Painful HIV-associated sensory neuropathy

Peter Kamerman

16th World Congress on Pain, Yokohama, Japan, 2016

Major neurological complications of HIV infection

Central nervous system

HIV-associated neurocognitive disorders (HAND)

Myelopathy

Peripheral nervous system

HIV-associated sensory neuropathy (HIV-SN)

Inflammatory demyelinating polyneuropathies

Polyradiculopathy

Mononeuritis multiplex

Global prevalence of HIV-SN (adults): 30-60%

Global prevalence of HIV-SN (children): 13-38%

Typical clinical features

SIGNS

Reduced:

Pin-prick sensitivity

Vibration sense

Reflexes

Temperature sense

SYMPTOMS

Pain

Numbness

Paraesthesias

Pathogenesis

Pathogenesis of HIV-SN

Macrophage infiltration from the skin to the DRG

DRG

Pardo et al., 2001

Nerve trunk

Pardo et al., 2001

Skin

Goullée & Price, *unpublished*

Typical clinical features

SIGNS

Reduced:

- Pin-prick sensitivity
- Vibration sense
- Reflexes
- Temperature sense

SYMPTOMS

Pain

- Numbness
- Paraesthesias

Pain is a common symptom of HIV-SN

HIV-SN is a major cause of chronic pain

- **Participants:**
324 HIV-positive out-patients with a diagnosis of chronic pain.

Primary source of pain

Painful peripheral neuropathy	45-48%
Low back pain	22-28%
Arthralgia	6-13%

The impact of painful HIV-SN

Having pain is associated with

being unemployed

↑ depression and anxiety

↑ severity of depressive symptoms

↑ sleep disturbance

↓ independence

↓ social functioning

Painful HIV-SN in children

- **Participants:**
 - 135 HIV-infected children
 - 50% female
 - Age: 7 (3 - 11) years
 - CD4: 1184 (927-1440) cells/ml
 - All exposed to stavudine (d4T)
- **SN diagnostic criteria:**
Bilaterally reduced / absent ankle reflexes OR vibration sense

Symptoms are typically moderate to severe

- **Participants:**
21 patients with painful HIV-SN
- **Assessment:**
Neuropathic Pain Symptom Inventory (NPSI)

Risk of painful HIV-SN

PAIN

Predictors of new-onset distal neuropathic pain in HIV-infected individuals in the era of combination antiretroviral therapy

Jemily Malvar^a, Florin Vaida^b, Chelsea Fitzsimons Sanders^b, J. Hampton Atkinson^b, William Bohannon^b, John Keltner^b, Jessica Robinson-Papp^c, David M. Simpson^c, Christina M. Marra^d, David B. Clifford^e, Benjamin Gelman^f, Juanjuan Fan^h, Igor Grant^b, Ronald J. Ellis^{b,*}, for the CHARTER Group

PAIN 156: 731-739, 2015. DOI: 10.1097/01.j.pain.0000461252.75089.bf

493
pain-free
HIV+

Median follow-up: 24 months
(IQR: 12-42; 1961 visits)

Assessment at each visit

- *Pain*: Yes / No
- *Signs*: Bilaterally reduced / absent pin-prick OR vibration sense OR ankle reflexes.

Incidence of painful HIV-SN

(incidence: 6.4 cases per 100 person years)

Risks for developing painful HIV-SN

Risks for having painful HIV-SN

- anxiety / depression
- total pain burden

Assessment:

- *Pain:* Yes / No
- *Signs:*
Bilaterally reduced / absent
pin-prick sensation OR
vibration sense OR
ankle reflexes.

Risks for having painful HIV-SN

Depression and anxiety

Painful HIV-SN (n = 129)

- I am not depressed or anxious
- I am moderately depressed or anxious
- I am extremely depressed or anxious

Non-painful HIV-SN (n = 72)

1 tile = 1%

Risks for having painful HIV-SN

Percent with other pain sites

Painful HIV-SN (n = 129)

Non-painful HIV-SN (n = 72)

1 tile = 1%

Pain intensity at other sites

Painful HIV-SN (n = 129)

Non-painful HIV-SN (n = 18)

1 tile = 1%

Cause or effect: reduced cortical volume?

- **Participants:**
*241 patients HIV-SN
from 5 study centres in
the USA (CHARTER)*

Pharmacological management

Treatment: there is a lack of evidence

Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis

Nanna B Finnerup*, Nadine Attal*, Simon Haroutounian, Ewan McNicol, Ralf Baron, Robert H Dworkin, Ian Gilron, Maija Haanpää, Per Hansson, Troels S Jensen, Peter R Kamerman, Karen Lund, Andrew Moore, Srinivasa N Raja, Andrew S C Rice, Michael Rowbotham, Emily Sena, Philip Siddall, Blair H Smith, Mark Wallace

Lancet Neurol 2015; 162-73

*“Pain due to **HIV-related painful polyneuropathy**...seems **more refractory** [to treatment] than other types of pain in our meta-analysis.”*

*“This difference might be due to **large placebo responses** in HIV-related neuropathy trials”*

Large placebo response

Large placebo response?

PT0213 A Systematic Review of Factors Influencing Placebo Response in Clinical Trials of Neuropathic Pain: A Comparison of HIV Associated Sensory Neuropathy and Diabetic Polyneuropathy H.Kemp¹, L. Vase², S. Nguyen³, A. Ben Abdallah⁴, A. Rice¹, N. Finnerup², S. Haroutounian⁴

What is being used to manage the pain?

- **Participants:**
130 adults with painful HIV-SN
- **SN diagnostic criteria:**
Bilaterally reduced / absent ankle reflexes OR vibration

* Median (IQR) amitriptyline dose: 25 (25-75) mg/day | APAP: Paracetamol

Summary

Acknowledgments

University of the Witwatersrand

Antonia Wadley
Zané Lombard
Prinisha Pillay
Liesl Hendry
Asma Shaikh

Burnet Institute, Melbourne

Kate Cherry

University of Western Australia

Patricia Price
Hayley Goullée
Constance Chew

Funding

- National Research Foundation, South Africa
- South African Medical Research Council
- International Association for the Study of Pain
- University of the Witwatersrand

...and

- *The Honey Badger*