

Treatment of pain in Transverse Myelitis

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Outline

- TM – general considerations in relation to pain
- Other spinal cord disease and pain (numerous, and important in relation to pain treatment)
- Causes and classification of types of pain in TM
- Mechanisms of pain (limited understanding is reason for inadequacies of currently available treatments)
- Co-morbidities of pain in TM
- Treatment
 - Nociceptive ('normal') pains
 - Neuropathic pains (ie pain due to spinal cord damage)
 - Non-drug physical treatments
 - Drugs
 - Surgical treatment
 - Psychological measures
- Access to treatment

TM – general characteristics

Definition: development of isolated spinal cord dysfunction (in a *single* area) due to inflammation / infection over hours or days in patients in whom no evidence exists of a compressive (or vascular) spinal cord lesion.

Epidemiology: incidence up to 1.34-4.6 per million population

Main symptoms, course and outcome of illness:

occurs in people aged 4-83 years

tingling, numbness, back pain, weakness, bladder and bowel disturbance

maximum symptoms in 37% within 1 day

45% in 1-10 days

18% in more than 10 days

outcome:	good in 42%]
	fair in 38%] this relates to function, and does not
	poor in 20%] necessarily include pain assessment

(approximately 7% later develop inflammation at other sites and are found to have MS)

Diagnosis can be difficult: similar acute presentation can be caused by many other diseases; investigation is needed to exclude other causes

TM & conditions that cause the same type of pain

Inflammation -

TM	viral infection:	herpes simplex & zoster (chicken pox, shingles), glandular fever, rabies, HIV, tick-borne viruses, (HTLV)
	'para-infectious':	preceding viral illness (flu, measles), recent immunisation
	other related -	ADEM, Devic's disease (NMO)
	[multiple sclerosis -	a common cause of <i>multiple</i> areas of inflammation in the spinal cord and brain]

Vascular: spinal 'stroke', vasculitis, abnormal blood vessels (AVM)

Trauma (*NB most trials of treatment for **pain** have been conducted in spinal cord injury*)

Spinal tumours

Congenital – spina bifida

Syringomyelia (development of a cavity in the spinal cord)

Vitamin B 12 deficiency

Pain in TM

- Presence of pain is not always recorded in acute stages – often overshadowed by paralysis etc
- Delayed onset – acute back pain common in early stages, but chronic pain often develops weeks or months after onset
- Two types of pain occur in TM -
 - *nociceptive* pain ('normal' pain): pain signalled by an intact nervous system. Several possible causes in TM.
 - *neuropathic* pain: pain caused by damage to the nervous system (spinal cord in TM)

Nociceptive ('normal') Pain

- Painful events signalled by an intact nervous system
- Rapid localisation and identification of nature of stimulus
 - exactly where it is
 - what type of harmful event it is (burn, stab, etc)
 - sensation rapidly perceived by the brain
- Allows avoidance / withdrawal from potentially tissue-damaging events (or immobilisation in the case of chest or abdominal pain)
- So, nociceptive pain has a clear protective function
 - *diseases causing severe loss of pain lead to tissue destruction, eg leprosy*

Neuropathic Pain

- Damage to the sensory pathways in the nervous system causes loss of sensation, and is sometimes associated with pain (this is neuropathic pain - NP)
- Apparent paradox: pain is experienced in an area where there is sensory loss
- NP can be regarded as 'gratuitous' pain: it has no biological protective function
- NP is often severe; the quality of the pain is difficult to describe, it can occur over wide areas and is poorly localised (may affect trunk and legs in TM)

Classification of Pain in TM

- Neuropathic Pain
 - ‘At level’ pain; at the level affected by TM in the spinal cord
 - ‘Below level’ pain: below the level affected in the spinal cord
- Nociceptive Pain
 - Musculoskeletal postural spinal pain (particularly with marked weakness)
 - Spasm in the legs
 - Pressure areas (buttocks, sacrum, hips)
 - Overuse pain of shoulders and arms
 - Visceral abdominal pain (may be poorly localised)
 - bladder pain: infection
 - bowel pain: constipation
- *Any of the nociceptive pains may exacerbate the neuropathic pains*

Description of neuropathic pain in TM

- At level pain:
 - spontaneous girdle or band-like distribution around one or both sides of trunk
 - electric shock-like, shooting, burning commonly reported
 - may be associated with an abnormal, unpleasant sensitivity of skin in affected area (allodynia)
- Below level pain:
 - spontaneous burning, aching, stabbing, or shock-like pain
 - allodynia may be present in a variable area of the pain

Description of neuropathic pain in TM

- Other features
 - delayed onset – weeks or months after onset of TM
 - pain occurs with TM at any level in spinal cord
 - severity of pain not related to severity of other features (eg weakness)
 - girdle pain tends to be worse with incomplete lesions in spinal cord (which is usually the case in TM)
 - allodynia tends to be worse when central part of spinal cord affected by TM

Mechanisms of pain in TM

- Damage to nerve cells (neurons) in spinal cord:
 - leads to abnormal excitability and production of nerve impulses, perceived as pain
- Loss of normal inhibitory controls in spinal cord:
 - the normal controls in the spinal cord prevent a lot of potentially 'painful' nerve impulses reaching the brain. These are lost or impaired with spinal cord damage
- Abnormal production of chemicals (neurotransmitters) in areas of damage caused by TM:
 - leads to increased excitability of nerve cells
- Abnormal spinal cord activity causes knock-on effects in the brain:
 - development of abnormal excitability and even altered connections in the thalamus (the main sensory relay station in the brain)

Co-morbidities of pain in TM

- Physical
 - weakness, loss of mobility, loss of sensation, bladder and bowel problems
- Depression]
 - complex relationship with chronic pain]
 - pain of TM is *not* psychogenic] all tend to exacerbate pain
- Anxiety]
- Disturbed sleep patterns]
- Fatigue]

- Effects on work
- Social withdrawal

- *Worst scenario with chronic neuropathic pain due to any cause-*
 - *Pain, with limited response to treatment, associated with reduced physical activity and a fear of making the pain worse through physical activity, fatigue, depression, inability to work, social isolation, which can lead to increasing dependence on medical services*
 - *Poor awareness of neuropathic pain can affect sympathetic response and delay access to appropriate services*

Treatment – non-neuropathic pains

- Musculoskeletal postural
 - Physio: maintain mobility; increase strength; gait and posture
- Spasms / spasticity
 - Baclofen, physio
- Attention to pressure areas
 - Particularly in those with severe weakness
- Bladder
 - Prompt diagnosis and treatment of infection
- Bowels
 - Prevention and treatment of constipation

Neuropathic pain treatment: non-drug physical measures

- Electrical stimulation
 - Transcutaneous electrical nerve stimulation (TENS) +/-
 - Spinal cord stimulation +/-
- Acupuncture +/-
- Physio

Neuropathic Pain drug treatment -1

- Relatively few randomised controlled trials: most performed in SC injury
- Antidepressant drugs
 - Uncertain action, but may work by increasing effective levels of NA and 5-HT – neurotransmitters, NMDA receptor antagonism, sodium channel blockade
 - Also effective if there is associated depression
 - amitriptyline (TCAD) + NNT=4.0
 - venlafaxine, duloxetine (SSRI, SNRI) +/-
- Antiepileptic (anticonvulsant) drugs
 - sodium valproate (Epilim) -
 - carbamazepine (Tegretol) -
 - lamotrigine (Lamictal) -
 - gabapentin (Neurontin) +
 - pregabalin (Lyrica) ?
 - topiramate (Topamax) +/-
- *Note: adverse side-effects common and often limiting; gabapentin least likely to cause problems, but there is considerable individual variation in susceptibility to side-effects*

NP drug treatment -2

- Membrane-stabilising drugs (sodium channel blockers)
 - lignocaine (intravenous) + short-lived effect
 - mexiletine (oral) -
 - Anaesthetic drugs
 - ketamine (intravenous) + short-lived effect *
 - propofol (intravenous) + short-lived effect *
 - Opioids
 - morphine (spinal injection) +/- *
 - alfentanil (intravenous) + *
 - morphine + clonidine (spinal injection) + *
 - Other classes of drug
 - baclofen (spinal injection) +/-
 - neuroleptic drugs (oral; used in schizophrenia) -
 - cannabinoids (oral; plant extract & synthetic) +/- * (trials in MS & brachial plexus avulsion)
 - Notes: * denotes likelihood of major side-effects
- Drug combinations** can be tried, but side-effects are more likely to occur
- Alternative drugs in the various classes of drug can be tried

Recommendations for drug treatment of NP in TM

1. Gabapentin or pregabalin
2. Amitriptyline or other TCAD
3. Trials of –
 - lamotrigine
 - tramadol (medium strength opioid, with fewer side effects than morphine)
 - Strong opioid (morphine)
 - cannabinoid (named patient basis)
4. Drug combinations

Is surgical treatment feasible or appropriate?

- Dorsal root entry zone (DREZ) lesioning (Nashold operation)
 - may help at-level pain and sensitivity
 - potential major adverse effects
 - cannot be performed for pain on both sides (because of high risk of permanent unintended damage to the spinal cord)
- Anterolateral cordotomy
 - may give temporary relief
 - high risk of **causing** neuropathic pain in the medium to long term
 - cannot be performed on both sides of the spinal cord
- *Conclusion*
 - ***Surgery is inadvisable***

Psychological measures

- Cognitive behavioural therapy (CBT)
 - Aims to
 - increase physical activity and fitness
 - reduce fear and anxiety
 - improve coping behaviour
 - reduce depression
 - help return to work

Evidence of effectiveness is lacking specifically in pain due to TM, but good evidence of effectiveness in groups of patients with a variety of chronic severe neuropathic and non-neuropathic pains

Access to treatment

- Multidisciplinary pain clinic encourages full assessment and a focus on individualised approach and treatment of the pain in context
- Some pain services are linked to neurorehabilitation services, but not all
- Local variation in available services in UK
- British Pain Society can provide information (www.britishpainsociety.org)
- Local neurologist should be able to advise
- ***Patient groups provide essential support and information***