**Ambulatory Block/ EBM session**

Eiyu Matsumoto 2/19/10

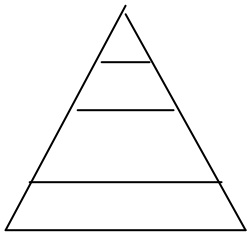
1. Case & Question

A 67 yo alcoholic male presented with 2-year-history of peripheral neuropathy.

-> What is the therapy for alcoholic neuropathy?

2. Method for article search

Evidence-Based Medicine 3rd edition



| | |
|---|---|
| Systems | ACP PIER, UpToDate, Best Evidence, Harrison online, BMJ clinical evidence |
| Synopses | ACP Journal club |
| Synthesis | Cochrane reviews |
| Studies | Original articles |

- Dynamed, ACP pier, BMJ clinical evidence, Cochrane: No information

- UpToDate

Alcohol abusers have a **high incidence of peripheral nerve disorders**, including symmetric polyneuropathy, autonomic neuropathy, and compression mononeuropathies. As an example, **peripheral neuropathy was detected in 32 percent** and autonomic neuropathy in 24 percent of 107 consecutively examined alcohol abusers in one report. The majority of patients in this series were middle class working men, and evidence of malnutrition was present in only a small minority. The prevalence of autonomic and peripheral neuropathy each **correlated best with lifetime alcohol consumption more than with nutritional deficiency**.

Pathogenesis — Detailed neuropathologic and electrophysiologic evaluation suggests that alcoholic peripheral neuropathy is **primarily an axonal neuropathy, complicated by demyelination when there is coexisting nutritional deficiency**. ….Taken together, these **data suggest that alcoholic peripheral neuropathy is caused by alcohol neurotoxicity, but it is sometimes complicated by vitamin deficiency**.

**Clinical features** — Alcoholic polyneuropathy is a **gradually progressive disorder of sensory, motor, and autonomic nerves**. The clinical abnormalities are usually **symmetric and predominantly distal**. Symptoms include **numbness, paresthesia, burning dysesthesia, pain, weakness, muscle cramps, and gait ataxia**. The most common neurologic signs are **loss of tendon reflexes**, beginning with the ankle jerks, defective perception of touch and vibration sensation, and weakness. **Loss of vibratory sensation can be demonstrated in asymptomatic alcohol abusers**.

**Treatment** — Specific treatments for alcoholic peripheral neuropathy are not available. Patients should receive thiamine supplementation since malnutrition may contribute to the development of the disorder. *Improved nutrition and cessation of drinking have been associated with symptom improvement in cohort studies* although complete recovery from severe neuropathy is uncommon. Low doses of tricyclic antidepressants, mexiletine [68], or gabapentin are sometimes effective in controlling the burning dysesthesias of alcoholic peripheral neuropathy.

- PUBMED, MeSH search with “Alcoholic neuropathy” OR “Alcoholic neuropathy/therapy” OR “Alcoholic neuropathy/drug therapy” ---- Not helpful

- PUBMED, clinical query “Alcoholic neuropathy” AND “Therapy” ---- 1 article

**1. Peripheral Nerve Functions Improve in Chronic Alcoholic Patients on Abstinence**

- This is the only one prospective study for the effect of abstinence on alcoholic neuropathy, conducted in 1991, in New Orleans over 6 mo.

PICO

Population:
- 32 patients from Alcohol rehab wards, they lost f/u 8 patients during research period. Age 46 +- 10, Total calorie intake 1850 kcal, Vit B intake on average, Duration of drinking 26 yrs, daily intake 207g
- See table 1

Intervention:
- Periodical evaluation: 10 days, 1 mo, 3 mo, 6 mo
- muscle strength, reflex, gait, sensory evaluation, skin temp, NCS, EMG

Comparison:
- None

Outcome:
- Vibration perception threshold improved from 1.00 ->0.50 over 6 mo. ( $p<0.001$)
- Sensory nerve action potential amplitude ($p<.01$)
- Sensory conduction velocities ($p<.01$)
- Motor conduction velocities ($p<.01$)
- Increase polyphasic motor units ($p<.05$)
- Normal spontaneous activity and recruitment of motor unis were seen with no change over 6 mo.
- See table 2

Conclusion
- Abstinence improved objectives of peripheral neuropathy without Vitamin B supplements.

Pros for this trial
- First prospective observational data with objective
- We can recommend the patient to stop drinking if they c/o peripheral neuropathy.
- No potential harm for stop drinking except for withdrawal symptoms.

Limitations
- No clinical evaluations for treatment effect (regarding gait unsteadiness, episode of fall, subjective changes etc..)
- Only 24 patients
- No placebo/randomization/blind
- Short study period
- Magnitude: medium

**2. Treatment of alcoholic polyneuropathy with vit B complex: a randomised controlled trial.**

- This is the only articles for effect of Vitamin B complex for alcoholic polyneuropathy as a multi-centre, randomized, double blind, placebo-controlled trial on 325 patients over 3mo in UK in 2005.

PICO

Population
- Pts who is alcoholic more than 2 years, consumed >50 units of alcohol/day with sensory symptoms who was diagnosed with peripheral neuropathy bia NCS.
- Exclusions: DM, Parkinson's disease, Wernicke-Korsakoff, epilepsy, non-alcoholic neuropathy, any significant cardiac disease, had skin eruptions, women who is pregnant or lacating, has HIV or syphilis, has allergy to meds, drug abuse/dependent, took Vitamins last 3 mo.
- Screening period (visit1), Randomization (visit 2), F/U at week 6 (visit 3), F/U 12(visit 4)
- A total 394 patients were screened and 325 patients were randomized. 109 received new B complex (with folate), 107 received old B complex (without folate), 109 received placebo.
- No difference of age, gender, duration of alcoholic polyneuropathy, prior alcohol usage, alcohol usage at visit 3 and visit 4
- 49 lost f/u

Interventions/ Comparison
- Goup1: Vitamin B1, 2, 6, 9, 12
- Goup2: Vitamin B1, 2, 6, 12
- Group3: Placebo
- One tab TID

Outcome
- Efficacy assessment: Vibration perception threshold, Pain questionnaire, Sensory function, finger to nose coordination, reflex response
- Improvement in both Group 1 and Group 2. No difference between Group 1 and 2.

Safety
- Dyspepsia+, otherwise pretty safe.

Pros
- The only multi-centred, double blinded control trial.
- Moderate-sized N.
- Patient has been drinking! Magnitude is big.
- Efficacy was evaluated from multiple measures including both subjective and objective standpoint.
- No major adverse event, excellent safety profile.
- Ubiquitous patient population. We can easily apply the study to our patients.

Cons
- No NCS or definitive objectives.
- No formulation/dose comparison except for folate.
- Effect of non-brand medication is unknown.