herbal Analgesics

- Pain associated with inflammation:
  - Arthritis
  - Tendonitis
  - Myalgia

- Pain associated with vascular spasm:
  - Migraine
  - Angina
  - Intermittent claudication

- Pain associated with visceral spasm:
  - Gall bladder
  - Urinary tract
  - Intestinal colic
  - Spasmodic dysmenorrhea

- Neuralgic pain (in limited cases)
  - Shingles
Analgesics

- Some traditional herbal analgesics include:
  - *Corydalis spp* (Corydalis)
  - *Eschscholzia californica* (Californian poppy)
  - *Salix alba* (Willow bark)
  - *Piscidia erythrina* (Jamaican Dog Wood)
  - *Anemone pulsatilla* (Pasque flower)
  - *Piper methysticum* (Kava)

- Topical Analgesics
  - *Mentha × piperita* (Peppermint essential oil)
  - *Capsicum minimum* (Cayenne)
  - *Arnica montana* (Arnica)
Corydalis ambigua

- Actions
  - Bitter, sedative, hypnotic, analgesic, cardioprotective, anti-arrythmic

- Uses
  - Pain, insomnia, cardiac arrythmia, myocardial ischemia

- Contraindications
  - Pregnancy
Treatment Considerations

- Reduce local and systemic inflammation
  - Topical anaesthetics – *Capsicum frutescans*, *Piper methysticum*, *Gaultheria procumbens* (Wintergreen oil), *Syzigium aromaticum*
  - Systemic - *Zingiber officinale*, *Serenoa repends*, *Curcuma longa*, *Glycyrrhiza glabra*, *Harpagophytum procumbens*, *Boswellia serrata*, *Marticaria recutita*, *Arnica montana*, *Salix alba*

- Support the immune system
  - Dysfunction may impact on autoimmune/infectious disease pain presentation (*Hemidesmus indicus*, *Tylophora indica*, *Echinacea spp.*, *Uncaria tomentose*, *Andrographis paniculata*, *Astragalus membranaceus*, medicinal fungi)

(Sinclair, 2014, pp.810-812)
Treatment Considerations

- Support the nervous system
  - Psychological consequence of pain exposure and specific painful diseases affecting the NS such as herpes zoster etc.
  - Adaptogens and nervine tonics
  - Address insomnia if present - Sedatives and hypnotics
  - Psychological – CBT referral, mindfulness/meditation, anti-depressants and/or anxiolytics

(Sinclair, 2014, p.812-814)
## Herbal Sedatives, Hypnotics & Anxiolytics

<table>
<thead>
<tr>
<th>Sedatives</th>
<th>Hypnotics</th>
<th>Anxiolytics</th>
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<tbody>
<tr>
<td>Withania, Bacopa</td>
<td>Californian poppy</td>
<td>Bacopa</td>
</tr>
<tr>
<td>Bugle weed</td>
<td>Hops</td>
<td>Californian poppy</td>
</tr>
<tr>
<td>Californian poppy</td>
<td>Kava</td>
<td>Oats Green</td>
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<tr>
<td>Chamomile, Cramp Bark</td>
<td>Mexican Valerian</td>
<td>Kava</td>
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<tr>
<td>Hops, Jamaican Dog Wood</td>
<td>Valerian</td>
<td>Lavender</td>
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<tr>
<td>Kava, Lemon balm</td>
<td>Passionflower</td>
<td>Mexican Valerian</td>
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<tr>
<td>Lime Flowers</td>
<td></td>
<td>Valerian</td>
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<tr>
<td>Mexican Valerian</td>
<td></td>
<td>Neem Leaf</td>
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<tr>
<td>Valerian, Mistletoe</td>
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<td>Passionflower</td>
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<tr>
<td>Passionflower</td>
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<td>Ziziphus</td>
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<tr>
<td>Peppermint, Skullcap</td>
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<tr>
<td>Ziziphus, Wild Cherry</td>
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It can be seen from this table that many of our nervine herbs cover a wide range of nerve related actions.
Herbal Sedatives, Hypnotics & Anxiolytics

- Indications
  - Modern tension and anxiety syndromes (short term or intermittent use)
  - Insomnia – difficulty getting to sleep first thing at night.
  - Weaning off conventional sedative prescriptions
  - Restlessness during convalescence
Herbal Sedatives, Hypnotics & Anxiolytics

- Contraindications
  - Generally milder than prescribed sedatives and should not be seen as immediate substitutes in more serious indications.
  - It would be unwise and possibly dangerous to stop strong medication without careful planning.
  - Insomnia marked by increasing restlessness during the early morning
  - Depression
Antispasmodics and Relaxants

- Some traditional herbal antispasmodics and relaxants:
  - *Viburnum opulus*
  - *Dioscorea villosa*
  - *Leonurus cardiaca*
  - *Matricaria chamomilla*
  - *Passiflora incarnata*
  - *Piper methysticum*
  - *Scutellaria lateriflora*
  - *Tilia spp*
  - *Valeriana officinalis*
Antispasmodics and Relaxants

- **Indications:**
  - Anxiety, irritability and restlessness, including in children
  - Sleeplessness due to anxiety and irritability
  - Nervous dyspepsia
  - Irritable bowel and intestinal colic
  - Tension headache
  - Spasmodic dysmenorrhoea
  - Antispasmodics and relaxants may be taken as hot infusions, though the ordinary tea bag may not be sufficiently strong compared with a tradition brew.
Nervine Tonics & Nervous Trophorestoratives

- Many conditions of tension are linked with fatigue, debility and depression

- A group of remedies have emerged to meet the needs of a modern stressed society

- Anti-depressants: *Hypericum perforatum, Lavandula officinalis, Crocus sativa, Rhodiola rosea*
Nervine Tonics & Nervous Trophorestoratives

• Avena sativa
• Hypericum perforatum
• Scutellaria laterifolia
• Turnera aphrodisiaca
• Verbena off.
• Withania somnifera
Nervine Tonics & Nervous Trophorestoratives

- Indications:
  - Nervous exhaustion
  - Neuralgia, herpes infections
  - Depressive states
  - Insomnia (waking in the small hours after getting to sleep easily)
  - Convalescence
  - Neurasthenia
Nervine Tonics & Nervous Trophorestoratives

- Contraindications:
  - True trophorestoratives are almost nutritive in their effects, with few risks of adverse effects except in those patients with extremely debilitated constitutions.

- Application:
  - May be taken as required or before food.
  - Long term therapy with trophorestoratives is generally the norm.
Pain Example: Headaches

- Headaches – pain located above the orbitomeatal line.
  **Primary:**
  - Tension-type
  - Cluster
  - Migraine - disabling, primary headache, characterised by unilateral pulsing pain. With or without aura

**Secondary:**
- Cranial or cervical vascular disorders, non-vascular disorders e.g. hypertension
- Substance or withdrawal, infection, homeostatic disorder, psychiatric

(Cottingham, 2014, p.330-331)
Pharmaceutical Management

**Non-Opioid Analgesics** - Paracetamol

**Mode of Action**
- Inhibits prostaglandin production within the CNS, with some COX inhibition (no anti-inflammatory benefits) giving it analgesic and antipyretic properties.

**Side Effects**
- Occasional incidences of skin rash & nausea if used within therapeutic dose.
- Paracetamol overdose (10-15gms or 20-30 tablets) will cause severe liver damage due to depletion of glutathione, and possibly lead to death. Doses of 50 tablets is usually fatal unless quickly antidoted with acetyl cysteine.
- Liver toxicity appears to be linked to the concomitant use of excessive quantities of alcohol, or overdose

(Bryant & Knights, 2007; Bullock et.al. 2007)
Pharmaceutical Management

Non-steroidal Anti-inflammatory Drugs (NSAIDs) – ibuprofen, aspirin, diclofenac, indomethacin, piroxicam

Mode of Action
- Non-selectively inhibit the synthesis and release of prostaglandins by inhibiting the cyclo-oxygenase (COX) enzymes in both COX-1 & COX-2 pathways. Also inhibits platelet aggregation.

Side Effects
- Gastro-intestinal (dyspepsia, nausea, vomiting, diarrhoea, constipation, gastritis, and may all potentially lead to ulceration and haemorrhage (COX-1 inhibition)
- Skin reactions, rash, sodium retention, may precipitate asthma attacks.

(Bryant, 2003)
Pharmaceutical Management

COX-2 selective NSAIDs – Celecoxib

Mode of Action
- COX-2 is formed in inflammatory conditions – thus it is this pathway that would seem most appropriate to target when trying to reduce inflammation and pain (Bryant, 2003).
- Don’t inhibit COX-1 so have no GIT side effects or alter platelet aggregation. Useful for patients that can’t use non-specific NSAIDs.

Side Effects
- Associated with an increased risk of cardiovascular and thrombotic adverse effects.
- Renal damage due to inhibition of vasodilator prostaglandins resulting in heart failure and hypertension in some patients.
  (Bryant & Knights, 2007; Bullock et.al. 2007)
Pharmaceutical Management

**Opioids** – Opium, Morphine, Codeine, Oxycodone, Pethidine, Tramadol etc...

**Mode of Action**
- Opioids stimulate opioid receptors inhibiting the release of substance P from the dorsal horn neurons reducing pain sensations and inhibiting local inflammatory reactions.
- Euphoric action inhibits pain perception.
- Opiate analgesics are useful for relieving intense pain, non-responsive to non-opioid analgesics
- The response can vary dramatically between different opioid drugs, with different rates of absorption
- The more lipophilic the agent, the better absorbed and the greater the ability to cross the blood-brain-barrier

(Bryant & Knights, 2007; Bullock et.al. 2007)
Treatment Aims

- Establish the type of headache and underlying cause
- Address of risk factors and triggers (e.g. food sensitivities and allergic responses)
- Reduce pain and inflammation
- Ensure optimal nutrition and hydration
- Consider detoxification programs to manage medication overuse headache syndrome
- Assess body mechanics and spinal alignment – refer
- Address lifestyle – exercise, stress reduction (work/life balance)

(Cottingham, 2014, pp.335-342)
<table>
<thead>
<tr>
<th>Herb</th>
<th>Action/Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coleus, Zingiber &amp; Turmeric</td>
<td>All work on prostaglandin pathway</td>
</tr>
<tr>
<td>Corydalis</td>
<td>Analgesic – very large doses required</td>
</tr>
<tr>
<td>Californian poppy</td>
<td>Analgesic</td>
</tr>
<tr>
<td>Willow Bark</td>
<td>Analgesic and anti-inflammatory</td>
</tr>
<tr>
<td>Chaste tree</td>
<td>If hormonal relationship</td>
</tr>
<tr>
<td>Rosemary</td>
<td>Migraine or hypertensive headache</td>
</tr>
<tr>
<td>Skullcap</td>
<td>Nervine</td>
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<tr>
<td>Valerian</td>
<td>Sedative, nervous excitability</td>
</tr>
<tr>
<td>Mistletoe</td>
<td>Hypertensive headaches and frequent headaches with flushing face</td>
</tr>
<tr>
<td>Lavender</td>
<td>For depression associated with digestive dysfunction</td>
</tr>
<tr>
<td>Catnip</td>
<td>Sedative and for nervousness</td>
</tr>
<tr>
<td>Passionflower</td>
<td>Nervousness, debility with fullness</td>
</tr>
</tbody>
</table>
Tanacetum parthenium

- Traditionally used for migraines (especially if better with warm applications)
- Serotonergic pathway addressed by inhibiting phospholipase, preventing release of 5-HT from platelets and polymorphonuclear leukocytes
- In-vitro – inhibits nitric oxide release (sensitise migraineurs to pain and activate vasodilation – trigger)
- May inhibit prostaglandin synthesis
- Long term treatment is necessary - can be up to six months before effects are noticed

(Cottingham, 2014, pp 335-343)
Neuralgia/Neuropathy

- Neuropathic pain pathophysiology is largely based on the causative aetiology in many instances; however, it is heavily characterised by dysfunction of pain fibres of the CNS.

Treatment considerations:

- Neuropathy
  - Neuro protective
    - *Ginkgo biloba*
  - Capillary protective
    - *Vaccinium myrtillus*

- Neuralgia
  - *Capsicum spp.*
**Capsicum minimum**

- Capsaicin is an active constituent from the fruit of *Capsicum minimum* and other species (Cayenne).
  - Binds to vanilllinoid receptors, promotes release of substance P, neurokinin, somatostatin and calcitonin from peripheral nerve fibres (particularly C fibres in the slow pain network). Initially worsens pain/itching
  - Repeated applications, C fibres are depleted of these neurotransmitters, and are no longer able to transmit pain or itch signals.
  - With continued use, this effect can be sustained indefinitely.

(Yarnell, Abascal 2008)
Capsicum minimum

- Conditions in which topical capsaicin has proven effective in double-blind trials include:
  - Various neuralgias
  - Diabetic neuropathy
  - Dialysis-induced pruritus
  - Psoriatic pruritus
  - Fibromyalgia
  - Osteoarthritis
  - Stump pain
  - Postmastectomy pain
  - Postherpetic neuralgia

(Yarnell, Abascal, 2008)
Herb-Drug Interactions

Opioids

*Panax ginseng*
- May reduce drug induced tolerance and decrease adverse effects (Stargrove et al. 2008)

Opioids – Codeine

Fiber
- May prevent gastric upset and constipation. Concurrent use of water, fibre, and water rich foods that assist with bowel motion may be beneficial.

Alcohol
- Impaired alertness, constipation, impaired judgment (Braun & Cohen, 2010)
Herb-Drug Interactions

Paracetamol
- Alcohol may have more potential to cause liver damage when taken together (Braun & Cohen, 2010)

- *Syzygium aromaticum* (Clove) oil due to potential hepatotoxicity of its eugenol content should not be used together (speculative) (Brinker 2010, p.104)

- *Cyamopsis tetragonolobus* (Guar gum seeds) and *Malus domestica* slows absorption due to slower gastric emptying (Brinker 2010, p.364)
Herb-Drug Interactions

**NSAIDs - Aspirin**

Capsaicin
- Found to protect gastric mucosa against aspirin-induced damage.

(Braun & Cohen, 2010)

Grapeseed extract
- Enhances antiplatelet and anti-inflammatory activity of aspirin and may ↑ risk of bleeding.

*Allium sativum, Zingiber officinalis, Curcumin longa*
- Inhibits COX & LOX pathways therefore enhancing the drug effectiveness. Additive effect.

(Sarris & Wardle, 2010)
Cognition Enhancement

- Cognition encompasses a broad range of brain processes, the health of which allows for social connectedness, a sense of purpose and the ability to function independently.

- Cognitive decline is significant in the elderly population. Alzheimer’s disease is the most common dementia. Cerebrovascular disease – brain lesions connected with cardiovascular health/risk factors

- Traditional herbal remedies address these
Bacopa monnieri

- A traditional Ayurvedic herb used as a brain tonic, and to improve memory and learning
- Also used to promote longevity, nervous deficit due to injury and stroke
- In India it is called Brahmi - as is Gotu Kola: *Centella asiatica*
- The two plants share similar uses, and they are sometimes confused in the literature
An Australian clinical trial examined the long-term effects of an extract of *Bacopa monnieri* on cognitive function in 54 healthy human volunteers (Calabrese et.al. 2008).

The study was of double-blind, placebo-controlled design in which subjects were randomly allocated to receive Bacopa or placebo.

Neuropsychological testing was conducted before treatment and at 5 and 12 weeks after treatment.
Bacopa monnieri

- After 12 weeks the largest cognitive change from Bacopa treatment was a time reduction for the Inspection Time (IT) test.

- IT is regarded as a measure of the integrity of the early stages of information processing and may act as a rate-limiting factor for cognition.

- This indicates that Bacopa significantly improved the speed of visual information processing.
Schisandra chinensis

- Lignans from *Schisandra chinensis* improved concentration, fine co-ordination and sensitivity in healthy young male adults as assessed by tasks such as threading a needle and telegraphic reception and transmission.
- Schisandra improved vision, enlarged the visual field, improved hearing and heightened skin sensory discrimination
- It was thought that those effects are central rather than peripheral.

(Chang HM 1987 as cited in Bone 2003, p.407)
Panax ginseng

- In a double-blind study on students given Ginseng over thirty-three days significant improvements in psychomotor ability and intellectual performance were observed.

- Nurses switching from day to night duty were evaluated for competence, mood, wellbeing and psychophysical performance in a double-blind clinical study of Ginseng versus placebo.

- Ginseng improved the scores for competence and mood, and performance on the psychophysical test.

(D’Angelo et al, 1986)
Pre-reading for next session


References


References


References


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